Investigations into the Effects of Middle Ear Surgery on Inner Ear Function

A Thesis Submitted in Partial Fulfilment
of the Requirements for the Degree of
Doctor of Philosophy

Melissa J. Babbage

Department of Communication Disorders

The University of Canterbury, Christchurch, New Zealand

March 2015

Abstract

Middle ear surgical procedures are typically associated with a high rate of improvement in air-conduction thresholds and a low rate of sensorineural hearing loss in the conventionally assessed frequency range (0.25 – 8 kHz). Hearing loss in the extended high-frequency (EHF) range (8 – 16 kHz), however, may be common, although its characteristics are not well understood. To elucidate the effects of middle ear surgery on auditory function, prospective investigations were performed to provide data that allowed transient and permanent changes in EHF hearing to be distinguished, and to establish the nature of EHF hearing loss.

Changes in hearing at 0.25 to 16 kHz were documented in 88 patients following stapedectomy, ossiculoplasty, and tympanoplasty. Hearing was measured preoperatively, and 1 week, 1, 3, 6, and 12 months postoperatively. Results showed that elevation of EHF air-conduction thresholds occurred frequently following all three surgeries and was most severe one week postoperatively. Although significant recovery of hearing was recorded by three months, 12 months after surgery, 50% of patients who underwent stapedectomy, 42% who had a tympanoplasty and 20% who underwent ossiculoplasty retained a reduction in their highest audible frequency. A TEAC HP-F100 bone-conduction transducer was modified for use in EHF audiometry and used in a small pilot study to demonstrate that EHF hearing loss following stapedectomy may be composed of both conductive and sensorineural elements.

It was hypothesised that changes to utricular responses reflective of trauma to the vestibular portion of the inner ear may also occur following middle ear surgery. Measurements of tap-evoked ocular vestibular evoked myogenic potentials (oVEMPs) were performed in the same group of patients in which audiometric data was collected. Overall, the oVEMP data provided no evidence of a postoperative change in utricular responses.

To assess clinical importance of EHF hearing loss, its role in one aspect of auditory function, localisation ability, was investigated in 46 participants; 23 with EHF hearing loss and 23 with normal EHF hearing. Overall, the results agreed with previous studies that localisation accuracy decreased when was EHF spectral content was removed by filtering, however the difference between hearing groups was significant only when speakers were positioned in the lateral vertical orientation.

Regardless of the clinical consequences, the increased vulnerability of EHF hearing acuity to the effects of middle ear surgery provides a useful model which could be used to efficiently assess the effect of technical factors of surgery or the efficacy of ototherapeutic treatments on hearing outcomes.

Acknowledgements

I would like to express my sincere gratitude to my supervisors for their support and encouragement throughout the last four years. Associate Professor Greg O'Beirne has patiently and enthusiastically provided guidance, advice, and technical expertise, for which I am extremely thankful. The surgical expertise and knowledge of Associate Professor Phil Bird have been invaluable, and this research would not have been possible without his assistance.

I wish to acknowledge the work of Dr Mike Bergin in the initial stages of data collection, and am thankful for his advice and assistance in getting this research underway. I am also grateful to the Audiology Department at Christchurch Hospital for their assistance in data collection and to Ms Sarah Gray for collecting the data for the study of localisation accuracy.

I am most appreciative of the statistical expertise of Ms Rodelyn Avila, and the assistance of Professor Jennifer Brown. I would also like to thank Dr John Pearse, Mr Ben Scott, and Mr David Healy from the School of Engineering for their advice and assistance in modifying and testing our bone-conduction transducer. Valuable assistance was also provided by Ms Tania Gargiulo and the administrators at the Otolaryngology Department at Christchurch Hospital with recruitment, accessing patient records, and arranging follow-up appointments.

I am very grateful to the participants in this research, many of who went out of their way to attend repeated assessments over the course of twelve months, and all of who were tolerant and generous with their time in taking part in this study.

I would like to acknowledge the Oticon Foundation in New Zealand, who provided a grant that funded this research and supported me through my doctoral studies.

I am forever grateful for the love and support of my family. To Mum, who is a constant source of reassurance, encouragement, and friendship, and Dad, whose confidence in me and my ability to complete this thesis has been unfailing, as is his ability to help me keep things in perspective (after all – it's just an ear!).

My most heartfelt thanks go to my partner, Bryan. I cannot thank him enough for his love, encouragement, and incredible patience during the last four years. His support and willingness to share in this with me (even on Saturday morning VEMP trips to the hospital) have made the completion of this thesis possible.

Abbreviations

ABR	Auditory brainstem response
ANOVA	Analysis of variance
ANSI	American National Standards Institute
B&K	Brüel & Kjær
BILD	Binaural intelligibility level difference
CI	Confidence interval
COM	Chronic otitis media
cVEMP	Cervical vestibular evoked myogenic potential
dB	Decibel
dB SL	Decibels sensation level
dB HL	Decibels hearing level
dB SPL	Decibels sound pressure level
DPOAE	Distortion product otoacoustic emission
EAC	External ear canal
ECochG	Electrocochleography
EHF	Extended high frequency
ENG	Electronystagmography
G.R.A.S	Gunnar Rasmussen Acoustic Systems
IAA	Interaural attenuation
IAC	Internal auditory canal
ICC	Intraclass correlation coefficient
IHC	Inner hair cell
IEC	International Electrotechnical Commission
ILD	Interural level differece
ITD	Interaural timing difference
LDV	Laser Doppler vibrometry
MD	Minimal difference
OAE	Otoacoustic emission
OHC	Outer hair cell
oVEMP	Ocular vestibular evoked myogenic potential
PORP	Partial ossicular replacement prosthesis
SCC	Semicircular canal
SCM	Sternocleidomastoid
SD	Standard deviation
SE	Standard error
SEM	Standard error of measurement
SNR	Signal to noise ratio
SVV	Subjective visual vertical
SVH	Subjective visual horizontal
TM	Tympanic membrane
TORP	Total ossicular replacement prosthesis
VSR	Vestibulospinal reflex
VOR	Vestibulo-ocular reflex
VCR	Vestibulo-collic reflex
VNG	Videonystagmography
VEMP	Vestibular evoked myogenic potential

Table of Contents

PART I: INTRODUCTION

Chapter 1: Introduction

Surgical procedures in the middle ear are generally performed to address the broad goals of eradicating disease and restoring the sound conduction pathway from the external ear to the cochlea. Middle ear surgeries aimed at improving sound transmission are typically associated with a high rate of success in improving air-conduction thresholds and a low rate of associated sensorineural hearing loss. However, any assessment of hearing outcome will be dependent on the sensitivity of the measurement tool selected to describe the result. It has been documented that when hearing thresholds are assessed postoperatively in the extended high-frequency range (8 – 20 kHz), hearing deterioration may be recorded relatively frequently following procedures that would be otherwise deemed successful based on a conventional assessment of hearing at lower frequencies (Bauchet St Martin, Rubinstein, & Hirsch, 2008; Doménech & Carulla, 1988; Mair & Laukli, 1986; Tange & Dreschler, 1990).

Using the most sensitive tool available to measure postoperative hearing deterioration gives the potential to efficiently examine the effect of technical factors of surgery, such as laser type, fenestra size, and prosthesis choice, and ototherapeutic treatments, on hearing outcomes. Subtle differences in audiometric outcomes that are obscured when data in the conventional frequency range is assessed may inform the debate regarding optimal surgical techniques and materials. This is of particular importance given the low rates of lower frequency sensorineural hearing loss following middle ear surgery, and thus the large numbers of patients that must be assessed to detect adverse outcomes using traditional methods. If a technique or treatment can be shown to significantly reduce the rate of extended high-frequency hearing loss, it is possible that the rate of rarer cases of significant hearing loss at frequencies below 8 kHz may also be reduced if a sufficient number of patients are tested.

Extended high-frequency audiometry must be more accurately described and understood if it is to be realised as a sensitive measure of the effect of middle ear surgery on the function of the peripheral auditory system. At present, while a postoperative elevation of air-conduction thresholds has been documented after several types of middle ear surgery (Bauchet St Martin et al., 2008; Doménech & Carulla, 1988; Mair & Laukli, 1986; Tange & Dreschler, 1990), complete, prospective, data has not yet been obtained for each type of surgery demonstrating whether this hearing loss is transient or permanent, or is conductive or sensorineural.

Overall hearing acuity is determined by the status of both the middle ear and the inner ear. Although middle ear surgery theoretically restores the anatomy of the middle ear closer to its physiological state than when pathology is present, it is possible that the reconstructed middle ear differs sufficiently from the normal anatomy that sound transmission at higher frequencies is permanently compromised (Mair & Hallmo, 1994). Temporary conductive hearing loss may also occur across all audiometric frequencies as a result of factors directly related to surgery in the middle ear cavity, such as the presence of blood, packing, and swelling (Robinson & Kasden, 1977). Alternatively, extended high-frequency hearing loss may be the result of trauma to the cochlea during surgery, manifesting as either temporary or permanent sensorineural hearing loss. Limitations imposed by equipment available for assessing bone-conduction thresholds above 4 kHz has meant that the majority of previous studies that have identified extended high-frequency hearing loss following middle ear surgery have failed to determine whether the loss is conductive or sensorineural in nature, or a combination of both. If extended high-frequency audiometry is to be used to detect operative harm, it is essential that it is identified whether the hearing deterioration is a result of cochlear injury, or to changes in the structure and movement patterns of the middle ear.

Hearing outcomes can differ significantly depending on the time relative to surgery that audiometry is performed (e.g. Sergi, Scorpecci, Parrilla, & Paludetti, 2010; Sperling, Sury, Gordon, & Cox, 2013). Previous studies have reported that high-frequency hearing loss is either more common or more severe in the early postoperative period (Bauchet St Martin et al., 2008; Hegewald, Heitman, Wiederhold, Cooper, & Gates, 1989), however inadequate follow-up assessments and the reporting of group mean hearing thresholds rather than rates of hearing loss has meant that the information we have regarding the relative rates of transient and permanent loss of high-frequency hearing acuity has remained limited. This is a critical issue to consider, from the perspective of providing the patient with complete information, to determine whether developing methods of reducing the incidence of extended high-frequency hearing loss are warranted, and to establish the optimal timing of assessments if extended high-frequency audiometry is to be used as a tool for future research into the effects of middle ear surgery on the function of the middle and/or inner ear.

If operative trauma to the inner ear occurs, balance as well as hearing function may be compromised following surgery. While it is widely acknowledged that varying degrees of balance disturbance are not a rare occurrence following middle ear surgery (Athanasiadis-Sismanis, 2010), objective measurements of balance dysfunction, and related changes in

hearing acuity, have rarely been documented following middle ear surgery. Most critically, there is a lack of data documenting vestibular function in the early postoperative period, when symptoms tend to be most common and most severe. The assessment of changes in vestibular responses may provide additional information regarding the impact of middle ear surgery on the function of the inner ear, and may corroborate audiometric findings.

The overarching purpose of this project was to investigate the influence of middle ear surgical procedures on short- and long-term hearing and balance function using measurement tools thought to be most sensitive to damage due to surgical trauma. Specifically, these tools included extended high-frequency audiometry and ocular vestibular evoked myogenic potentials. In particular, this research was designed to i) provide detailed, prospective data that allowed transient and permanent changes in postoperative hearing and balance to be distinguished; and ii) to develop methods to reliably determine whether the cause of extended high-frequency loss was changes to middle ear transmission characteristics, or iatrogenic cochlear damage.

Part I of this thesis provides an introduction to the relevant anatomy of the peripheral auditory and vestibular systems, types of hearing loss and the anatomical structures involved, and an overview of middle ear surgical procedures. Parts II and III present a series of clinical and methodological studies performed to investigate the effect of middle ear surgery on postoperative hearing function. The methodological investigations presented in Part II and III aimed to strengthen the interpretation of the data collected in the clinical study by addressing the reliability and sensitivity of the measurement tools used.

The aim of the clinical study described in Chapter 3 was to establish the patterns of hearing change following middle ear surgery in terms of audiometric frequency and timing of any recovery or deterioration occurring over the first postoperative year. Principally, we were interested in documenting extended high-frequency air-conduction thresholds in order to examine the hypothesis that hearing at these frequencies is a more sensitive measure of operative trauma.

The reliability and validity of extended high-frequency audiometry as a measurement tool is discussed and assessed in Chapter 4. Ideally, this methodological study would have preceded clinical data collection, however concerns regarding the validity of these audiometry in this frequency range were raised during the course of the clinical study. The study presented in Chapter 4 was therefore conducted in parallel with the extended high-frequency threshold

measurements performed in patients undergoing middle ear surgery described in Chapter 3. Implications from the methodological study have, however, been incorporated into the interpretation of results from the clinical study.

Potential mechanisms of hearing loss and their relationship to the pattern of increasing loss with rising frequency observed postoperatively are discussed in Chapter 5. In order to address questions about whether high-frequency postoperative hearing loss is conductive or sensorineural, a transducer developed to assess high-frequency bone-conduction thresholds is described in Chapter 6. Presented in that chapter are studies in otologically healthy subjects aimed at developing optimal protocols for the use of the bone-conduction transducer and determining the reliability associated with measurements using the device. A pilot study of extended high-frequency bone-conduction measurements performed with the transducer in patients who had undergone middle ear surgery is documented in Chapter 7.

The effect of middle ear surgery on vestibular function is discussed and investigated in Part IV of this thesis. A review of the literature regarding balance disturbance following middle ear surgery and the assessment of balance function is followed by a study of changes in vestibular responses in patients who have undergone middle ear procedures. Measurements of vestibular responses were performed in the same group of participants in which audiometric data was collected and presented in Chapter 3. This allowed the relationship between postoperative hearing loss and balance disturbance to be explored and the implications for the cause of changes in these measurements to be considered.

The increased vulnerability of extended high-frequency hearing acuity to the effects of middle ear surgery certainly provides a useful model on which to efficiently assess the efficacy of interventions aimed at improving hearing. However, the clinical importance of extended high-frequency hearing loss is less clear. Chapter 9 provides a detailed review of the literature regarding the role of spectral content above 8 kHz in auditory perception and presents a study performed in participants with normal hearing and with extended high-frequency hearing loss designed to assess the impact of extended high-frequency hearing acuity on auditory localisation abilities.

A grand summary of results obtained and concluding remarks considering the research presented in all the preceding sections is provided in Part IV. Implications of these results for patients and potential methods of prevention and treatment of postoperative hearing and balance symptoms are also discussed in detail.

Chapter 2: An introduction to hearing, balance, and middle ear disease

2.1 Overview

The purpose of this chapter is to introduce the anatomy, physiology, disease processes, and surgical procedures that underpin the research contained in this thesis. To understand the effects of middle ear disease and middle ear surgery on hearing and balance function, it is necessary to first have an understanding of the normal anatomy and physiology of the peripheral auditory and vestibular systems. This chapter therefore first presents an overview of the normal peripheral auditory and vestibular systems and methods of assessing their function, followed by a description of pathologies commonly affecting the middle ear and surgical procedures used in the treatment of these diseases.

2.2 The peripheral auditory system and the measurement of hearing acuity

2.2.1 Anatomy and physiology of the peripheral auditory system

The peripheral auditory system can be divided into three sections; from most lateral to most medial, the external ear, the middle ear, and the inner ear (Figure 1). Each component of the peripheral auditory system is described in detail in the following sections.

2.2.1.1 The external ear

Afferent auditory transmission begins with collection and filtering of acoustic stimuli by the pinna. The pinna is the portion of the ear visible externally, and is composed of a frame of fibroelastic cartilage covered by skin and attached to the temporal bone by ligaments and muscles. The prominences and depressions of the lateral surface of the pinna act as resonators and reflectors that differentially affect signals arriving from various locations in space. The spectrum of the sound that reaches the tympanic membrane (TM) therefore varies systematically with the location of the acoustic stimulus, providing high-frequency spectral cues for localisation, particularly in the median plane (Blauert, 1997; Carlile, 1996; Hofman & Van, 2003; Shaw, 1974; Wightman & Kistler, 1989).

Sound waves collected by the pinna are channelled to the TM through the external auditory canal (EAC), an s-shaped tube bounded medially by the TM. The lateral one-third of the

EAC is composed of cartilage and lined with epidermal tissue that contains hair follicles and cerumen producing sebaceous and ceruminous glands. In contrast, the medial two-thirds of the canal have an osseous foundation formed by the temporal bone and an epidermal lining devoid of hair and glands. The geometry of the EAC results in the reinforcement of energy in the incoming acoustic signal in the frequency range 3 – 4 kHz, providing a boost in amplification of 10 – 15 dB for those frequencies (Dallos, 1973).

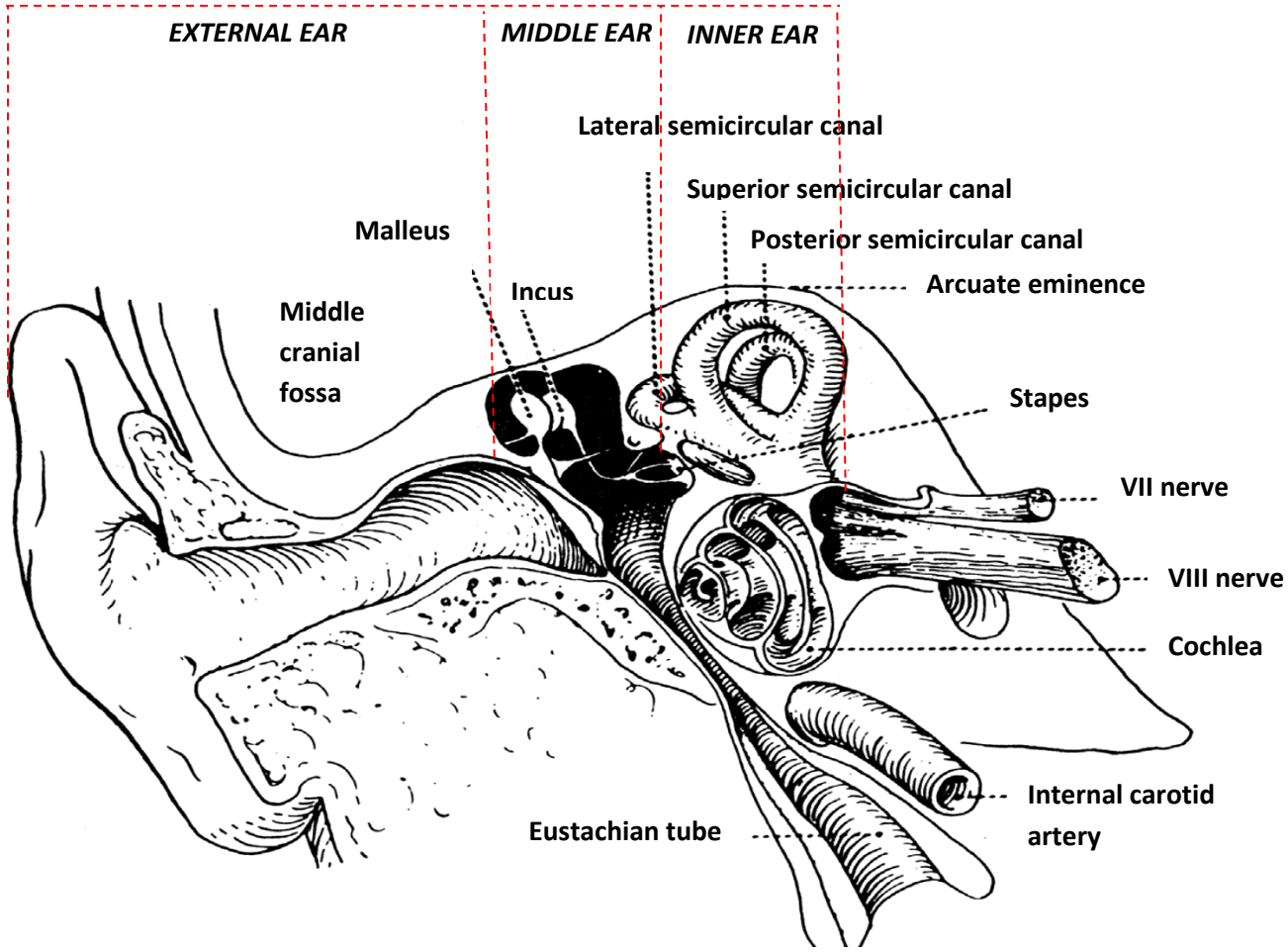

Figure 1. The external, middle, and inner ear sections of the peripheral auditory system. Adapted from Chapter 3: The nature of hearing loss (p.23), by R.T. Sataloff and J. Sataloff, (2006). In *Occupational hearing loss* (3rd ed.), by R. T. Sataloff and J. Sataloff (Eds.) Copyright 2006 by CRC Press. Adapted with permission.

2.2.1.2 The middle ear

The first component of the middle ear; the TM, is a conically-shaped structure, with the apex of the cone pointing medially. Somewhat broader superiorly, the adult TM is tilted

anteroinferiorly, is approximately oval in shape, and has a surface area of approximately 55 to 90 mm^2 (Yost, 2000; Zemlin, 1998). The TM is composed of three strata: the lateral epidermal layer, the medial mucosal layer, and a fibrous layer between the two. The outer, epidermal layer is covered in stratified squamous epithelium and is continuous with the epidermis of the EAC, whereas the mucosal layer is a thin, flat epithelium, continuous with the mucosal lining of the middle ear cavity. The intermediate fibrous layer of the TM, known as the lamina propria, consists of two primary types of collagen fibres (Figure 2); radial fibres that radiate outwards from the centre of the TM, and concentric circumferential fibres, which become more plentiful and thickened towards the periphery of the TM (Møller, 2000; Zemlin, 1998). The larger, inferior portion of the lamina propria; the pars tensa, also contains transversal fibres, which run horizontally across the inferior quadrant of the TM (Ferrazzini, 2003). In the superior part of the TM, referred to as the pars flaccida, the collagen and elastic fibres of the lamina propria are fewer in number and arranged in a looser fashion (Zemlin, 1998). The lamina propria thickens at the periphery of the TM to form the fibrocartilaginous tympanic annulus, which is anchored into a groove in the bony EAC known as the tympanic sulcus around the circumference of the TM, with the exception of the most superior portion.

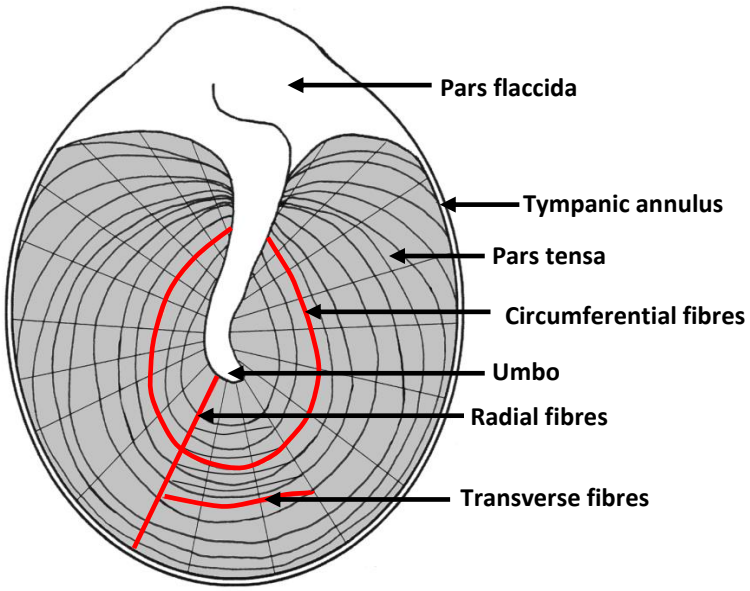

Figure 2. The structure of the tympanic membrane. The types of collagen fibres that make up the lamina propria of the pars tensa are shown in red.

The acoustic pressure funnelled through the EAC is transformed into a mechanical stimulus when sound waves hit the TM. Studies of vibratory patterns of the human tympanic membrane using laser Doppler vibrometry (LDV) (e.g. Ferrazzini, 2003; Koike, Wada, &

Kobayashi, 2002; Konrádsson, Ivarsson, & Bank, 1987) and stroboscopic holography (Cheng et al., 2010) have shown that in response to frequencies of less than 2 kHz, the motion of the TM is simple, with one to three displacement maxima moving approximately in phase with each other (Cheng et al., 2010). More complex spatial displacement patterns of the TM are seen above 2 kHz, with highly fragmented movement patterns that significantly reduce movement at the centre of the TM in response to high-frequency stimuli (Cheng et al., 2010; Ferrazzini, 2003). The anisotropy, shape, and thickness of the TM have an important influence on its vibratory patterns and transmission of that vibration to the middle ear (Funnell & Laszlo, 1982; Williams, Blayney, & Lesser, 1997; Williams & Lesser, 1990).

The middle ear space, also known as the tympanic cavity or tympanum, is divided by the margins of the TM into three sections (Figure 3); the mesotympanum adjacent to the TM, the epitympanum above the level of the superior TM attachment, and the hypotympanum below the TM (Gelfand, 1997; Musiek & Baran, 2007). The TM forms the majority of the lateral wall of the cavity, with the remaining portion in the epitympanic region formed by part of the squamous section of the temporal bone. The remainder of the middle ear cavity is surrounded by portion of the temporal bone. A thin plate of bone known as the tegmen tympani separates the middle ear from the cranial cavity superiorly while the tympanic plate of the temporal bone isolates the middle ear from the jugular fossa inferiorly. The tegmen tympani and the mucosal lining of the middle ear extend to form the roof of the mastoid antrum, where there is an indirect communication between the mastoid air cells and the tympanic cavity (Zemlin, 1998). The medial wall of the middle ear cavity is formed by the dense portion of temporal bone that encases the inner ear and includes the promontory; a lateral protrusion of the basal turn of the cochlea into the middle ear space, and the two membrane covered openings to the inner ear; the oval and round windows. The total volume of the adult middle ear cavity is approximately 2 cm^3 (Musiek & Baran, 2007). In its healthy state, the space is filled with air conveyed from the nasopharynx via the Eustachian tube, which opens into the middle ear at the anterior wall.

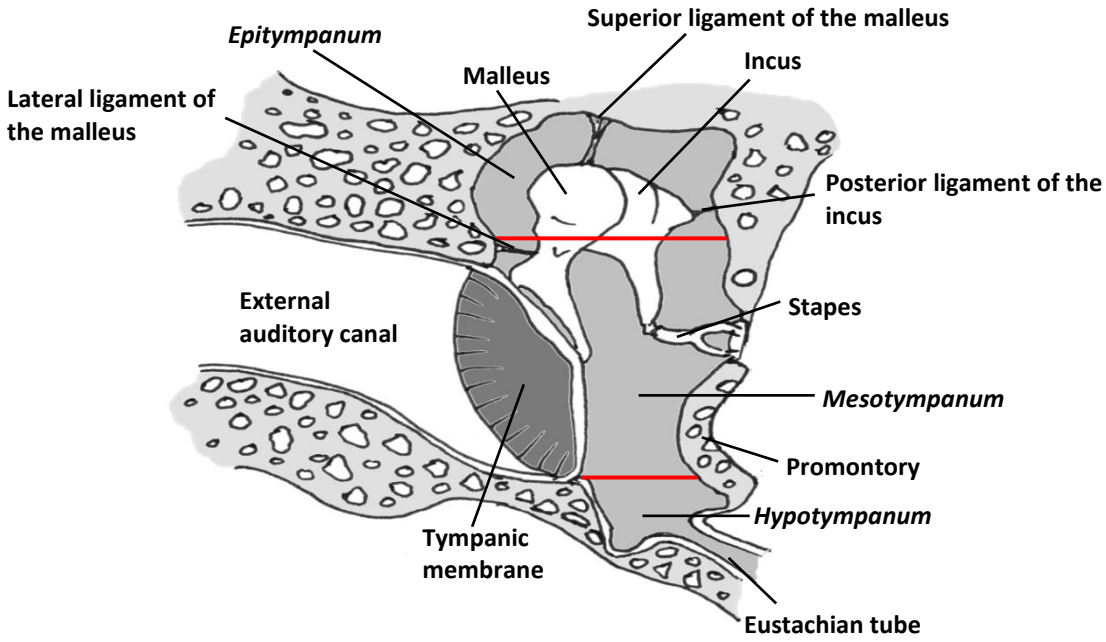

Figure 3. Schematic of the middle ear showing the positions of key structures and the division of the tympanic cavity into the epitympanum, mesotympanum, and hypotympanum (boundaries are indicated in red).

Three bones; the malleus, incus, and stapes, collectively known as the ossicles, are contained within the middle ear cavity. Most laterally, the malleus has a head, neck, manubrium, a lateral process, and an anterior process. The manubrium of the malleus is embedded in the TM. This firm attachment point of the manubrium at the centre of the TM; the umbo, draws the TM in towards the tympanic cavity, creating the TM's conical shape. The head and neck of the malleus are contained within the epitympanum where the synovial malleoincudal joint articulates the head of the malleus with the body of the incus. Extending from the anterior process, the anterior ligament of the malleus, together with the posterior incudal ligament, creates the axis of ossicular rotation (Gulya, 2010). In addition to the anterior ligament, the position of the malleus is maintained by the superior, anterior suspensory, and lateral ligaments of the malleus (Wolff & Bellucci, 1956).

The largest of the ossicles, the incus, has three processes; the long, short, and lenticular processes, and, as described above, a body that articulates with the head of the malleus. The long process of the incus descends from the epitympanum in a posterior direction parallel to the malleal manubrium, then turns medially within the mesotympanum and ends in the lenticular process. The lenticular process articulates with the head of the stapes to form the synovial incudostapedial joint. The posterior incudal ligament attaches to the short process of the incus, anchoring it into the incudal fossa of the epitympanum (Wolff & Bellucci, 1956).

Positioned most medially in the ossicular chain is the stapes. The smallest of the ossicles, the stapes has a head that articulates with the incus, a footplate, and an arch composed of an anterior and a posterior crus, that link the head to the footplate. The footplate of the stapes is positioned in the oval window at the intersection of the middle ear and the inner ear, and is held in place by the annular ligament (Wolff & Bellucci, 1956).

Other important structures housed within the middle ear cavity include the tympanic section of the facial nerve, the chorda tympani - a branch of the facial nerve, and two muscles; the tensor tympani and stapedius muscles. Innervated by the trigeminal nerve, the tensor tympani originates from the Eustachian tube at the anterior wall of the middle ear and sweeps across the space and around the cochleariform process to attach to the medial aspect of the neck and manubrium of the malleus. The stapedius muscle emerges from the pyramidal eminence on the posterior wall of the middle ear cavity and inserts into the posterior crus or, less frequently, the head of the stapes (Gulya, 2010). Innervation of the stapedius muscle is received from the facial nerve. Both the tensor tympani and stapedius muscles perform important functions in pulling the ossicles away from the tympanic membrane and oval window, respectively, to dampen vibration and prevent excessive pressure transfer to the inner ear.

Acoustic signals must travel from the relatively low-impedance medium of the air in the EAC to the fluid-filled cochlea, which has markedly higher impedance. The middle ear acts as an acoustic transformer to overcome this impedance mismatch and ensure efficient transmission of energy to the cochlea. Three middle ear mechanisms combine to increase the sound pressure level at the stapes footplate relative to that at the TM. The principle transformer mechanism of the middle ear results from the area difference between the TM and the stapes footplate, with the footplate being approximately 17 times smaller than the TM (Rose, 1978; Zemlin, 1998). As the force from the acoustic stimulus gathers across the entire tympanic membrane and is then coupled to the smaller footplate, the sound pressure applied to the cochlea should be approximately 17 times greater than that applied to the TM. An additional increase of sound pressure to the inner ear is provided by the lever action resulting from the different lengths of the manubrium of the malleus and the long process of the incus. The two ossicles are articulated by an encapsulated joint and therefore move together as a unit. As the manubrium is approximately 1.3 times longer than the long process of the incus (Rose, 1978), a corresponding increase in force is applied to the footplate. A third, less important, mechanism is provided by the buckling effect of the curved TM (Gelfand, 1997). Combined,

these mechanisms increase the energy at the oval window by approximately 27 dB; however this increase varies with the unique dimensions of an individual's middle ear. Laboratory measurements of middle ear sound pressure gain in human temporal bones indicate that the maximum gain is approximately 20 dB, and therefore smaller than predicted by the transformer model (Puria, Peake, & Rosowski, 1997). The level of pressure gain is also frequency dependent, and is maximal at 1 kHz and reduced at higher and lower frequencies (Puria et al., 1997).

2.2.1.3 The inner ear

The inner ear consists of a bony labyrinth of interconnected passages or cavities, and is positioned within the petrous apex of the temporal bone. The auditory portion of the inner ear; the cochlea, is a broad-based, conical structure, that spirals approximately two and three quarter turns around a bony core, known as the modiolus, and narrows from the base to the apex. Within the bony cochlear shell is the membranous labyrinth, which is attached to the bony labyrinth medially by the osseous spiral lamina and laterally by the spiral ligament. The osseous spiral lamina projects outwards from the modiolus to divide the coiled tube of the cochlea into two ducts along most of its length. The division of the cochlea into two main compartments is completed by the basilar membrane. Above the osseous spiral lamina, the scala vestibuli duct connects with the tympanic cavity at the oval window, whereas the lower duct; scala tympani, opens into the tympanic cavity at the membrane-covered round window. The separation into two compartments is absent only at the helicotrema; a small opening at the apex of the cochlea where scala tympani and scala vestibuli communicate (Figure 4).

Extending superiorly and laterally from the osseous spiral lamina to the spiral ligament is Reissner's membrane, which forms the superior boundary of a third duct; scala media. Inferiorly, scala media is bounded by the basilar membrane. Scala vestibuli and scala tympani both contain perilymph, a fluid high in sodium, while scala media is filled with potassium-rich endolymph. Scala media is bordered laterally by stria vascularis, a highly vascular pumping epithelium responsible for the maintenance of endolymph and the +95 mV endocochlear potential, which is the driving force for cochlear transduction (Tasaki & Spyropoulos, 1959).

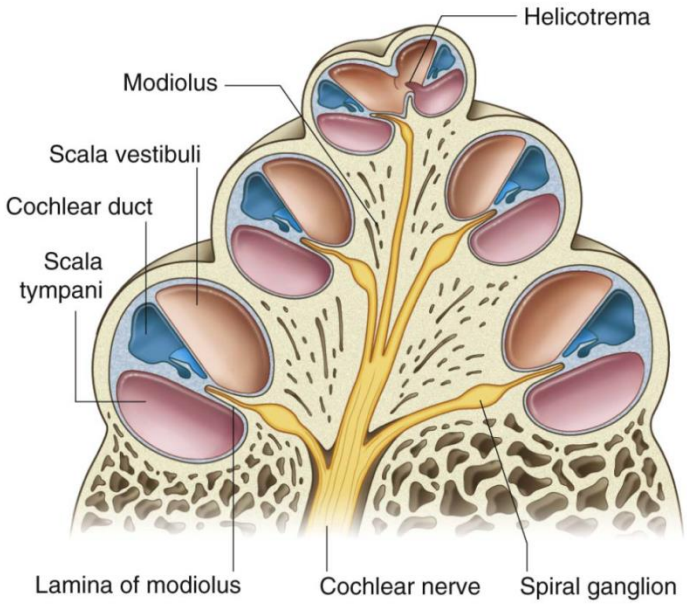

Figure 4. Mid-modiolar section of the cochlea illustrating the three ducts: scala tympani, scala vestibuli, and scala media (cochlear duct). From *Gray's Anatomy for Students* (p.966), by R. L. Drake, A. W. Vogl and A. W. M. Mitchell, (2009). Copyright 2010 by Churchill Livingstone. Reprinted with permission.

Running longitudinally atop the basilar membrane is the organ of Corti, a sensory epithelium divided into inner and outer portions by the pillars of Corti. On the modiolar side of the inner pillar is one row of inner hair cells (IHCs) and on the spiral ligament side of the outer pillar are three (or occasionally four) rows of outer hair cells (OHCs). Bundles of stereocilia containing mechanically-gated mechanoelectrical transduction channels protrude from the apical surface of each hair cell and, in the case of the OHCs, have their tips embedded in the tectorial membrane; an acellular matrix overlying the hair cells.

In contrast to the bony cochlea which decreases in cross-sectional from base to apex, the basilar membrane widens from base to apex. The width of the adult human basilar membrane progressively broadens from approximately 0.16 mm at the base of the cochlea to 0.52 mm near the helicotrema at the apex (Wrightson & Keith, 1918). The stiffness and tension of the basilar membrane also changes along its length; from flaccid at the apical end, to stiffer and slightly tensed at the basal end (Yost, 2000).

Movement of the stapes footplate in the oval window of the cochlea provokes a longitudinal wave in the cochlear fluids that sets up a transverse travelling wave on the basilar membrane (von Békésy, 1960). The transverse wave propagates from the base to the apex of the cochlea, with maximum displacement obtained at the basal end of the cochlea for high-frequency stimuli and at the apex for low-frequency stimuli. This tonotopic arrangement is the result of

the structural characteristics of the cochlea, in particular the stiffness gradient along the basilar membrane (von Békésy, 1960). Upward displacement of the basilar membrane causes a radial shearing of the OHC stereocilia, opening the mechanically-gated ion channels and allowing an influx of potassium ions from the endolymph in scala media into the hair cell. The alternating current of potassium ions into the cell as the ion channels open and close results in an alternating receptor potential, that causes active contractions of the OHC. This process, known as electromechanical transduction, acts to partially cancel the friction of the travelling wave, boosting basilar membrane movement (Brownell, Bader, Bertrand, & de Ribaupierre, 1985; Dallos, 1992). IHCs perform mechanoelectrical transduction, transducing the movement of the basilar membrane in response to sound into an electrochemical signal that stimulates the primary afferent neurons. As occurs in OHCs, shearing of the IHC stereocilia results in an influx of potassium, which depolarises the cell. The reduction in the membrane potential of the cell triggers the release of glutamate and initiates an action potential in the primary afferent cochlear nerve fibre that innervate the IHCs (Pickles, 2008).

The electrochemical signals from the hair cells are carried to the auditory centres of the brain by the primary afferent neurons via the cochlear branch of the vestibulocochlear nerve. The cochlear neurons are bipolar cells, with one process synapsing to the hair cells (primarily the IHCs) and the other process travelling through the internal auditory canal (IAC) together with the vestibular and facial nerves, and the labyrinthine artery, to the brainstem. The electrical impulses of the cochlear nerve then travel through the auditory brainstem to the primary auditory cortex located in the temporal lobe.

The vascular supply to the cochlea is derived from the labyrinthine artery, which arises from the anterior inferior cerebellar branch of the basilar artery. The common cochlear branch of the labyrinthine artery gives rise to the main cochlear artery and the vestibulocochlear artery. The main cochlear artery ascends spirally around the modiolus to supply the upper three-quarters of the cochlea. Within the modiolus, the cochlear artery divides into the external and internal arterioles, which supply the structures of the lateral and medial walls of the cochlea respectively. The cochlear ramus artery arises from the vestibulocochlear artery to supply the remaining basal quarter of the cochlea and adjacent modiolus. The amount of vascularisation is greater in the base than the apex of the cochlea, consistent with greater physiological activity of the cochlea at its base (Axelsson & Ryan, 2001).

2.2.2 Hearing assessment

Pure-tone audiometry is used to quantify hearing acuity at discrete frequencies in each ear. Its aim is to identify hearing impairment, and determine its type, degree, and configuration for the purposes of diagnosis and (re)habilitation. Frequency-specific thresholds, defined as the lowest intensity at which an individual will reliably respond to the presence of a stimulus, are plotted on an audiogram to show how hearing sensitivity varies across the frequency range tested. Hearing thresholds are plotted in decibels hearing level (dB HL), an audiometric unit with a reference level that varies according to the ear's sensitivity to sound at a given frequency. Audiometric zero (0 dB HL) is based on the mean frequency-specific thresholds of average, normal hearing, young people. Thresholds plotted in dB HL on an audiogram therefore show the degree of deviation of an individual's hearing thresholds from what is considered normal.

Customarily, hearing thresholds are assessed at octave frequencies from 0.25 to 8 kHz. The rationale behind the selection of these frequencies is that the spectral information considered most critical for the perception of speech is contained within this frequency range (Harrell, 2000). However, human hearing sensitivity may extend up to 20 kHz and it is possible to measure thresholds above 8 kHz and up to at least 16 kHz (the extended high-frequency (EHF) range) using specialised audiometric equipment. The topic of EHF audiometry is discussed in detail in Part II of this thesis.

Diagnosis of the type of hearing loss present is made by comparing the pure-tone thresholds obtained via air-conduction with those recorded via bone-conduction stimulation. Air-conduction audiometry refers to threshold measurement in response to stimuli presented by a headphone placed over the pinna, or inside the EAC. Airborne stimuli are presented to the external ear and must travel through the external ear, middle ear, and cochlea to be detected as sound. Dysfunction of any part of the afferent auditory pathway may therefore be responsible for an increase in thresholds to air-conducted stimuli. Bone-conduction audiometry aims to bypass the external and middle ear to directly measure the level of cochlear sensitivity. Stimulation is achieved by way of a bone-vibrator applied to the skull. This vibratory stimulus is transmitted through the bones of the skull, as well as the cartilage, skin, soft tissues, and fluids of the body, to produce a pressure difference between scala vestibuli and scala tympani, and ultimately a travelling wave on the basilar membrane (Khanna, Tonndorf, & Queller, 1976; Stenfelt, Puria, Hato, & Goode, 2003). It is generally accepted that bone-conduction hearing involves several pathways of cochlear stimulation. A

summary of those mechanisms considered to be the most important to bone-conduction sound perception follows:

2.2.2.1 Osseotympanic component

The contribution of the external ear to bone-conduction hearing is termed the osseotympanic component. In response to the presentation of a bone-conducted stimulus, the skull, and therefore the walls of the EAC, vibrates. These vibrations result in deformation of the walls of the EAC which produces an alternating sound pressure in the canal that mobilises the TM and is transmitted to the cochlea via the air-conduction pathway. At stimulus frequencies below the first resonance of the skull (0.8 – 1 kHz), the cartilage and soft tissue of the lateral part of the EAC vibrate, and this portion of the canal is principally responsible for sound radiation at low-frequencies (Stenfelt, Wild, Hato, & Goode, 2003; Tonndorf, 1966). At higher frequencies, the sound pressure produced by the vibration of the bony portion of the canal is likely to be the primary source of airborne sound generation, however the canal essentially acts as a high-pass filter, and the effect of the osseotympanic mechanism at these frequencies is negligible (Tonndorf, Campbell, Berstein, & Reneau, 1966).

In a normal, open EAC, the contribution of the osseotympanic mechanism to bone-conduction hearing is minimal at approximately 10 dB below that of other mechanisms for frequencies below 2 kHz, and even less at higher frequencies (Stenfelt, Wild, et al., 2003). However, when the entrance to the canal is occluded, the sound pressure level in the EAC in response to bone-conducted stimuli is elevated, and the osseotympanic pathway becomes dominant for frequencies between 0.4 and 1.2 kHz (Stenfelt, Wild, et al., 2003); a phenomenon known as the occlusion effect (Tonndorf, 1964). Sound pressure level in the occluded ear canal in response to bone-conducted stimuli has been shown to increase by up to 20 dB for frequencies below 2 kHz (Stenfelt & Goode, 2005), although the effect on hearing thresholds is typically 5 – 10 dB smaller, and limited to frequencies at and below approximately 1 kHz (Stenfelt & Reinfeldt, 2007).

2.2.2.2 Inertial component

The inertial, or inertial-ossicular, component of bone-conduction hearing refers to the transmission of bone-conducted stimulation to the cochlea via the vibration of the ossicular chain. Mechanically, the ossicular chain may be viewed as a mass-spring system, in which

the TM, muscles and ligaments act as springs supporting the mass of the ossicles (Stenfelt, 2011). When the skull vibrates at low-frequencies in response to bone-conduction excitation, the spring elements force the ossicles to move in phase with the vibrations of the surrounding bone. At frequencies above the resonance frequency of the intact ossicular chain; around 1.5 kHz, the mass of the ossicles overcomes the stiffness of the spring components, resulting in a relative motion between the ossicles and the surrounding bone (Homma, Du, Shimizu, & Puria, 2009; Stenfelt, Hato, & Goode, 2002). As with air-conduction stimulation, the movement of the ossicular chain out of phase with the skull results in the movement of the stapes footplate in the oval window, thus producing fluid displacement within the cochlea and stimulating the hair cells to produce a sensation of sound. The inertial component of bone-conduction occurs most efficiently in the mid-frequencies, with the greatest contribution to bone-conduction hearing at 1.5 – 3 kHz (Stenfelt, 2006).

2.2.2.3 Cochlear mechanisms of bone-conduction

When the skull is set into motion by a bone-conduction stimulus, the bones of the skull compress and expand in synchrony with the alternating polarities of the transverse waves. The effect of this distortion of the bony walls of the otic capsule is an alteration of the cochlear fluid spaces, causing a fluid motion that gives rise to displacement of the basilar membrane. This pathway of bone-conduction stimulation is known as the inner ear compression (von Békésy, 1932), or distortional mechanism (Tonndorf, 1966).

The theoretical basis of the compression mechanism is that the physical asymmetries between the impedances of the oval and round windows and between the fluid volumes of scala tympani and scala vestibuli, allow the incompressible cochlear fluids move in response to distortion of the cochlear shell (Kirikae, 1959). Upon otic capsule compression, fluid is forced from the larger scala vestibuli side to the scala tympani side of the cochlea, where the membranous window is more compliant. Expansion of the otic capsule results in fluid flow in the opposite direction. The movement of perilymph pushes the basilar membrane upward and downward, thus opening and closing the mechanoelectrical transduction channels in the hair cell stereocilia (Stenfelt, 2011). Stenfelt (2011) suggests that effective cochlear compression is limited to frequencies with a wavelength less than ten times the size of the cochlea. This restricts effective cochlear stimulation by compression to frequencies of 4 kHz and above.

Inertial forces also act on the cochlear fluids when the temporal bone vibrates in response to a bone-conduction stimulus. The product of these forces is a pressure gradient across the basilar membrane that produces a flow of fluid between scala vestibuli and scala tympani, initiating a travelling wave on the basilar membrane. This inertial displacement of cochlear fluids therefore provides a second cochlear pathway for bone-conduction stimulation, and is believed to be the most important bone-conduction component for frequencies below 4 kHz (Stenfelt, 2011).

Movement of the cochlear fluids is possible only when compliant structures are present on both sides of the basilar membrane, providing both an inlet and outlet for the displaced fluid. In the normal cochlea, the oval window on the scala vestibuli side and the round window of the scala tympani side act as compliant pathways, however other structures, such as the vestibular and cochlear aqueducts, nerve fibres, veins, and microchannels entering the cochlea, may also perform this function (Küçük et al., 1991). These structures collectively act as a third window to the cochlea allowing fluid to flow when a pressure gradient over the basilar membrane is created.

Theoretically, bone-conduction testing allows the separation of the component of a hearing loss due to pathology of the external or middle ear, from that due to cochlear or neural dysfunction. However, as is evident from the mechanisms that contribute to bone-conduction hearing described above, the status of the external and middle ear may also influence the level at which bone-conduction thresholds are recorded. Despite this, the alteration of bone-conduction thresholds due to an external or middle ear lesion is small relative to the change in air-conduction thresholds (Stenfelt & Goode, 2005) and comparison of hearing sensitivity measured via the air- and bone-conduction pathways can therefore be used to broadly determine the site of lesion.

2.2.2.4 Conductive hearing loss

A conductive component to a hearing loss is diagnosed based on the presence of a significant positive air-bone gap. An air-bone gap occurs when the bone-conduction threshold is better (lower) than the air-conduction threshold at a given frequency and is defined as significant when the difference is 15 dB HL or greater (Figure 5). As air-conduction thresholds represent hearing acuity as measured through the entire afferent auditory pathway, and bone-

conduction thresholds represent hearing acuity measured primarily from the level of the cochlea onwards, an air-bone gap indicates that the pathology responsible for the increase in air-conduction thresholds is at the level of the external or middle ear.

Any disruption to the normal transmission of sound along the air-conduction pathway prior to the point of cochlear stimulation may cause a conductive hearing loss. The degree and configuration of hearing loss depends on the nature and location of the disruption to the conductive mechanism. As a rule, pathologies that increase the mass of the middle ear system have a greater effect on high-frequency hearing, whereas disorders that increase stiffness tend to increase low-frequency thresholds. A wider range of thresholds will be affected if both mass and stiffness properties of the middle ear are altered (Stach, 2010).

Conductive hearing losses can often be treated surgically and closure of a significant air-bone gap is a primary goal of many middle ear surgeries.

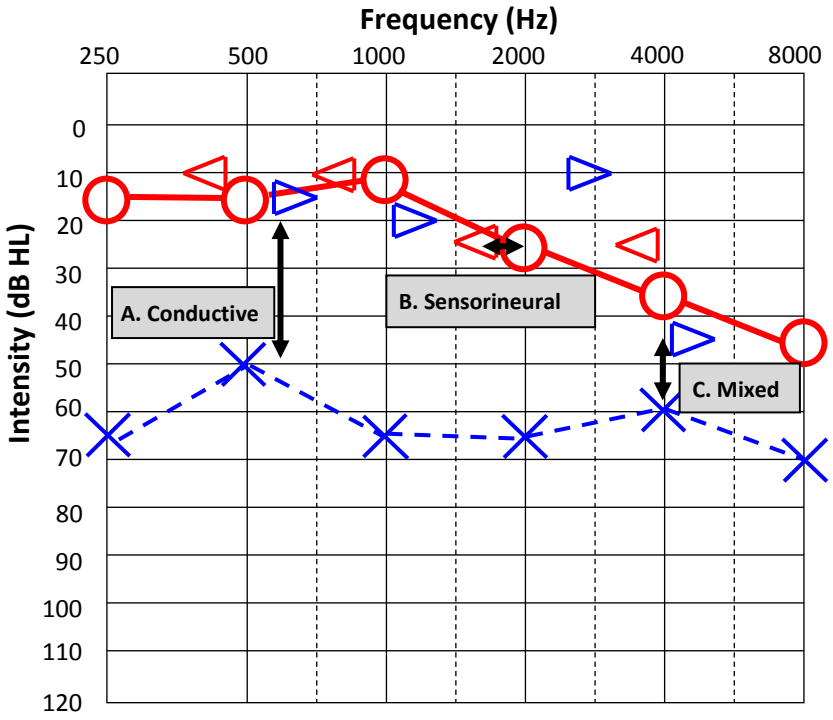

Figure 5. Conductive hearing loss (A) is characterised by an air-bone gap of 15 dB HL or greater, with a bone-conduction threshold of less than 20 dB HL. Sensorineural hearing loss (B) is defined as both air- and bone-conduction thresholds greater than 15 dB HL with a difference between the two values of less than 15 dB HL. A mixed hearing loss (C) is diagnosed when an air-bone gap of 15 dB HL or greater is present, with a bone-conduction threshold of greater than 15 dB HL.

2.2.2.5 Sensorineural hearing loss

Sensorineural hearing loss occurs when the sensory or neural mechanisms within the cochlea, auditory nerve, or central auditory pathways are absent or dysfunctional. In the majority of cases, the lesion is localised to the OHCs and/or IHCs of the cochlea, and the result is a failure of the affected structures to transduce mechanical stimulation to the electrochemical signals that are transmitted to the cochlear nerve (Moore, 1995). Cochlear damage may result in decreased auditory sensitivity as well as impaired frequency selectivity, temporal resolution, temporal integration, and loudness perception (Moore, 1996).

A sensorineural hearing loss will result in an increase in bone-conduction thresholds at the pure-tone frequencies associated with the cochlear and/or neural damage. In the presence of normally functioning external and middle ear conductive mechanisms, a sensorineural hearing loss will not typically produce a significant air-bone gap, i.e. air- and bone-conduction thresholds will both be increased and will be within 10 dB HL of each other (Figure 5). The frequencies affected and the configuration of the loss are dependent on the location of the damage. In cases where hearing loss results from cochlear pathology, the frequencies at which hearing is impaired generally correspond to the region of cochlear damage (e.g. Moody, Stebbins, Hawkins, & Johnsson, 1978; Schuknecht & Neff, 1952). High-frequency hearing loss therefore provides a gross indication that pathology is localised to the basal cochlea, whereas low-frequency hearing loss would indicate a more apical site of injury. At present, a hearing loss due to impairment of the cochlear structures cannot be reversed surgically.

2.2.2.6 Mixed hearing loss

Sensorineural and conductive pathologies may co-occur, resulting in both a significant air-bone gap and elevated bone-conduction thresholds (Figure 5). This pattern of results is termed a mixed hearing loss.

2.3 The peripheral vestibular system and measurement of vestibular function

The posterior portion of the labyrinth houses the five vestibular end organs; three semicircular canals (SCCs), and two otolithic organs; the utricle and the saccule (Figure 6). These organs act as static and dynamic force sensors and convey information to the central

nervous system regarding angular head velocity and linear acceleration. This information is integrated with inputs from the proprioceptive and visual systems at the level of the spinal cord, cerebellum, and higher cortical centres, and used in the maintenance of balance and equilibrium.

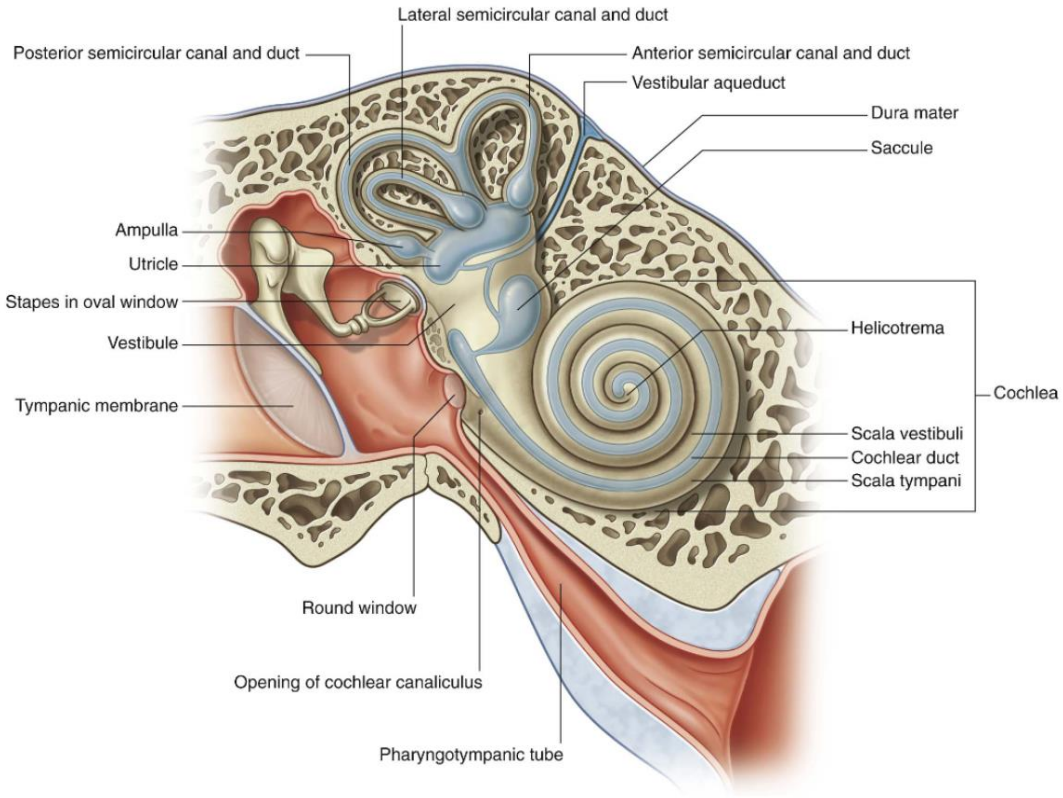

Figure 6. Illustration of the membranous labyrinth showing the relative positions of the cochlear and vestibular apparatuses in the inner ear. From *Gray's Anatomy for Students* (p.966), by R. L. Drake, A. W. Vogl and A. W. M. Mitchell, (2009). Copyright 2015 by Churchill Livingstone. Reprinted with permission.

2.3.1 Otolithic organs

The utricle and saccule are sensitive to linear acceleration, including the direction and magnitude of gravity, and transient linear acceleration due to movement (Fernández & Goldberg, 1976a, 1976b, 1976c). The endolymph-filled otolithic organs are positioned in recesses of the medial wall of the vestibule, between the cochlea and SCCs. The smaller of the two organs, the saccule, is connected anteriorly to the cochlea via the ductus reunions, and posteriorly to the endolymphatic duct (Figure 6). The utricle lays posterosuperiorly to the saccule and contains six openings; five which connect to the three SCCs, and another that

connects the utricle to the endolymphatic duct via the utriculosaccular duct. The sensory units of both the otolithic organs; the maculae, consist of neuroepithelium with hair cells that project into an overlying gelatinous matrix which contains solid calcium carbonate crystals known as otoconia. The otoconia give the otolithic membrane a specific gravity nearly three times that of the surrounding endolymph (Lim, 1984), causing the maculae to be highly sensitive to both linear head motion and static tilt with respect to the direction of gravity. When the otolithic organs are subjected to linear acceleration, the tilting of the macula pulls the otolithic masses downward and away from their resting positions, carrying the cilia embedded in the gelatinous matrix with them and initiating a change in the generator potential of the hair cells (Goldberg & Fernández, 1984).

The orientation of the macula of each otolithic organ corresponds to the plane in which the organ responds to acceleration. In an upright human, the saccular macula is located on the anterior vertical wall of the saccule and responds to linear acceleration in the vertical plane. The macula of the utricle lies mainly on the floor of the utricle, and responds to motion within the horizontal plane. Within each macula a line of demarcation known as the striola separates the epithelium approximately down the centre into two regions with opposite hair-bundle orientation and therefore opposite directional polarisation (Hain & Helminski, 2007; Wersäll & Bagger-Sjöbäck, 1974). Consequently, linear acceleration in almost any direction will result in hair cell depolarisation of hair cells in a section of hair cells in one of the otolithic organs. Although the utricle and saccule are primarily stimulated by linear acceleration, they may also respond to pressure changes resulting from high-intensity sound, vibration, or electrical stimulation (Welgampola & Colebatch, 2005).

2.3.2 Semicircular canals

Whereas the otolithic organs are sensitive to the effects of gravity and linear acceleration of the head, the SCCs are stimulated by angular (rotational) acceleration and are insensitive to gravity. The SCCs are circular, narrow-bore tubes filled with endolymph, which communicates with the endolymph of the utricle. Each labyrinth has a set of three SCCs arranged approximately orthogonal to each other so the superior and posterior canals are each at 45 degree angles to the saggital plane, but perpendicular to each other, and the lateral canal is oriented at 30 degrees to the transverse plane. Each canal is maximally sensitive to angular rotations in its own plane and is paired with a parallel SCC in the same plane from the

contralateral labyrinth. These functional pairings between the two lateral canals and each superior canal with the contralateral posterior canal means that rotation in the plane of each coplanar pair will be excitatory to one member of the pair and inhibitory to the other (Brandt & Strupp, 2005). This arrangement allows the combined input of all three canals to be used by the higher auditory centres to determine both the vector and amplitude of head rotation in any direction.

One end of each SCC is dilated to form the ampulla (Figure 6), which contains the sensory epithelium of the SCCs, termed the crista. Like the otolithic maculae, the crista consists of an epithelium from which hair cells project into a gelatinous mass known as the cupula. When the head is subjected to angular acceleration, the inertia of the endolymph causes the fluid to lag behind the movement of the canal walls. The inertial mass of the endolymph pushes on the cupula and billows outward under the pressure, causing deflection of the hair bundles embedded within it (Hillman & McLaren, 1979; McLaren & Hillman, 1979).

2.3.3 Vestibular transduction and afferent innervation

Unlike the hair cells in the cochlea, vestibular hair cells retain a kinocilium throughout life (Wersall, 1961). Each hair cell bears a single long kinocilium on its apical surface, positioned at one side of a bundle of stereocilia arranged in order of height, with the tallest stereocilia closest to the kinocilium. Deflection of the cilia towards the kinocilium will result in depolarisation of the hair cell and an increase in the rate of neurotransmitter release and consequent neural firing. When the hair bundle is bent in the opposite direction, hyperpolarisation of the hair cell will occur, causing a decrease from the basal rate of neural discharge in the postsynaptic afferent neurons (Correia & Dickman, 1991; Goldberg & Fernández, 1984).

The basal surfaces of the vestibular hair cells synapse with the primary afferent vestibular neurons. Vestibular nerve fibres are the afferent projections of bipolar neurons, the cell bodies of which form Scarpa's ganglion at the medial end of the IAC. The vestibular nerve is divided into superior and inferior portions which innervate the sensory epithelia of the vestibular end organs. The superior vestibular nerve innervates the cristae of the superior and lateral SCCs, the utricular maculae and the anterosuperior portion of the saccular maculae. The inferior portion of the nerve innervates the remaining vestibular end organs; the posterior SCC cristae and the balance of the saccular maculae. The superior and inferior divisions of

the vestibular nerve merge medial to Scarpa's ganglion and come together with the axons from the cochlear afferent neurons to form the eighth cranial nerve (Gacek, 1968; Schuknecht, 1993). Afferent vestibular neurons enter the brainstem of the pontomedullary junction and most terminate in the vestibular nuclei, from which nerves relay the information to the neural structures that control eye movement, body position, and head stability.

2.3.4 Vascular supply

The main blood supply to the peripheral vestibular apparatus is through the labyrinthine artery, which branches into the anterior labyrinthine and common cochlear arteries after entering the labyrinth (Schuknecht, 1993). The anterior labyrinthine artery provides the arterial supply to the cristae of the superior and lateral SCCs, the utricular macula, and a small portion of the saccule. The second branch, the common cochlear artery further divides into two branches; the proper cochlear artery and the vestibulocochlear artery, the latter of which gives rise to the cochlear ramus and the posterior vestibular artery. The posterior vestibular artery supplies the crista of the posterior SCC and the majority of the saccule (Schuknecht, 1993).

2.3.5 Vestibular reflexes

Projections from the vestibular nuclei to the extra-ocular muscles, spinal cord, and skeletal muscles serve three key reflexes; the vestibulo-ocular reflex (VOR), the vestibulocollic reflex (VCR), and the vestibulospinal reflex (VSR). The input of the vestibular end organs, predominantly the SCCs, is combined to modulate the VOR, the output neurons of which are the motor neurons of the ocular motor nuclei. These nuclei drive the extra-ocular muscles, which produce compensatory movements during head and body movement to maintain a stable image on the retina. The contribution of the SCCs to this reflex is well defined, however, although the otolithic organs are also thought to contribute to the VOR, the pathway from the labyrinth to the extra-ocular muscles in not yet clear (Murofushi & Kaga, 2009a). Sensory input about linear acceleration provided by the otolithic organs is also used to modulate the VCR, which acts on the neck musculature to maintain head stability during movement (Murofushi & Kaga, 2009a). Head and postural stability is further maintained by compensatory muscle movements mediated via the VSR (Pompeiano, 1975).

2.3.6 Assessment of vestibular function

The maintenance of balance, equilibrium, and a clear visual image relies on the integration of sensory information from the five vestibular end-organs of each labyrinth, the visual system, and proprioceptive signals from muscles and joints. As stated above, integration of these inputs occurs at the level of the spinal cord and cerebellum, and ultimately in the frontal, parietal, and occipital lobes of the cerebral cortex. Impairment to any of these sensory or neural structures in the pathway may result in imbalance, therefore a primary goal of balance assessment is to isolate the site of lesion. This section will provide a brief overview of objective methods of isolating and assessing the function of the vestibular end organs and their associated reflex pathways. The tests used in this study, vestibular evoked myogenic potentials (VEMPs) will be discussed in greater detail in Chapter 8.

2.3.6.1 Tests of SCC and VOR function

The majority of available tests of vestibular function assess the SCCs, in particular the lateral SCC. The functional status of the SCC is assessed through the evaluation of involuntary eye movements (nystagmus) mediated by the VOR and evoked in response to vestibular stimulation. Eye movements can be observed directly, or more accurate and objective measurements can be made using electronystagmography (ENG) or videonystagmography (VNG). ENG and VNG test batteries include assessments of spontaneous nystagmus, smooth pursuit tracking, saccadic eye movements, and optokinetic nystagmus. Important information suggesting whether the cause of balance disturbance is more likely central or peripheral in origin can be gained using these tests, however it is often not possible to clearly determine the site of pathology, and an additional stimulus must be used to more directly assess the function of the peripheral vestibular organs (Vitte & Semont, 1995).

The two most commonly used methods of stimulation of the vestibular apparatus are bithermal caloric irrigation and rotation, both of which examine the function of the lateral SCCs and VOR. Caloric testing involves infusing water or air of different temperatures into the EAC while the patient is lying supine with the head tilted so that the lateral SCC is oriented vertically. The temperature difference between the body and the infused water creates a convective current in the endolymph of the temperature of the lateral SCC, which projects into the middle ear space. The maximum velocity of the slow component of nystagmus in response to each caloric stimulus in each ear can be used to identify

asymmetrical vestibular function (Jongkees & Philipszoon, 1964). The comparison of responses from each vestibule means that bithermal caloric testing is highly reliable in detecting unilateral vestibular loss associated with the lateral SCC and VOR (Aschan, Bergstedt, & Stahle, 1956; Baloh & Honrubia, 1989; Bhansali & Honrubia, 1999).

Rotational testing has an advantage over caloric testing in it enables testing at multiple stimulus frequencies (Hess, Baloh, Honrubia, & Yee, 1985). With the subject seated in darkness in a rotating chair, rotational testing involves rotating or oscillating the chair while the subject's eye movements are measured using ENG or VNG (Brandt & Strupp, 2005). Rotation of the head simultaneously stimulates the lateral SCCs on each side of the head; increasing neural discharge from the labyrinth towards which the head is turned and decreasing neural discharge from the opposite labyrinth (Jacobson & Newman, 1991). The slow phase of nystagmus produced may show asymmetry in some cases of unilateral vestibular loss (Baloh, Honrubia, Yee, & Hess, 1984; Maire & van Melle, 2000), however both labyrinths will always be stimulated during rotational testing, and the ability to diagnose the site and side of unilateral vestibular hypofunction is limited (Baloh, Sills, & Honrubia, 1979).

2.3.6.2 Tests of otolithic organ function

Assessment of the function of the otolithic organs is more rarely performed as part of the vestibular test battery. Static otolithic function, specifically that of the utricle, can be examined indirectly using the subjective visual vertical (SVV) or subjective visual horizontal (SVH) tests. The otolithic organs function as sensors of gravity and head tilt and SVV and SVH tests assess this function by measuring the angle between perceived vertical or horizontal and true (gravitational) vertical or horizontal (Kingma, 2006).

SVV and SVH tests are performed by having a subject seated with the head upright in a dark room adjust a luminous line to what they perceive is vertical (SVV) or horizontal (SVH) (Halmagyi & Curthoys, 1999). Subjects with healthy otolithic systems can correctly position the line within a standard deviation of approximately 1.1 degree (Kingma, 2006), however patients with unilateral loss of peripheral function show a deficit in this ability. In the acute stage of loss of vestibular function, for example, immediately following unilateral vestibular deafferentation, patients will demonstrate a tilt of the SVV or SVH towards the lesioned side of around 10 to 20 degrees (Bohmer & Rickenmann, 1995; Curthoys, Dai, & Halmagyi,

1991; Gomez Garcia & Jauregui-Renaud, 2003; Vibert, Häusler, & Safran, 1999). Although small abnormalities may remain, the SVH and SVV generally return to normal within weeks or months of the initial injury as central compensation occurs (Pinar, Ardic, Topuz, & Kara, 2005; Tabak, Collewijn, & Boumans, 1997; Tribukait, Bergenius, & Brantberg, 1998; Vibert & Häusler, 2000). The recovery of the ability to perform these tasks limits the utility of SVV and SVH tests to diagnose otolithic abnormalities in cases of long-term vestibular weakness.

Dynamic otolith function can be assessed through the measurement of the VEMP. VEMPs can be recorded either the cervical muscles (cVEMP), or the extra-ocular muscles (oVEMP) and are short-latency electromyograms generated by the otolithic organs by sound or vibratory stimulation, independent of cochlear function (Colebatch & Halmagyi, 1992). cVEMPs, recorded from surface electrodes over the tonically contracted sternocleidomastoid muscle, are well established as a clinical test of ipsilateral saccular and inferior vestibular nerve function when evoked by high-intensity air-conduction stimuli (Colebatch, 2001; Colebatch, Halmagyi, & Skuse, 1994; Murofushi, Curthoys, Topple, Colebatch, & Halmagyi, 1995). cVEMP thresholds in response to bone-conducted stimuli are typically lower than those for air-conducted stimuli, possibly reflecting activation of utricular afferents in addition to saccular ones (Curthoys, 2010; Curthoys, Kim, McPhedran, & Camp, 2006).

In contrast to cVEMPs, oVEMPs reflect predominantly contralateral otolithic function (Rosengren, McAngus Todd, & Colebatch, 2005). oVEMPs are recorded from electrodes positioned beneath the eyes (over the inferior ocular muscles) and require only that the patient fix their gaze upward to bring the inferior oblique muscle close to the active electrode (Iwasaki et al., 2009). oVEMPs are considered to reflect function of the utricle and superior vestibular nerve when evoked by both air- and bone-conducted stimuli (Iwasaki et al., 2009; Rosengren & Kingma, 2013).

VEMP waveforms may be analysed with regards to their latency, amplitude, threshold, and asymmetry ratio. Abnormalities in responses vary with the type of pathology present, however, absent responses or large asymmetry ratios are often observed in cases of unilateral peripheral vestibular lesions (Brandt & Strupp, 2005; Young, 2006). Although VEMPs are not affected by the status of the cochlea, responses to air-conducted stimuli will usually be absent or reduced in cases of conductive hearing loss, with preserved responses to bone-conduction stimulation (Sheykholeslami, Murofushi, Kermany, & Kaga, 2000). The origins and clinical uses of VEMPs are discussed in much greater detail in Chapter 8, however,

depending on the type of VEMP tested, they provide a useful tool for the identification of unilateral dysfunction of the otolithic organs and/or their associated neural structures.

2.4 Common disorders requiring middle ear surgery

Indications for performing middle ear surgery may include the presence of a conductive hearing loss and signs and symptoms of chronic middle ear disease, such as TM perforation, otorrhea, otalgia, and inflammation. Given that the type and extent of disease can greatly influence both the specific surgical procedure performed and the short- and long-term success rates for improving hearing, a brief review of common middle ear pathologies indicating the need for reconstructive middle ear surgery is provided here.

2.4.1 Chronic otitis media

Chronic otitis media (COM) is a persistent inflammatory disease of the middle ear space and/or mastoid. COM typically results from long-term Eustachian tube dysfunction with abnormal middle ear pressure and poor aeration of the middle ear space, together with an inflammatory stimulus, such as multiple episodes of acute otitis media, or persistent bacterial infection of the middle ear (Gopen, 2010). The inflammatory process of COM causes long-term, often permanent, pathologic changes in the TM, middle ear space and in the mastoid. Mucosal inflammation, granulation tissue formation, and bone erosion are frequently noted in the diseased middle ear and changes in the TM may include atelectasis, perforation, retraction pocket development, and tympanosclerosis (Merchant & Rosowski, 2010).

The range of disease states described as COM can be divided into two groups based on the presence or absence of cholesteatoma. Cholesteatoma is an erosive growth consisting of keratinising squamous epithelium that can be destructive to the structures of the middle ear and mastoid. Erosion of bone generally begins with the ossicular chain and may progress to other structures surrounding the middle ear cavity, such as the otic capsule and tegmen tympani, as the cholesteatoma expands (Gopen, 2010). The severity of the infection, the pathologic changes present, whether cholesteatoma is present, and the time course of COM manifestation will determine the clinical presentation of COM, which may vary widely. The primary symptoms are conductive hearing loss of up to 60 to 70 dB HL and otorrhea (Merchant & Rosowski, 2010).

The pathologic changes present in an ear with COM indicate a need for surgery, but may also limit the success of surgical procedures. There is a significant risk of recurrent disease, often associated with persistent Eustachian tube dysfunction and abnormal middle ear static pressure. These characteristics of the diseased ear can result in less than optimal results initially following surgery, or deterioration in hearing even months or years after the surgical procedure (Black, 1992; Merchant & Rosowski, 2010).

2.4.2 Otosclerosis

Otosclerosis is a disease of the otic capsule that is characterised by disordered resorption and deposition of bone. Abnormal remodelling of bone creates sclerotic foci, which may occur in any portion of the otic capsule, but are particularly prevalent in the area just anterior to the oval window and insertion point of the stapes footplate (Schuknecht & Barber, 1985). In the majority of cases of otosclerosis, the footplate is initially fixed anteriorly by remodelled bone with subluxation of the posterior portion of the footplate. As the otosclerotic lesion expands to involve the stapediovestibular joint, the stapes footplate may become completely fixed in the oval window, reducing the transmission the vibrations of the ossicles to the cochlea (Handzel & McKenna, 2010).

Hearing loss is conductive in the vast majority of cases and typically progresses with the expansion of otosclerotic foci from affecting primarily the low-frequencies to becoming apparent across the audiometric frequency range. The maximum conductive hearing loss that occurs due to stapes fixation is approximately 60 dB HL (Maureen, 1993). Although a depression of bone-conduction thresholds centred around 2 kHz termed “Carhart’s notch” is often observed, this is considered to be due to a loss of the external and middle ear contributions to bone-conduction hearing, rather than a true sensorineural component (Carhart, 1971; Tonndorf, 1971). An asymmetrical conductive hearing loss is common, as although approximately 75% of cases will be bilateral, the extent and time course of the disease is likely to vary between the ears (Handzel & McKenna, 2010). A preliminary diagnosis is generally made based on the audiogram, case history, and otoscopic examination, with the definitive diagnosis made at the time of surgery.

Unlike in ears with COM, the tympanic membrane, malleus, incus, and mucosa of the middle ear and mastoid are unaffected by the presence of otosclerosis at the footplate. Chronic abnormalities in Eustachian tube function and static pressure of the middle ear are also not

associated with otosclerosis. Short- and long-term hearing outcomes following surgery to mobilise the fixed stapes in otosclerosis will therefore not be compromised by persistent abnormalities of the ear, and results are generally very good (Merchant & Rosowski, 2010).

2.5 Surgical categorisation

The procedure performed to correct conductive hearing loss depends strongly on the type and extent of disease present, the presence of anatomical defects to the structures of the middle ear, the anatomy of the individual, and the preference of the surgeon, among other factors. The following paragraphs provide an overview of surgeries performed to reconstruct the conductive mechanism based on the way each procedure is performed in the hospitals used in this study and the most common descriptions provided in the literature.

2.5.1 Tympanoplasty

The term tympanoplasty has been used to describe a wide range of surgical procedures that aim to reconstruct the tympanic membrane, ossicular chain, or both. Traditionally, Wullstein's classification system was used to categorise tympanoplasty procedures as types I through V (Wullstein, 1956). With the exception of type I tympanoplasty, also known as a myringoplasty, which describes the repair of only the TM, this classification system is now rarely used, and instead tympanoplasty procedures are typically described based on the structures involved or the type of reconstruction performed. In the present study, only procedures that involved repair of a TM perforation without repair of the ossicular chain were classified as tympanoplasties. The primary indication for tympanoplasty is therefore TM perforation, with or without middle ear pathology.

The technique and graft material employed in surgical repair of the tympanic membrane varies depending on the size and location of the perforation, the presence or absence of middle ear pathology, anatomical considerations (such as the width of the EAC), and the surgeon's preference (Athanasiadis-Sismanis, 2010). Tympanoplasty can be performed using a transcanal, postauricular, or endaural approach. The postauricular approach is typically preferred for large and anterior TM perforations and small EACs, while the transcanal approach provides adequate visualisation of the perforation and TM for smaller, posterior perforations (Athanasiadis-Sismanis, 2010).

Grafts can be constructed of synthetic, or more often, autologous materials, including temporalis fascia, loose areolar fascia, tragal perichondrium, periosteum, cartilage, or adipose tissue (Athanasiadis-Sismanis, 2010; Dornhoffer, 2003). There are two main grafting techniques used in tympanoplasty; the underlay and overlay techniques, which differ in the position of the graft in relation to the tympanic annulus. When the underlay technique is employed, the graft is positioned medial to the tympanic annulus and manubrium of the malleus, whereas in the overlay technique the graft is placed lateral to the fibrous annulus and any TM remnant and medial to the manubrium (Athanasiadis-Sismanis, 2010). Results associated with both techniques are very good, although the overlay technique is associated with a higher risk of complications such as graft lateralisation, formation of granulation tissue and epithelial pearls, and delayed healing (Athanasiadis-Sismanis, 2010; Glasscock, 1973).

2.5.2 Ossiculoplasty

Ossiculoplasty refers to reconstruction of all or part of the ossicular chain with the aim of re-establishing the link between the tympanic membrane and cochlea, and optimising the middle ear transformer mechanism (Athanasiadis-Sismanis & Poe, 2010). Surgical reconstruction of the ossicular chain is indicated in cases of conductive hearing loss clinically suspected to be due to discontinuity or fixation of the ossicular chain. The procedure may be performed in otherwise healthy ears, or in ears with COM, often in conjunction with tympanoplasty and/or mastoidectomy. When COM is active, treatment of middle ear and mastoid disease is prioritised and ossiculoplasty may be delayed to a second stage procedure following surgical management of the active disease (Athanasiadis-Sismanis & Poe, 2010).

The wide range of surgical techniques and types of prostheses in current use for ossicular reconstruction has led to procedures generally being described in terms of the type of prosthesis used, how it was positioned relative to the ossicular defect, and the use of any other stabilising or grafting materials, rather than in terms of a classification system (Athanasiadis-Sismanis & Poe, 2010). The choice regarding the surgical procedure is based on the extent of ossicular deficiency, the type of any additional mastoid surgery performed, and the preference and experience of the surgeon (Merchant & Rosowski, 2010).

Materials used in ossiculoplasty include autografts, such as autologous ossicles, cartilage, and bone. For example, where the incus is relatively healthy, this ossicle can be removed and reshaped, then interpositioned into the ossicular chain to restore the link between the

tympanic membrane and inner ear is (Pennington, 1983). In cases where the ossicles are absent, extensively eroded, or diseased, synthetic prostheses are used to reconstruct the ossicular chain. Synthetic prosthetic materials will ideally be highly biocompatible, stable, and easy to manipulate with minimal handling required during surgery (Moon et al., 2007). Materials currently in common use include hydroxyapatite, polyethylene, and titanium (Moon et al., 2007; Shinohara, Gyo, Saiki, & Yanagihara, 2000).

Two main types of synthetic prosthesis are used, depending on the remaining middle ear structures. A partial ossicular replacement prosthesis (PORP) is used when the stapes superstructure is present to connect the head of the stapes to the tympanic membrane or manubrium (Brackmann & Sheehy, 1979). If the stapes superstructure is absent, a total ossicular replacement prosthesis (TORP) is placed between the stapes footplate in the oval window and the tympanic membrane or manubrium (Figure 7). A cartilage buffer is often positioned between the prosthesis and the tympanic membrane to prevent extrusion of the prosthesis (Merchant & Rosowski, 2010).

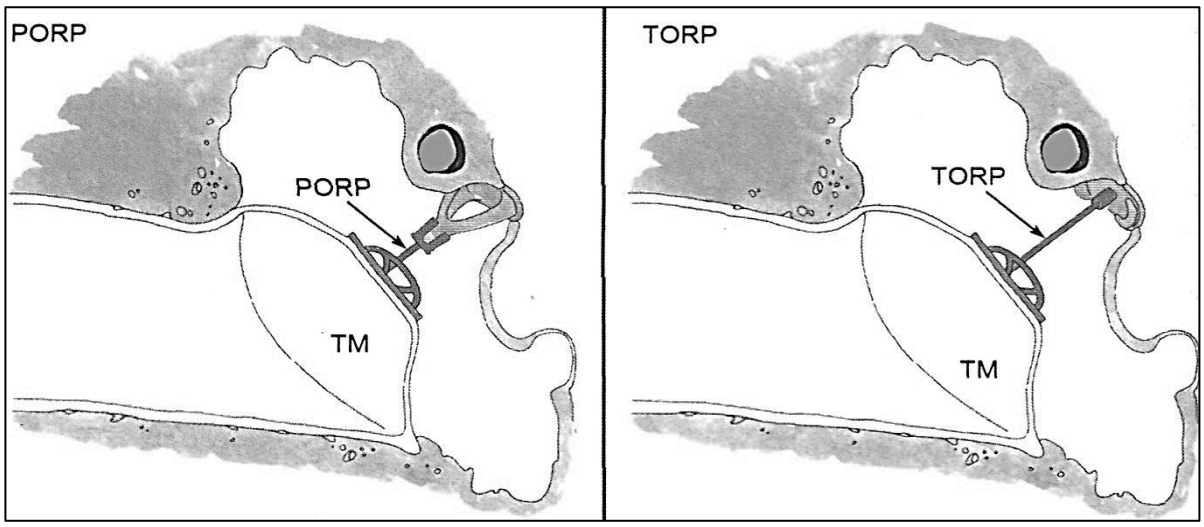

Figure 7. Schematic diagram showing positioning of the prosthesis in partial ossicular replacement prosthesis (PORP) and total ossicular replacement (TORP) procedures. From Chapter 9: Surgical reconstruction and passive prostheses (p.258), by S.N. Merchant and J.J. Rosowski, (2010). In *The middle ear: Science, otosurgery, and technology*, by S. Puria, R. Fay, and A. Popper (Eds.). Copyright 2013 by Springer Science+Business Media. Reprinted with permission.

2.5.3 Mastoidectomy

Mastoidectomy refers to surgical procedures in which the mastoid bone is opened and the air cells are removed by drilling. Typically, mastoidectomy is performed to control COM, either

with or without cholesteatoma, within the mastoid and middle ear space. The procedure provides access to remove disease from anatomical areas which are challenging to visualise, particularly the epitympanum and air cells (Bennett, Warren, & Haynes, 2006). The primary goals of mastoidectomy are to eradicate disease and prevent disease recurrence, while the preservation or restoration of hearing is the secondary goal (Haynes & Wittkopf, 2010). Tympanoplasty and/or ossiculoplasty are often performed in conjunction with mastoidectomy, either during a single operation, or as a second-stage procedure to restore the middle ear conductive mechanism and improve hearing.

Mastoidectomy procedures can be broadly divided into two types; canal wall-up (CWU) and canal wall-down (CWD) mastoidectomies. CWU procedures involve complete removal of the mastoid air cells along the tegmen, sigmoid sinus, and presigmoid dural plate, with preservation of the posterior wall of the bony external ear canal (Bennett et al., 2006). Healthy tissues of the middle ear and EAC are restored to their anatomical positions following disease removal (Haynes & Wittkopf, 2010). CWU mastoidectomies often require a second-look procedure 6 to 12 months after the initial surgery to check for disease recurrence and to reconstruct the ossicles, if this was not done initially. Disease recurrence is not uncommon and is often not visible on clinical examination when the canal wall is left intact (Syms, Syms, & Sheehy, 2010).

In CWD procedures the posterior osseous EAC wall is removed in addition to the mastoid air cells, so that the EAC and mastoid converge to form a common cavity. CWD mastoidectomy includes meatoplasty, which entails removing a varying amount of conchal cartilage and skin of the membranous EAC, and reconstruction of the TM to separate the middle ear space from the mastoid cavity (Kveton, 2010). Ossicular reconstruction may or may not be performed, depending on the specific type of procedure undertaken (Syms et al., 2010).

The purpose of creating an open cavity by removing the EAC is to exteriorise the mastoid cavity and any unresectable disease to facilitate monitoring of recurrent or persistent disease (Kveton, 2010). Surgical exposure to the epitympanum and more difficult to access areas of the middle ear may also be improved when the CWD procedure is used compared to the canal-wall up procedure (Palva, 1987). The procedure is therefore indicated over CWU mastoidectomy in cases such as unresectable disease on the facial nerve, stapes footplate or sinus tympani, or limited access to the epitympanum (Haynes & Wittkopf, 2010).

2.5.4 Stapes surgery

In cases of clinically diagnosed stapedial fixation, stapedectomy is indicated when the conductive loss is of a degree that there is a reasonable expectation that the patient will obtain a perceptible benefit from surgery. In general, an air-bone gap of at least 25 dB HL at 0.25 to 1 kHz is considered adequate to justify surgery (Handzel & McKenna, 2010).

The term stapedectomy is often used to broadly describe surgical procedures involving the removal of all or part of the stapes footplate, and its replacement by a prosthesis (Merchant & Rosowski, 2010). More specifically, stapedectomy refers to the removal of the entire footplate (or part of the footplate in the case of partial stapedectomy). Stapedotomy involves the creation of a small opening in the footplate using a pick, drill, or laser, rather than the removal of the entire footplate. In both cases, the prosthesis is positioned between the oval window and the incus to create a mobile structure for the transfer of vibration from the tympanic membrane to the inner ear. Stapedotomy is a more recently developed procedure compared to stapedectomy, and is currently the procedure of preference (Handzel & McKenna, 2010). For the purposes of this thesis, patients undergoing either stapedectomy or stapedotomy procedures were recruited as participants in the studies described. Information regarding the type of procedure performed was recorded to allow later sub-group data analysis based on procedure type.

Both stapedectomy and stapedotomy may be performed using either a postauricular or a transmeatal approach. To briefly summarise the procedures as described by Handzel and McKenna (2010), the initial step following opening of the middle ear cavity is gentle palpation of the ossicles to establish mobility. When stapedial fixation and incus and malleus mobility are confirmed, the surgeon proceeds with separation of the incudostapedial joint and cutting of the stapedial tendon. The posterior crus of the stapes is then divided and the suprastructure is removed. At this point in stapedotomy a fenestration is made in the footplate to allow placement of the prosthesis within it. In stapedectomy the entire footplate is removed, leaving the membrane below intact, and the oval window is sealed with a tissue graft. A prosthesis is then attached to the incus and inserted into the fenestration. Many stapes prostheses of various designs and materials have been described, with pistons constructed of Teflon and titanium currently in common use (Merchant & Rosowski, 2010).

2.6 Conclusion

The peripheral auditory and vestibular systems, the sensory organs of which are housed in the inner ears, are both delicate and complex. Middle ear disease, as well as surgical procedures to eradicate such disease and correct conductive hearing loss, can potentially impact both hearing and balance function. Where this chapter has discussed the normal anatomy, physiology, and assessment of hearing and balance, the following chapters will review and investigate how these systems may be affected by middle ear disease, and particularly the short and long-term effects of middle ear surgery on auditory and vestibular function.

PART II: HIGH-FREQUENCY HEARING LOSS FOLLOWING MIDDLE EAR SURGERY

Chapter 3: Hearing loss following middle ear surgery

3.1 The prevalence and patterns of hearing loss following middle ear surgery

3.1.1 Quantifying hearing loss following middle ear surgery

Sensorineural hearing loss is a well-known complication of middle ear surgery and one that patients are informed of as part of the process of obtaining informed consent. Typically, across a variety of middle ear procedures, patients are advised of a rate of some degree of permanent hearing loss of 0.6 – 5% (Ayache, Lejeune, & Williams, 2007; Dawes & Curry, 1974; Palva, Kärjä, & Palva, 1973; Sheehy, 1984; Tos, Lau, & Plate, 1984) and an incidence of anacusis in the operated ear of approximately 0.5% (Dawes & Curry, 1974; Shea, 1998; Tos et al., 1984). However, reported rates of postoperative hearing loss vary widely and a review of the literature documenting hearing outcomes of middle ear surgery shows significant variation in the way in which data are reported. The success of surgery may be established and reported using several outcome measures, including the improvement in average air-conduction thresholds, bone-conduction thresholds, and/or air-bone gaps at 0.5, 1, and 2 kHz, or 0.5, 1, 2, and 3 or 4 kHz. Other studies fail to report the criteria by which rates of success or failure of surgery are calculated (Berenholz, Rizer, Burkey, Schuring, & Lippy, 2000; Hodgson & Wilson, 1991). This variability in reporting persists despite the publication of guidelines for the reporting of hearing results following surgery to correct conductive hearing losses by the Committee on Hearing and Equilibrium, American Academy of Otolaryngology – Head and Neck Surgery (AAO-HNS) in 1995.

Middle ear surgery does not alter hearing thresholds equally at all audiometric frequencies, therefore the choice as to which frequency or frequencies will be used to report the hearing outcome of a surgery has the potential to significantly alter the reported rates of success and complications. Analysis of bone-conduction thresholds following various types of middle ear surgery has demonstrated that two separate phenomena occur. Successful reconstruction of the conductive mechanism may restore the external and middle ear contribution to bone-conduction hearing, thus improving thresholds at 0.5, 1, and particularly 2 kHz (Harder, Jerlvall, Kylén, & Ekvall, 1982; Lee, Hong, Hong, Cho, & Chung, 2008; Linstrom, Silverman, Rosen, & Meiteles, 2001; Mair, Pedersen, & Laukli, 1989; Moscillo, Imperiali, Carra, Catapano, & Motta, 2006; Toner, Smyth, & Kerr, 2007; Tuz, Dogru, Uygur, & Gedikli, 2000). Conversely, the threshold at 4 kHz appears to be both the least likely to

improve upon restoration of the middle ear mechanism and most sensitive to iatrogenic cochlear damage. Threshold elevation thought to be reflective of cochlear trauma is therefore most commonly seen at this frequency postoperatively (à Wengen, Pfaltz, & Uyar, 1992; Aslam, 2010; Lesinski & Stein, 1989; Palmgren, 1979; Palva et al., 1973; Persson, Harder, & Magnuson, 1997; Ragheb, Gantz, & Mccabe, 1987; Redaelli de Zinis, Cottelli, & Koka, 2010; Vartiainen & Seppa, 1997).

Given the differential effects of middle ear surgery on high- and low-frequency bone-conduction thresholds, one would expect that rates of loss reported in studies that use lower frequencies to quantify hearing loss will be less than studies that use higher frequencies. Indeed, this effect is demonstrated in a meta-analysis of 29 studies reporting the incidence of sensorineural hearing loss following stapes surgery conducted by Bergin (2011). Using a criterion of greater than 10 dB to define a significant change in hearing, Bergin found that across the studies, the incidence of hearing loss was 2.0% when calculated as the average bone-conduction threshold change at 0.5, 1, and 2 kHz. The addition of 4 kHz to the average increased the rate to 2.5%, while ignoring 0.5 kHz and limiting the average to 1, 2, and 4 kHz increased the apparent incidence slightly further to 2.8%. A markedly higher rate of hearing loss of 5.0% was identified when only the change in the 4 kHz bone-conduction threshold was considered. As well as showing the greater sensitivity of high-frequency thresholds to surgical harm, Bergin's data demonstrates that when pure-tone averages are used, the mutually neutralising elements of the improvement of bone-conduction thresholds at lower frequencies and the increase in the 4 kHz threshold are likely to mask each other out, reducing the apparent rate of hearing change.

Another key reason for the high variability in the reported rates of postoperative sensorineural hearing loss is the lack of consistency in the magnitude of threshold change that is deemed a hearing loss. In some reports documenting a low incidence of postoperative sensorineural loss, the threshold significance levels chosen are as high as 30 – 40 dB (Kamal, 1996; Lippert et al., 2001; Mann, Amedee, Fuerst, & Tabb, 1996), which will clearly lower the apparent incidence of hearing loss compared to studies using lower threshold shift criteria to define a significant change in hearing. Such high significance criteria exclude potentially significant, but smaller, hearing losses from being reported.

3.1.2 Rates of sensorineural hearing loss following middle ear surgery

If we focus only on hearing at 4 kHz, the rate of sensorineural hearing loss following surgery is often markedly higher than that reported to patients. A retrospective chart review conducted by Bergin (2011) in order to determine the incidence of sensorineural hearing loss following middle ear surgeries performed at Christchurch Hospital and through the private practices of two otologists between 1998 and 2009, identified complete audiometric records for 834 stapedectomy/stapedotomy, tympanoplasty/myringoplasty, mastoidectomy, and ossiculoplasty procedures. Using criteria of greater than a 10 dB increase in the bone-conduction threshold at 4 kHz to define a significant hearing loss, 8.3% of the procedures were found to have resulted in a sensorineural loss.

Studies that have quantified sensorineural hearing loss in the same way as Bergin (2011) have generally shown similar rates of sensorineural hearing loss. Following 111 TORP and PORP ossiculoplasties, Schmerber, Troussier, Dumas, Lavieille, and Nguyen (2006) documented a rate of sensorineural hearing loss at 4 kHz of 3.6%, identical to the rate of loss shown by Bergin (2011) for 140 comparable procedures. A higher rate of postoperative hearing loss has been shown following stapes surgery, and Bergin reported an incidence of postoperative deterioration at 4 kHz 11.2% in 196 primary stapes surgeries. In a much smaller series, Häusler, Schär, Pratisto, Weber, and Frenz (1999) reported hearing loss in 20% of their 15 stapedotomy patients two months postoperatively, with the incidence decreasing to 7% when patients were reassessed one year after surgery.

One finding of note was the relatively high rate (10%) of sensorineural hearing loss following tympanoplasty/myringoplasty identified by Bergin (2011). Given that this is a procedure that typically involves less ossicular manipulation than other surgeries studied, it is interesting that the rate of postoperative hearing loss was higher than the overall rate of 8.3%. Redaelli de Zinis et al. (2010) calculated sensorineural hearing loss following tympanoplasty/myringoplasty in the same manner as Bergin, and published a slightly lower rate of 4 kHz bone-conduction deterioration of 7% for their series of 134 subjects. Although it is possible that these results reflect genuinely high rates of sensorineural hearing loss following tympanoplasty/myringoplasty, it is also possible that these findings result from incomplete data collection. In Bergin's chart review, pre- and postoperative audiometry with 4 kHz bone-conduction thresholds was not available for 75.3% of patients who underwent tympanoplasty/myringoplasty procedures, relative to 63.5% for all procedures. If patients who experience more problems postoperatively are more likely to attend follow-up

appointments or have postoperative audiometry performed, the sample will be biased towards patients with poorer outcomes.

3.1.3 Stability of bone-conduction hearing thresholds following middle ear surgery

As exemplified by Häusler et al.'s (1999) study, postoperative hearing loss may be either transient or permanent. In agreement with the data reported by Häusler et al., partial recovery of hearing over the early postoperative period was documented in a prospective study by Somers, Vercruysse, Zarowski, Verstreken, and Offeciers (2006), who monitored the evolution of bone-conduction thresholds from two days to six months following 336 stapedotomy procedures. Two days after surgery, a mean drop was found at all bone-conduction test frequencies, the largest reaching 7 dB at 4 kHz. Despite significant recovery at other frequencies, a residual mean hearing loss of 1.6 dB at 250 Hz and 2.7 dB at 4 kHz was measured six months postoperatively. Seventeen patients who showed an increase in bone-conduction thresholds at least 15 dB at the first postoperative assessment were administered methylprednisolone and intravenous vasodilators following surgery. Four of these patients retained sensorineural hearing losses ranging from mild to severe. It is unclear whether the recovery of cochlear function was a result of the intervention, or whether bone-conduction thresholds would have improved naturally over the postoperative course.

Initial deterioration and delayed improvement of mean bone-conduction thresholds following stapes surgery has also been demonstrated in several prospective studies and retrospective chart reviews without pharmaceutical intervention (Antonelli, Gianoli, Lundy, LaRouere, & Kartush, 1998; Gerard, Serry, & Gersdorff, 2008; Keck, Wiebe, Rettinger, & Riechelmann, 2002; Sergi et al., 2010), For example, Gerard et al. (2008) found that mean bone-conduction thresholds at 1, 2, and 4 kHz, but not 0.5 kHz, had deteriorated significantly from preoperative levels when assessed 24 hours after surgery in 147 cases in which stapedotomy was performed. Thresholds returned to preoperative levels at 1 and 2 kHz by the final assessment 2 - 6 months postoperatively, however, despite minor improvement following the initial assessment, the mean threshold at 4 kHz remained significantly poorer than before surgery. Similarly, Sergi et al. (2010) showed that while mean bone-conduction thresholds remained stable at 0.5 and 1 kHz, and improved by 1 dB at 2 kHz, a loss of 5 dB was recorded at 4 kHz two days following CO_2 laser stapedotomy. When reassessed an average of

3.7 months postoperatively, the mean 4 kHz bone-conduction threshold had recovered to within 1 dB of the preoperative mean.

The use of group means in each of the studies discussed does not make it clear whether the improvement is due to complete resolution of hearing loss in some cases, partial resolution in most cases, or a combination of both phenomena. A more recent chart review by Sperling et al. (2013) addressed some of the questions remaining from previous studies by comparing the *rates* of bone-conduction threshold deterioration of greater than 10 dB measured five days after primary stapedotomy, to the rate of threshold deterioration six months after surgery. Based on the closure of the mean air-bone gap from 30 dB before surgery to 7 dB five days after surgery and 6 dB six months postoperatively, the surgeries can be considered successful. However, at the early postoperative assessment, 28 of the 45 patients presented with a loss of bone-conduction sensitivity of at least 10 dB at one or more frequencies. Six months after surgery, significant postoperative threshold shifts persisted in 10 of the 28 patients with an early bone-conduction loss, and were also documented in six patients who had initially experienced no threshold increase. Both early and late bone-conduction threshold shifts tended to be larger and occurred more frequently at 4 kHz than at lower frequencies. Sperling et al. hypothesise that such early loss of hearing may reflect more subtle labyrinthine trauma that, although often recoverable, may still have the potential to affect overall cochlear health and impact hearing years later.

Given the variability in results over the postoperative course, the timing of the postoperative audiometric assessments from which data is reported warrants consideration when comparing results across studies. It is also important to note that the heterogeneity across studies is not limited to the way in which results are reported. Different populations and patient series will have different characteristics in terms of the extent of disease, and centres will manage cases differently using different surgical techniques and equipment. The extent of the influence of many of these factors on hearing outcomes is uncertain, however, they certainly limit the comparisons that can be made across the literature. Although all the factors and measurement parameters discussed create uncertainty regarding the typical rate of hearing loss following middle ear surgery, what is evident is that when sensitive measures of sensorineural hearing loss are considered, for example the change in the 4 kHz bone-conduction threshold, the rate of postoperative hearing loss is often greater than the risk quoted to patients.

3.1.4 High-frequency hearing loss following middle ear surgery

3.1.4.1 Surgery for chronic middle ear disease

Few studies of middle ear surgery outcomes report postoperative thresholds above 4 kHz, however, those that do frequently note the increased rate of postoperative hearing loss in the high-frequency range (Antonelli et al., 1998; Barbara, Monini, de Seta, & Filipo, 1994; Bauchet St Martin et al., 2008; Bellucci, 1979; Choi et al., 2011; Dawes, 1999; Desai, Aiyer, Pandya, & Nair, 2004; Just, Guder, & Pau, 2011; Meyer, 1999; Palva et al., 1973; Shaan et al., 1995; Strömbäck, Kobler, & Rask-Andersen, 2012). An increased incidence of postoperative hearing loss in the high-frequencies was first identified by Palva et al. (1973). In their analysis of hearing outcomes following 1680 surgeries for chronic ear disease, Palva et al. found that the rate of "high-tone" hearing loss was 4.5%. In 57% of those cases, the hearing loss was limited to the 4 – 8 kHz range. The authors are not clear in their definition of a "high-tone" loss; however it appears that in all cases hearing dropped to profound levels at the frequencies in question. In 27 patients with hearing loss, Palva et al. employed a series of special tests, including loudness balancing and the forward and reverse Békésy tests, which were designed to clarify the nature of the hearing losses. The results were taken to unanimously indicate that the site of lesion was the cochlea in all cases.

Hearing deterioration in the high-frequency range may occur either with or without a concurrent increase in the bone-conduction threshold at 4 kHz. Whereas a loss in bone-conduction sensitivity at 4 kHz provides a strong case that the loss in higher frequencies is at least partially sensorineural, the explanation is not as clear when an isolated increase in air-conduction thresholds at 6 or 8 kHz is documented. In agreement with Palva et al. (1973), an increased susceptibility of hearing thresholds at 4 kHz and above to deterioration following surgery for chronic middle ear disease was demonstrated by Dawes (1999). Reporting data collected from 145 ears within six weeks of surgery, Dawes found an elevation in the 8 kHz threshold in 11% of cases. Of these 16 patients, five patients also experienced a drop in bone-conduction sensitivity at 4 kHz. Only two patients with an increase in 4 kHz bone-conduction and 8 kHz air-conduction thresholds also had bone-conduction threshold elevation at lower frequencies. Although no details are given, the author comments that "some" patients with a postoperative elevation of bone-conduction or 8 kHz air-conduction thresholds showed an improved pure-tone average across the frequencies often used for reporting surgical outcomes. This comment highlights the need to consider higher frequencies when reporting rates of surgical success or harm.

Similar findings of an increased incidence of hearing loss following surgery for chronic ear disease when frequencies above 4 kHz are examined have been published by Shaan et al. (1995) and Choi et al. (2011). Of the 11% of 37 patients that experienced a loss at 8 kHz described by Shaan et al. (1995), all also showed an increase in the 4 kHz bone-conduction threshold. In contrast, Choi et al. (2011) present mean data from a large series of 559 patients undergoing surgical management of COM that show a limited association between an increase in high-frequency air-conduction thresholds and bone-conduction hearing at 4 kHz. Mean data across tympanoplasties and mastoidectomies showed significant improvement in postoperative air-conduction thresholds at all frequencies except 6 kHz (the highest frequency tested), which was aggravated by 3.4 dB. In this series, the loss at 6 kHz was associated with only a 0.1 dB increase in the mean bone-conduction threshold at 4 kHz. Given that only group mean data is reported by Choi et al., it is possible that a small number of patients who did experience a loss at 4 kHz are obscured by the larger number who experienced an improvement or little change.

Palva et al. (1973) stated that some recovery of hearing sensitivity occurred during the first three postoperative months, following which there was no appreciable change in thresholds. However, the rate and degree of recovery of high-frequency hearing following middle ear surgery for chronic middle ear disease have not been documented in any detail. Dawes (1999) present hearing outcomes from within six weeks of surgery, Choi et al. (2011) performed the final assessment at a mean of five months postoperatively, and Palva et al. (1973) are not clear regarding when the presented data was recorded. In order to determine the relative rates of transient and permanent high-frequency postoperative hearing loss it is necessary to obtain audiological data from both early and late in the postoperative course in the same group of patients.

3.1.4.2 High-frequency hearing loss following surgery for otosclerosis

Stapes surgery for otosclerosis has also been shown to produce a higher rate of deterioration at frequencies above 4 kHz than at lower frequencies (Antonelli et al., 1998; Barbara et al., 1994; Bauchet St Martin et al., 2008; Bellucci, 1979; Just et al., 2011; Meyer, 1999; Strömbäck et al., 2012). It is apparent that high-frequency hearing loss occurs more frequently in early postoperative assessments and that recovery begins within the first month of surgery (Antonelli et al., 1998; Barbara et al., 1994; Just et al., 2011). For example,

Barbara et al. (1994) reported that hearing loss at 8 kHz documented three and five days following stapedotomy recovered more slowly and to a lesser degree than early postoperative hearing loss at 4 kHz. In a more recent study of hearing following 48 stapedotomies, Just et al. (2011) documented a non-significant increase in mean bone conduction thresholds at 4 – 8 kHz present 2 – 3 weeks postoperatively that they described as temporary. However, at the final postoperative assessment six weeks after surgery, an increase of greater than 5 dB in the bone-conduction threshold was found in 10% of patients at 4 kHz, 19% at 6 kHz, and 25% at 8 kHz. This represents a marked decrease in the rate of bone-conduction deterioration compared to the early postoperative assessment, but certainly appears to indicate that the hearing loss was not transient in all cases.

While the patterns and timing of changes in hearing postoperatively are of significant interest and importance in determining the likely pathogenesis of the hearing loss and for counselling patients, more important for the patient is the likelihood that any high-frequency hearing loss will be permanent. In a large series of 338 patients undergoing surgery for primary otosclerosis published by Strömbäck et al. (2012), the reported rate of high-frequency hearing loss one year postoperatively was 6.5%. In that report, a high-frequency loss was defined as an increase of greater than 10 dB in the average threshold at 4, 6, and 8 kHz. An increase of greater than 10 dB was also found for the 4 kHz bone-conduction threshold in 3.8% of patients, however the number of patients who experienced both a 4 kHz bone-conduction loss and an increase in high-frequency air-conduction thresholds, as opposed to only one of the two, is not reported.

Long-term hearing outcomes are also reported in a retrospective review of 61 CO_2 laser assisted stapedectomy or stapedotomy procedures by Bauchet St Martin et al. (2008). The initial postoperative assessment performed 4 – 6 weeks after surgery showed a mean improvement in thresholds at 2 kHz and below, accompanied by a worsening of the 4 kHz bone-conduction thresholds and 8 kHz air-conduction thresholds. By the follow-up assessment, at least nine months after surgery, partial improvement in mean hearing thresholds were found, although a mean loss of 4.2 dB at 8 kHz persisted. In this series, deterioration of greater than 5 dB from preoperative thresholds was documented at the final assessment in 23% of ears at the bone-conduction threshold at 4 kHz and in 38% of ears at the 8 kHz air-conduction threshold. Although these rates appear markedly higher than those reported by Strömbäck et al. (2012), this can be primarily accounted for by the use of a 10 dB threshold for reporting change by Strömbäck et al., compared to the 5 dB threshold chosen by

Bauchet St Martin et al.. In addition, both these studies report an increasing level of hearing loss with increasing frequency. The use of the average threshold at 4, 6, and 8 kHz by Strömbäck et al., would therefore be expected to result in a smaller number of patients being reported with a significant high-frequency hearing loss than when only the change at 8 kHz is reported, as was done by Bauchet St Martin et al.

A review of the extant literature highlights several key methodological issues that limit our understanding of postoperative high-frequency hearing loss. In particular, the reporting of only early or only long-term outcomes, a lack of consistency in follow-up schedules that makes comparisons between studies difficult, and published reports that fail to state at what point in the postoperative course the reported data was collected. Addressing these methodological limitations to ensure data is obtained that captures both transient and permanent hearing losses, and the rates and degrees to which they occur, is a necessary step in determining the aetiologies of such losses and devising ways to reduce it.

3.1.5 Extended high-frequency hearing loss following middle ear surgery

It is clear from the preceding discussion that the rates of sensorineural hearing loss reported following middle ear surgery are dependent on the sensitivity of the tool used to quantify the hearing outcome. Evidence of decreased hearing improvement with increasing frequency within the conventional frequency range (0.25 – 8 kHz) suggests that testing higher frequency thresholds at 8 – 20 kHz (the "extended high-frequency" (EHF) range) may be a more sensitive measure of operative harm. Indeed, it has been documented that although hearing thresholds in the conventionally measured frequency range may improve following middle ear surgery, a concomitant increase of thresholds in the EHFs may be observed (Bauchet St Martin et al., 2008; Doménech & Carulla, 1988; Mair & Laukli, 1986; Tange & Dreschler, 1990).

An elevation of thresholds in the EHF range following middle ear surgery was first reported by Mair and Laukli (1986). Audiometry performed 1 – 3 years after 36 myringoplasties and 28 stapes surgeries (stapedotomy and partial stapedectomy) showed that while both types of surgery resulted in significant improvements in hearing in the conventional frequency range, a significant mean increase in air-conduction thresholds was evident at 10 – 16 kHz. Although these changes were significantly larger following stapes surgery, a significant worsening of thresholds was also seen at 10 – 16 kHz following myringoplasty. That

significant hearing loss was limited to the EHFs was interpreted as evidence that high-frequency audiometry may be a more sensitive test of damage to hearing following middle ear surgery.

Mair and Laukli's (1986) finding of a depression in mean EHF air-conduction thresholds following otherwise successful stapes surgeries has been replicated by Doménech and Carulla (1988), and Tange and Dreschler (1990). The type of stapes procedure performed was also shown to impact the degree of high-frequency hearing loss recorded by Tange and Dreschler (1990), who demonstrated a larger decrement in mean thresholds at 10 – 18 kHz following 13 partial stapedectomies (11.9 dB SPL), compared to 40 stapedotomy (5.5 dB SPL) procedures. Audiometry was reportedly performed preoperatively and at 3 months, 6 months, and 12 months postoperatively, although it is unclear which set of postoperative data is presented, and therefore whether the hearing loss may be considered permanent. Tange and Dreschler suggest the variation in results with surgery type is the result of stapedotomy being a less traumatic procedure to the cochlea than stapedectomy. It is not reported; however, what dictated the choice of surgical procedure. It is possible that the degree of hearing loss observed postoperatively may not bear a direct relationship to the type of surgery performed and the level of trauma the cochlea was subjected to, but rather be related to the physical condition of the ossicles and inner ear and that led that type of surgery to be selected. It is also unclear whether either the preoperative EHF hearing loss, which was found to be greater when more than one otosclerotic focus was present or if the oval window niche was obliterated, or the postoperative EHF loss, were in fact due to cochlear damage.

A key limitation of Mair and Laukli (1986) and Tange and Dreschler (1990) studies investigating postoperative changes in air-conduction thresholds in the EHFs is the absence of bone-conduction threshold measurements across the same frequency range. Using conventional bone-conduction transducers it is only possible to test thresholds up to 6 kHz due to a sharp drop in the output of the transducer above 4 kHz (Richards & Frank, 1982). These previous studies have hypothesised, presumably based on the frequencies at which the hearing loss was observed, that the loss of EHF hearing acuity following middle ear surgery is the result of trauma to the cochlea. However, there are many mechanisms by which middle ear surgery may produce a conductive hearing loss, either transiently through factors directly related to surgery in the tympanic cavity, such as oedema, transudates, and microhaemorrhage (Robinson & Kasden, 1977), or more permanently, as a result of changes in middle ear transmission characteristics through alteration of the mass and stiffness

properties of the middle ear structures (Mair & Hallmo, 1994). It cannot be determined based on frequencies affected alone whether the hearing loss is conductive or sensorineural – bone-conduction measurements are required.

The first attempts to measure extended high-frequency cochlear function following middle ear surgery were made using an Audimax 500 high-frequency electrostimulation audiometer capable of measuring thresholds up to 20 kHz (Doménech & Carulla, 1988; Doménech, Carulla, & Traserra, 1989; Hegewald et al., 1989). This technique uses electrical stimulation delivered through cutaneous electrodes to provoke auditory sensations in the cochlea and is thought to provide auditory stimulation similar to that evoked with conventional bone-conduction testing (Tonndorf & Kurman, 1984). Using this technique to examine changes in cochlear function at 6 – 19 kHz in 24 patients following stapedectomy, Doménech and Carulla (1988) demonstrated a "moderate" hearing loss in 20 patients, and a lowering of the highest frequency at which a hearing threshold was measureable in 16 patients. No downward shift in either air- or bone-conduction thresholds was recorded at any of the conventional frequencies. These results were interpreted as indicating that even what is traditionally considered a successful stapedectomy, frequently causes inner ear damage. Two major methodological limitations of Doménech and Carulla's study undermine this conclusion. The first is that postoperative high-frequency audiometry was performed a few days after stapedectomy, whereas conventional audiometry was performed approximately three weeks postoperatively. Using only this early postoperative data it cannot be determined whether the EHF hearing loss was transient or permanent, nor is it clear whether if conventional audiometry was similarly performed within a few days of surgery, a comparable hearing loss would have been observed. The second flaw, the failure to mask thresholds in the EHF range, is discussed in further detail below.

Electrostimulation thresholds elicited using the Audimax 500 audiometer have also been shown to deteriorate following tympanoplasty (Doménech et al., 1989) and mastoidectomy (Hegewald et al., 1989) procedures. Doménech et al. (1989) demonstrated a measurable hearing loss (defined as more than five electrostimulation units at one or more frequencies) in the EHFs in nine of 24 patients following tympanoplasty. Audiometry in the conventional frequency range showed no deterioration of hearing at 4 kHz, and a loss at 8 kHz was present in only one case. Again, the relative rates of transient and permanent hearing loss are unknown, as the timing of follow-up assessments is not stated.

Hegewald et al. (1989) found evidence of only temporary mean threshold shifts following 25 mastoidectomies. High-frequency electrostimulation audiometry performed 48 hours postoperatively showed significant mean threshold changes at 2, 4, 5, 6, and 16 kHz. By the second postoperative assessment one month after surgery, no statistically significant threshold deterioration was evident at any frequency. A significant change was, however found in the mean highest frequency at which a threshold could be measured before the limit of the audiometer was reached. This value decreased from that measured preoperatively by an average of 890 Hz at one month after surgery, which Hegewald et al. suggest indicates that this measure is a more sensitive test of surgical trauma than individual threshold changes. The use of mean threshold changes may be particularly insensitive in the EHF range due to the reduced dynamic range of the audiometer at these frequencies and the higher probability of a preoperative hearing loss being present.

As stated above, the electrostimulation bone-conduction technique used by Doménech and Carulla (1988), Doménech et al. (1989), and Hegewald et al. (1989) did not include masking of bone-conduction thresholds. Effective contralateral masking procedures are vital in both air- and bone-conduction audiometry to accurately determine the ear responding to the stimulus. The omission of masking when performing bone-conduction audiometry results in simultaneous stimulation of both cochleae, and in theory, measures only the thresholds in the better hearing ear (Studebaker, 1967). Doménech and Carulla (1988) attempted to verify that they were assessing the threshold of the operated ear by asking patients to report lateralisation of the stimulus. They concluded that as no patient reported hearing the tone in the contralateral ear, they were most likely measuring the threshold of the ipsilateral ear. Hegewald et al. (1989) assert that due to the minimal interaural attenuation (IAA) of the skull, both the operated and non-operated ears should be similarly exposed to drill noise during mastoid surgery. They propose that it is therefore unnecessary to obtain individual ear bone-conduction thresholds to document iatrogenic damage, as thresholds from both ears should be affected. This assertion does, however, rely on the assumption that any surgical trauma is solely the result of noise and/or vibration from drilling and suctioning, rather than from other mechanisms, such as manipulation of the ossicular chain, which would be expected to affect only the operated ear.

Although the absence of masked bone conduction data may certainly be considered a limitation of all three studies, it is interesting to note that such a high rate of hearing loss was documented in the EHF range by Doménech and Carulla (1988) and Doménech et al. (1989)

in what may be the better hearing ear. This finding may support the theory that the component of surgery resulting in hearing deterioration in this series did affect both ears, suggesting that noise and/or vibration from drilling, suctioning, or a combination of both, may be responsible for the hearing loss. Alternatively, such results may indicate that, unlike conventional bone-conduction testing, electrostimulation audiometry in the EHF range gives an indication of the threshold in the ipsilateral ear only.

To our knowledge, only one previous study has been published that has included both masked air- and bone-conduction audiometric data in the EHF range following middle ear surgery. Mair and Hallmo (1994) used the Präcitronic KH-70 electromagnetic high-frequency bone-conductor to examine the changes in EHF hearing acuity following myringoplasty. Although mean air-conduction thresholds across the 22 patients were elevated by 2 – 11 dB at all frequencies from 6 to 18 kHz when assessed an average of 4.5 months postoperatively, masked bone-conduction thresholds were not significantly altered in the EHF range. This suggests that the mean high-frequency hearing loss documented following myringoplasty in this group was due to impaired middle ear transmission, presumably due to structural changes to the tympanic membrane and/or the ossicular chain, rather than damage to the cochlea.

Limited change in masked bone-conduction thresholds has also been documented following ear surgery involving the use of a high-speed drill (osteoma removal, attico-antrotomy, and various types of mastoidectomy) (Hallmo & Mair, 1996). Comparison of pre- and postoperative bone-conduction thresholds obtained with Präcitronic KH-70 bone-conductor in 46 ears showed no significant change in threshold at any individual frequency three months postoperatively. However, the octave 8 – 16 kHz did show a marginally significant overall change of 1.4 dB, whereas comparable measurements in the contralateral ear (performed on 15 patients) showed no significant changes in bone-conduction thresholds following surgery. Hallmo and Mair (1996) do not consider the small increase in the mean bone-conduction high-frequency octave threshold to be evidence of surgically induced trauma, but rather the result of difficulty with correct placement of the bone conductor on the operated side following surgery. They comment that size of the Präcitronic KH-70 made it cumbersome and difficult to obtain correct retroauricular placement when defects were present in the mastoid cortex. This is likely to have resulted in poorer transmission from the transducer to the skull when the vibrator was placed on the ipsilateral, but not the contralateral, side and is proposed to be the reason for the slight increase in bone-conduction

thresholds from the operated ear postoperatively. The authors therefore conclude that their results show no evidence of cochlear damage following drilling in temporal bone surgery.

The few published reports investigating postoperative changes in hearing acuity in the EHF range have varied considerably in methodology, and in particular there is a lack of reliable data documenting changes of high-frequency bone-conduction thresholds specific to the operated ear. To summarise the results from the extant literature, a significant increase in air-conduction thresholds has been documented in the EHF range following stapes surgery (Mair & Laukli, 1986; Tange & Dreschler, 1990), and myringoplasty (Mair & Hallmo, 1994; Mair & Laukli, 1986). Only Mair and Hallmo (1994) have assessed masked bone-conduction thresholds in the same frequency range to demonstrate that the measured hearing loss was conductive in origin. One other study also employed high-frequency masked bone-conduction, and documented only a 1.4 dB increase in thresholds following ear surgery involving the use of a high-speed drill (Hallmo & Mair, 1996). No air-conduction thresholds were reported for this series. A significant elevation of high-frequency bone-conduction thresholds obtained using electrostimulation has been reported following stapedectomy (Doménech & Carulla, 1988), tympanoplasty, (Doménech et al., 1989), and transiently following mastoidectomy (Hegewald et al., 1989), although the conclusions that can be drawn from these results are limited by methodological issues, in particular the failure to mask the contralateral ear.

Although several studies published thus far have shown that hearing thresholds in the EHFs may be susceptible to elevation following various middle ear surgeries, complete and accurate data for each type of surgery demonstrating whether this hearing loss is of a transient or permanent nature, or is conductive or sensorineural in origin has not yet been obtained. No previous report of this data has documented a systematic, prospective study that is capable of detecting both transient and permanent changes to high-frequency hearing acuity and determining whether these changes are due to iatrogenic inner ear damage, altered middle ear transmission properties, or a combination of both.

3.1.6 Aims and hypotheses

A primary goal of this research was to collect prospective data describing the patterns and prevalence of hearing loss following middle ear surgery using the most sensitive measurement tools available clinically. Based on the review of the literature above, we

considered that EHF audiometry was a promising method of obtaining a more sensitive measure of changes in hearing acuity postoperatively and therefore in this phase of the study we aimed to confirm this hypothesis. Specific goals in the present study were:

- To determine the prevalence of hearing loss following middle ear surgery performed to reconstruct the conductive mechanism;
- To assess if and how hearing is differentially affected across the entire audiometric test frequency range;
- To determine the extent and time course of any recovery in hearing over the first postoperative year;
- To determine the relative rates of transient and permanent postoperative hearing loss; and
- To compare differences in each of these measurements across three types of surgery: stapes surgery (stapedectomy and stapedotomy), ossiculoplasty, and tympanoplasty/myringoplasty.

The other key aim of this research was to determine whether EHF hearing loss post-middle ear surgery was conductive or sensorineural in origin, however that aim was addressed in a separate, later study (presented in Chapter 7) following the development of the required measurement equipment.

It was hypothesised that whereas hearing would improve at 2 kHz and below following all of the procedures included in this study, we would see increasing hearing loss as the test frequency increased from 4 kHz up to 16 kHz. We expected that in the majority of cases this high-frequency hearing loss would recover over the first 1 to 3 months after surgery, but that in a smaller proportion of cases some degree of hearing loss would be retained. Tympanoplasty was hypothesised to be associated with the lowest rate of postoperative hearing loss, due to the reduced ossicular manipulation and drilling compared to stapes surgery and ossiculoplasty. We predicted that the forces transmitted to the inner ear at the stapes footplate during stapes surgery would result in the highest rate of hearing loss after this procedure.

3.2 Method

3.2.1 Participants

This prospective, observational study was conducted in association with the Department of Otolaryngology Head and Neck Surgery, Christchurch Hospital, and one otologist working in the private sector in Christchurch. Patients scheduled to undergo either primary or revision middle ear surgery under general anaesthetic at Christchurch Hospital or St George's Hospital were considered for eligibility based on the following inclusion criteria:

a) 16 years of age or older

b) Scheduled to undergo one of the following middle-ear surgical procedures:

   i. Stapedectomy/stapedotomy

   ii. Tympanoplasty/myringoplasty

   iii. Ossiculoplasty

c) An average preoperative bone-conduction threshold of 50 dB HL or less at 0.5, 1, and 2 kHz

d) No other known disorders which might affect the auditory or vestibular system

e) Available for postoperative assessments

Patients meeting the eligibility criteria were given an information sheet regarding the study (Appendix A) at the time of their preadmission assessment and invited to participate either by the surgeon or another researcher. Written consent (see Appendix A) was obtained from all patients who agreed to participate, in accordance with the ethical approval obtained for this phase of the study from the University of Canterbury and the Health and Disability Ethics Committee (Upper South B Ethics Committee, ethics reference number URB/09/07/029). Demographic information collected at the preoperative assessment included age, sex, history of previous otologic surgery, proposed surgery, and otologic symptoms.

Ninety-six participants who underwent 107 middle ear surgical procedures satisfied the inclusion criteria and were enrolled in this study. Forty-five of the surgeries were stapedectomies or stapedotomies, 33 were tympanoplasties, and 30 ossiculoplasties. Where participants underwent both tympanoplasty and ossiculoplasty during a single surgery, the surgery was categorised as ossiculoplasty to reflect that the ossicles were manipulated.

As only surgeries aimed at reconstructing the conductive mechanism were included, patients undergoing mastoidectomy procedures alone were not eligible for inclusion. Where mastoidectomy was performed in conjunction with tympanoplasty or ossiculoplasty as a single surgery aiming to improve hearing, patients were invited to participate in the study. In these cases the procedure was recorded as tympanoplasty or ossiculoplasty for the purpose of analysis with a notation that mastoidectomy was performed simultaneously.

3.2.2 Equipment

Tympanometric measures were obtained using a calibrated Grason-Stadler GSI Tympstar tympanometer (Grason-Stadler, Eden Prairie, MN) and pure-tone audiometry was performed using a calibrated diagnostic audiometer, the GSI 61 (Grason-Stadler, Eden Prairie, MN). Air-conduction stimuli in the conventional frequency range were presented via ER-3A insert earphones (Etymotic Research Inc., Elk Grove Village, IL) whenever possible, or via TDH-39 supra-aural headphones (Telephonics Corporation, Farmingdale, NY) if the EAC was not adequately clear of wax, discharge, blood, or other matter. For the presentation of air-conduction stimuli in the EHF range, Sennheiser HDA200 circumaural headphones were used (Sennheiser electronic GmbH & Co., Wennebostel, Germany). Bone-conduction stimuli were presented using a Radioear B-71 (Radioear Corporation, New Eagle, PA) bone-conduction vibrator. All audiometric testing was carried out in sound treated rooms meeting the criteria of ISO 8253-1 (2010), either at Christchurch Public Hospital, or at the University of Canterbury.

3.2.3 Procedure

3.2.3.1 General procedure

All participants underwent a preoperative assessment no more than one month before their scheduled surgery. This assessment included otoscopy, tympanometry, bilateral air- and bone-conduction audiometry at the conventional pure-tone frequencies, and bilateral air-conduction audiometry in the EHFs. We aimed to repeat the full preoperative examination battery at approximately 1 - 2 weeks, 1 month, 3 months, 6 months and 1 year postoperatively, with the exception of tympanometry, which was not carried out within the first three months following middle ear surgery. The exact timing of postoperative testing was dependent on when follow-up appointments with otolaryngologists were scheduled.

3.2.3.2 Pure-tone audiometry

Following otoscopic assessment to assess for occlusion of the EAC, pure-tone audiometry was performed using the appropriate air-conduction transducer. Thresholds for continuous pure-tone stimuli in decibel hearing level (dB HL) were measured in 5 dB steps using the modified Hughson-Westlake technique (Carhart & Jerger, 1959). In the conventional frequency range, air-conduction thresholds in each ear were measured at octave frequencies from 0.25 to 8 kHz, as well as at 3 kHz. In the EHF range, air-conduction thresholds were measured at 1/6th octave frequencies from 9 to 16 kHz. Bone-conduction thresholds were measured at 0.5, 1, 2, 3, and 4 kHz, regardless of air-conduction thresholds. "No response" was recorded when the participant did not respond to a tone presented at the limits of the audiometer for the frequency and ear being tested.

During air-conduction testing, narrow-band masking noise was applied to the contralateral ear via the selected air-conduction transducer when the difference between the air-conduction threshold in the test ear and the air- or bone-conduction threshold non-test ear exceeded the relevant minimum IAA values published by Yacullo (1996). The IAA in the EHF range was conservatively estimated as 40 dB based on the data reported by Brannstrom and Lantz (2010). Contralateral masking using narrow-band noise was always applied during bone-conduction testing. Air- and bone-conduction masking were performed using a step masking method (Yacullo, 1996).

3.2.3.3 Tympanometry

Tympanometry was performed using a 226 Hz probe tone, with a sweep rate of 50 daPa per second. The recorded traces were compared to normative data published by ASHA (1990). A Type A tympanogram, consistent with normal middle ear pressure and compliance, was classified as a trace with a static admittance between 0.3 and 1.4 mmho, and a peak pressure between -100 and +100 daPa. Traces with normal volumes and peak pressures, but static admittance values above or below the normal range were classified as Type Ad and Type As respectively. A peak pressure of less than -100 daPa was interpreted as evidence of a retracted tympanic membrane. A trace with no peak was classified as Type B, and was interpreted in conjunction with otoscopy and the equivalent EAC volume metric to distinguish between a tympanic membrane perforation (high EAC volume), middle ear dysfunction (normal volume), and EAC occlusion (low volume) (ASHA 1990).

3.2.4 Data-analysis

3.2.4.1 Assessment brackets

As exact timing of assessments varied across participants, assessments were bracketed according to the number of days after surgery they were performed and labelled as follows:

1 week = 1 – 20 days after surgery

1 month = 21 – 59 days after surgery

3 months = 60 – 134 days after surgery

6 months = 135 – 300 days after surgery

12 months = 301+ days after surgery

3.2.4.2 Conventional frequencies

Hearing outcomes in the conventional frequency range were calculated according the AAO-HNS (1995) recommendations. The air-conduction pure-tone average (AC PTA) was calculated as the average of thresholds at 0.5, 1, 2, and 3 kHz for each participant and the bone-conduction pure-tone average (BC PTA) was the average of the bone-conduction thresholds at the same frequencies. The difference between the AC PTA and the BC PTA recorded at the same assessment was taken as the air-bone gap. Additionally, as recommended by the AAO-HNS (1995) as a more sensitive measure of cochlear harm, the high-frequency bone-conduction pure-tone average (HF BC PTA) was calculated using the thresholds at 1, 2, and 4 kHz.

For each of these values, the mean, standard deviation, and range was calculated at each assessment according to surgery type. HF BC PTAs, air-bone gaps, and AC PTAs were also analysed in terms of the mean change relative to the preoperative value by subtracting the postoperative value from the preoperative value. Changes consistent with poorer hearing were therefore negative values and hearing improvements were positive, indicating a gain in hearing sensitivity. Air-bone gaps were further assessed by calculating the percentage of patients with air-bone gaps of 10 dB or less and 20 dB or less at each assessment.

Statistical analyses of changes in mean PTAs and air-bone gaps across assessments were performed using mixed model analyses with post-hoc pairwise comparisons. Bonferroni

corrections were used due to multiple comparisons. For these and all other statistical tests in this study, the significance criterion was $p < .05$.

Bone-conduction thresholds were also assessed using the threshold at 4 kHz alone. This threshold was analysed in terms of the percentage of patients presenting with a change in the threshold of greater than 10 dB and greater than 20 dB, and the mean threshold recorded at each assessment. A repeated measures ANOVA with pairwise comparisons was used to test for changes in the mean 4 kHz threshold across assessments.

All of the analyses described above were performed using IBM SPSS version 22 (2013, IBM Corp., Armonk, NY).

3.2.4.3 EHF hearing thresholds

Changes in the highest frequency at which a hearing threshold could be measured before the limits of the audiometer were reached were assessed to determine the percentage of patients who experienced a postoperative loss in EHF hearing at each assessment. This metric does not take into consideration the degree of high-frequency hearing loss, but does provide some indicator that hearing loss has occurred when hearing thresholds become unmeasurable. The percentage of patients with a loss, gain, or no change in the highest measureable frequency were calculated at each assessment for each surgery. The rate of measurable frequency loss was also calculated for the non-operated ear as a control measure. In cases where measureable thresholds were lost, the number of test frequencies that became inaudible were calculated. For example, if a threshold was measureable at 16 kHz before surgery, but the highest threshold was 14 kHz postoperatively, one test frequency was loss.

3.2.4.4 Mixed effects model analysis

A linear mixed effects model analysis was performed using the statistical software package R (R Development Core Team 2010, Vienna, Austria), to assess postoperative changes in thresholds across all frequencies and all three surgeries.

Prior to analysis, test frequencies were aggregated into groups of four to simplify the analysis. Frequency levels were:

1 = 0.25 – 1 kHz

2 = 2 – 8 kHz

3 = 9 – 11.2 kHz

4 = 12.5 – 16 kHz

Where thresholds were recorded as no response at the limits of the audiometer, the threshold was taken as 5 dB above the maximum output level at that frequency. This method was based on the assumption that this value was the minimum level the threshold could be recorded at if the audiometer output range was extended. This enabled us to detect when a change had occurred if a “no response” was present postoperatively at the same level a threshold was measured preoperatively.

The model analysis explored the individual relationships between threshold change relative to the preoperative value (dependent variable) and frequency, assessment time, surgery type, and revision/primary surgery. Other surgical variables were not included as observation numbers were too low, leading to a risk of overfitting. Further examination of the differences between frequency bands and assessment brackets was achieved using pairwise analyses comparing the mean postoperative threshold change in each frequency band to each other for each of the three surgeries. The criterion for statistical significance was set at $p < .05$.

3.3 Results

3.3.1 Patient characteristics

Of the 96 patients recruited, 88 had data available from at least one follow-up assessment and were therefore included in the data analyses. As long as at least one set of postoperative data was recorded, all available audiometric data for a given participant was included regardless of whether all postoperative assessments were completed. The number of participants tested therefore differed in each follow-up bracket. Forty-eight participants were male and 59 were female, with a mean age at the time of surgery of 46.0 years (*SD* = 13.9, range = 16.1 – 70.0 years). Participant characteristics are presented according to surgery type in Table 1.

Three patients had two different types of procedures at different times; one on each ear, therefore the total number of ears undergoing surgery was 91. Overall, the 91 ears underwent 44 stapedectomies, 28 ossiculoplasties, and 27 tympanoplasties. Of these procedures, 52 were primary surgeries, 31 were revisions of previous surgeries, and 16 were the second step of planned two-stage procedures. The majority of surgeries; 38 stapedectomies, 17 ossiculoplasties, 11 tympanoplasties, and were performed by one otologist with approximately 18 years of experience. The remaining procedures were performed by several surgeons in various levels of training.

Table 1. Patient characteristics according to surgery type.

Surgery	Ears *n*	Procedures *n*	Procedure type			Mean age (years) *(SD)*	Sex		Ear	
			Primary	Revision	Second stage		*M*	*F*	*R*	*L*
Stapedectomy	39	44	30	14	-	49.2 (*12.2*)	13	31	26	18
Ossiculoplasty	28	28	5	7	16	41.6 (*13.7*)	18	10	18	10
Tympanoplasty	27	27	17	10	-	45.6 (*15.9*)	14	13	18	9
Total	91	99	52	31	16	46.0 *(13.9)*	45	54	62	37

3.3.2 Hearing in the conventional frequency range

3.3.2.1 Stapedectomy

Of the 44 stapes surgeries included in this study, 31 were performed using an argon laser, 12 with a CO_2 laser, and one using a microdrill only. Surgeries included 30 primary procedures and 14 revisions. Pre- and postoperative descriptive statistics according to the type of laser used and whether surgeries were primary or revision procedures are provided in Appendix B.

As shown in Figure 8 and Table 2, the mean AC PTA decreased by an average of 16.6 dB from preoperative levels to 40.6 dB (*SD* = 16.2) by the first assessment after stapes surgery.

Gradual improvement occurred until 3 months after surgery and a minimum mean AC PTA of 27.5 dB (*SD* = 10.7) was documented 6 months postoperatively. A small increase in the mean AC PTA to 29.2 dB (*SD* = 14.8) and a 20 dB increase in the maximum AC PTA were recorded at the 12 month assessment as a result of the failure of two surgeries by this assessment. The mean AC PTA at the preoperative assessment was significantly higher than at all postoperative assessments (all $p < .001$). The mean AC PTA at the first postoperative assessment was also significantly higher than the values recorded at all subsequent assessments (all $p < .05$).

The mean BC PTA was slightly but significantly lower than the preoperative mean at assessments from 3 months onward (all $p < .005$) (Figure 8). At the first postoperative assessment, however, the mean BC PTA increased to 27.3 dB (*SD* = 10.6), which was significantly greater than mean values documented at later assessments (all $p < .05$).

Table 2. Summary of pre- and postoperative hearing in patients undergoing stapedectomy.

	Approximate time since surgery					
	Preop	1 week	1 month	3 months	6 months	12 months
n	44	39	42	36	35	34
AC PTA						
Mean *(SD)*	57.1 *(11.8)*	40.6 *(16.2)*	30.9 *(11.3)*	28.6 *(10.7)*	27.5 *(10.7)*	29.2 *(14.8)*
Range	36.3 – 95.0	17.5 – 81.3	12.5 – 60.0	11.3 – 57.5	10.0 – 58.8	7.5 – 78.8
HF BC PTA						
Mean *(SD)*	24.7 *(10.3)*	27.9 *(10.8)*	22.8 *(11.9)*	20.6 *(9.9)*	20.0 *(10.5)*	20.6 *(10.3)*
Range	6.7 – 48.3	8.3 – 46.7	5.0 – 43.3	5.0 – 40.0	3.3 – 45.0	3.3 – 43.3
Air-bone gap						
Mean *(SD)*	31.3 *(10.5)*	13.3 *(10.2)*	8.2 *(6.1)*	7.1 *(6.2)*	7.0 *(6.8)*	8.2 *(10.1)*
Range	10.0 – 59.2	-1.3 – 38.8	-3.8 – 23.3	-3.8 – 26.3	-5.0 – 30.0	-2.5 – 53.8
4 kHz BC change						
>10 dB	-	36%	19%	0%	0%	3%
>20 dB	-	18%	5%	0%	0%	0%

All thresholds are given in dB HL.

The mean air-bone gap decreased significantly by 18.0 dB by the first assessment and by a further 5.1 dB by the second assessment, after which it remained reasonably stable (Table 2). The mean air-bone gap was significantly lower at all postoperative assessments compared to the preoperative mean (31.3 dB, *SD* = 10.5) (all $p < .001$) and the mean air-bone gap at the 1 week assessment (13.3 dB, *SD* = 10.2) was significantly higher than that at the 1, 3, and 6 month assessments ($p < .05$). At the final assessment, 80% of patients had an air-bone gap of 10 dB or less, compared to 2% preoperatively (Figure 9). Nine per cent of patients retained an air-bone gap of greater than 20 dB 12 months after surgery.

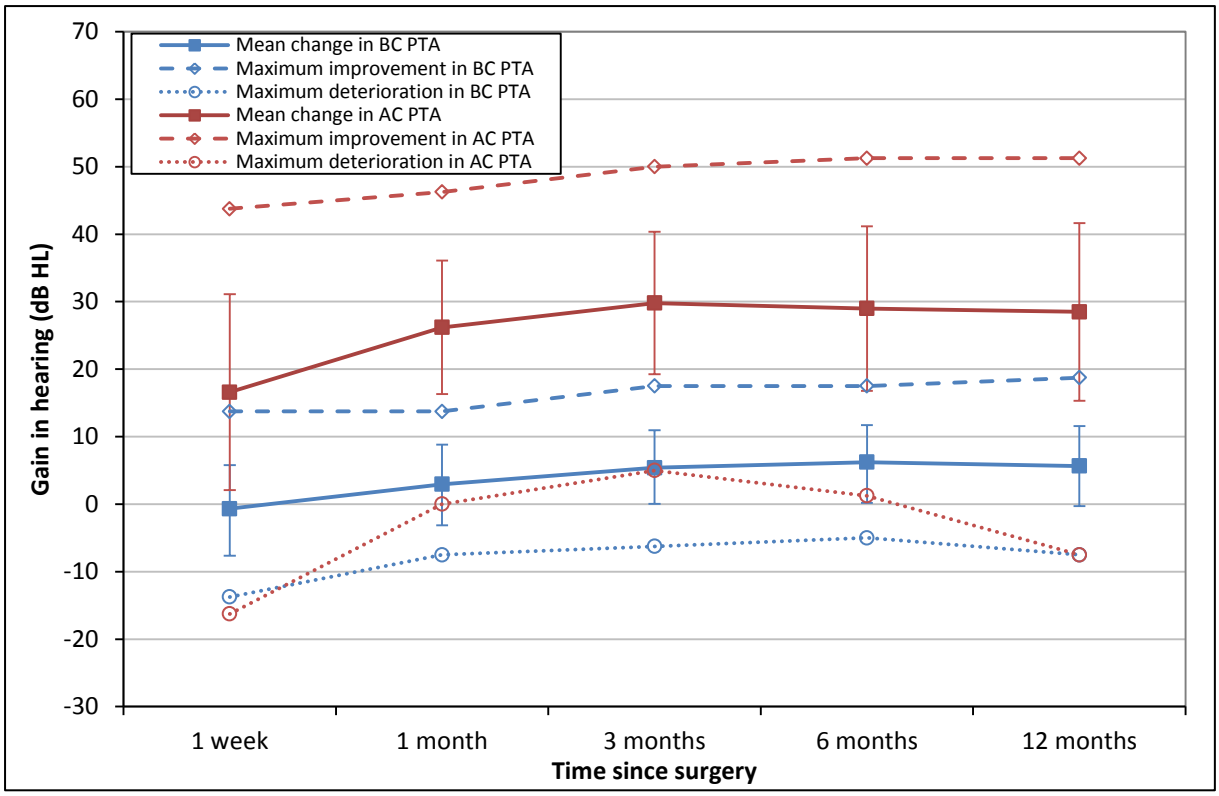

Figure 8. The mean gain, maximum improvement, and maximum deterioration of air- and bone-conduction pure-tone averages at 0.5, 1, 2, and 3 kHz at each follow-up assessment following stapes surgery.

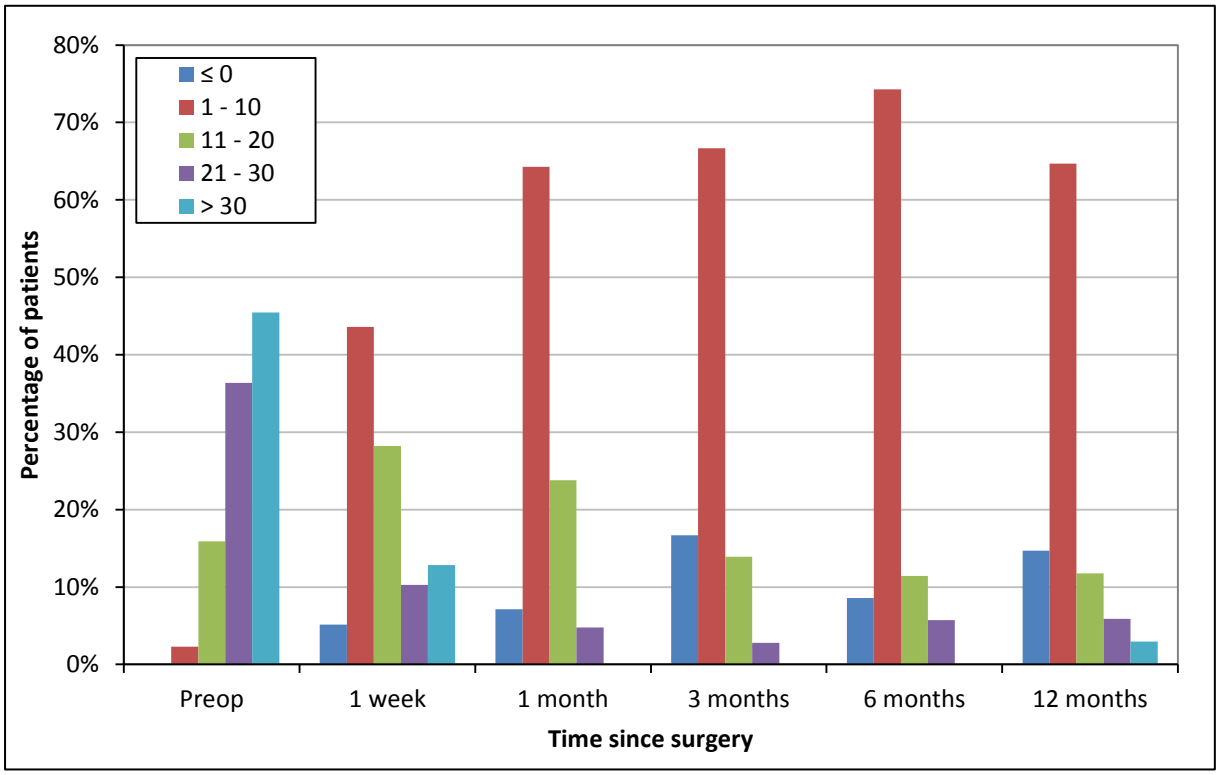

Figure 9. The percentage of patients with air-bone gaps falling within each of five brackets: ≤ 0 dB, 1 – 10 dB, 11 – 20 dB, 21 – 30 dB, and >30 dB preoperatively and at each follow-up assessment following stapes surgery.

Figure 10 shows both the change in the HF BC PTA and the change at 4 kHz alone. The mean HF BC PTA increased by 3.2 dB at the initial postoperative assessment, before recovering to an average approximately 4 dB better than the preoperative level by 3 months after surgery. A mixed model analysis with pairwise comparisons showed that the mean HF BC PTA was significantly higher at the 1 week follow-up compared to the preoperative assessment ($p = .03$) and all subsequent assessments (all $p < .001$). The mean HF BC PTAs at assessments from 3 months onwards were significantly better than the preoperative mean (all $p < .05$).

The bone-conduction threshold at 4 kHz showed greater postoperative deterioration than the HF BC PTA. One week after surgery 36% of patients presented with a 4 kHz bone-conduction threshold increase of greater than 10 dB, and 18% with an increase greater than 20 dB (Table 2). Recovery in some patients was documented by 1 month, at which time 19% had a 4 kHz loss of greater than 10 dB and 5% had losses of greater than 20 dB. From 3 months onward, no cases of sensorineural loss of greater than 20 dB were recorded at 4 kHz. At 12 months one patient (3%) presented with a 4 kHz threshold increase of 15 dB.

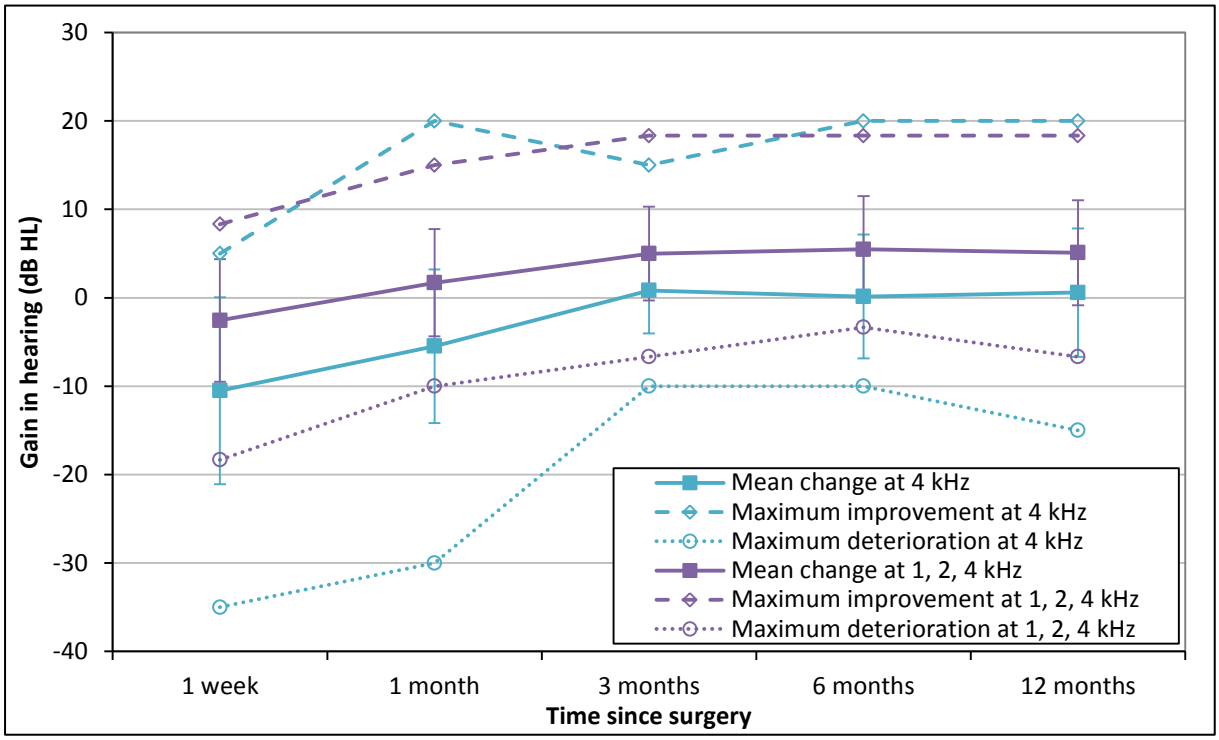

Figure 10. The mean change, maximum improvement, and maximum deterioration of the bone-conduction pure-tone average at 1, 2, and 4 kHz (HF BC PTA) and at 4 kHz alone at each follow-up assessment following stapes surgery.

3.3.2.2 Ossiculoplasty

Of the 28 ossiculoplasties studied, 19 involved placement of a PORP and nine used a TORP. The majority (57%) of patients undergoing ossiculoplasty had the procedure performed as a planned second stage operation. Of the remaining 12 surgeries, five were primary procedures and seven were revisions. Cholesteatoma was identified and removed intraoperatively during five procedures. Pre- and postoperative hearing summary statistics according to each of these variables are provided in Appendix B.

The greatest reductions from the mean preoperative AC PTA of 48.2 dB (*SD* = 11.1) were recorded 3 and 6 months after ossiculoplasty, when the average thresholds were 37.7 dB and 37.6 dB, respectively (Table 3, Figure 11). As with stapedectomy, failures of the surgical repair or recurrence of disease several months after surgery caused an elevation of the mean AC PTA in later follow-up brackets. Mixed model statistical analyses showed a significant improvement in the mean AC PTA compared to the preoperative value only at the 1 month postoperative assessment ($p = .01$).

Table 3. Summary of pre- and postoperative hearing in patients undergoing ossiculoplasty.

	Approximate time since surgery					
	Preop	1 week	1 month	3 months	6 months	12 months
n	28	21	20	16	22	20
AC PTA						
Mean *(SD)*	48.2 *(11.1)*	42.1 *(16.8)*	37.7 *(10.4)*	37.6 *(16.1)*	38.3 *(11.3)*	39.3 *(13.7)*
Range	30.0 – 76.3	18.8 – 80.0	15.0 – 55.0	13.8 – 86.3	21.3 – 61.3	17.5 – 72.5
HF BC PTA						
Mean *(SD)*	18.0 *(10.6)*	17.5 *(10.3)*	13.3 *(7.3)*	17.3 *(10.6)*	15.9 *(9.1)*	16.9 *(11.2)*
Range	5.0 – 43.4	1.7 – 38.3	1.7 – 25.0	1.7 – 41.7	0.0 – 38.3	0.0 – 41.7
Air-bone gap						
Mean *(SD)*	29.8 *(12.6)*	24.9 *(10.5)*	23.9 *(10.5)*	19.5 *(9.9)*	22.4 *(10.6)*	22.4 *(10.3)*
Range	9.6 – 52.5	5.0 – 43.8	2.5 – 46.3	-2.5 – 42.5	7.5 – 52.5	6.3 – 46.3
4 kHz BC change						
>10 dB	-	10%	5%	13%	0%	10%
>20 dB	-	5%	0%	0%	0%	0%

All thresholds are given in dB HL.

The maximum deterioration of the BC PTA was 22.5 dB documented at the first follow-up, after which all patients maintained bone conduction thresholds a maximum of 8.7 dB poorer than their preoperative PTA (Figure 11). The mean BC PTA did not change significantly across the preoperative and postoperative assessments ($F(5, 69) = .92$, $p = .47$).

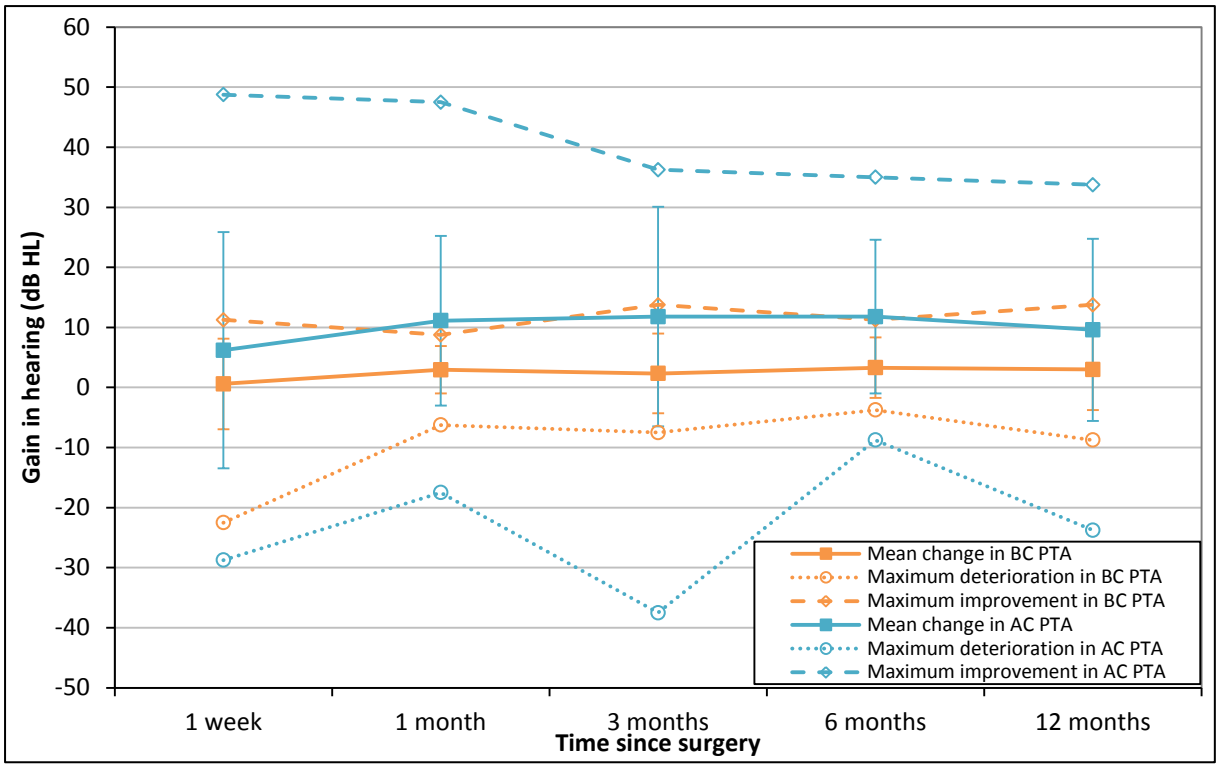

Figure 11. The mean change, maximum improvement, and maximum deterioration of air- and bone- conduction pure-tone averages at 0.5, 1, 2, and 3 kHz at each follow-up assessment following ossiculoplasty.

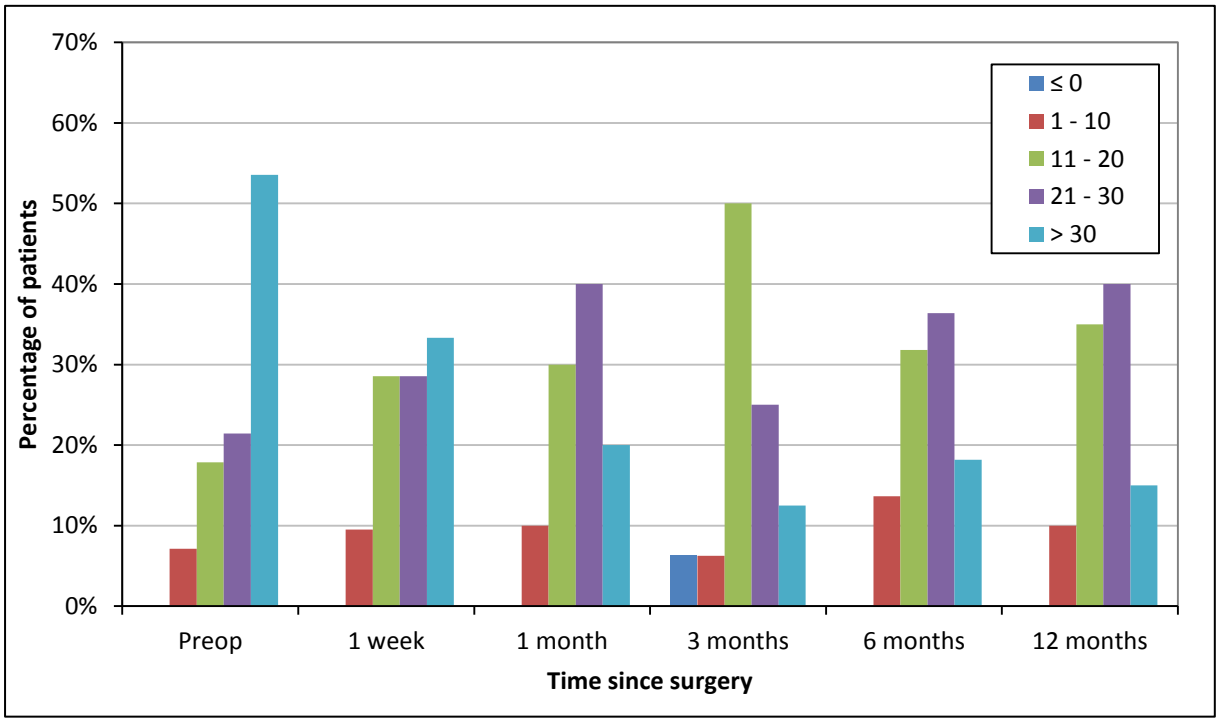

Figure 12. The percentage of patients with air-bone gaps falling within each of five brackets: ≤ 0 dB, 1 – 21- dB, 11 – 20 dB, 21 – 30 dB, and >30 dB preoperatively and at each follow-up assessment following ossiculoplasty.

The average air-bone gap following ossiculoplasty decreased from 29.8 dB (*SD* = 12.6) before surgery to a minimum of 22.4 dB at the 6 and 12 month postoperative assessments (Table 3). This decrease was not statistically significant, and no significant differences between any pair of assessment brackets were detected. The percentage of patients with air-bone gaps of greater than 30 dB decreased from 54% before surgery to 15% at the final assessment (Figure 12), and the percentage of patients with an air-bone gap of 20 dB or less increased from 25% before surgery to 45% 12 months after surgery. There was a trend for hearing to improve until three months after surgery, with a higher rate of air-bone gaps of greater than 30 dB recorded 1 week postoperatively compared to later follow-up brackets.

No statistically significant differences in the mean HF BC PTA or the mean 4 kHz threshold were found between any assessment brackets (Figure 13). One week after surgery, 10% experienced a loss in bone-conduction hearing at 4 kHz of between 10 and 19 dB, and 5% (1 patient) presented with a loss of greater than 20 dB (Table 3). No losses of greater than 20 dB were recorded at subsequent assessments.

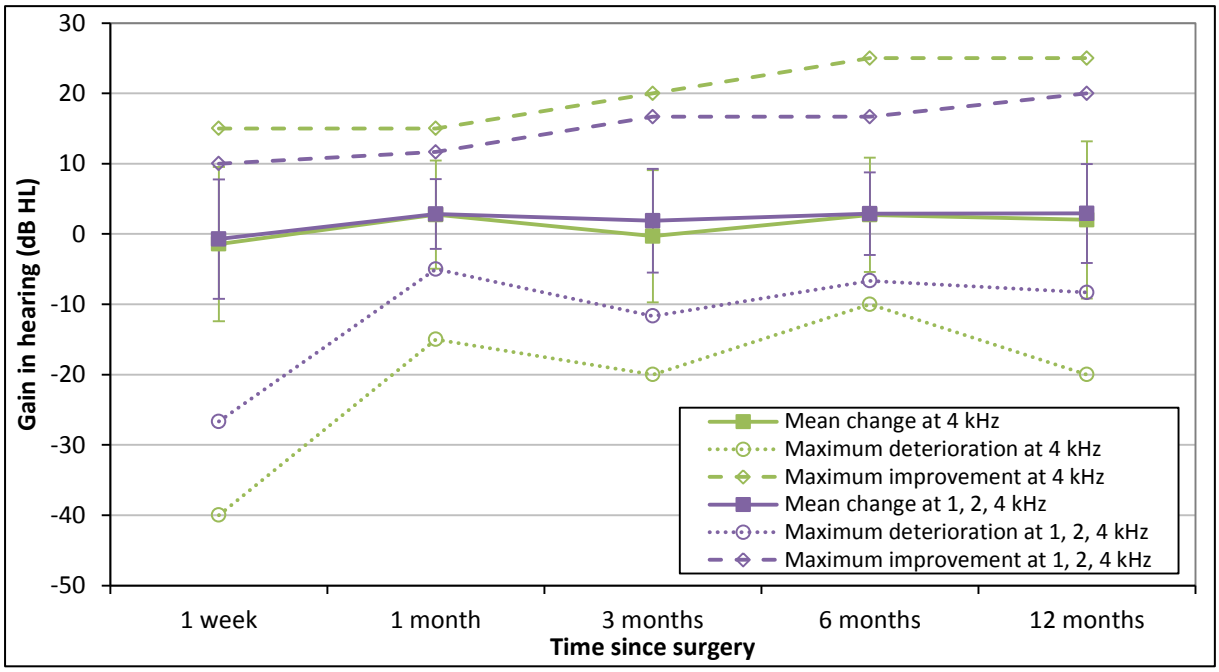

Figure 13. The mean change, maximum improvement, and maximum deterioration of the bone-conduction pure-tone average at 1, 2, and 4 kHz (HF BC PTA) and at 4 kHz alone at each follow-up assessment following ossiculoplasty.

3.3.2.3 Tympanoplasty

Cholesteatoma was found and removed intraoperatively during six tympanoplasties. Seventeen of the 27 tympanoplasties included in this study were primary procedures and 10 were revisions. Mastoidectomy was performed in conjunction with tympanoplasty in five cases. Audiometric results according to these surgical variables are provided in Appendix B.

Patients undergoing tympanoplasty had the best mean preoperative air-conduction PTA of any of the surgery groups (M = 36.6 dB, SD = 15.7), however, improvements in hearing postoperatively were limited (Table 4). At the initial postoperative assessment the mean AC PTA increased significantly by 10.6 dB (Figure 14) and the minimum postoperative mean AC PTA of 24.5 dB (SD = 10.8) was recorded 6 months after surgery. The mean at 1 week was significantly higher than the mean AC PTAs recorded at all further assessments (all $p < .05$). Although the lowest mean AC PTA was recorded at the 6 month assessment, it must be noted that only 13 of the 27 patients attended this assessment; fewer than any other assessment (Table 4). Aside from the statistically significant increase in the mean PTA at 1 week (p = .002), analyses showed no differences between the preoperative mean AC PTA and means in any other postoperative brackets.

The mean bone-conduction threshold at 0.5, 1, 2, and 3 kHz remained within 2 dB of the preoperative mean BC PTA throughout the postoperative course. Maximum BC PTA deterioration across all assessments did not exceed 8.8 dB (Figure 14).

Table 4. Summary of pre- and postoperative hearing in patients undergoing tympanoplasty.

	Approximate time since surgery					
	Preop	1 week	1 month	3 months	6 months	12 months
n	27	16	17	21	13	19
AC PTA						
Mean *(SD)*	36.6 *(15.7)*	47.2 *(15.6)*	37.0 *(14.4)*	32.9 *(14.4)*	24.5 *(10.8)*	35.6 *(16.2)*
Range	16.3 – 77.5	25.0 – 72.5	16.3 – 73.8	15.0 – 72.5	11.3 – 41.3	11.3 - 76.3
HF BC PTA						
Mean *(SD)*	17.4 *(12.8)*	21.9 *(13.6)*	17.7 *(11.8)*	16.1 *(12.4)*	13.2 *(9.1)*	17.6 *(10.2)*
Range	-3.3 – 43.3	0.0 – 45.0	1.7 – 41.7	1.7 – 38.3	3.3 – 31.7	3.3 – 40.0
Air-bone gap						
Mean *(SD)*	18.6 *(11.1)*	26.6 *(10.4)*	20.5 *(10.3)*	16.1 *(9.3)*	11.5 *(8.4)*	17.3 *(10.5)*
Range	2.5 – 48.8	8.8 – 43.8	3.8 – 43.8	6.3 – 41.3	1.3 – 30.0	3.8 – 43.8
4 kHz BC change						
>10 dB	-	25%	18%	0%	15%	0%
>20 dB	-	13%	0%	0%	0%	0%

All thresholds are given in dB HL.

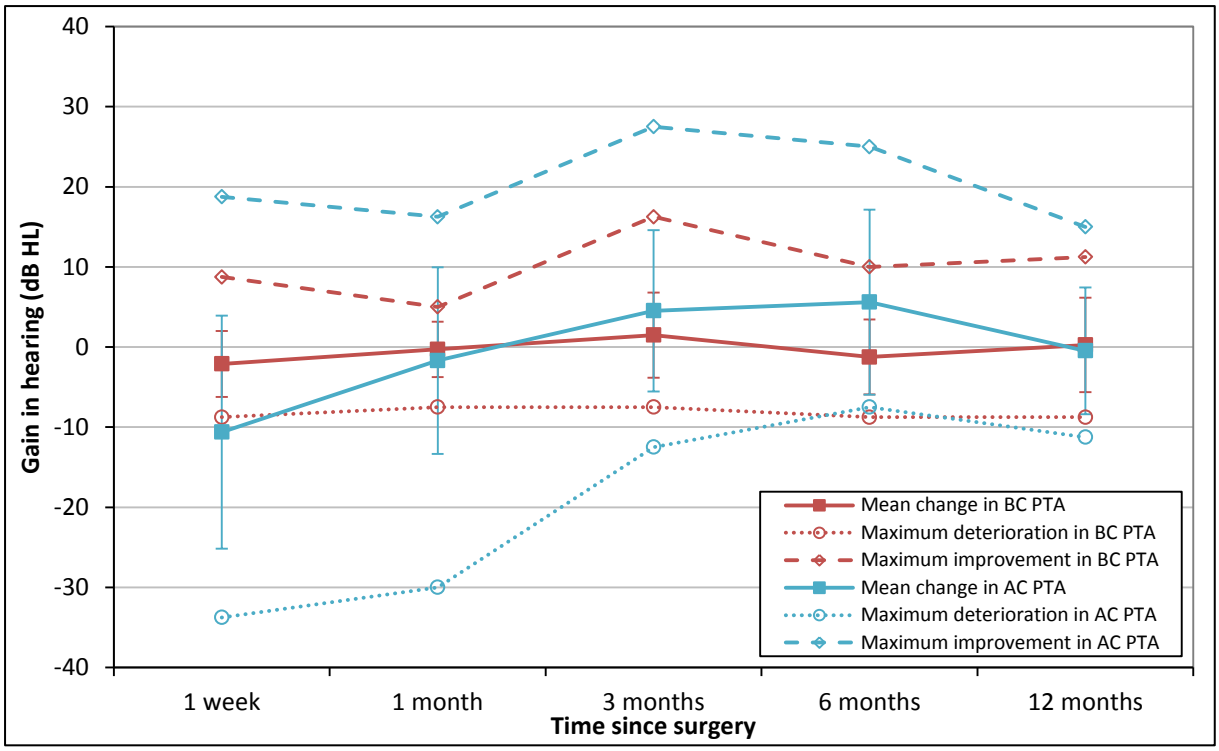

Figure 14. The mean change, maximum improvement, and maximum deterioration of air- and bone-conduction pure-tone averages at 0.5, 1, 2, and 3 kHz at each follow-up assessment following tympanoplasty.

The average air-bone gap initially increased from 18.6 dB (*SD* = 11.1) to 26.6 dB (*SD* = 10.4) (Table 4). Partial recovery was documented 1 month after surgery, and the average air-bone gap remained smaller than it had been before surgery for the remainder of the follow-up period. The final mean air-bone gap was slightly smaller than that measured preoperatively at 17.3 dB (*SD* = 10.5 dB). A mixed model analyses revealed a significant main effect of assessment time ($F(5, 51) = 5.66$, $p < .001$). Similar to analyses for AC PTA, pairwise analyses the only significant difference between the preoperative and postoperative assessments occurred 1 week after surgery ($p = .03$). The mean air-bone gap one week after surgery was significantly greater than that at postoperative assessments at 3, 6, and 12 months.

An increase in the percentage of patients with air-bone gaps of no greater than 20 dB was noted by the final follow-up; from 59% before surgery to 68% 12 months later (Figure 15). Again, although results appear much better at the 6 month assessment, the smallest number of patients was retested in this time bracket, likely skewing the data.

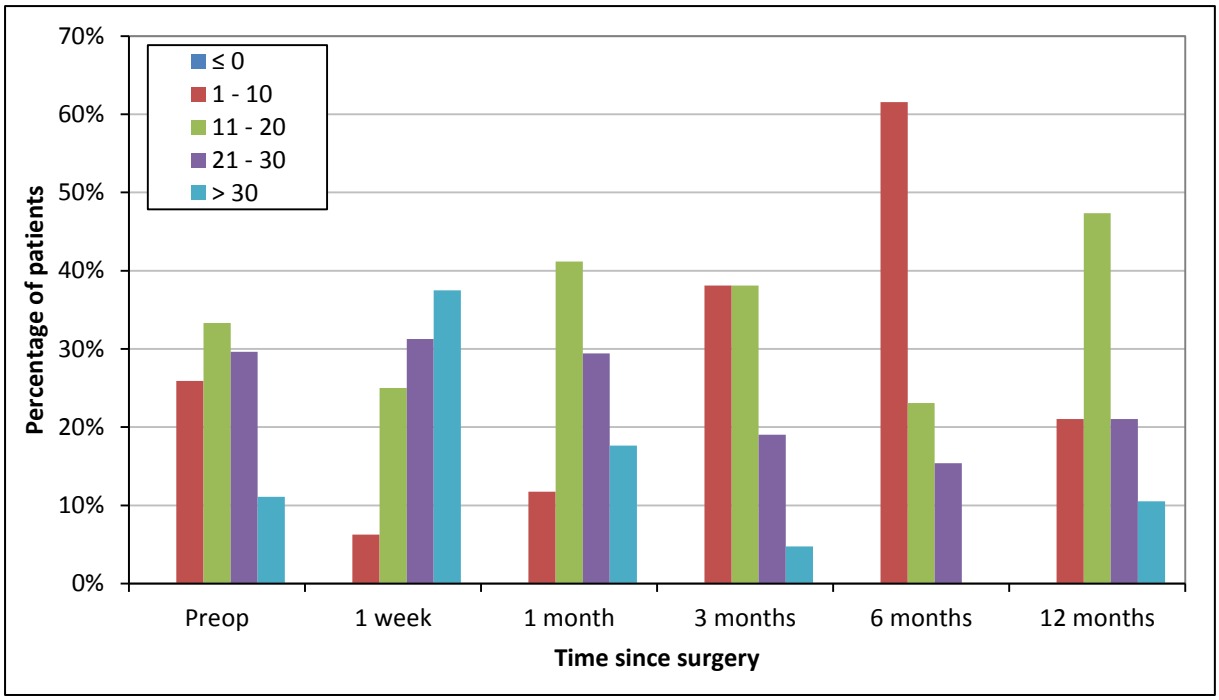

Figure 15. The percentage of patients with air-bone gaps falling within each of five brackets: ≤ 0 dB, 1 – 21- dB, 11 – 20 dB, 21 – 30 dB, and > 30 dB preoperatively and at each follow-up assessment following tympanoplasty.

As shown in Figure 14, increases of approximately 4 dB and 7 dB were seen in the mean HF BC PTA and the mean bone-conduction threshold at 4 kHz, respectively, at the first postoperative assessment. Mean thresholds for both measures returned to close to preoperative levels by the 3 month assessment. As noted for ossiculoplasty and stapedectomy, maximum deterioration was greater at 4 kHz alone than at the average of 1, 2, and 4 kHz. Also in agreement with other procedures, deterioration was greatest 1 week after surgery. Statistical analyses showed a significant difference compared to the preoperative mean only at the 1 week postoperative assessment for both the mean 4 kHz bone-conduction threshold (p = .01) and the mean HF BC PTA (p = .002).

The percentage of tympanoplasty patients presenting with a loss of bone-conduction sensitivity at 4 kHz of greater than 20 dB was 13% 1 week after surgery, recovering to 0% across the remaining assessments (Table 4). Losses greater than 10 dB were recorded in 25% of the 16 patients assessed 1 week after surgery, with recovery evident by 3 months after surgery. At the final assessment none of the 19 patients seen had a loss at 4 kHz of greater than 10 dB.

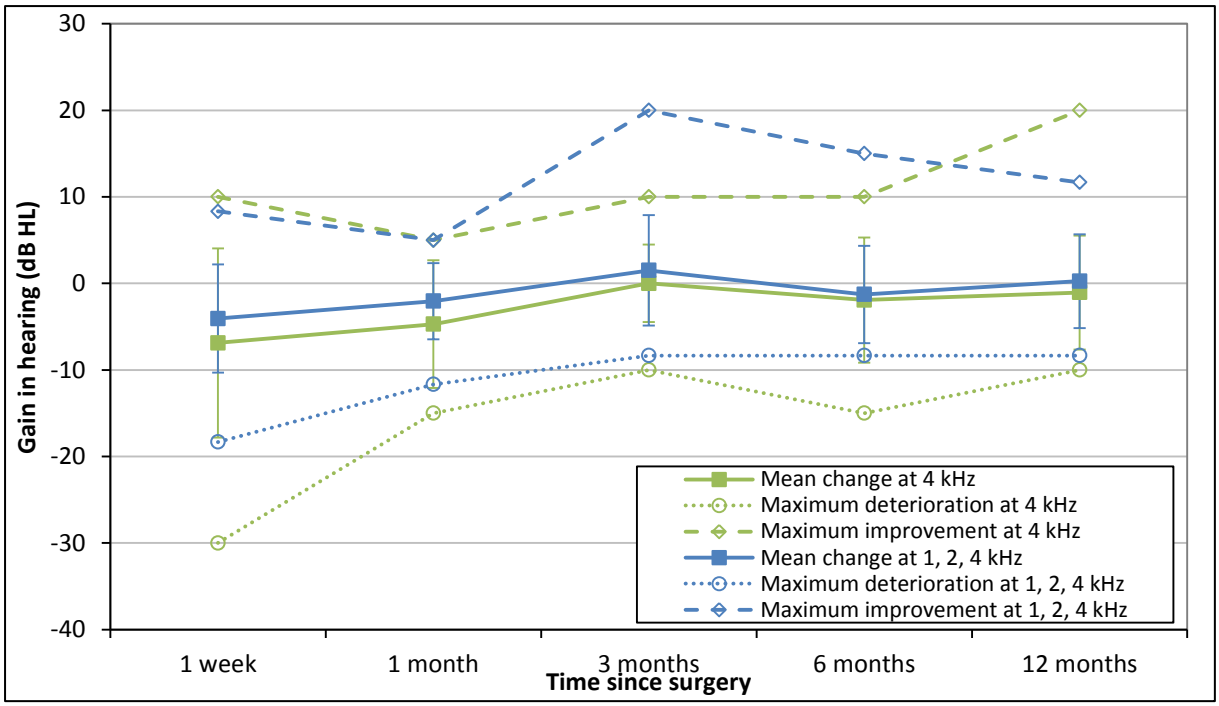

Figure 16. The mean change, maximum improvement, and maximum deterioration of the bone-conduction pure-tone average at 1, 2, and 4 kHz and at 4 kHz alone at each follow-up assessment following tympanoplasty.

3.3.3 Audiometric results across test frequencies

Exploratory data analysis was performed so that changes in hearing across the entire audiometric frequency range could be examined graphically. As trends in the data were not consistent across surgery types, data from each surgery was analysed separately.

Mean thresholds at each test frequency for each surgery and assessment are presented in Figures 17 and 18. Although mean absolute thresholds at each assessment are less informative than mean changes in thresholds, when evaluating EHF thresholds in particular, it is critical to evaluate how close thresholds are to the limits of the audiometer. Thresholds that are closer to the maximum output levels preoperatively will not be able to increase by the same amount as better preoperative thresholds, even if iatrogenic damage is identical.

It is evident from Figures 17 and 18 that thresholds at 4 kHz and below were poorest preoperatively in the stapedectomy group, but best at the final assessment for this group. In the EHF range, preoperative thresholds were highest in the ossiculoplasty group, and already at or close to the limits of the audiometer in many patients. EHF thresholds in this group changed little of the postoperative course, potentially at least in part because in some patients there was little range for threshold elevation to be recorded. Postoperative EHF threshold elevation occurred in both the stapedectomy and tympanoplasty groups, with the greatest increase at the first postoperative assessment and partial recovery occurring over time. The error bars show that the range of preoperative and postoperative thresholds recorded for all surgeries was very large across all test frequencies.

All mean audiograms show an apparent recovery of thresholds at 16 kHz. As the audiometer output is more restricted at 16 kHz than at 14 kHz, in most cases this pattern occurred because a threshold could not be measured before the limits of the audiometer were reached at 16 kHz. Other potential causes for such audiometric patterns are, however, addressed in Chapter 4.

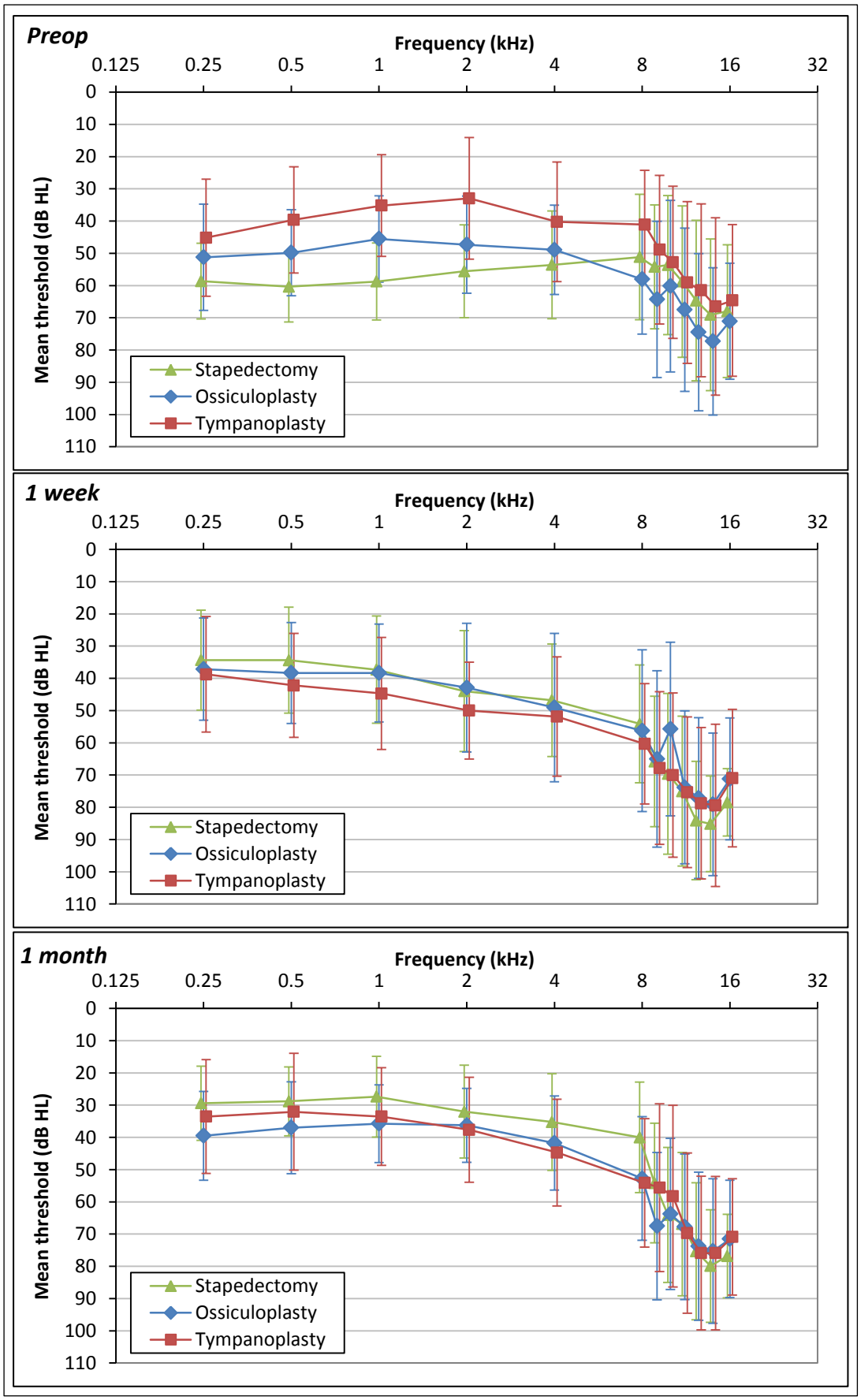

Figure 17. Mean pure-tone thresholds measured for each surgery group preoperatively and at postoperative assessments at 1 week and 1 month. Errors bars show standard deviation. Data points for different surgery types are slightly offset for clarity.

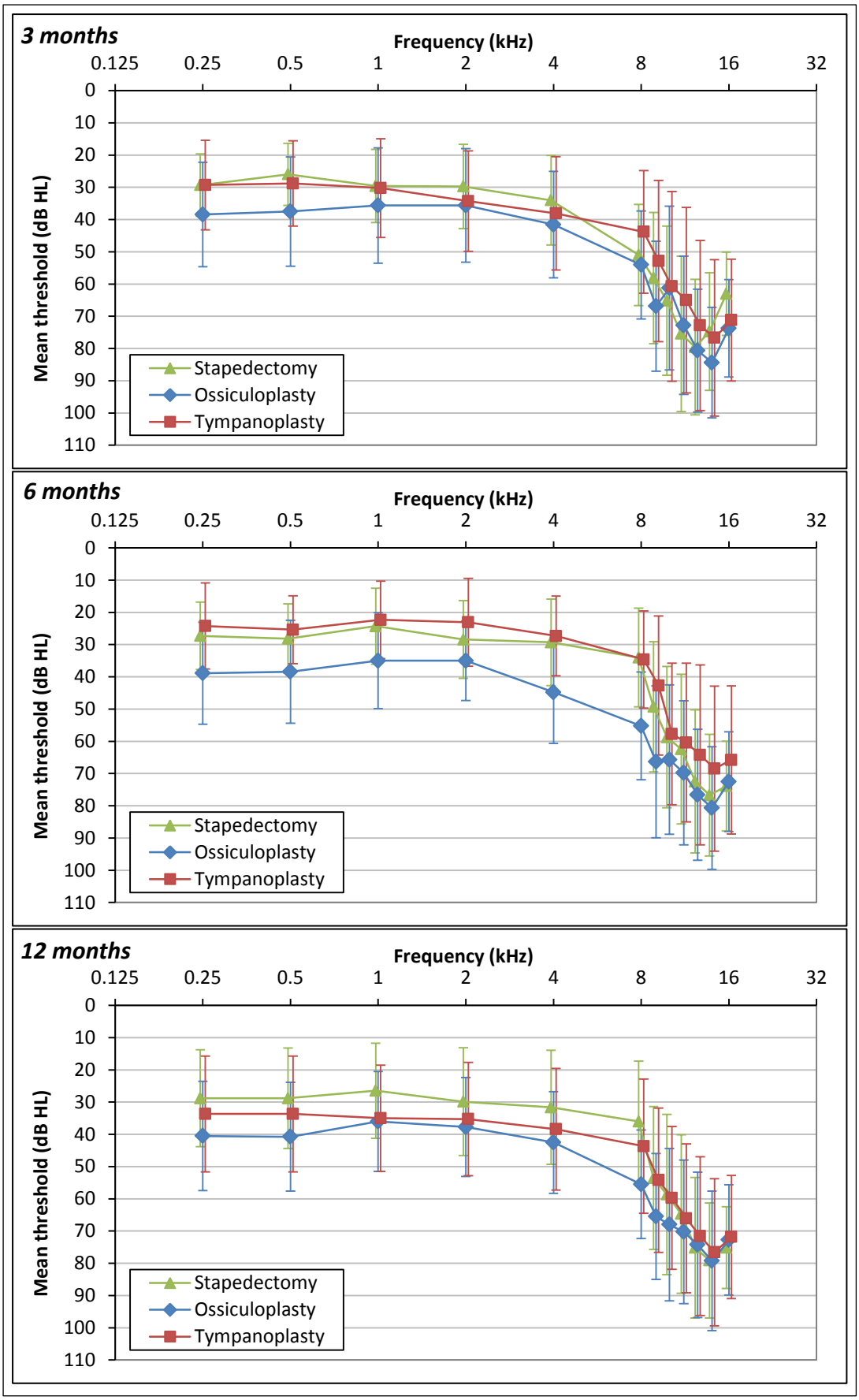

Figure 18. Mean pure-tone thresholds measured for each surgery group at postoperative assessments at 3, 6, and 12 months. Errors bars show standard deviation. Data points for different surgery types are slightly offset for clarity.

3.3.3.1 Changes in hearing across all frequencies post-stapedectomy

Figure 19 shows the distribution of changes in hearing over time after stapedectomy. It is clear that the greatest improvements in hearing were achieved in frequency Band 1 (0.25 – 1 kHz). Improvements in this band were apparent from the first assessment, with continued improvement until 3 months after surgery. In Band 2 (2 – 8 kHz) most patients experienced hearing improvement by 3 months, however this was not as extensive as in Band 1, and hearing took longer to improve following surgery in this band. Hearing loss was greatest in Band 3 (9 – 11.2 kHz), particularly 1 week after surgery, with gradual, partial recovery by 3 months. At the highest frequencies, 12.5 – 16 kHz, the median loss in hearing was not as great as in Band 3 and the range of changes recorded was smaller. It is likely that this difference in the EHF bands is related to the reduced ability to detect changes when thresholds were more elevated preoperatively, as they were in the highest frequency band. Incomplete hearing recovery was also documented across the group in Band 4, although a high percentage of patients retained a hearing loss in both EHF bands at the final assessment.

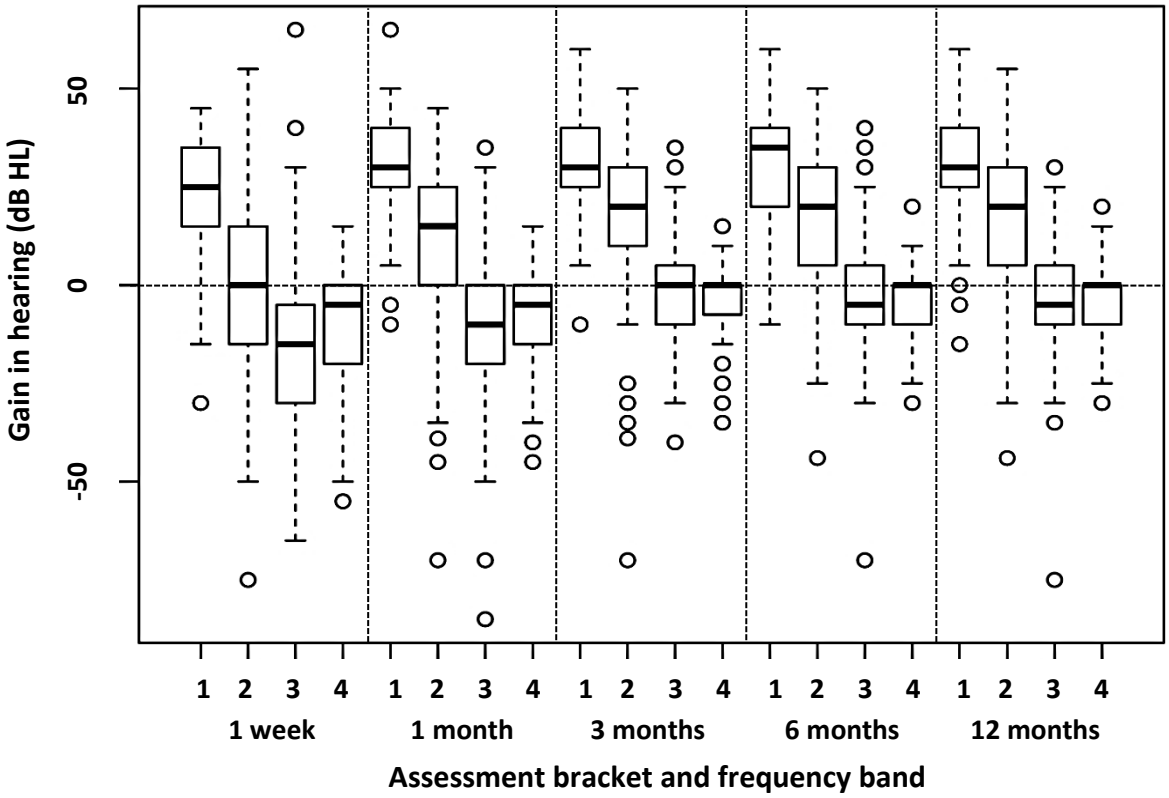

Figure 19. Distribution of changes in hearing relative to the preoperative assessment for patients undergoing stapedectomy. Frequency bands 1 and 2 describe changes in the conventional frequency range, and bands 3 and 4 the EHF range. Outlier data, calculated as Quartile 1- 1.5*interquartile range and Quartile 3 + 1/5*interquartile range, are indicated by open circles.

Figure 20 tracks postoperative changes in hearing in individual stapedectomy patients through time. Data from each postoperative assessment bracket is presented in two figures, divided into a low-frequency range of 0.25 – 6 kHz, and a high-frequency range of 8 – 16 kHz. Hearing improvement relative to preoperative thresholds is indicated by markers above the horizontal line at 0 dB, and hearing deterioration is indicated by markers below 0 dB.

From the graphs showing hearing change in the lower frequency range, it is apparent that most patients experienced hearing improvement in the conventional frequency range by the second assessment. Only three individuals experienced persistent hearing deterioration at 4 – 8 kHz. Variability in hearing change was much greater at 8 kHz and above than at lower frequencies. The majority of patients presented with a loss of high-frequency hearing at the first postoperative assessment, with limited recovery occurring by the second assessment, 1 month after surgery. Greater recovery was evident by the third and fourth postoperative assessments. At the final assessment, approximately 12 months after surgery, at frequencies from 8 to 11.2 kHz, there appears to be a relatively even distribution of patients experiencing either no change in thresholds, hearing improvement, or hearing loss. At the three highest test frequencies more patients experienced hearing loss than hearing gain.

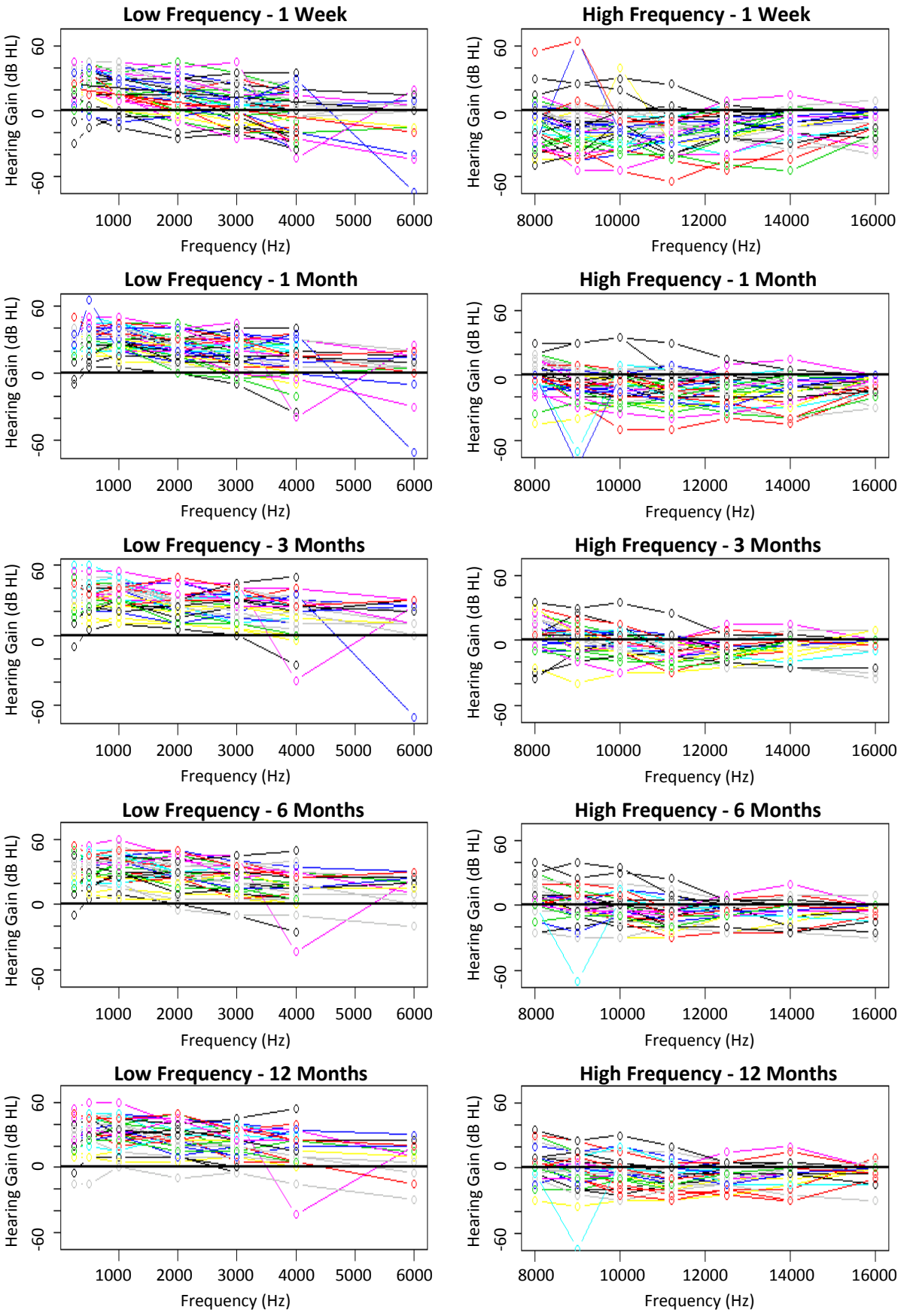

Figure 20. Hearing gain in low-frequencies (0.25 – 6 kHz) and high-frequencies (8 – 16 kHz) in individual stapedectomy patients across all postoperative assessments.

3.3.3.2 Changes in hearing across all frequencies post-ossiculoplasty

Consistent with the data described in the conventional frequency range, median changes in hearing were smaller in all frequency bands following ossiculoplasty compared to stapedectomy (Figure 21). In agreement with stapedectomy results, improvements were consistently greatest at the lowest frequencies and smallest at the highest test frequencies. Some further improvement in thresholds was noted after the initial postoperative assessment, particularly in Bands 1 and 2, with optimal results recorded at the 3 month assessment. Unlike stapedectomy, surgery rarely resulted in deterioration of thresholds in Band 4, although, interestingly the poorest results in Band 4 were present at the final assessment. Again, hearing outcomes were poorest in Band 3.

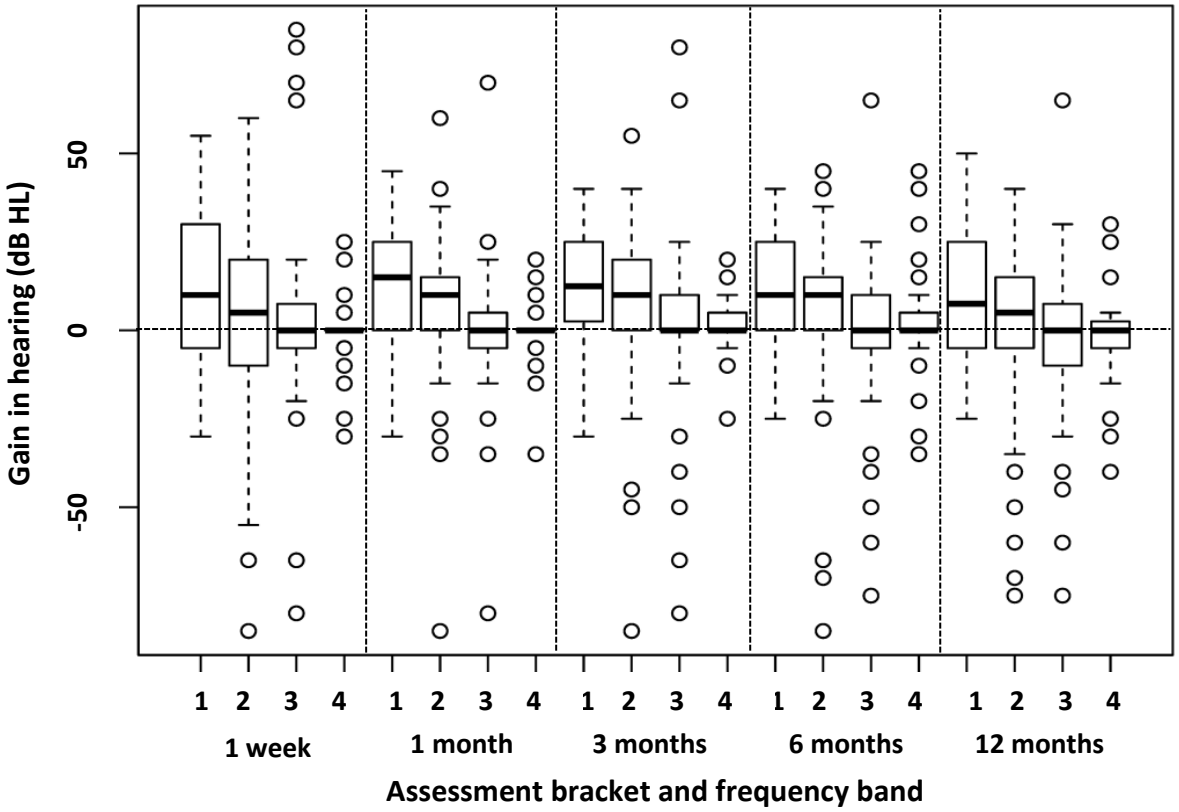

Figure 21. Distribution of changes in hearing relative to the preoperative assessment for patients undergoing ossiculoplasty. Frequency bands 1 and 2 describe changes in the conventional frequency range, and bands 3 and 4 the EHF range. Outlier data, calculated as Quartile 1- 1.5*interquartile range and Quartile 3 + 1/5*interquartile range, are indicated by open circles.

It is evident from the changes in hearing in individual patients presented in Figure 22, that hearing outcomes following ossiculoplasty were much more variable than those following stapedectomy. The majority of patients experienced improved hearing acuity in the lower frequency range, generally by approximately 1 month after surgery. There were, however, several patients that experienced a deterioration in hearing in the conventional frequency range following surgery. Fluctuation in hearing and delayed deterioration after an initially positive result also evident in some cases.

The high rate of high-frequency deterioration observed following stapedectomy is not evident following ossiculoplasty. Results in the high-frequency range show significant variability across assessments, with no clear pattern of recovery over the postoperative course. At all postoperative assessments there were a reasonably even number of patients with hearing loss and hearing gain in the high-frequency range.

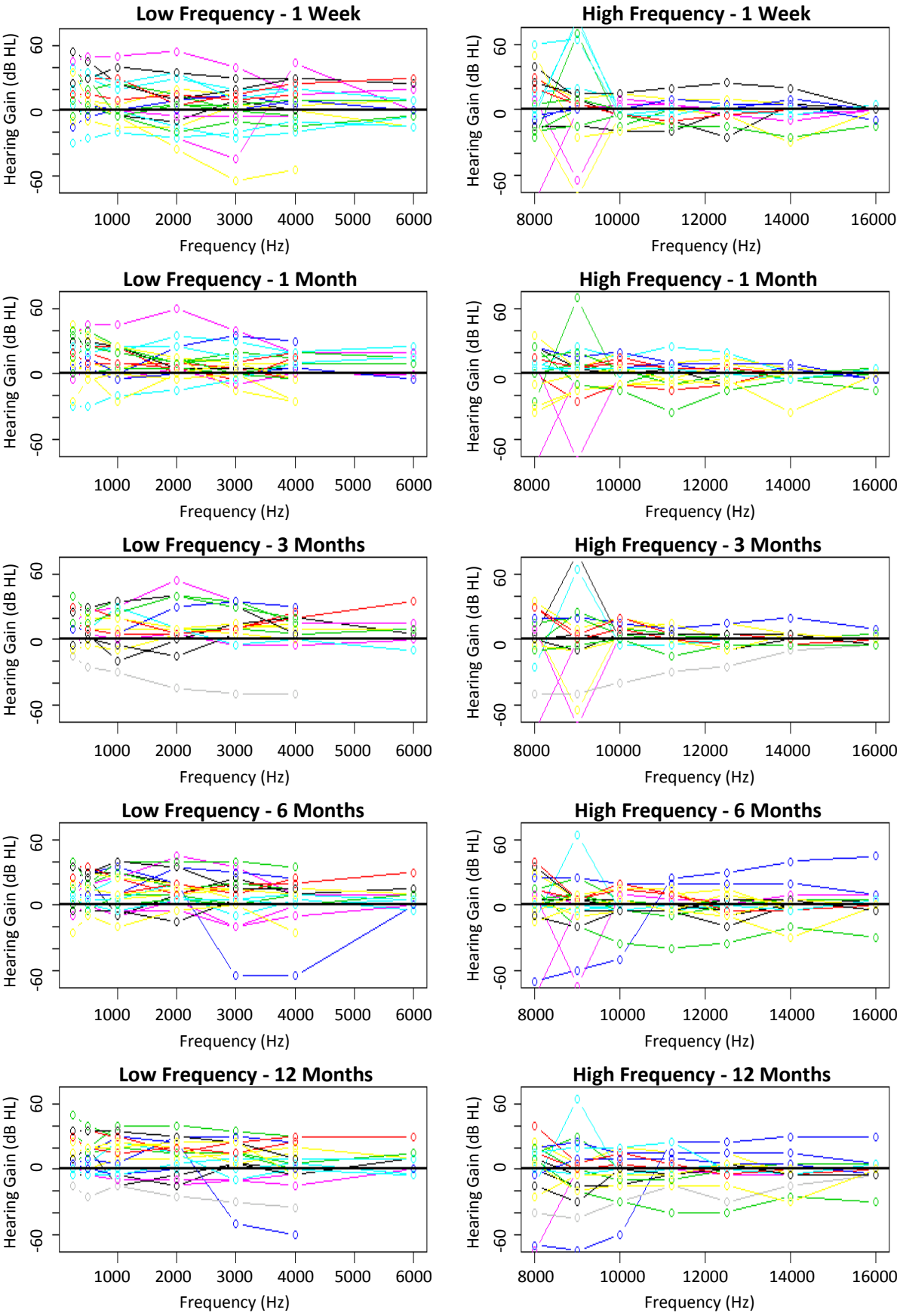

Figure 22. Hearing gain in low-frequencies (0.25 – 6 kHz) and high-frequencies (8 – 16 kHz) in individual ossiculoplasty patients across all postoperative assessments.

3.3.3.3 Changes in hearing across all frequencies post-tympanoplasty

The initial audiometric results following tympanoplasty showed deterioration of median thresholds in all frequency bands (Figure 23). Deterioration was initially similar in Bands 2 and 3, however greater improvement over time was found for Band 2. Improvement was greatest in Band 1, although some late deterioration was documented in this band and in Band 2 by 12 months. In the EHF bands, median threshold increases were again greatest in Band 3, although across the group smaller increases in thresholds were also found in Band 4. Unlike lower frequency bands, the results in Band 4 change little across the postoperative course.

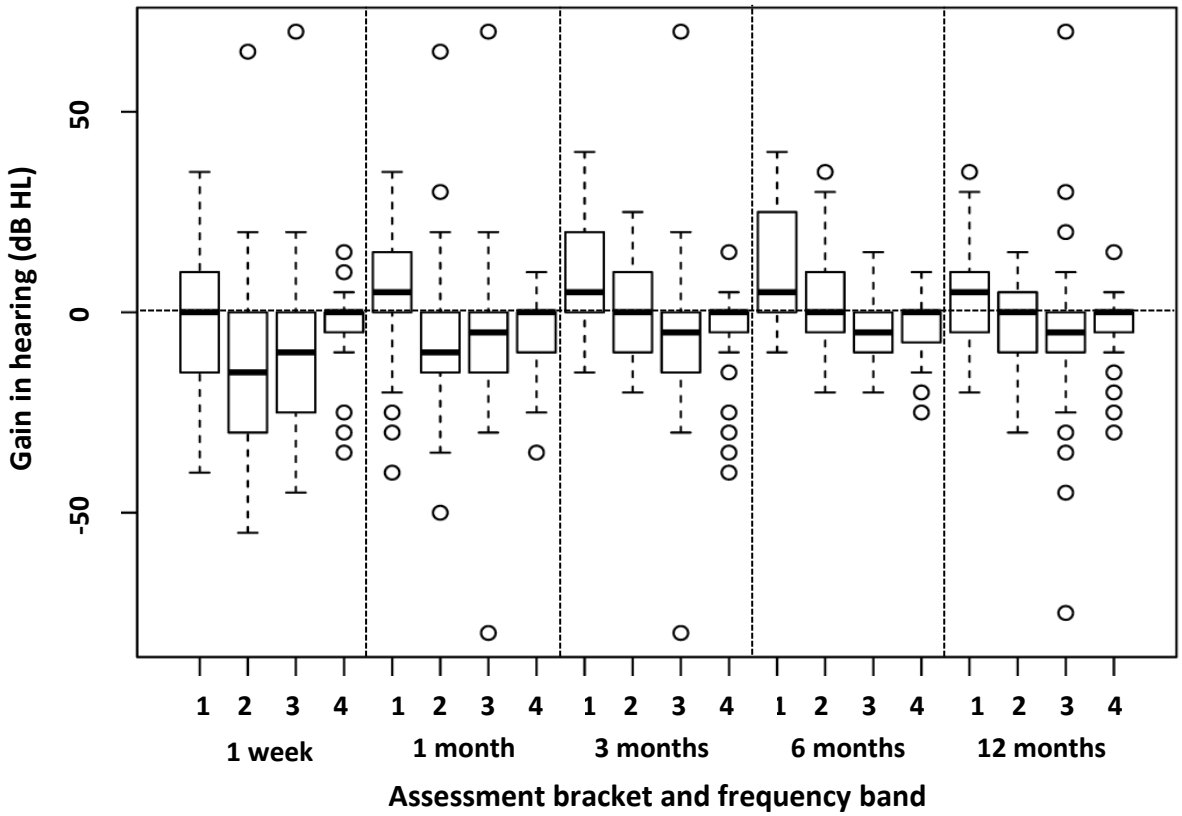

Figure 23. Distribution of changes in hearing relative to the preoperative assessment for patients undergoing tympanoplasty. Frequency bands 1 and 2 describe changes in the conventional frequency range, and bands 3 and 4 the EHF range. Outlier data, calculated as Quartile 1- 1.5*interquartile range and Quartile 3 + 1/5*interquartile range, are indicated by open circles.

As shown in Figure 24, hearing initially decreased following tympanoplasty across all frequencies tested in the majority of patients. Recovery in some cases occurred by the 1 month assessment, and optimal hearing results in the lower-frequency range were achieved around 3 to 6 months post-tympanoplasty, at which time hearing had improved in the

majority of patients. Hearing deterioration following initial recovery occurred in several cases, and affected lower frequencies more than high-frequencies.

At all postoperative assessments except that 6 months after surgery, more patients showed some degree of high-frequency deterioration than the number that showed improvement. When improvement did occur, it was more likely to be present at lower frequencies within the high-frequency range than at the highest test frequencies.

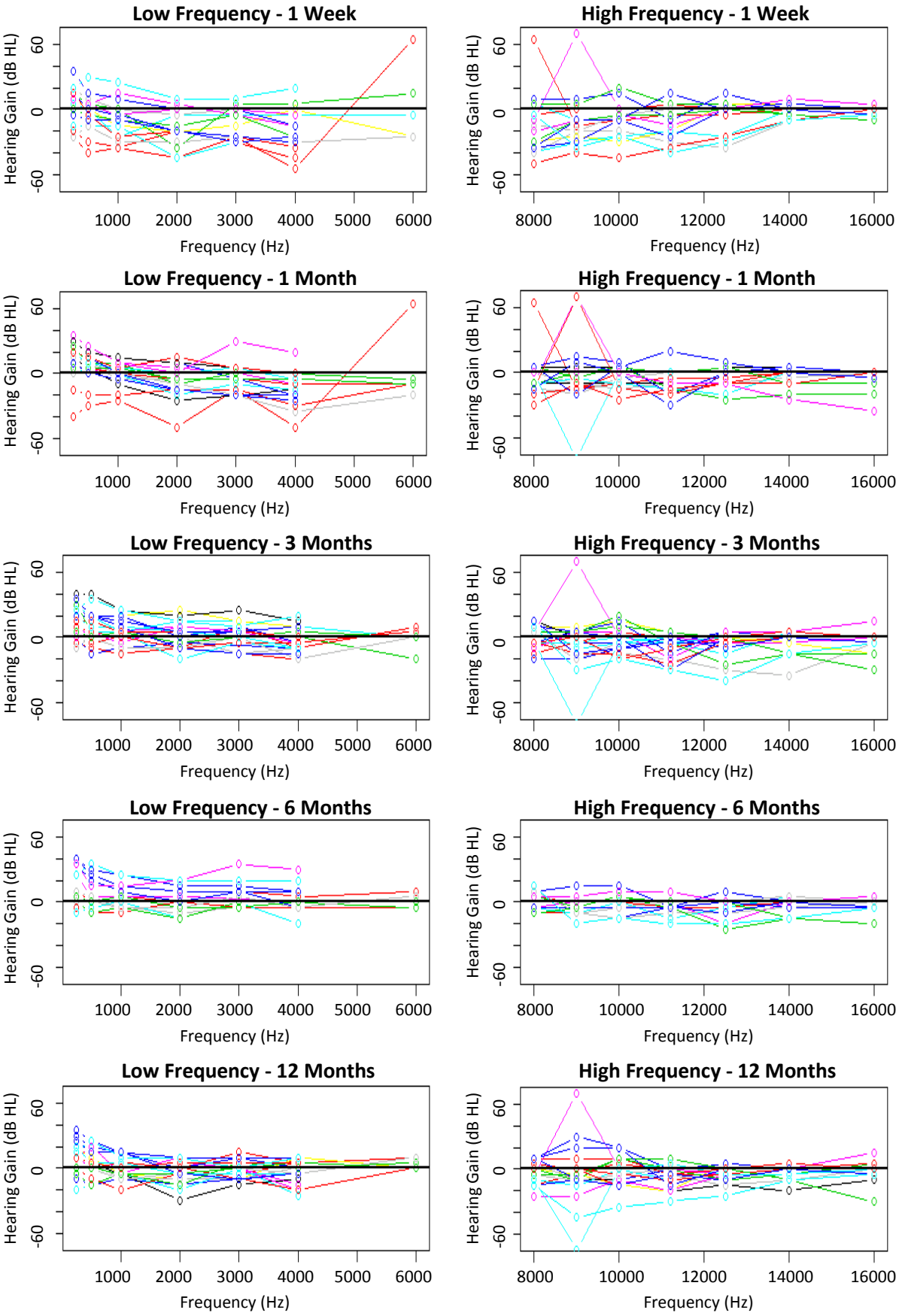

Figure 24. Hearing gain in low-frequencies (0.25 – 6 kHz) and high-frequencies (8 – 16 kHz) in individual tympanoplasty patients across all postoperative assessments.

3.3.4 Linear mixed effects model

A mixed effects model was used to analyse the audiometric data across all three surgeries. Such a model is capable of describing the relationship between the response (change in hearing) and the study variables, while taking into account the correlated data resulting from repeated measurements on each participant over time. A mixed effects model consists of fixed effects and random effects, which are estimated separately. Fixed effects show how each of the variables of primary interest (frequency band, assessment bracket, and surgery type) contribute to the mean response (the average change in hearing across patients). These fixed effects have levels that are of primary interest; in this case assessment brackets 1 – 5 (1 week, 1 month, 3 months, 6 months, and 12 months), frequency bands 1 – 4 (0.25 – 1 kHz, 2 – 8 kHz, 9 – 11.2 kHz, and 12.5 – 16 kHz), and surgery type (stapes, tympanoplasty, and ossiculoplasty).

Random effects are a way to accommodate the variation across individual patients. The assumption is that, on average, this variation has a mean of zero, so that across all patients the average trend for change in hearing over time can be described by the fixed effect. However, the trend for hearing change across assessments for any individual patient may differ from the average. This random variation is of interest as it measures how different the individual trends are across all patients. Random effects are assumed to be normally distributed with a mean of 0 and a variance of σ^2 with residual ε.

3.3.4.1 Model analysis across surgeries

Two models were investigated, and their performance assessed so that the optimal model could be selected.

In these models, a random effect for Subject ID was created for "Band" (frequency) and "Bracket" (assessment time). This enabled us to examine the patient specific effect as the data for each patient was allowed to react differently for each Band and Bracket. The random effect is shown as Band/Bracket|SubjectID.

In model 1 the fixed effect "status" was added to assess for a relationship between whether the surgery was a primary or revision procedure and the degree of hearing change. For this analysis second stage ossiculoplasties were included in the revision group to ensure numbers in each group were sufficient and that variables were consistent across all surgeries.

Model 1:

Hearing change = Status + Surgery + Bracket + Band + Bracket|SubjectID + Band|SubjectID

Model 2:

Hearing change = Surgery + Bracket + Band + Bracket|SubjectID + Band|SubjectID

In model 1, the effect of "status" was not significant ($p > .05$) and therefore was dropped from model 2. To formally test which model was superior, an ANOVA was performed to assess for differences between the models. This ANOVA showed no significant difference between the models, indicating that model with the lowest number of parameters should be selected. The model fitted to the data was therefore model 2, shown in Tables 5 and 6.

Table 5. Model 2: fixed effects results across surgeries.

Variable	Estimate	Standard Error	*t* value
Intercept	13.23	2.05	6.47*
Bracket (2)	5.5	0.79	6.97*
Bracket (3)	8.42	0.98	8.56*
Bracket (4)	8.53	1.12	7.63*
Bracket (5)	7.75	1.18	6.56*
Band (2)	-12.21	1.16	-10.55*
Band (3)	-24.26	2.03	-11.94*
Band (4)	-23.04	1.96	-11.06*
Surgery (Stapes)	1.06	1.58	0.67
Surgery (Tymp)	-4.46	1.80	-2.48*

Statistically significant results (< .05) are marked with an asterisk (*).

The fixed effects of a model are considered to be significant when the *t* -value is greater than ±2, which is approximately the 95% quartile value. The results for model 2 show that all fixed effects, except for the stapes surgery variable, are significant.

In this model, the intercept is the baseline for comparison and is regarded as the average response for Bracket 1, Band 1 and ossiculoplasty.

When significant, the coefficients (estimates) can be interpreted as the change in the response with all other factors held constant. For example, the change in hearing experienced in Bracket 2 is on average 5.5 times higher than that in Bracket 1. The positive coefficients for all brackets indicate that, on average, across time brackets, hearing improves across all

surgeries relative to Bracket 1. The negative coefficients for the frequency bands show that hearing improvement decreases at frequency band increases above Band 1 (0.25 – 1 kHz). Greater negative coefficients are associated with Bands 3 (9 – 11.2 kHz) and 4 (12.5 – 16 kHz). Additionally, it is evident that of all surgeries, change in hearing is poorest following tympanoplasty, as the coefficient is negative, and best following stapes surgery, where a positive coefficient was calculated. It must however be noted that, surprisingly, across all variables, stapes surgery was not significantly different to ossiculoplasty.

Fixed effects describe the average change in hearing across patients and are additive. For example, holding all other factors constant, if an ossiculoplasty patient was being tested in frequency Band 4 (12.5 – 16 kHz) at time Bracket 1 (1 – 2 weeks after surgery), then on average we can expect the change in hearing relative to the preoperative mean to be:

Change in hearing = 13.23 (intercept) − 23.04 (Band 4 coefficient) = −9.81 dB

If we were to test another patient who underwent stapes surgery in the same frequency band and time bracket then the result would be:

Change in hearing = 13.23 − 23.04 + 1.06 (Stapes coefficient) = −8.75 dB

Similarly, for a tympanoplasty patient:

Change in hearing = 13.23 − 23.04 − 4.46 (Tympanoplasty coefficient) = −13.21 dB

This shows that for the frequency band 12.5 – 16 kHz measured approximately 1 week after surgery, hearing deteriorates relative to mean preoperative thresholds following all surgeries, with the greatest deterioration occurring in tympanoplasty patients, followed by ossiculoplasty and then stapedectomy.

If this comparison is repeated for the final assessment, Bracket 5, the model predicts that the degree of hearing loss at 12.5 – 16 kHz will have decreased to an average of -1.00 dB for stapedectomy, -2.06 for ossiculoplasty, and -6.52 for tympanoplasty. In this case, the improvement in hearing over in time (by Bracket 5) is offset by the negative coefficient of Band 4. This illustrates that while we expect change in hearing to continue to be poorer in the in the higher frequency bands than in bracket 1, this effect will decrease over time.

Table 6. Model 2: random effects results.

Variable	Variance	Variance explained
Bracket (1)	80.36	0.09
Bracket (2)	36.75	0.04
Bracket (3)	37.32	0.04
Bracket (4)	54.56	0.06
Bracket (5)	53.86	0.06
Band (1)	184.31	0.22
Band (2)	120.57	0.14
Band (3)	108.7	0.13
Band (4)	31.14	0.04
Residual	146.15	0.17
Total	853.72	1.00

Table 6 shows how the additional variation in change in hearing is explained by allowing a random component to accommodate for the variation among individual patients. The variance listed for each of the variables in the table shows how much the individual responses deviate from the overall mean for the variable, which is given by the fixed effect. Higher numbers indicate greater variability across patients in responses. The variability of the responses demonstrates a convex type of behaviour.

Across assessment brackets, variability is highest in Bracket 1, decreases in Brackets 2 and 3, and increases somewhat in the final two brackets. This indicates that some patients show greater improvement over time than others and that some experience a decline in hearing acuity over time. The random effects for band show that the highest response variability is experienced in Band 1. The variability in response then declines in the higher frequency bands, and is particularly low in Band 4. It is highly likely that the reduced variability in Band 4 is from the number of responses in this band that occurred at the limits of the audiometer, and were therefore all recorded as the same threshold level. The residual is the proportion of variance that is unexplained in the model, and in this case is 17%.

3.3.4.2 Model analysis by surgery

While the model described above provided an interesting comparison of data across surgeries, we were concerned that the different patterns of results observed between surgery types, as illustrated in Section 3.3.3, were not accurately reflected when the model was fitted to the combined dataset. Mixed model analyses were therefore performed for each type of surgery individually.

3.3.4.2.1 Stapedectomy

As shown in Table 7, the results for the stapes model show that all fixed effects are significant. In this model, the intercept is the baseline for comparison and is regarded as the average response for Bracket 1, Band 1. As in the model fitted to the combined dataset, the positive coefficients for all brackets indicate that, on average, hearing improves over the postoperative period, relative to Bracket 1. The highest coefficient was calculated for Bracket 3, suggesting that hearing improvement is maximal by three months after surgery, with a small decrease by the 12 month assessment.

The negative coefficients for the frequency bands show that hearing improvement decreases at frequency band increases above Band 1 (0.25 – 1 kHz), up to Band 3 (9 – 11.2 kHz). The highly negative coefficients are very similar for Bands 3 and 4, consistent with a plateau in the increasing hearing loss with increasing frequency.

Table 7. Model 2: fixed effects results for stapes surgeries.

Variable	Estimate	Standard Error	*t* value
Intercept	22.05	1.96	11.25*
Bracket (2)	7.30	0.96	7.62*
Bracket (3)	11.49	1.26	9.09*
Bracket (4)	11.48	1.45	7.90*
Bracket (5)	10.32	1.78	5.80*
Band (2)	-16.75	1.30	-13.03*
Band (3)	-37.79	1.97	-19.20*
Band (4)	-37.19	2.18	-17.09*

Statistically significant results (< .05) are marked with an asterisk (*).

Table 8 shows the results of the random effects analysis, with the variance calculated for each of the variables showing how much the individual responses deviate from the overall mean for the variable.

In contrast to the overall data, this analysis shows that across assessment brackets, variability is highest in Bracket 5. This is consistent with our observations of elevated thresholds due to failure of the surgical repair in two patients late in the postoperative monitoring period. Variance is lowest in Bracket 3, consistent with the optimal results recorded at that point in the postoperative course when recovery appeared to be complete and no prosthesis failures had occurred. The random effects for band show that the highest response variability is experienced in Band 1, closely followed by Band 3. The variability in response is particularly

low in Band 4. As noted above, this is most likely due to the absence of measureable thresholds in many cases in the highest frequency band. The proportion of variance that is unexplained in the model is 20%.

Table 8. Model 2: random effects results for stapes surgeries.

Variable	Variance	Variance explained
Bracket (1)	67.91	0.10
Bracket (2)	36.60	0.06
Bracket (3)	32.72	0.05
Bracket (4)	59.62	0.09
Bracket (5)	76.86	0.12
Band (1)	77.75	0.12
Band (2)	64.73	0.10
Band (3)	77.72	0.12
Band (4)	31.21	0.05
Residual	128.73	0.20
Total	653.85	1.00

Pairwise comparisons were performed to further investigate the effect of frequency band on postoperative change in hearing thresholds. The comparisons of frequency bands collapsed across all assessments is shown in Table 9. The negative differences again indicate that hearing improvement is, on average, greater in the lower frequency bands. Comparisons between all bands are highly statistically significant, except that between the two highest frequency bands; Bands 3 and 4. Overall, these comparisons suggest that although hearing improvement decreases with increasing frequency band, there is a point at which the change with frequency plateaus. As discussed, this is likely to be at least partially due to the inability to accurately record the extent of threshold deterioration in the highest frequency band.

Table 9. Pairwise comparisons of frequency bands for the stapedectomy group.

Bands compared	Estimate	Standard error	*p*-value
2-1	-16.95	1.20	< .001*
3-1	-37.79	1.97	< .001*
4-1	-37.19	2.18	< .001*
3-2	-20.84	1.43	< .001*
4-2	-20.24	1.92	< .001*
4-3	0.60	1.70	.98

Statistically significant results (< .05) are marked with an asterisk (*).

3.3.4.2.2 Ossiculoplasty

The model analysis of the ossiculoplasty data shows much weaker effects of both time and frequency than the analysis of the stapedectomy data. The positive coefficients for all brackets indicate that hearing did improve postoperatively, but these coefficients are not statistically significant for Brackets 2, 3, and 4 (Table 10). This suggests that, on average, hearing did not change significantly after the first assessment.

In agreement with the stapedectomy data, the fixed effects for band in ossiculoplasty show that, on average, as frequency increases, hearing deterioration increases, at least up to Band 3. These results are statistically significant. Again, the small decrease in the coefficient for Band 4 compared to Band 3 is documented.

Table 10. Model 2: fixed effects results for ossiculoplasty.

Variable	Estimate	Standard Error	*t* value
Intercept	9.43	3.19	2.96*
Bracket (2)	2.04	1.58	1.29
Bracket (3)	2.81	2.20	1.28
Bracket (4)	2.98	2.16	1.38
Bracket (5)	2.42	2.34	1.04
Band (2)	-7.24	2.81	-2.58*
Band (3)	-13.16	3.86	-3.41*
Band (4)	-11.90	3.21	-3.71*

Statistically significant results (< .05) are marked with an asterisk (*).

Analysis of random effects, shown in Table 11, indicated that variance across patients was greatest at the first postoperative assessment and decreased at the second assessment. Variability increased in Bracket 3, but was relatively stable at subsequent assessments. The random effects for band show the greatest response variability in Band 2, followed by Band 1, 3, and finally 4. The markedly lower variance across patients in Band 4 is consistent with the stapedectomy data. The proportion of variance unexplained by this model, as indicated by the residual, is 19%.

Table 11. Model 2: random effects results for ossiculoplasty.

Variable	Variance	Variance explained
Bracket (1)	68.44	0.07
Bracket (2)	33.81	0.03
Bracket (3)	56.29	0.06
Bracket (4)	45.09	0.05
Bracket (5)	50.25	0.05
Band (1)	167.80	0.17
Band (2)	213.60	0.22
Band (3)	149.76	0.15
Band (4)	13.53	0.01
Residual	188.69	0.19
Total	987.26	1.00

The pairwise comparisons between frequency bands (Table 12), like stapedectomy, showed that average hearing change was more negative as test frequency increased. However, following ossiculoplasty, there is no significant difference between Band 2, 3, and 4. Statistically significant differences were present between Band 1 and all other frequency bands. These results suggest that the average degree of change in thresholds postoperatively is not significantly different in the band at 2 – 8 kHz to that at higher frequencies.

Table 12. Pairwise comparisons of frequency bands for the ossiculoplasty group.

Bands compared	Estimate	Standard error	*p*-value
2-1	-7.24	2.81	.045*
3-1	-13.16	3.86	.003*
4-1	-11.90	3.21	.001*
3-2	-5.92	2.99	.18
4-2	-4.66	3.61	.54
4-3	1.26	2.91	.97

Statistically significant results (< .05) are marked with an asterisk (*).

3.3.4.2.3 Tympanoplasty

Finally, the model was applied to the tympanoplasty data. Here, the positive fixed effects for Bracket show that hearing improves significantly over time in all brackets in comparison to Bracket 1 (Table 13). The intercept is, however, not statistically significant, indicating that hearing in Bracket 1, Band 1, was not significantly different to that before surgery. The significant negative coefficients for Bands 2, 3, and 4 are consistent with those for stapedectomy and ossiculoplasty, in showing that hearing outcomes become poorer with

increasing frequency up to Band 3. The decrease in the coefficient in Band 4 compared to Band 3 is again documented.

Table 13. Model 2: fixed effects results for tympanoplasty.

Variable	Estimate	Standard Error	*t* value
Intercept	1.00	2.90	0.35
Bracket (2)	4.86	1.89	2.58*
Bracket (3)	7.67	1.98	3.89*
Bracket (4)	8.79	2.27	3.87*
Bracket (5)	7.52	2.14	3.52*
Band (2)	-9.74	1.78	-5.46*
Band (3)	-13.20	3.12	-4.24*
Band (4)	-10.94	2.73	-4.01*

Statistically significant results (< .05) are marked with an asterisk (*).

Analysis of random effects (Table 14) indicated that variance across patients was greatest at the first postoperative assessment and decreased dramatically at the second assessment. Variability increased again in Bracket 3, and continued to increase in subsequent assessment brackets. Following tympanoplasty, variance was greatest in Band 1, followed by Band 3. As with the other surgeries, variability appears to be lowest in the highest frequency band. The proportion of variance unexplained by this model is 25%.

Table 14. Model 2: random effects results for tympanoplasty.

Variable	Variance	Variance explained
Bracket (1)	41.25	0.08
Bracket (2)	3.44	0.01
Bracket (3)	14.49	0.03
Bracket (4)	24.48	0.05
Bracket (5)	31.66	0.06
Band (1)	125.08	0.24
Band (2)	55.46	0.11
Band (3)	88.20	0.17
Band (4)	10.44	0.02
Residual	133.35	0.25
Total	527.85	1.00

Pairwise comparisons of frequency Bands for the tympanoplasty group produced very similar results to those seen following ossiculoplasty. Significant differences were present between

Band 1 and all higher frequency bands, consistent with greater hearing improvement at 0.25 – 1 kHz than at higher frequencies (Table 15). No statistically significant difference in the average change in hearing across assessments was present between the higher frequency bands. Comparisons between frequency bands showed the poorest results in Band 3. The non-significant positive difference between Bands 3 and 4 suggests less deterioration in the highest frequency band compared to 9 – 11.2 kHz. Likely explanations for this finding have been noted above, although it is interesting that this pattern was evident for all surgery types.

Table 15. Pairwise comparisons of frequency bands for the tympanoplasty group.

Bands compared	Estimate	Standard error	*p*-value
2-1	-9.74	1.78	< .001*
3-1	-13.20	3.11	< .001*
4-1	-10.94	2.73	< .001*
3-2	-3.46	2.51	.49
4-2	-1.21	2.28	.95
4-3	2.25	2.28	.74

Statistically significant results (< .05) are marked with an asterisk (*).

3.3.5 Changes in the highest frequency with a measureable threshold

3.3.5.1 Stapedectomy

One week after stapes surgery, 77% of the 39 patients tested experienced a decrease in the highest frequency at which a hearing threshold could be measured compared to their preoperative audiogram. As shown in Figure 25, the percentage of patients with a loss of measureable EHF hearing thresholds decreased to a minimum of 47% by the assessment at approximately 3 months postoperatively and remained reasonably stable from this point onwards. At the final assessment, 50% of patients retained a decrease in the hearing frequency heard. Few patients (5 – 12%) presented with an increased range of measureable frequencies after surgery and this value changed little over the postoperative course.

The contralateral ear acted as a control for each participant for the effects of test-retest reliability and deterioration unrelated to the surgical procedure. Plotted for comparison to changes in the operated ear in Figure 25, the percentage of patients who lost measureable EHF thresholds in the contralateral ear after surgery ranged from 8% to 21% across the one year follow-up period. At all assessments the percentage of patients with a decrease in the non-operated ear was at least 29% below the percentage with a decrease in the operated ear.

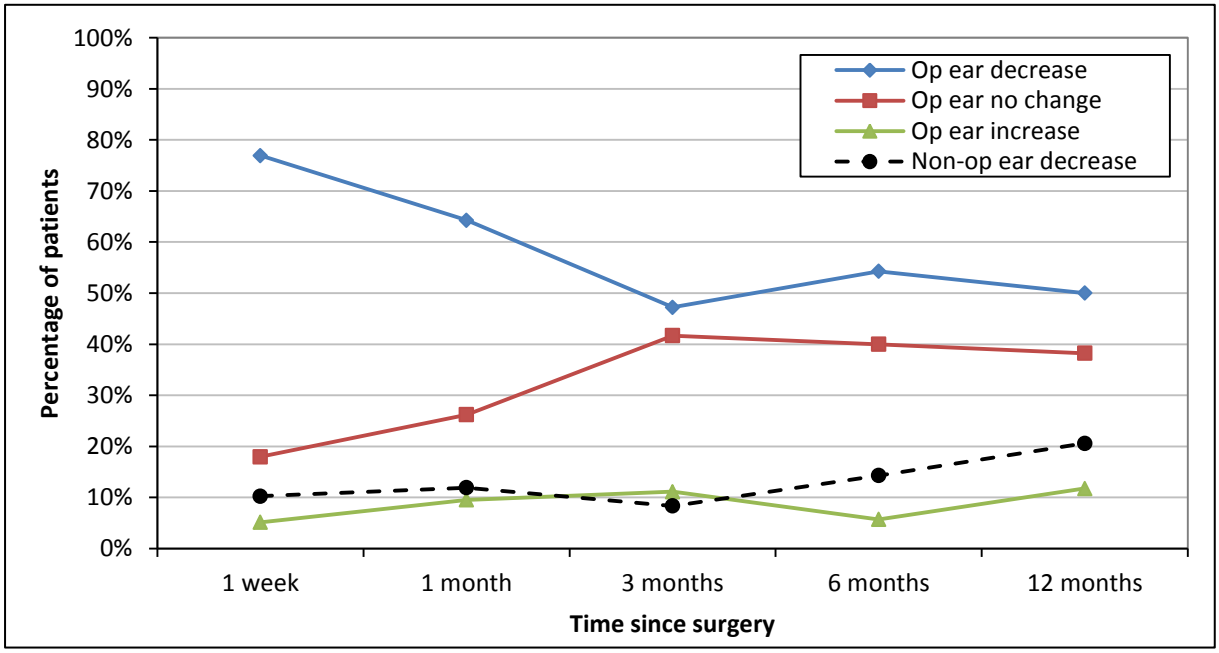

Figure 25. The percentage of post-stapedectomy patients showing a change in the highest frequency at which a threshold was measureable compared to that measured before surgery. The percentage of patients demonstrating a decrease in hearing in the contralateral ear at each assessment is presented for comparison.

In the majority of cases in which the highest frequency with a measureable threshold decreased, the extent of the decrease was one test frequency (e.g. 11.2 kHz to 10 kHz). This pattern was particularly evident at later postoperative assessments where 14%, 9%, and 12% of all patients tested had a loss of more than one frequency at 3, 6, and 12 months, respectively (Figure 26). At the first postoperative assessment, a loss of a measureable threshold at one test frequency was documented in 31% of all patients, whereas 46% lost two to four frequencies. A marked reduction in patients losing multiple measureable thresholds occurred by 1 month, with 21% of cases of two or more lost frequencies at this assessment.

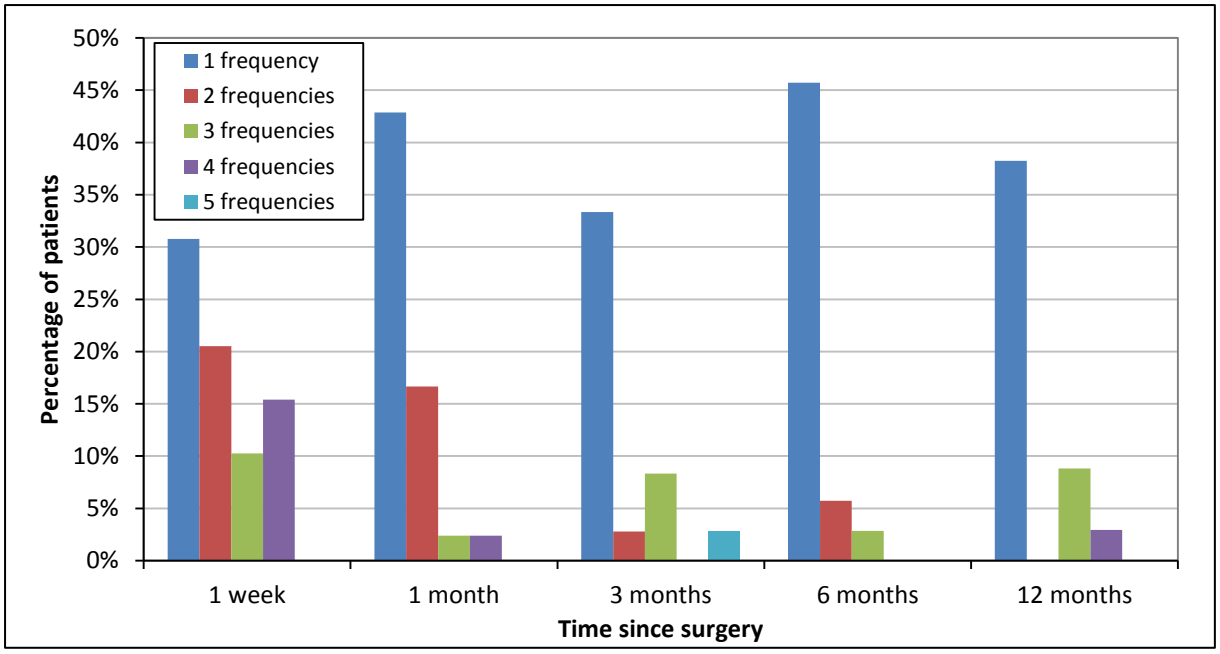

Figure 26. The percentage of all post-stapedectomy patients showing a change of 1, 2, 3, 4, or 5 test frequency steps in the highest frequency at which a threshold was measureable.

3.3.5.2 Ossiculoplasty

The percentage of patients showing a postoperative reduction in the highest frequency with a measureable threshold was much lower following ossiculoplasty than stapedectomy. At the initial postoperative assessment, 38% of the 21 patients tested presented with a decrease in the highest measureable frequency (Figure 27). As shown in Figure 28, in the majority (24% of all patients) of these cases only one test frequency was lost. The percentage of patients with a decrease in the highest measureable test frequency dropped to a minimum of 15% 1 month after surgery (equal with the rate of increased measureable test frequencies), and then

increased at 3 months to remain between 20% and 38% for the remainder of the follow-up period. At the final assessment, 20% of patients retained a decrease in the hearing frequency heard, with two of these four patients losing one test frequency and two losing two test frequencies (Figure 28).

Assessing the rate of measureable frequency loss in the contralateral ear following ossiculoplasty indicates that, with the exception of the first postoperative assessment, the majority of the decrease is the highest frequency heard in the operated ear is unlikely to be the result of surgery. The incidence of a decrease in the highest audible frequency in the non-operated ear ranged from 10% to 31%, and at the final assessment exceeded the decrease rate in the operated ear by 10%. At the first postoperative assessment the difference between the operated and non-operated ears was 19%, however this difference decreased to between only 5% and 9% at the three subsequent assessments.

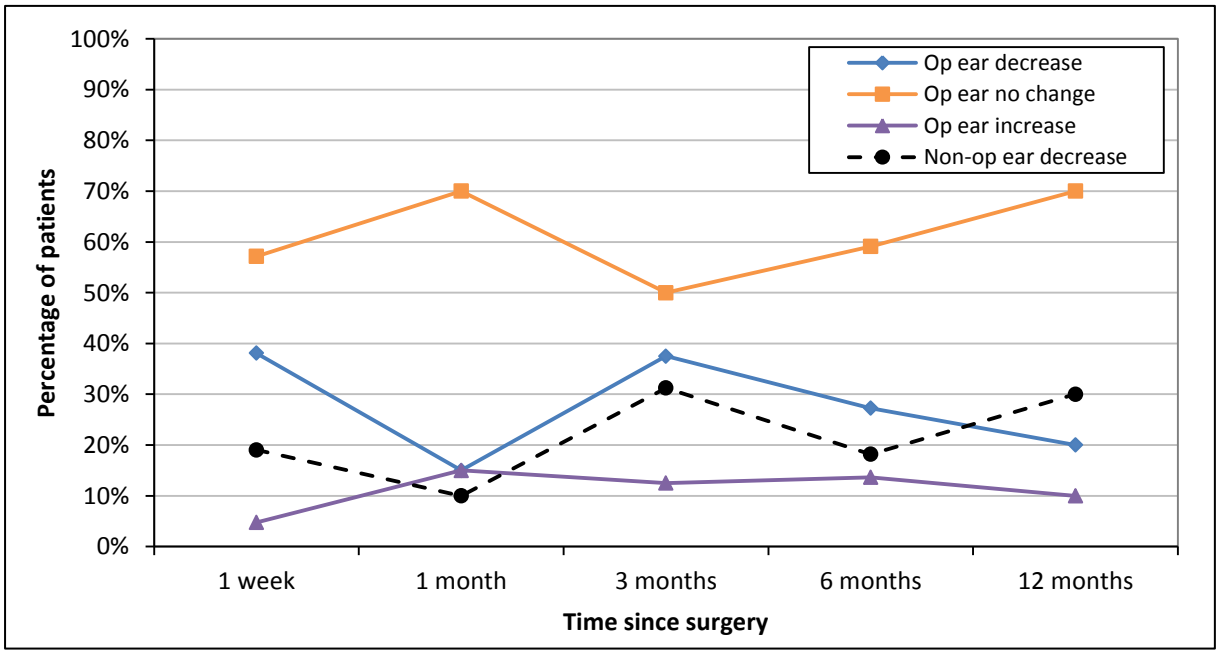

Figure 27. The percentage of post-ossiculoplasty patients showing a change in the highest frequency at which a threshold was measureable. The percentage of patients demonstrating a decrease in hearing in the contralateral (non-operated ear) at each assessment is also presented for comparison.

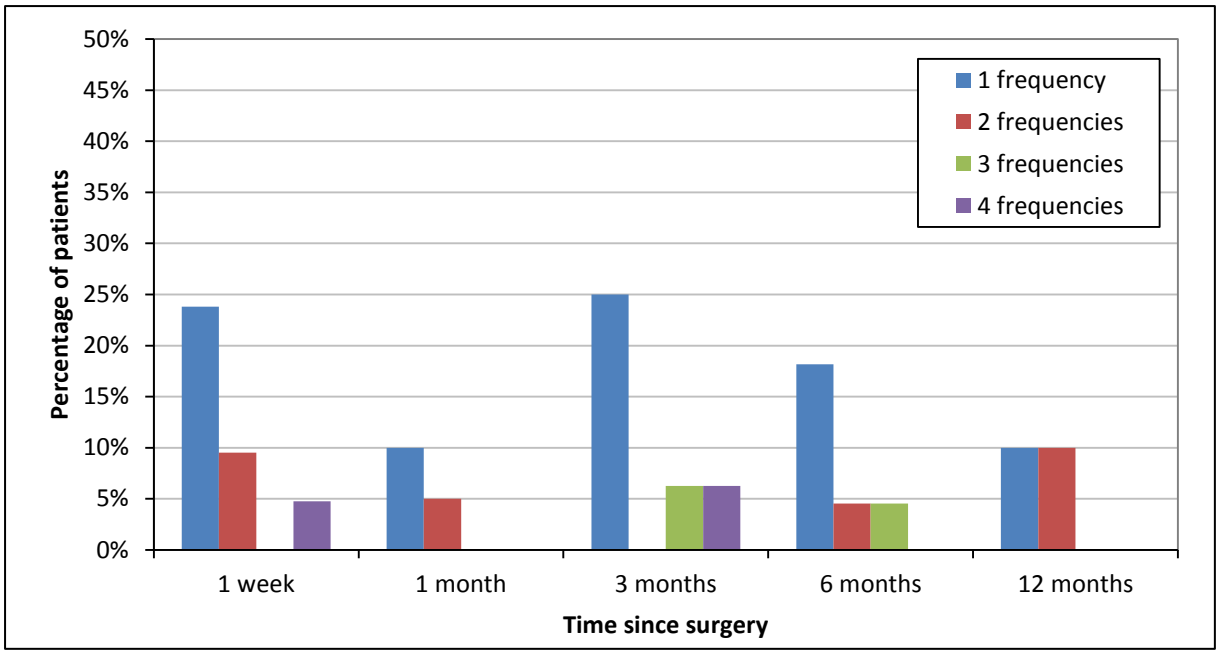

Figure 28. The percentage of all post-ossiculoplasty patients showing a change of 1, 2, 3, 4, or 5 test frequency steps in the highest frequency at which a threshold was measureable.

3.3.5.3 Tympanoplasty

Following tympanoplasty, the rate of decrease in the highest frequency with a measurable threshold was consistently at least 15% higher in operated ears than in the contralateral ears (Figure 29). At the first assessment post-tympanoplasty, 56% of patients had a loss of measureable thresholds. This decreased to a minimum of 38% six months after surgery. Twelve months after surgery, 42% retained a decrease in the highest measureable frequency. The rates of decreased measureable thresholds and no change in the highest frequency heard remained very similar throughout the postoperative course.

At the first postoperative assessment, 32% of all patients had a loss of two or more frequencies, however this rate decreased over the postoperative course. One month after surgery the rate of multiple frequencies lost decreased to 18% and at the final assessment 11% of patients lost measureable thresholds at the two highest frequencies heard preoperatively (Figure 30). No cases of three or more frequencies lost were recorded at the assessments at either six or 12 months after surgery.

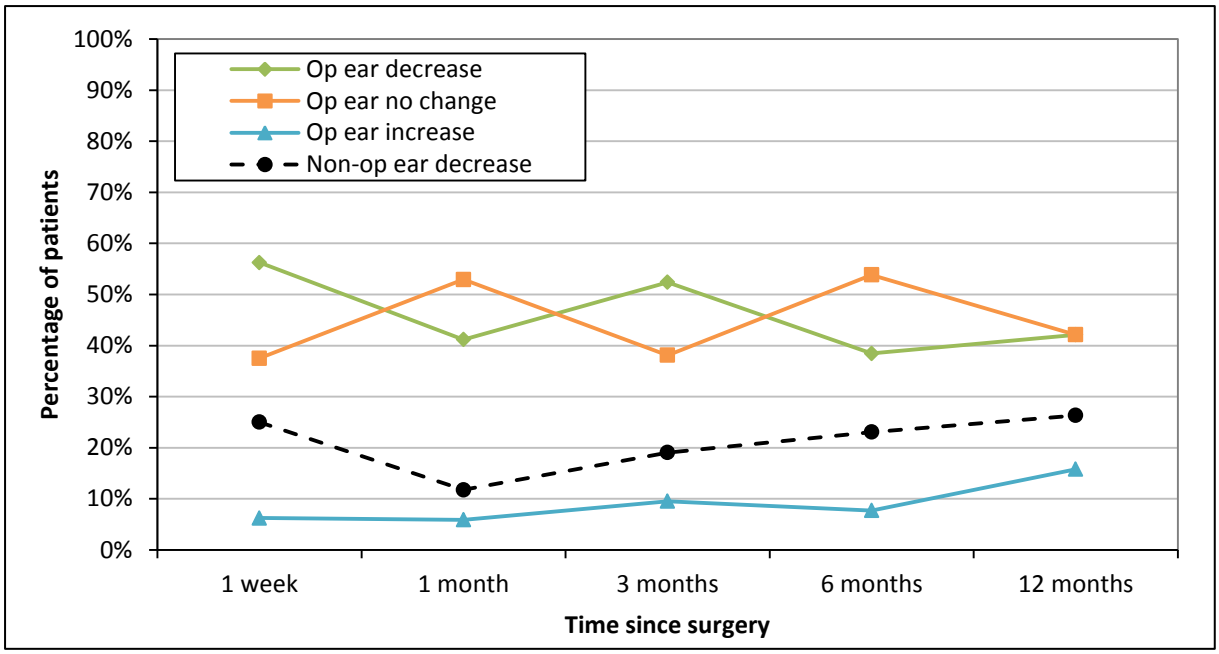

Figure 29. The percentage of post-tympanoplasty patients showing a change in the highest frequency at which a threshold was measureable compared to that measured before surgery. The percentage of patients demonstrating a decrease in hearing in the contralateral (non-operated ear) at each assessment is also presented for comparison.

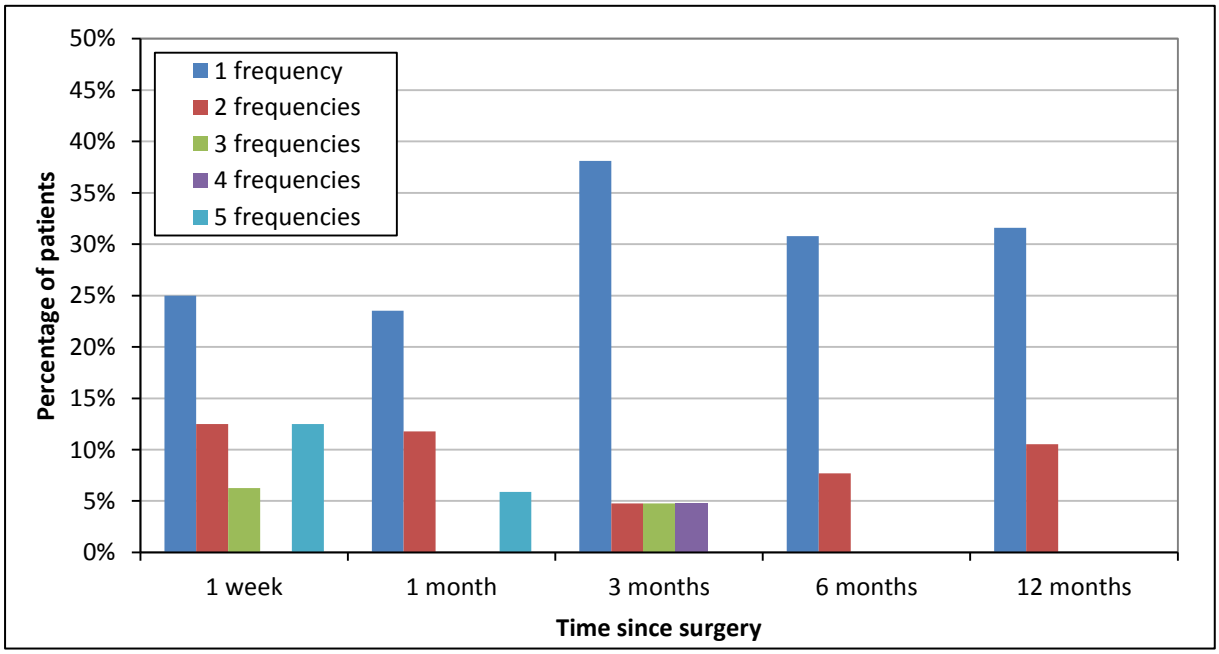

Figure 30. The percentage of all post-tympanoplasty patients showing a change of 1, 2, 3, 4, or 5 test frequency steps in the highest frequency at which a threshold was measureable.

3.4 Discussion

The primary aim of the present study was to determine the prevalence of hearing loss across the entire audiometric test frequency range following surgery performed to reconstruct the middle ear conductive mechanism. Whereas previous reports have identified that hearing in the EHF range often deteriorates on average after surgery (Bauchet St Martin et al., 2008; Doménech & Carulla, 1988; Mair & Laukli, 1986; Tange & Dreschler, 1990), these studies have not clearly described the relative incidence of transient and permanent loss. By monitoring the evolution of audiometric thresholds at 0.25 to 16 kHz from one week until 12 months after surgery, our study was designed to address this gap in the literature and quantify hearing loss and recovery in both the conventional and EHF ranges following stapedectomy, ossiculoplasty, and tympanoplasty.

In agreement with our hypothesis, postoperative audiometry clearly showed that hearing loss frequently occurs in the EHF range following middle ear surgery, often despite successful closure of the air-bone gap and an absence of sensorineural hearing loss in the conventional frequency range. The differential effect of surgery on hearing sensitivity at high and low frequencies was particularly strong following stapes surgery, with weaker trends apparent following tympanoplasty and more limited, short term effects documented in patients undergoing ossiculoplasty. EHF hearing loss was more prevalent and threshold shifts larger in the early postoperative period, however a significant proportion of patients retained an EHF hearing loss when tested 12 months after surgery, most commonly after stapedectomy.

3.4.1 Early postoperative hearing loss and recovery of hearing

3.4.1.1 Conventional frequency range

It is well known that audiometric results immediately after middle ear surgery are poorer than those obtained at least one to three months postoperatively (Sergi et al., 2010; Sperling et al., 2013). Much of the improvement over time is presumed to be related to the resolution of factors such as swelling, bleeding, and packing in the middle ear space that produce a temporary conductive hearing loss (Cho et al., 2007; Robinson & Kasden, 1977). The present audiometric results after stapedectomy and ossiculoplasty follow this expected pattern, and showed an initial improvement in the mean AC PTA and air-bone gap by the 1 week postoperative assessment, with gradual continued improvement until the assessment 3 months after surgery. Unlike stapedectomy and ossiculoplasty, the mean AC PTA and air-bone gap

initially significantly worsened following tympanoplasty. While the initial outcome of this surgery was poorer, again, partial recovery of both values was documented 1 month after surgery, and the average AC PTA and air-bone gap remained smaller than preoperatively from 3 months onwards.

In addition to factors that cause conductive hearing losses to persist in the early postoperative period, short-term changes in bone-conduction thresholds suggestive of transient cochlear trauma have been widely reported after otologic surgery (Antonelli et al., 1998; Gerard et al., 2008; Keck et al., 2002; Sergi et al., 2010). In agreement with Bergin's (2011) meta-analysis, our results indicated that the most sensitive measure of loss of bone-conduction sensitivity was the evaluation of the change in the 4 kHz threshold in isolation. Following all surgeries, a mean increase in the 4 kHz bone-conduction threshold was recorded 1 week after surgery, although results were significant only for stapedectomy and tympanoplasty. The rate of patients presenting with a loss of greater than 10 dB at 4 kHz was also greatest 1 week postoperatively, with recovery in most cases occurring within three months of surgery, in line with air-conduction threshold improvement. The documented pattern of temporary sensorineural hearing impairment following stapedectomy, particularly at 4 kHz, is in agreement with group mean shifts in bone-conduction thresholds documented in previous studies, confirming that this series is not unique in terms of early postoperative changes in audiometric thresholds (Antonelli et al., 1998; Gerard et al., 2008; Keck et al., 2002; Sergi et al., 2010).

3.4.1.2 EHF range

Sperling et al. (2013) posit that early losses of bone-conduction sensitivity, such as those observed at 4 kHz in this study, may reflect surgical trauma to the labyrinth that, although not evident later in the postoperative course, may have a long-term effect on the overall cochlear health. They suggest that early hearing outcomes following stapes surgery may provide a more sensitive indicator of cochlear trauma that could be used to inform the debate regarding technical factors of surgery, such as laser type, fenestra size, and prosthesis choice. We propose that such questions can be addressed with greater efficiency by measuring EHF thresholds which, according to the present results, are impaired in a higher percentage of patients and are more likely to be impaired long-term than thresholds in the conventional frequency range. Indeed, one week after surgery the percentage of patients with a decrease in

the highest test frequency at which a threshold was measureable was more than twice as high as the percentage of patients with a loss of greater than 10 dB in the 4 kHz bone-conduction threshold at the same assessment.

Median thresholds in the EHF range increased relative to the preoperative assessment in the early postoperative period following both stapedectomy and tympanoplasty. Increases were largest in the frequency band from 9 to 11.2 kHz, with smaller increases recorded in the analysis at 12.5 to 16 kHz. Given that preoperative thresholds were generally higher, and therefore closer to the more restricted maximum output of the audiometer at 12.5 to 16 kHz than at 9 to 11.2 kHz, the most parsimonious explanation for the greater shift in the lower EHF frequency band is that there was a greater ability to record these changes. If thresholds at frequencies associated with the basal cochlear turn, where we hypothesise trauma occurs, are very elevated preoperatively, we are more limited in our ability to detect the degree of damage that occurs postoperatively. This is certainly a limitation of EHF audiometry. The changes recorded in median EHF thresholds after ossiculoplasty may have been limited due to this same issue, as mean preoperative thresholds in the ossiculoplasty group were higher than in patients undergoing other surgeries.

We attempted to address the limitations of assessing mean or median threshold changes in the EHF range where audiometer output is restricted by calculating the percentage of patients who experienced a decrease in the highest frequency at which a threshold could be measured. Consistent with the median data, the rate of EHF hearing loss, as calculated using this metric, was highest post-stapedectomy, followed by tympanoplasty, with the lowest rate of hearing loss after ossiculoplasty. A decrease in the highest frequency at which a threshold was measureable occurred frequently initially after surgery, and loss of at least one test frequency was documented one week after surgery in 77% of stapedectomy cases, 56% of tympanoplasties, and 38% of ossiculoplasties. That such a high rate of measureable frequency loss could be measured after ossiculoplasty in the absence of changes in median EHF thresholds supports our assertion that the absence of significant findings in the model analysis was related to the high preoperative EHF thresholds.

Questions regarding exactly what is being measured using high-frequency electrostimulation and methodological limitations in studies using this technique restrict comparisons that can be made to the results of the present study. Such studies do, however, provide evidence of at least temporary early EHF changes after middle ear surgery that is in agreement with the current findings (Doménech & Carulla, 1988; Doménech et al., 1989; Hegewald et al., 1989).

Doménech and Carulla (1988) demonstrated a "moderate" increase in unmasked electrostimulation thresholds at 6 – 19 kHz in 20 of 24 patients, and a lowering of the highest frequency at which a hearing threshold was measureable in 16 patients a few days after stapedectomy. Hegewald et al. (1989) found similar evidence of a temporary mean unmasked threshold shifts 48 hours following 25 mastoidectomies that recovered, on average, by the second postoperative assessment one month after surgery. In that series, a significant decrease of an average of 890 Hz was however found in the mean highest frequency at which a threshold could be measured one month after surgery, despite the improvement in the mean threshold. Our results showed a similar trend for improvement in mean thresholds and recovery over time, with persistence of a loss of at least one measureable EHF threshold in a high percentage of patients.

Tracking thresholds in individual patients indicated that partial recovery of EHF hearing occurred in the vast majority of cases, rather than complete recovery in some patients and no improvement in others. Evidence of temporary worsening of EHF hearing acuity indicates that if the cause of hearing loss is trauma to the cochlea, the injury is limited and recoverable (at least in part). If the hearing loss is conductive in nature, it appears that in most cases the factors causing the hearing loss, perhaps oedema or effusion, at least partially resolve over time.

3.4.2 Late postoperative hearing loss

Despite some recovery of EHF hearing thresholds after the initial postoperative increase, many patients retained a loss of at least one measureable test frequency 12 months postoperatively. Again, this percentage was highest for patients who had undergone stapes surgery, after which 50% retained a loss of measureable EHF thresholds one year after surgery. Long-term EHF loss after tympanoplasty was also common, with 42% retaining a decrease in the highest frequency heard. At all assessments following stapedectomy and tympanoplasty the percentage of patients with a decrease in the non-operated ear remained well below the percentage operated ear, strongly supporting the theory that the decrease in measureable thresholds was a result of the surgery. In contrast, with the exception of the results from the one week assessment, rates of hearing loss in the ear contralateral to that in which ossiculoplasty was performed were close to the rate of loss in the operated ear. These results suggest that in the majority of cases the long-term decrease in the highest frequency

heard in the operated ear following ossiculoplasty is the result of other variables affecting test-retest reliability or EHF hearing, rather than the surgery itself.

In agreement with the early postoperative results, the rate of measureable EHF frequency loss and the increase in median EHF thresholds was markedly higher than the rate of 4 kHz bone-conduction elevation one year after surgery. At 12 months, sensorineural hearing loss was identified, according to the criterion of an increase of greater than 10 dB at 4 kHz, in 3% of stapedectomy patients (1 patient), 10% of ossiculoplasty cases (2 patients), and no patients who had undergone tympanoplasty. In all three patients with a significant loss at 4 kHz, the threshold was elevated by 15 dB from the preoperative threshold, and in all three cases the loss developed over the course of the 12 month follow-up period, rather than developing immediately after surgery and persisting for one year. This suggests the cause of sensorineural loss was not related to acute surgical trauma to the inner ear. Again, if the EHF loss is sensorineural in origin, the comparison of EHF loss and 4 kHz bone-conduction threshold increases suggests that measuring EHF hearing loss is a much more sensitive indicator of long-term cochlear trauma.

The literature describing EHF hearing loss following middle ear surgery is sparse, particularly in terms of documenting the rate of hearing loss, rather than only changes in mean group thresholds. Mair and Laukli (1986) performed postoperative testing 1 – 3 years after myringoplasty and stapedectomy, therefore their findings are most comparable to our final 12 month results. In that study, EHF hearing loss is reported as a mean change in air-conduction thresholds at 10 – 16 kHz only. Deterioration was significantly greater in the 36 patients of theirs who underwent myringoplasty than their 28 stapes surgery patients, in agreement with the present study. A deterioration of mean EHF thresholds was also reported after stapes surgery by Tange and Dreschler (1990). Although it is not clear from that study at what point in the postoperative course the reported data was collected, assessments were performed 3, 6, and 12 months after surgery, at least suggesting that hearing loss was present that persisted beyond the immediate postoperative period. Our results showing the persistence of many cases of EHF hearing loss beyond the initial recovery period following stapedectomy and tympanoplasty are in accordance with these two previous studies. We expand on this previous research by showing the progression of EHF hearing loss across the 12 months after surgery and clarify the incidence of significant EHF hearing deterioration.

While the current results present unique information regarding the initial deterioration and incomplete recovery of EHF thresholds in the months following surgery, we cannot from

these results distinguish whether transient and permanent hearing losses result from the same causal mechanisms. It is possible that transient and permanent hearing losses are two separate phenomena; potentially, the more severe early hearing loss could be due to surgical factors that impair the conductive mechanism during healing, and long-term hearing loss could be the result of cochlear injury. Indeed, even the reverse could be true, with initial hearing loss the result of acute inner ear trauma, and long-term hearing loss caused by permanent changes in the structural anatomy and therefore the transmission properties of the middle ear apparatus. The converse of these possibilities is that both early and late hearing loss are usually due to the same mechanism, with the injury or abnormality recovering completely in some patients and partially in others, causing hearing thresholds to improve over time. In no cases did we find no improvement at all in thresholds at 8 kHz and above following the one week assessment, consistent with the idea that the immediate postoperative injury or obstruction always recovered, at least to some degree, over time.

3.4.3 Nature of the hearing loss

The major limitation in the present study and in previous reports by Mair and Laukli (1986) and Tange and Dreschler (1990) is the inability to distinguish between conductive and sensorineural hearing loss. This limitation was addressed in a study by Mair and Hallmo (1994) in which assessment of masked air- and bone-conduction around thresholds 4.5 months following myringoplasty indicated that the hearing loss was conductive. It is interesting that threshold increases in mean air-conduction thresholds of 2 – 11 dB at 6 – 18 kHz were documented by Mair and Hallmo at a time in the postoperative course when any mean EHF hearing loss following tympanoplasty had resolved in the present study. While their data certainly provides evidence that EHF hearing loss several months after middle ear surgery can be conductive, at least following myringoplasty, the issue of early postoperative EHF loss remains unaddressed. The reporting of mean thresholds only in this study also potentially obscures individual cases in which bone-conduction thresholds may have deteriorated.

We attempted to address the lack on EHF bone-conduction measurements in a limited manner by testing bone-conduction thresholds in the conventional frequency range. The assumption here is that if the air-bone gap is closed at 4 kHz and below, indicating the absence of a conductive hearing loss, an isolated conductive EHF hearing loss is less likely.

The recovery of the 4 kHz bone-conduction threshold in a time frame similar to the EHF thresholds could suggest that the initial, more severe, temporary EHF loss was cochlear in nature, however, there is uncertainty regarding the contribution of external and middle ear transmission pathways to high-frequency bone-conduction thresholds (Cho et al., 2007). If other bone-conduction pathways are influencing the results, the 4 kHz bone-conduction threshold elevation may in fact be due to conductive factors, and give no insights into the cause of EHF hearing loss.

Tympanometry was performed in an additional effort to estimate the function of the conductive mechanism. Tympanometric data provided some evidence of normal middle ear function for a 226 Hz input tone in all stapedectomy cases, however frequently after tympanoplasty and ossiculoplasty, acoustic immittance measures showed Type B tympanograms, consistent with abnormal middle ear function. In some cases such a result was recorded even in the presence of successful closure of the air-bone gap within the conventional frequency range. We did not attempt to correlate tympanometry results with changes in EHF hearing and the results are not reported in this chapter, primarily because tympanometry could not be performed until at least 3 months after surgery when many cases of EHF hearing loss had improved. It may be that abnormal tympanometry results after some middle ear procedures, although not correlative with abnormal middle ear function in the conventional frequency range, could indicate that sufficient structural change has occurred that EHF transmission through the middle ear is affected. Wideband tympanometry, which uses a broad range of probe tone frequencies to more accurately assess the status of the middle ear (e.g. Sanford, Hunter, Feeney, & Nakajima, 2013) may also be useful to address this question. Certainly, this is an issue that requires further investigation.

3.4.4 Differences between surgeries

Loss of EHF hearing occurred much more frequently following stapes surgery than tympanoplasty, and especially ossiculoplasty. If the hearing loss is due to cochlear damage rather than middle ear transmission characteristics, these results suggest that the injurious surgical manoeuvre is more common during stapes surgery than other middle ear procedures. The most obvious candidate is direct manipulation of the stapes footplate, which is exclusively performed in stapes surgery. Side effects from the use of lasers on the footplate are also a possibility, as is drilling on the footplate. However, if transmission of force to the

inner ear through direct manipulation of the ossicular chain is a major cause of hearing loss, we would have expected that rates of EHF threshold elevation would have been highest following stapedectomy and ossiculoplasty, with much lower rates after tympanoplasty. That this was not found to be the case and EHF hearing loss after ossiculoplasty was rarely identified indicates that this may not be a common cause of EHF hearing loss.

Other factors particular to the groups of patients undergoing each type of surgery may have influenced the ability to detect EHF hearing loss, although not necessarily its occurrence. In particular, patients undergoing ossiculoplasty had poorer mean EHF thresholds preoperatively than those undergoing stapedectomy or tympanoplasty. These patients were also more likely to have undergone one or more previous otologic surgeries, which may have resulted in greater EHF hearing loss prior to the surgery included in this series. It was also noted that patients undergoing ossiculoplasty often had a lower number of measureable thresholds before their procedure. Measuring the number of frequencies that become inaudible after surgery goes some way towards addressing the limitations associated with calculating mean change in the EHF range, but if EHF thresholds are not measureable preoperatively, we cannot detect their loss postoperatively. If the hearing loss is due to injury only at the basal turn of the cochlea, it may be the case that more subtle trauma results only in loss at the highest test frequencies. Therefore if, for example, thresholds at 12.5 kHz and above cannot be measured before surgery, trauma cannot be detected postoperatively. In such cases, only when trauma was severe enough that a greater number of increasingly lower frequencies were affected would we expect to see significant results. Although all participants had measureable frequencies at least up to 10 kHz, this may not have been adequate to detect less severe iatrogenic damage.

Conductive hearing loss is still a possibility that has not been eliminated, and it is certainly possible that differences in the way in which surgeries altered the normal structural anatomy of the middle ear could be the cause of differences in the rates of EHF hearing loss between surgeries. In particular, it may be that changes at the stapes-oval window interface had a greater effect on transmission of EHF stimuli than changes in the structure of the ossicles. In the same manner, perhaps changes to the microanatomy of the TM also influenced EHF hearing more than alteration of the movement patterns of the ossicles. These possibilities are discussed further in Chapter 5.

3.4.5 Hearing outcomes in the conventional frequency range

The focus of this study was on postoperative hearing deterioration, particularly in the EHF range, however the assessment of hearing outcomes in the conventional range using traditional criteria is an important step to ensure that our overall hearing outcomes are comparable to those in other studies.

Analyses of audiometric outcomes following stapes surgery using traditional AAO-HNS (1995) criteria indicate that in the majority of cases the surgery was successful. Approximately 12 months after surgery the mean AC PTA was found to have decreased significantly to 29.2 dB (*SD* = 14.8) from 57.1 dB (*SD* = 11.8) before surgery. The mean air-bone gap also decreased significantly from 31.3 dB (*SD* = 10.5) before surgery to 8.2 dB (*SD* = 10.1) at the final assessment. Air-bone gaps of 10 dB or less were achieved in 80% of patients, and of 20 dB or less in 91%. Comparison across studies is difficult given differences in timing of assessments, however, overall our results are in accord with others reported from at least three months after surgery. Large, recently published series of stapes surgeries (primary or both primary and revision) have documented rates of air-bone gap closure to 10 dB or less in 63% to 97% of patients and to 20 dB or less in between 87% and 98% of cases (Fayad, Semaan, Meier, & House, 2009; Marchese, Scorpecci, Cianfrone, & Paludetti, 2011; Massey, Kennedy, & Shelton, 2005; Sergi et al., 2010; Sorom, Driscoll, Beatty, & Lundy, 2007; Sperling et al., 2013; Tenney, Arriaga, Chen, & Arriaga, 2008; Vincent, Bittermann, Oates, Sperling, & Grolman, 2012; Vincent, Sperling, Oates, & Jindal, 2006).

As expected, the postoperative improvement in average air-conduction thresholds was smaller following ossiculoplasty and tympanoplasty than for stapedectomy. In the group of patients undergoing ossiculoplasty, the mean AC PTA improved from 48.2 dB (*SD* = 11.1) before surgery to 39.3 dB (*SD* = 13.7) 12 months after surgery, and the mean air-bone gap decreased from 29.8 dB (*SD* = 12.6) to 22.4 dB (*SD* = 10.3). However, neither improvement reached statistical significance. Approximately one year after surgery, the percentage of patients with an air-bone gap of 20 dB or less was 45%; an increase from the 25% documented before surgery. These results are within the, admittedly wide, range reported in other recent studies, in which mean postoperative air-bone gaps have been reported of 11 to 29 dB, with closure to 20 dB or less reportedly achieved in 44% to 89% of cases (Alaani & Raut, 2010; Demir et al., 2012; Fayad, Ursick, Brackmann, & Friedman, 2014; Galy-Bernadoy et al., 2014; Gardner, Jackson, & Kaylie, 2004; Iniguez-Cuadra et al., 2010; Mardassi et al., 2011; Martin & Harner, 2004; Meulemans, Wuyts, & Forton, 2013; Neff,

Rizer, Schuring, & Lippy, 2003; Quérat, Martin, Prades, & Richard, 2014; Schmerber et al., 2006; Vassbotn, Moller, & Silvola, 2007; Woods, Fata, & Saliba, 2009).

In contrast to stapedectomy, for which hearing improvement was always the primary goal, and ossiculoplasty, which was in many cases performed to improve hearing, improvement of hearing was generally a secondary goal when tympanoplasty was performed in the current study. Surgery was indicated by the presence of cholesteatoma in six of the 27 ears, and in the remaining cases was performed to repair a TM perforation, the causes of which varied. Reflecting the different reasons that surgery was performed, the group of patients undergoing tympanoplasty had a lower mean preoperative AC PTA than the other surgery groups. Data from the final assessment showed a mean AC PTA of 35.6 dB (*SD* = 16.2); 1 dB lower than before surgery, and a non-significant decrease in the mean air-bone gap from 18.6 dB (*SD* = 11.1) preoperatively to 17.3 dB (*SD* = 10.5). At 12 months, 68% of patients had an air-bone gap of less than or equal to 20 dB, compared to 59% before surgery. A review of recent studies reporting the results of primary and revision tympanoplasties reveals marked variation in techniques as well as both preoperative hearing and postoperative hearing outcomes. Most recent studies report mean postoperative air-bone gaps similar to those found in the present study (e.g. Gamra et al., 2008; Lee, Lee, Nam, Lee, & Kwon, 2012; Yawn, Carlson, Haynes, & Rivas, 2014), however, at 78 – 91%, recently reported rates of air-bone gap closure to within 20 dB are slightly higher than in our series (Gamra et al., 2008; Kim et al., 2014; Yilmaz, Guven, Kayabasoglu, & Varli, 2013). Given the variability across the literature in terms of patient and pathology characteristics, and surgical techniques, the finding that our rate of postoperative air-bone gap closure is somewhat poorer than others in the recent literature is not unexpected.

With regard to the few other studies that have also quantified sensorineural hearing loss as an increase of greater than 10 dB at 4 kHz, again our results are comparable. Häusler et al. (1999) reported a significant threshold shift at 4 kHz in 20% of their 15 stapedotomy patients two months postoperatively, and 7% one year after surgery. Higher rates of sensorineural loss at 4 kHz were documented by Boonchoo and Puapermpoonsiri (2007) following 30 stapedotomies, with loss greater than 10 dB measured for 20% of patients 1 to 3 months after surgery, and 23% of patients one year or more postoperatively. In a retrospective chart review performed at our institution, Bergin (2011) found a loss of greater than 10 dB in the 4 kHz bone-conduction threshold of 11.2% of 196 primary stapes surgeries. Although this rate seems higher than the present study, Bergin used the most recent audiogram performed in the

year after surgery, therefore in some cases results may have been obtained early in the postoperative period where thresholds would be expected to be poorer. Using the same criteria, Bergin (2011) and Schmerber et al. (2006) both reported rates of sensorineural hearing loss of 3.6% following ossiculoplasty, and the equivalent rate of sensorineural loss reported following tympanoplasty by Redaelli de Zinis et al. (2010) was 7% 6 – 12 months after surgery in 134 patients.

Overall, evaluation of the results in the conventional frequency range indicates that our series is not unique in terms of the success rates or rates of sensorineural hearing loss. These measures provide no evidence that the incidence of EHF hearing loss or cochlear trauma should be any greater in our study group than in other populations.

3.4.6 Limitations of the present study

The major limitation of the present study is, as noted, that EHF bone-conduction thresholds were not measured in the study population. Although this impacts our ability to determine the cause of hearing loss, it does not prevent the aims of the study; to document the rates of EHF hearing loss following middle ear surgery and describe changes in patterns of hearing loss over the 12 months after surgery, from being addressed. Further research is described later in this thesis that was performed to investigate whether hearing losses in the EHF range, as described here, are conductive or sensorineural.

In terms of addressing the hypotheses in this study, we consider that the primary limitations were related to the limited dynamic range available for testing in the EHF range. The effectiveness of measuring changes in EHF thresholds is much more limited in patients that have a pre-existing EHF hearing loss before surgery. This is particularly common in older patients, as hearing tends to deteriorate with age at the highest audible frequencies first (e.g. Ahmed et al., 2001; Dreschler, van der Hulst, Tange, & Urbanus, 1985; Laukli & Mair, 1985; Lopponen, Sorri, & Bloigu, 1991; Northern, Downs, Rudmose, Glorig, & Fletcher, 1972; Rocha, Atherino, & Frota, 2010; Rosen, Plester, El-Mofty, & Rosen, 1964; Schechter, Fausti, Rappaport, & Frey, 1986; Stelmachowicz, Beauchaine, Kalberer, Kelly, & Jesteadt, 1989; Wiley et al., 1998; Zislis & Fletcher, 1966), but also, as we noted, in patients with a long history of ear disease. As noted above, if reasonably good thresholds cannot be recorded before surgery, significant changes in these thresholds cannot be documented postoperatively. In the EHF range the output of the audiometer is much more restricted than at lower

frequencies, therefore even reasonably small hearing loss can shift a measureable threshold into the “no response” range, making an accurate estimate of how much hearing sensitivity has changed impossible.

We dealt with this limitation in two ways. The first was to calculate the percentage of patients in which thresholds that were measureable before surgery increased beyond the limits of the audiometer postoperatively. While by no means an ideal measure, as the extent of hearing loss is still not conveyed, we did find that this enabled us to demonstrate that EHF hearing loss had occurred in patients that had large preoperative hearing losses and thresholds that were already nearing the limits of the audiometer. For the purposes of statistical modelling, we added 5 dB to the maximum presentation level at which no response was recorded to obtain a postoperative threshold. Again, this does not represent the true threshold or the extent of the threshold shift, but does provide a value that indicates a change from the preoperative threshold has occurred, as is required for statistical analysis.

As with many clinical studies, recruiting an adequate number of participants and retaining those participants throughout the one year follow-up period was a significant issue in this study. The geographical area serviced by the public hospital at which surgeries were performed was large, and often patients had to travel some distance to appointments. We expect that this reduced the number of patients that returned for follow-up appointments. Further patients were lost to follow-up and recruitment slowed dramatically due to the large earthquakes that affected Christchurch in 2010 and 2011. We chose to manage the smaller than hoped for number of participants that returned for all postoperative appointments by including data for all participants as long as at least one complete postoperative audiogram was available. This increased numbers in each bracket substantially, as the majority of participants missed only one or two appointments. The degree to which individual patient data could be tracked over time was, however, more limited than was ideal. In addition, as with all postoperative studies, there is potentially a bias towards either better or worse outcomes in patients who choose to attend follow-up appointments compared to those that fail to attend.

It was our original intention to investigate whether factors such as the type of prosthesis used in ossiculoplasty, or the type of laser used in stapedectomy, had an effect on EHF hearing thresholds that was perhaps larger than that seen in the conventional frequency range. Unfortunately, the small participant numbers in each group meant that statistical power was too low for these analyses to be accurately performed. Certainly, further investigation of

these factors in a larger population would be a valuable future study. In the same manner, difficulties in recruiting large numbers of participants meant that our study population was not a homogenous group. Many factors varied across participants, any and all of which may have affected hearing outcomes or our ability to detect changes in EHF function. In particular, ossiculoplasty and tympanoplasty procedures were heterogeneous and the reasons for surgery were also varied, and included COM with or without cholesteatoma, reconstruction following mastoidectomy, traumatic perforation. These factors all influenced surgical variables such as the degree of ossicular manipulation and drilling required, which may have in turn influenced the likelihood of inner ear trauma.

3.4.7 Directions for future research

The primary focus for future research should be clarifying whether EHF hearing loss is conductive or sensorineural. This is the necessary step in developing methods of preventing such loss and in determining the utility of EHF audiometry clinically in middle ear surgery patients. We propose that the value of EHF audiometry in middle ear surgery is its potential to be used as a tool to more sensitively measure the effect of surgical variables, such as the type of laser or prosthesis used, on either cochlear function or middle ear transmission. We must therefore first establish whether the loss that obviously occurs frequently, at least in the early postoperative period, is the result of changes in middle ear transmission characteristics, or cochlear injury. If the loss is conductive, EHF audiometry could prove a useful gauge of the success with which new prostheses or grafts simulate the normal function of the middle ear. Alternatively, if EHF hearing loss is a highly sensitive indicator of inner ear trauma, it could be used both to determine the effects of manoeuvres and instruments on cochlear function, and to efficiently measure the success of interventions designed to protect the cochlea from injury.

3.4.8 Conclusions

The results of this study clearly show that hearing in the EHF range frequently deteriorates following middle ear surgery. EHF hearing loss is most common and severe in the early postoperative period, and typically recovers over the same timeframe as air- and bone-conduction thresholds in the conventional frequency range, over the first one to three months after surgery. Despite recovery, approximately half of patients who have undergone

stapedectomy and 42% of patients who have undergone tympanoplasty, presented with a residual EHF loss 12 months after surgery, even in the presence of complete air-bone gap closure at lower frequencies and an absence of bone-conduction hearing loss.

These results demonstrate that EHF audiometry is a highly sensitive test of changes in the auditory system that results from middle ear surgery. This could provide a sensitive tool that could be used to inform future debate regarding the effects of surgical techniques, devices, or pharmaceuticals designed to prevent iatrogenic damage to the inner ear.

Chapter 4: Extended high-frequency audiometry

4.1 Reliability, validity, and utility of EHF audiometry

In the previous chapter the use of EHF audiometry was discussed as a more sensitive measure of postoperative deterioration in hearing. There are, however, limitations to EHF audiometry, as noted in the interpretation of the results in Chapter 3, and these limitations, as well as issues regarding the reliability and validity of thresholds measurements above 8 kHz, warrant further consideration. The purpose of this chapter is to address issues affecting the clinical validity of EHF audiometry to ensure that the results presented in the previous chapter, and later in this thesis, are interpreted accurately and with appropriate consideration given to any significant weaknesses identified in the measurement tool.

4.1.1 Clinical applications of EHF audiometry

The measurement of hearing thresholds in the EHF range (above 8 kHz and up to 16 – 20 kHz) is well recognised as a tool that enables early detection of cochlear damage following administration of ototoxic drugs (Dreschler et al., 1985; Fausti, Frey, Henry, Olson, & Schaffer, 1992; Fausti et al., 1999; Fausti, Mitchell, Frey, Henry, & O'Connor, 1994; Fletcher, Cairns, Collins, & Endicott, 1967; Jacobson, Downs, & Fletcher, 1969; Tange, Dreschler, & van der Hulst, 1985). The premise for monitoring EHF thresholds for changes following the introduction of ototoxic agents is that cochlear trauma in response to such stressors will occur in the basal region first, and thus threshold shifts will initially be evident only at the highest audible frequencies (Ahmed et al., 2001; Beahan, Kei, Driscoll, Charles, & Khan, 2012; Fausti et al., 1992; Fausti et al., 1993). Extending the test frequency range therefore increases the sensitivity of audiometry to detect cochlear damage and allows the opportunity to assess the potentially permanent ototoxic effects of drugs versus their therapeutic effects (Beahan et al., 2012).

Evidence suggests that monitoring of EHF hearing acuity also provides an earlier indication of noise-induced cochlear trauma than threshold measurement restricted to the conventional frequencies (Ahmed et al., 2001; Buchler, Kompis, & Hotz, 2012; Corliss, Doster, Simonton, & Downs, 1970; Fausti et al., 1979; Kiukaanniemi, Lopponen, & Sorri, 1992; Morton & Reynolds, 1991; Northern et al., 1972; Rocha et al., 2010; Sataloff, Vassallo, & Menduke,

1967; Somma et al., 2008). As is discussed in detail in Chapter 3, EHF audiometry also appears to be a more sensitive tool for detecting the detrimental effects of middle ear surgery on auditory function (Bauchet St Martin et al., 2008; Doménech & Carulla, 1988; Mair & Laukli, 1986; Tange & Dreschler, 1990).

It is well documented that age-related deterioration in hearing thresholds is first evident in the EHF range and that hearing continues to deteriorate further within this frequency range with increasing age (e.g. Ahmed et al., 2001; Dreschler et al., 1985; Laukli & Mair, 1985; Lopponen et al., 1991; Northern et al., 1972; Rocha et al., 2010; Rosen et al., 1964; Schechter et al., 1986; Stelmachowicz, Beauchaine, Kalberer, Kelly, et al., 1989; Wiley et al., 1998; Zislis & Fletcher, 1966). As both the age of listeners and test frequency increase, the percentage of individuals for whom a threshold cannot be measured before the maximum output of the audiometer is reached rises (Ahmed et al., 2001; Matthews, Lee, Mills, & Dubno, 1997; Northern et al., 1972; Osterhammel & Osterhammel, 1979; Rosen et al., 1964; Schechter et al., 1986). The inability to determine threshold in these cases is a limiting factor on the clinical value of EHF audiometry, particularly above 14 kHz, in listeners from around 50 to 60 years of age (Hallmo, Sundby, & Mair, 1994; Osterhammel & Osterhammel, 1979).

4.1.2 EHF pure-tone audiometry stimuli

While the clinical applications of testing in the EHF range are impressive, concerns have arisen regarding difficulties in the accurate production of signals of a known intensity in this frequency range. When an acoustic stimulus is presented, a portion of the energy travelling medially through the EAC is reflected back into the canal at the TM (Stinson & Shaw, 1982). Where a quarter of the wavelength of an acoustic signal is equal to or less than the dimensions of the EAC, standing waves are formed in the canal by the interaction of incident waves and these reflected sound waves (Khanna & Stinson, 1985; Stinson, 1985). The wavelengths of signals below approximately 1 kHz easily exceed the structural dimensions of the EAC; however as test frequency increases, wavelength decreases and the short wavelengths of pure-tone signals in the EHF range create a risk of standing waves developing. For example, one quarter of the wavelength of a 10 kHz pure-tone is approximately 9 mm; similar to the diameter of the adult TM (Stinson, 1985). This tone may therefore set off resonances and antiresonances in the transverse plane, in addition to standing waves produced by reflections between the transducer and the TM along the length of the

canal (Tonndorf & Kurman, 1984). The locations of pressure maxima and minima shift with frequency and the geometry of the individual EAC, therefore the sound pressure level will be highly dependent on the location of measurement within the canal (Khanna & Stinson, 1985; Stinson, 1985; Stinson & Shaw, 1983). Further variation in the sound pressure level present at the TM is created by the angle of the TM at the terminal end of the EAC (Stelmachowicz, Beauchaine, Kalberer, Langer, & Jesteadt, 1988), and the overall result is pressure variations along the canal and across the TM surface of up to 10 dB SPL (Stevens, Berkovitz, Kidd Jr, & Green, 1987; Stinson, 1985; Stinson & Shaw, 1982; Tonndorf & Kurman, 1984). The sound pressure level at the TM, and thus the level of sound transmitted to the inner ear, is therefore difficult to predict.

Although there is considerable variation in the sound pressure level measured at different points across the TM for stimuli above 8 kHz, it is hypothesised that the net pressure responsible for the motion of the ossicular chain and cochlear stimulation is the product of integration of pressures across the entire surface of the TM (Hunter et al., 1996). Based on this theory, the sound pressure level transmitted to the middle ear should not vary as much across individuals as the pressure measured at single reference points at the TM will vary. The problem does however remain of how to account for such variations in sound pressure level at the TM when specifying the input level required to deliver a controlled stimulus. Most transducers for EHF audiometry are calibrated using a standard coupler (e.g. Ahmed et al., 2001; Buren, Solem, & Laukli, 1992; Dreschler et al., 1985; Frank, 1990; Hallmo et al., 1994; Osterhammel & Osterhammel, 1979; Sakamoto, Sugasawa, Kaga, & Kamio, 1998), which measures the output of the transducer, but does not take into account the deviations imposed on the signal by an individual's unique EAC acoustics.

Whereas accurate calibration is certainly a concern when comparing results across a group a subjects where canal characteristics will vary, a more important consideration for determining intra-subject reliability is the effect of earphone placement. The effective geometry of an individual's EAC may be altered by changes in the position of a transducer, which may in turn influence the position of resonances and antiresonances formed in response to high-frequency stimuli (Hickling, 1966; Stelmachowicz, Beauchaine, Kalberer, Kelly, et al., 1989; Stelmachowicz et al., 1988). It is therefore vital that care is taken to position transducers as accurately and consistently as possible, with the diaphragm of the earphone centred at the canal entrance, when performing audiometry in the EHF range.

4.1.3 Reliability of audiometry in the EHF range

An increase in inter-subject threshold variability with increasing test frequency has been well documented (Dreschler & van der Hulst, 1987; Frank, 2001; Matthews et al., 1997; Schechter et al., 1986; Stelmachowicz, Beauchaine, Kalberer, & Jesteadt, 1989; Stelmachowicz, Gorga, & Cullen, 1982). This trend may be partially a consequence of the interactions between high-frequency signals and individual EAC acoustics, although given that the degree of inter-subject threshold variability appears to increase with age (Schechter et al., 1986), lifestyle factors such as the level of long-term noise exposure probably also play an important role. As discussed above, EHF audiometry is most widely employed in the serial monitoring of hearing in patients who are undergoing treatment with ototoxic medications. The most important issue in the evaluation of the clinical validity of EHF audiometry is therefore the intra-subject, or test-retest reliability, rather than the degree of variability across the population. It is essential that intra-subject reliability is high enough so that significant changes from baseline threshold measurements can accurately be detected.

Despite the concerns regarding reliable production of pure-tone stimuli above 8 kHz, several studies have shown the intra-subject variability of audiometric thresholds in the EHF range (at least up to 14 kHz), although higher than that for the conventional frequency range, is within a clinically acceptable range of ±10 dB HL in 94 to 98% of ears (e.g. Frank, 1990, 2001; Frank & Dreisbach, 1991; Gordon, Phillips, Helt, Konrad-Martin, & Fausti, 2005; Matthews et al., 1997; Schmuziger, Probst, & Smurzynski, 2004; Valente, Valente, & Goebel, 1992). In one such study, Frank (2001) found that test-retest reliability across four sessions was within 10 dB HL at 8 – 14 kHz for approximately 98% of 100 adults with normal hearing below 8 kHz. Variability increased slightly at 16 kHz and 95% of subjects had test-retest differences of 10 dB HL or less at that frequency. Other groups have reported mean standard deviations of differences between EHF thresholds assessed on two separate occasions of around 3.5 – 5.5 dB HL (Fausti, Frey, Henry, Knutsen, & Olson, 1990; Hallmo et al., 1994; Laukli & Mair, 1985).

Intrasubject reliability does become poorer at 16 kHz and above (Frank, 2001; Schmuziger et al., 2004) and although young people with no significant otologic history are capable of perceiving pure-tones at frequencies of up to 20 kHz (Beiter & Talley, 1976; Buren et al., 1992; Fausti, Erickson, Frey, Rappaport, & Schechter, 1981; Fausti et al., 1990; Frank, 1990), the reduced reliability of thresholds obtained above 16 kHz sets an upper limit on the range of frequencies that are typically tested in clinical settings. The highest frequency that can be

tested is also limited by the increasingly high sound pressure levels required to reach threshold as frequency increases towards 20 kHz (Reuter, Schonfeld, Mansmann, Fischer, & Gross, 1998). Given the poorer test-retest reliability at 16 kHz and above, any changes in thresholds at these frequencies should be interpreted conservatively (Schmuziger et al., 2004).

Assessments of test-retest reliability of audiometric thresholds in any frequency range will be affected by the interval between tests. The trend for a decrease in test-retest reliability of pure-tone thresholds as the interval between tests in increased from one hour to one month has been demonstrated in the EHF range (Green, Kidd, & Stevens, 1987). Given that many of the published studies reporting test-retest reliability rates compare thresholds for assessments repeated over a short time frame, often within a single session or day (e.g. Ahmed et al., 2001; Matthews et al., 1997; Schmuziger et al., 2004), caution may be required when applying these test-retest reliability rates to clinical situations. In a clinical setting, such as monitoring thresholds over the course of chemotherapy treatment sessions, or assessing long-term outcomes of middle ear surgery in the EHF range, inter-test intervals will be longer, and therefore test-retest variability may be expected to increase to some degree.

In a similar manner, reliability rates will be affected by whether headphones are removed and replaced between assessments. This factor is of particular importance in the EHF range where the alterations in canal acoustics caused by a change in headphone position may alter the sound pressure level across the canal. Hunter et al. (1996) demonstrated that mean test–retest reliability of EHF thresholds increased from between 0.5 and 4 dB HL across all frequencies in seven children when headphones were not removed between two assessments, to between 4 and 8 dB HL when headphones were removed and carefully replaced between assessments of 14 children. Although this sample is small and included only children, whose smaller canals may increase the vulnerability to changes in sound pressure due to differences in headphones placement, this study certainly illustrates the increase in variability that may occur with slight changes in headphone position.

4.1.4 Unwanted noise in EHF audiometry

There is a wealth of literature discussing the test-retest reliability of EHF audiometry thresholds; however few reports have investigated the *validity* of such measures. The issue that must be addressed when evaluating the validity of thresholds in the EHF range is

whether the responses we are recording are a true reflection of hearing sensitivity at the frequency of the test-tone. Fausti, Rappaport, Schechter, and Frey (1982) used a release from masking paradigm to demonstrate that the thresholds they recorded in young adults with normal hearing sensitivity from 0.25 to 14 kHz were a true response to the test stimulus and not a lower frequency distortion tone. However, whether this is also the case when presenting EHF tones at the sound levels required to elicit a response in people without normal hearing sensitivity has been questioned. We and other authors have noted that some listeners report hearing additional tones when testing is performed using EHF, and particularly 16 kHz, stimuli. Sakamoto et al. (1998) remarked that several of their subjects with normal hearing in the conventional frequency range reported an intermittent "noise" during testing at 19 and/or 20 kHz using a Demlar Model 20K EHF audiometer. The authors suggested that an amplified noise floor may have been responsible for the reported noise.

The reference equivalent threshold sound pressure levels (RETSPLs) for calibration of audiometers in dB HL at 8 – 16 kHz are specified in an international standard (International Organization for Standardization, 2006). Due to the decreasing sensitivity of the auditory system as frequency increases (Fletcher & Munson, 1933; Robinson & Dadson, 1956), RETSPLs (which correspond to 0 dB HL, or the average threshold of young, otologically normal adults at the test frequency) increase with frequency from less than 10 dB SPL at 0.5 – 6 kHz up to 56 dB SPL at 16 kHz (ISO, 2006). As thresholds are often much poorer than RETSPLs in the EHF range, particularly in older adults, presentation at or near the maximum output of the audiometer is often required as frequency increases towards 16 kHz (Schmuziger, Brechbuehl, & Probst, 2007). Presentation at such high sound pressure levels increases the likelihood that additional spectral information will be produced at lower frequencies, and that this may be detected by listeners with a significant hearing loss at very high frequencies, but near normal hearing at lower frequencies. Although unwanted noise may also be produced when testing at lower frequencies, it is unlikely to adversely affect results as audiometric configurations seldom occur that require conventional frequencies to be presented at maximum sound pressure levels, but where hearing acuity is good enough to detect unwanted noise at lower frequencies near in frequency to the test tone.

The presence of unwanted sounds in the audiometer output compromises the validity of EHF audiometry, at least at the highest frequencies tested, in that what we record as threshold may not be a true representation of the listener's hearing acuity at that frequency. If the listener is responding to spurious noise or tones at a lower frequency where hearing sensitivity is better,

we will underestimate the degree of high-frequency hearing loss. Illustrating the potential effect of responses to off-frequency noise on the audiogram, Kurakata, Mizunami, Matsushita, and Shiraishi (2010) show three cases in which thresholds increase with increasing frequency over the EHF range, but then recover to some degree as the highest test frequency approaches. Recovery is evident at 14 and 16 kHz in one case and at 16 kHz only in the remaining two cases presented. Although there is a clause in IEC 60645-4 (2012) noting that unwanted sounds may occur during testing at 14 and 16 kHz that may be detected by listeners with significant hearing loss at those frequencies, causing audiograms to be recorded such as those described by Kurakata et al. (2010), the problem seems to have gone widely unacknowledged by clinicians and researchers. Two papers have, however, recently documented the presence and described the characteristics of unwanted sounds during tone presentation in EHF audiometry.

Schmuziger et al. (2007) identified unintended lower frequency sounds in the acoustic output of one of two commercially available audiometers when EHF stimuli were presented. Analysis of the acoustic output of one Madsen Itera II and one GSI 61 audiometer, both calibrated with Sennheiser HDA 200 circumaural headphones, showed that unwanted lower frequency signals were more prominent during the output of signals at 8 kHz and 16 kHz in the Madsen Itera II than for the GSI 60 audiometer. For the Madsen audiometer, the presentation of an 8 kHz pure-tone signal at an intensity of 121 dB SPL was accompanied by additional spectral peaks of a maximum of 31.6 dB SPL at harmonics of 4.1 kHz, 2.9 kHz, and 0.3 kHz. Unwanted noise was present at a lower presentation level of 114.6 dB SPL for the 16 kHz test tone, with signals of nearly 50 dB SPL at the harmonic frequency of 8 kHz and at approximately 0.4 kHz. These unwanted signals were significantly reduced to just a few decibels above the noise floor when the test signal was reduced in intensity to a maximum of 111.5 dB SPL for the 8 kHz tone and 106.1 dB SPL for the 16 kHz tone. No unwanted signals were identified in the acoustic output of the GSI 61 audiometer, despite their presence being clearly recognised during a subjective listening check by the author of a 16 kHz test stimulus presented at 107.3 dB SPL. This highlights that a significant limitation in the assessment of the output of EHF audiometers is the inadequate dynamic range of many signal analysers to cover the complete range of outputs from EHF to low-frequency signals.

Unwanted low-frequency signals were also identified by Kurakata et al. (2010) in the output of a Siemens UNITY 2 audiometer during presentation of EHF pure-tones, suggesting that the problem of spurious noise identified by Schmuziger et al. (2007) may be widespread

across commercially available audiometers. A comparison of the acoustic signal output of the audiometer through Sennheiser HDA 200 headphones and the electric signal output, measured directly from the audiometer while the headphones were connected, indicated that the unwanted lower-frequency noise and spectral peaks were generated electrically by the audiometer, as opposed to during the transduction of electrical to acoustic signals by the headphones. In the Karakata et al. (2010) study, measurements of both electric and acoustic output were performed at intensities increased in 5 or 10 dB HL increments from the minimum to the maximum output level of the audiometer at the seven audiometric frequencies from 8 to 16 kHz. They provided the power spectra of the acoustic and electric outputs at 8, 12.5, and 16 kHz only and show that for all three frequencies the unwanted sounds increased in intensity in an almost linear manner when the intensity of the test signal was increased beyond a certain presentation level. Unwanted broadband and pure-tone like components were recorded during presentation of test tones at each frequency shown, but were particularly apparent for 16 kHz stimuli, with significant spectral peaks occurring at approximately 2 and 4 kHz for presentation levels above 40 dB HL. Like Schmuziger et al., Kurakata et al. found that a reduction in the intensity of the test signal by 15 to 20 dB SPL reduced the levels of unwanted signals in the audiometer output to below threshold levels, however reducing or limiting the audiometer output will consequently reduce the power to detect and describe the level of hearing loss at the test frequencies.

An evaluation of the audibility of the unwanted sounds was performed by Kurakata et al. (2010) based on a comparison between the relevant RETSPLs and a calculation of the sound pressure levels of the unwanted sounds in the equivalent rectangular bandwidth of the auditory filter (ERB) for young people with normal hearing (based on the equations of (Glasberg & Moore, 1990). For pure-tones of 16 kHz presented at 60 dB HL, the ERB levels for the unwanted sounds exceeded the RETSPL curve by 10 – 15 dB HL at 0.6 – 4 kHz. This suggests that these unwanted sounds will be audible during 16 kHz test tone presentation for listeners with thresholds of 10 – 15 dB HL or less at these lower frequencies.

4.1.5 Aims and hypotheses

The present study was designed to determine whether unwanted spectral content was present in the power spectra of two GSI 61 audiometers when stimuli were presented audiometric test frequencies in the EHF range. These audiometers were used for the acquisition of data

presented in Chapter 3. It was considered important that the output of these audiometers be assessed given that the acoustic output GSI 61 was measured by Schmuziger et al. (2007), but, despite subjective reports of spurious noise in the audiometer output during EHF testing, the noise could not be quantified in the objective measurements. Several participants we had tested had made comments similar to those reported by Schmuziger et al. regarding "noise" during testing at 16 kHz, highlighting the need for this issue to be clarified. We also intended to verify whether the output was consistent across two audiometers of the same model that had been calibrated to the same standards.

Sakamoto et al. (1998) reported an "intermittent noise" during EHF testing, however it is unclear from their description of the issue whether "intermittent" is used to refer to occasions when the test tone is presented, as opposed to continuously, or whether the authors found that the noise was not consistently audible every time the test tone was presented. The present study was therefore also designed to determine whether any noise recorded was present on every presentation of the tone, or occurred intermittently. Although any unintended noise in the output of the audiometer is undesirable, it was a particular concern that if noise was present intermittently, test-retest reliability of pure-tone thresholds would be reduced.

Based on subjective reports that off-test frequency tones could be heard during testing at 16 kHz with both audiometers we assessed, we hypothesised that spectral output measurements would provide objective verification that these tones were present at lower frequencies at a level audible to listeners with normal or near normal hearing below approximately 8 kHz. We anticipated that unwanted spectral output would be a particular issue at 16 kHz and less of a concern at lower EHF frequencies.

4.2 Method

4.2.1 Audiometric equipment

The electrical output of two commercially available two-channel GSI 61 audiometers (Grason-Stadler, Eden Prairie, MN) designed for audiometric testing at 0.125 – 20 kHz were evaluated. Both audiometers were equipped with Sennheiser HDA 200 circumaural headphones (Sennheiser electronic GmbH & Co., Wennebostel, Germany). Calibration was performed by the same accredited testing facility in both cases, and in accordance with the relevant IEC and ISO standards for audiometers and pure-tone audiometry in the frequency range 0.125 to 16 kHz (IEC 60645-1 (2012), ISO 389-1 (1998) and 389-5 (2006)).

4.2.2 Output measurement equipment

Given Kurakata et al.'s (2010) data showing that low-frequency noise was generated electrically by the audiometer, only the electrical output to the Sennheiser HDA200 headphones was measured in the present study. Measurement of the averaged power spectrum of the electrical output of the audiometer while loaded by the headphones was performed using an NI USB 6009 data acquisition device (National Instruments, Austin, TX) connected to an HP Compaq nw9440 laptop (Hewlett Packard, Palo Alto, CA) running power spectrum measurement software programmed in LabVIEW 2012 (National Instruments, Austin, TX).

4.2.3 Procedure

Prior to measurements being made, all nonessential electronic equipment and lighting was turned off and the laptop used was run off the battery power supply. Measurements were made in the sound treated booths in which each audiometer is usually used. Recordings were made from Channel 1 only and no stimulus was presented through Channel 2 during recordings. The voltage drive to the HDA 200 headphones was sampled in parallel (i.e. with the headphones connected to the audiometer) with the audiometer set to deliver the signal to the left headphone only. The power spectrum of the drive was measured over a 0.5 second period and windowed with a Hanning function. Each average contained 2400 samples, obtained using a sample rate of 48 kHz, and the spectrum for each frequency contained 100

averages. The noise floor of the measurement equipment was estimated by recording the power spectrum of the drive when no tone was presented.

For audiometer 1, measurements were made at $1/6^{th}$ octave frequencies from 8 to 16 kHz at the intensity corresponding to the thresholds of one of the researchers; G.O'B. ("the listener"), who reported hearing "off-frequency" tones and noise during testing at 16 kHz. For audiometer 2, measurements were performed at 14 and 16 kHz only. The voltage drive associated with the listener's thresholds was measured at each frequency to allow comparison of the audiometer output and the pure-tone audiogram for the listener.

As the spectrum of the output at 16 kHz was our primary concern, at this frequency measurements were made at each output level from the minimum to the maximum output of the audiometer. The output level was increased in 5 dB steps from -10 dB HL to 55 or 60 dB HL (depending on the maximum output level of the audiometer), the power to the audiometer was turned off and then on again, and the measurements were repeated in descending intensity order. The purpose of repeating measurements was to check for any intermittent noise or change in the output across measurements at the same test frequencies. To ensure the power spectrum was accurately obtained without clipping of the signal, when intensity series were performed the measurement equipment was set to a 1 V range at lower intensities, and then increased to 10 V at and above the intensity at which clipping was noted.

The raw data was transferred into Microsoft Excel 2010 spreadsheets (Microsoft, Washington D.C, WA) for storage and analysis.

4.3 Results

4.3.1 Frequency series

4.3.1.1 Control frequencies: 8 – 12.5 kHz

Figures 31a and b show the voltage drive from channel 1 of audiometer 1 to the left HDA 200 headphone for the test frequencies 8, 9, 10, 11.2 and 12.5 kHz, at which the listener did not report hearing any spurious noises or off-test-frequency tones. At each frequency the signal was presented at the threshold of the listener to determine whether any unwanted noise that would have been audible with this particular audiometric configuration were present. Audiometric thresholds are plotted against the audiometer output for comparison. Figure 31a) shows frequency plotted linearly on the x-axis to improve visibility of higher frequency components of the output and Figure 31b) shows frequency plotted on a logarithmic scale to emphasise low-frequency components in the spectrum of the output. Visual inspection of the data shows that at these relatively low intensity levels, unintended spectral peaks are present at approximately 5700, 10000, 14000, and 18000 Hz, the most prominent of which is centred at 14000 Hz. The peaks are also present in the noise floor recording and therefore seem to be intrinsic in the measurement system. Such tones are less likely to result in false threshold measurements as they are constant throughout the testing, rather than appearing only when the audiologist presents the test tone. However, examination of lower frequency output at the EHF frequencies in Figure 31b, shows an additional three peaks in the power spectrum at 50, 100, and 150 Hz that do not shift in frequency or level depending on the frequency of the test tone, and which are not present in the noise floor recording. Audiometric thresholds were not measured at these frequencies, therefore it is not clear whether this low-frequency noise present only on presentation of the tone could be audible to the listener.

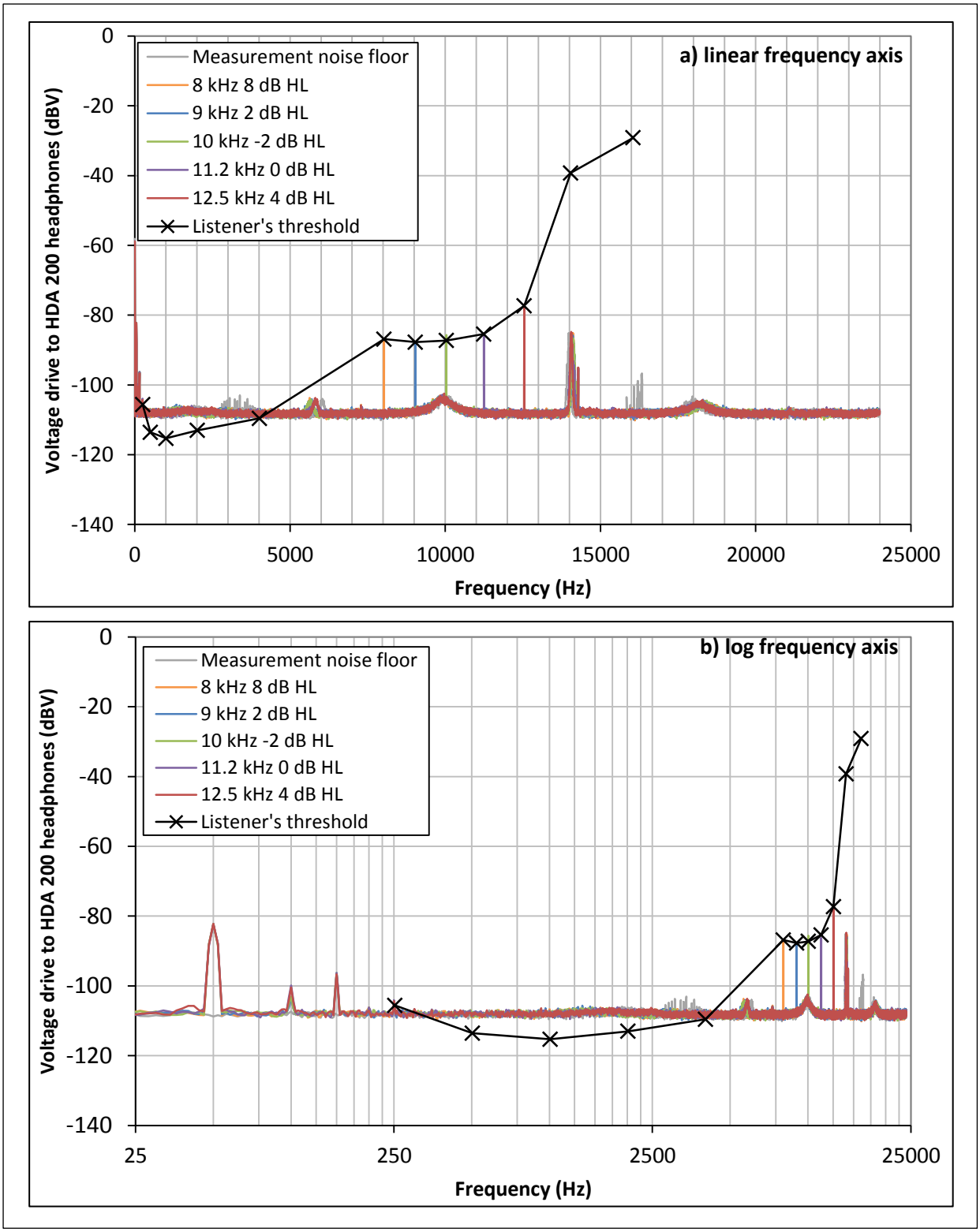

Figure 31. The voltage drive of audiometer 1 to the HDA 200 headphones at audiometric frequencies from 8 to 12.5 kHz. Test tones were presented at the level of the listener's pure-tone threshold at each frequency. The listener did not report being aware of any noise or off-test-frequency tones during testing of these frequencies.

4.3.1.2 Problematic frequencies: 14 and 16 kHz

4.3.1.2.1 Audiometer 1

The spectra of the electrical output of audiometer 1 at the level of the listener's pure-tone thresholds at 14 and 16 kHz are shown in Figures 32 a and b, using the same format described above for Figure 31. With this audiometer, the listener reported hearing audible lower-frequency tones when the 16 kHz test tone was presented, but not when 14 kHz was tested. However, the recordings made at both these frequencies show unwanted noise at frequencies lower than the test tone. Of particular note in the voltage drive spectrum for 14 kHz is the narrow peak at approximately 5880 Hz that rises above the listener's audiometric thresholds. Although the listener did not report hearing this particular pure-tone-like component when 14 kHz was presented, the recordings suggest it may be audible to listeners with good hearing acuity at this frequency. Also present in the 14 kHz output were peaks at approximately 50, 150, and 18000 Hz similar to those noted in the spectra of the five lower EHF frequencies. None of these additional components of the spectrum were present in the noise floor.

The test-tone presented at 24 dB HL at 16 kHz produced a voltage drive to the headphone that differed markedly from the output recorded at lower frequency test tones. Figure 32a shows prominent spectral peaks associated with stimulus presentation that were recorded at approximately 8000 and 14000 Hz. In particular, the broad peak at around 8000 Hz reaches a level close to the listener's threshold at that frequency. In Figure 32b, the 50 Hz peak found in the 14 kHz test tone output is again present, as is a peak at around 140 Hz. Also notable is the rise in the output level of the spectrum below around 2000 Hz. The voltage drive gradually increases down to approximately 300 Hz, after which it plateaus at this elevated, potentially audible, level. It was unable to be ascertained which of these lower-frequency tones were heard by the listener, but the fact that they appear only when the test tone is being presented by the audiologist increases the likelihood that false thresholds could be recorded for this frequency.

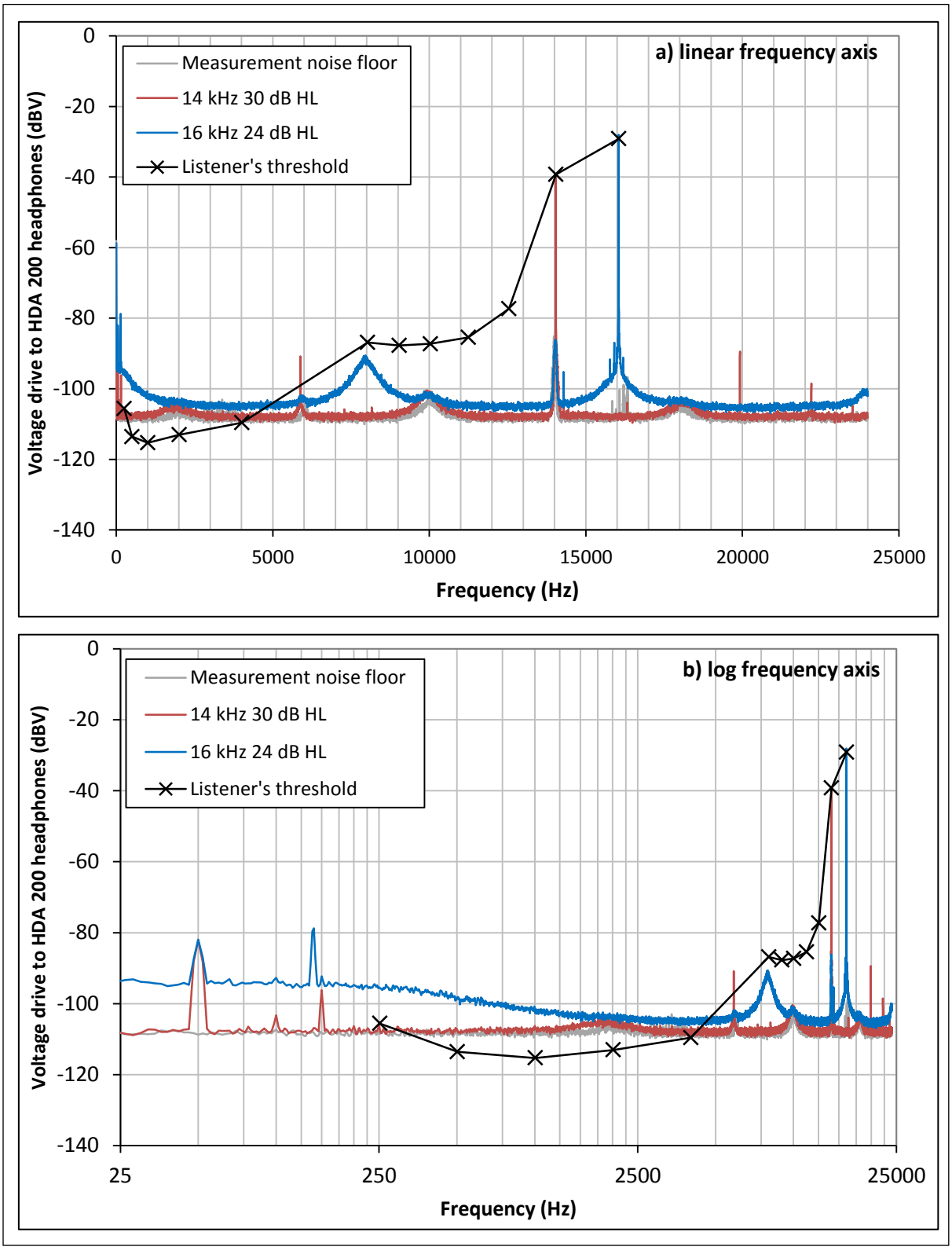

Figure 32. The voltage drive of audiometer 1 to the HDA 200 headphones at 14 and 16 kHz. Test tones were presented at the level of the listener's pure-tone threshold at each frequency. Note the potentially audible increase in low-frequency noise when the 16 kHz test tone is presented.

4.3.1.2.2 Audiometer 2

The measurements at 14 and 16 kHz are shown for audiometer 2 in Figure 33 a and b. Similar to the power spectra of audiometer 1, the electrical output of audiometer 2 for a 14 kHz test tone showed unwanted spectral peaks at around 5900 to 6100 Hz.

The voltage drive from audiometer 2 for a 16 kHz tone has more peaks than that recorded for the same signal from audiometer 1, in particular, the prominent peak at around 8000 Hz. Above the test frequency, small to medium peaks unlikely to influence the audiogram were present at approximately 17000, 21500 Hz, and 23500 Hz. Below the test frequency, a large peak was recorded at 30 Hz and a very broad increase in energy was present from approximately 700 to 1700 Hz. While the broad increase in output below 2 kHz is present in the voltage drive recordings of audiometer 1 is absent in audiometer 2, the peaks in the low-frequency response of both audiometers for the 16 kHz tone are a concern. At 16 kHz, "noise" was audible to listeners with both audiometers, however differences in the subjective properties of the "noise" were not assessed.

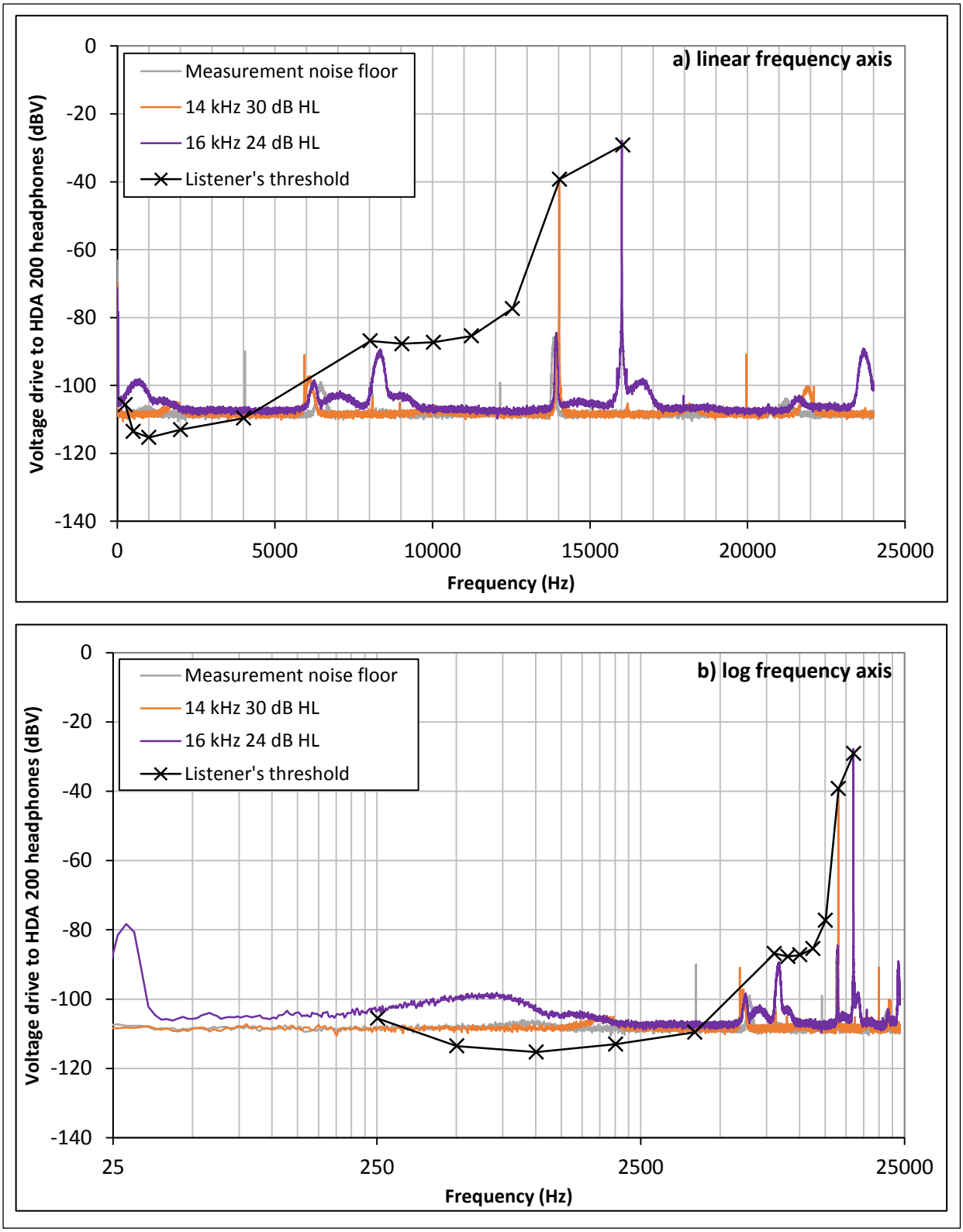

Figure 33. The voltage drive of audiometer 2 to the HDA 200 headphones at 14 and 16 kHz. Test tones were presented at the level of the listener's pure-tone threshold at each frequency. Note the potentially audible increase in noise around 1200 Hz when the 16 kHz tone is presented.

4.3.2 16 kHz intensity series

4.3.2.1 Audiometer 1

Figures 34a and b show the voltage drive to the HDA 200 headphones from audiometer 1 for output levels from -10 to the maximum presentation level of 55 dB HL. Stimuli were presented in 10 dB HL steps from -10 to 40 dB HL and in 5 dB HL steps from 45 dB HL to 55 dB HL. As in the frequency series, the output is shown in two panels; with frequency plotted linearly in panel a) and logarithmically in panel b). From these figures it is clear that overall, when the intensity of the test tone was increased in 5 or 10 dB steps, the level of the output across the entire frequency range increased approximately linearly. The exception is the peaks at 50, 100, and 150 Hz, which remain at the same level and frequency until they are covered by the rise in the overall level of the low-frequency output at 40 dB HL for 50 Hz, and at 30 dB HL for 100 Hz and 150 Hz. The spectral peaks at 130 and 8000 Hz are recordable from the lowest intensity level and increase with the rest of the spectrum, so that the level of these peaks above the level of other noise is maintained across all intensity levels.

It is clear from Figure 34 a and b that the low-frequency noise floor greatly exceeds the low-frequency hearing thresholds of the participant acting as the listener, even at low to moderate presentation levels of the 16 kHz tone.

4.3.2.2 Audiometer 2

In contrast to audiometer 1, when the intensity of the 16 kHz test tone was increased using audiometer 2, the frequency of unwanted spectral peaks shifted. As for audiometer 1, Figure 35a and b show the voltage drive for the audiometer as the intensity of the 16 kHz tone was increased in 10 dB steps from -10 dB HL to 40 dB HL, and in 5 dB steps from 45 dB HL to the maximum output level of 60 dB HL. Overall, the power spectrum of the output is less consistent across intensity than that for audiometer 1. In particular, the centre frequency of peaks at around 400 – 1100, 85000, 165000 and 23000 Hz shift slightly with intensity (Figure 35a). The shift in the centre frequency of peaks is clearly illustrated in Figure 35b, where a large spectral peak shifts from approximately 150 Hz at the lowest stimulus intensity to 100 Hz at the highest intensity. The broad rise in energy around 500 – 1000 Hz also varies markedly with intensity in regards to the centre frequency of the peak. This rise below 2 kHz plateaus at the higher intensities more than at lower intensities, for example at 30 dB HL, the voltage drive initially rises below 2 kHz, but returns to the level of the noise floor by 500 Hz.

The pattern of this increase in energy at higher intensities, particularly 60 dB HL is more similar to the pattern recorded at all intensities for audiometer 1, with no return of the voltage drive to the level of the noise floor with decreasing frequency. Again, the low-frequency noise-floor increases well above the noise floor of the measurement equipment and the pure-tone thresholds of the listener at stimulus presentation levels of 30 dB HL and above.

4.3.3 Repeatability

Repeated measurements of the voltage drive to the HDA 200 headphones at each intensity level at 16 kHz (data not shown) showed no evidence that the unwanted peaks in the output spectrum were intermittent in either audiometer.

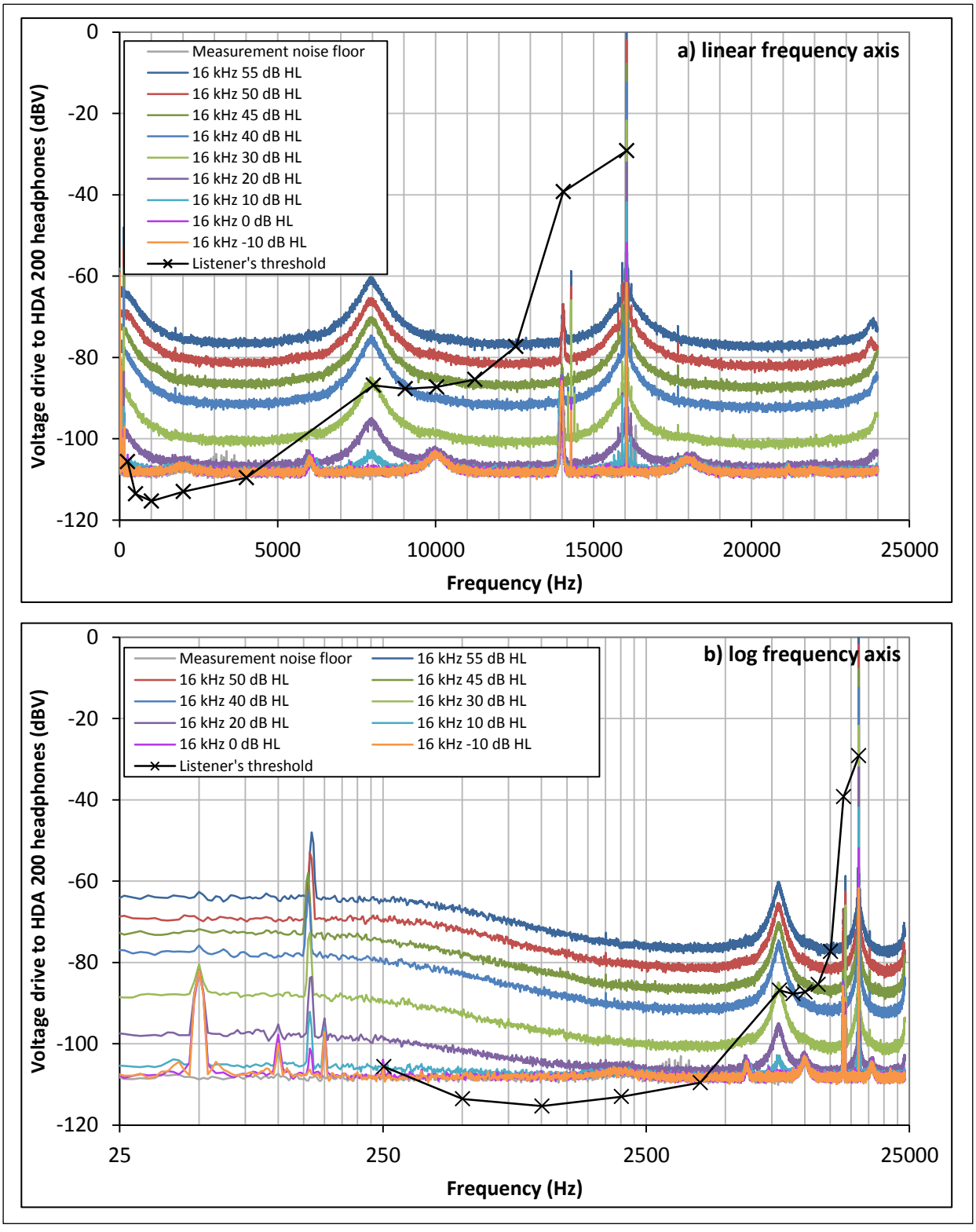

Figure 34. The voltage drive of audiometer 1 to the HDA 200 headphones for a 16 kHz tone at intensity levels from -10 dB HL to 55 dB HL. Note the increase in the level of the low-frequency noise floor with increasing presentation level of the 16 kHz tone. The listener's thresholds are plotted for comparison.

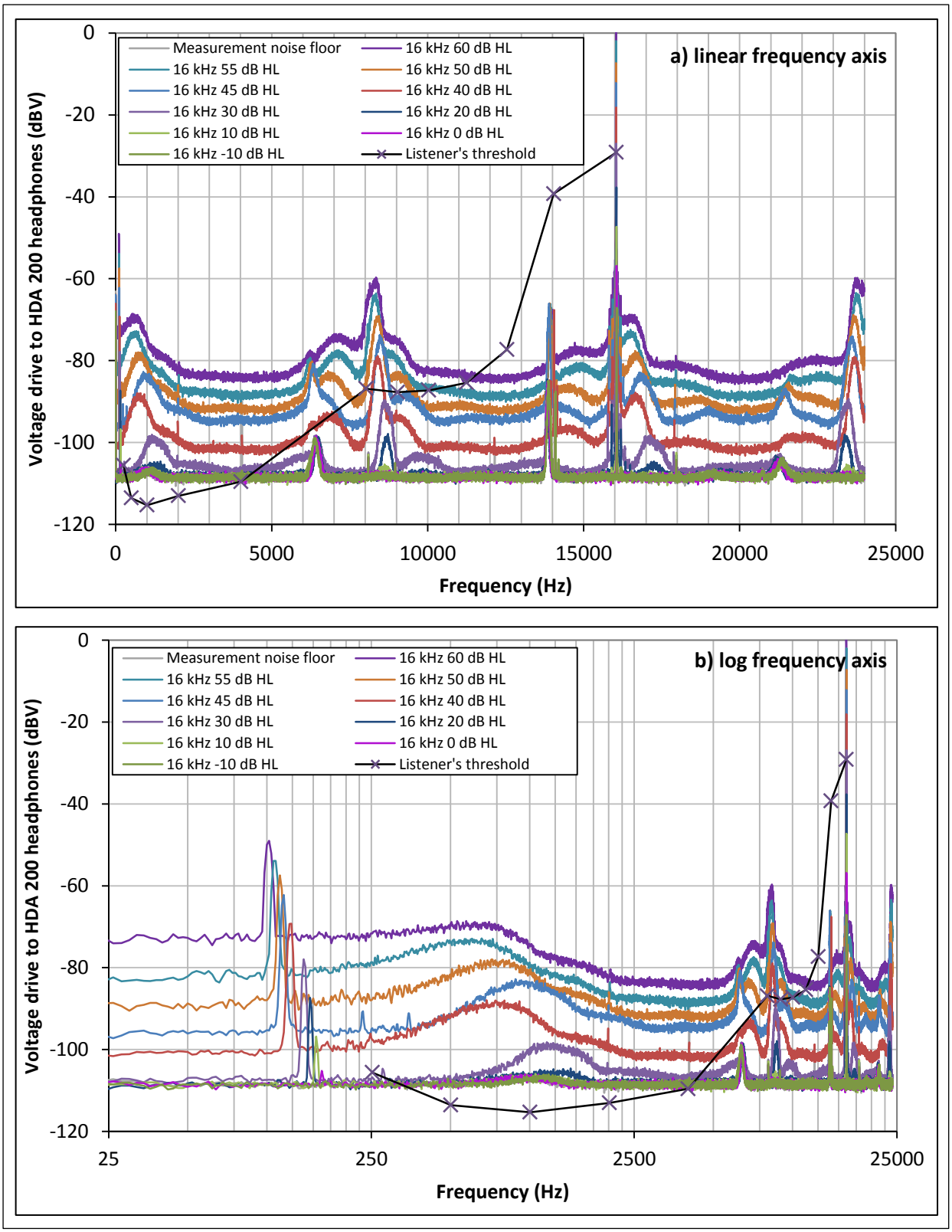

Figure 35. The voltage drive of audiometer 2 to the HDA 200 headphones for a 16 kHz tone at intensity levels from -10 dB HL to 60 dB HL. Note that the multiple noise peaks rise and shift in frequency with increasing presentation level of the 16 kHz tone. The listener's thresholds are plotted for comparison.

4.4 Discussion

The measurements of the spectra of the voltage drive to the headphones performed for two calibrated GSI 61 audiometers showed clear evidence of unwanted noise in the output when tones of 14 and 16 kHz were presented. The purpose of these measurements was not to conduct an exhaustive investigation of the characteristics of the output of the audiometer at each test frequency and presentation level, but instead to identify whether the spurious noise in the output of the audiometer previously reported by Schmuziger et al. (2007) and Kurakata et al. (2010) was an issue for the particular audiometers being used for EHF testing throughout the studies reported in this thesis. It was considered especially important that we perform these measurements given that one of the investigators, as well as several listeners tested during data collection for the study presented in Chapter 3, reported hearing "other noises" during pure-tone threshold seeking at 16 kHz. Although Schmuziger et al. provided similar subjective reports; they could not identify any unwanted noise in the acoustic output of their GSI 61 audiometer, prompting the need to clarify this issue.

The frequency series conducted showed that when pure-tones at each of the EHF test frequencies were presented at the level of the listener's thresholds, unwanted noise in the conventional frequency range was primarily a concern at 14 and 16 kHz for both audiometers. Although some spectral peaks at 150 Hz and below were recorded for lower frequency test tones, their impact is unclear as audiometric thresholds were not available for these frequencies. Given our results showing the presence of unwanted sounds with two GSI 61 audiometers and the subjective presence of such noise in Schmuziger et al. (2007) study, it seems likely that the absence of unwanted noise in the acoustic output measurements of their audiometer was a result of limitations in the measurement equipment.

When a 14 kHz pure-tone was presented the feature of primary concern in the output of both our audiometers was a spectral peak at around 5.9 kHz. This peak exceeded the listener's audiometric threshold, however it could not be detected as a separate tone during testing. For the 16 kHz test tone, concerning characteristics of the spectral output included an increase in both narrow- and broad-band components below approximately 2 kHz. While both audiometers showed unwanted spectral energy below 2 kHz, the frequency and intensity characteristics of this noise varied significantly between the two audiometers, particularly at lower presentation levels. Specifically, the centre frequency of peaks varied markedly across presentation levels in the output of audiometer 2, but not audiometer 1. Additionally, the rise in energy below approximately 2 kHz plateaued to a consistent level across frequencies

below approximately 300 Hz in the output of audiometer 1, but returned to the level of the noise floor at low stimulus intensities for audiometer 2. Overall, the output of audiometer 2 was less consistent and contained more unwanted peaks than the output of audiometer 1.

In agreement with the present results, Schmuziger et al. (2007) showed a rise in the acoustic output of the Madsen Itera II audiometer below about 2 kHz, although they did not comment on this. However, the centre frequencies of other unintended spectral peaks documented by Schmuziger et al. varied from the frequencies of peaks found in the output of either of our audiometers. Also conflicting with the present results, Kurakata et al. (2010) documented spectral peaks at 2 and 4 kHz in the electrical output of their Siemens UNITY 2 audiometer which were not present in our recordings. Given our data showing that the characteristics of unwanted noise vary between two audiometers of the same model, it is not surprising that the properties of the noise would be different in audiometers of different models.

Certainly the presence of unwanted noise in the output of calibrated audiometers is a concern when assessing the validity of EHF measurements; however whether such noise will be a problem during a given test session will depend on the particular audiometric configuration of the listener. Our listener's audiogram provides a particularly good example of the type of audiogram in which noise is likely to be an issue; thresholds are very good across most frequencies, with a rise to above 20 dB HL only at 14 and 16 kHz. It is this much better sensitivity for unwanted tones than for the test-tone that creates a problem as the lower-frequency tones could be detected before the test tone, leading to the recording of an artificially lower threshold for the test tone. Such an audiometric configuration would be expected to be relatively common given that thresholds typically decrease at the highest audible frequencies first with increasing age (e.g. Ahmed et al., 2001; Stelmachowicz, Beauchaine, Kalberer, Kelly, et al., 1989). Schmuziger et al. (2007) suggest that unwanted noise is more likely to be a concern for listeners with EHF hearing loss than those with normal hearing, as low-frequency tones will usually occur only near maximum output levels of the audiometer. However, our measurements show that unwanted noise is present at relatively low intensity levels, and therefore may be detected when thresholds at the highest test frequencies are similar or only slightly elevated compared to those at lower frequencies.

The differences in the output of the two audiometers of the same model shown in our measurements are particularly concerning. If more than one audiometer is being used to collect data to be compared over time, for example in patients being monitored during administration of ototoxic drugs, differences in the electrical output of each audiometer could

cause threshold changes to be identified that do not reflect true changes in hearing acuity. This possibility should be noted by any clinician performing monitoring of EHF thresholds. It is somewhat reassuring that we found no evidence that the noise present was intermittent, suggesting that when repeated audiograms are measured using the same audiometer, as they were for all participants tested in Chapter 3, they can be reliably compared over time.

Schmuziger et al. (2007) suggested that the introduction of steady, low-level noise to the test ear could be used to mask unwanted noise or tones and reduce their effect on thresholds. While this is a good suggestion, it is complicated by the fact that the characteristics of the spurious noise and tones varies across audiometers, and in some cases across presentation levels, necessitating the creation of either individualised masking noise for each audiometer, or the use of a relatively broadband masking noise. If a broadband noise is used, the intensity will need to be higher to effectively mask peaks in the spectrum of the audiometer output, which could potentially increase the difficulty of the task and discomfort for the listener. Further research is needed to investigate the viability of masking noise as a solution for unwanted peaks in the output of audiometers.

Alternatively, in accordance with IEC 60645-1 (2012), the output of the audiometer at 14 and 16 kHz could be limited to a level at which any noise present will not be audible. Given that noise above normal thresholds was found for a 14 kHz tone presented at 30 dB HL, this method would severely limit our ability to measure any threshold outside the normal range at these high-frequencies and therefore detect hearing loss.

4.4.1 Conclusion

At a minimum, the present results confirm that the issue of unwanted lower-frequency energy in the output of audiometers at 14 and 16 kHz is widespread and should be acknowledged when interpreting EHF audiograms and changes in thresholds at these frequencies over time. Given that off-frequency tones are not intermittent, we conclude that, when the same audiometer is used for repeated testing, changes in recorded thresholds are likely to be genuine, and not the result of differences in the spectra of the output over time. However, whether changes in 14 and 16 kHz thresholds, particularly in listeners with near-normal conventional frequency thresholds, reflect a true change in hearing sensitivity at 14 and 16 kHz, is less certain.

In the majority of cases of postoperative EHF hearing loss documented in the previous chapter, thresholds at lower frequencies improved. If listeners were responding to newly audible lower frequency tones, we would expect an improvement in EHF thresholds that corresponded with the improvement at conventional frequency thresholds. Given that the opposite of this prediction was true, we conclude that, at least in the majority of patients, EHF threshold changes reported in Chapter 3 were not the result of unintended tones in the audiometer output. However, in cases in which conventional frequency thresholds deteriorated so that unwanted tones that may have influenced the preoperative EHF audiogram became inaudible, we cannot exclude the possibility that inaccuracies in the audiometer output influenced the results. Fortunately, such cases were few in number, particularly following stapedectomy, where the greatest EHF losses were recorded.

Chapter 5: Literature review – Potential causes of extended high-frequency hearing loss following middle ear surgery

5.1 The site of lesion causing postoperative hearing loss

The patterns of EHF air-conduction threshold elevation described following middle ear surgery in Chapter 3 may be due to cochlear trauma resulting from surgery, to changes in the biomechanical properties in the middle ear, or a combination of both. This chapter presents a review of the insults and changes to the inner ear and the middle ear that have the potential to alter hearing thresholds, particularly in the EHF range, either temporarily or permanently following middle ear surgery.

5.2 Causes of postoperative high-frequency cochlear hearing loss

If hearing loss following middle ear surgery is due to inner ear injury, the mechanism of insult and the degree of risk to the cochlea will be specific to the procedure performed and the technique used. The level of risk may also be affected by individual patient factors such as the specific anatomy, previous otologic procedures, and the disease status of the middle ear (Wiet, Harvey, & Bauer, 1993). Many experimental and clinical studies have attempted to isolate the individual elements that threaten the cochlea intraoperatively and the factors that appear to present the greatest risk to cochlear function are discussed in detail in the following sections.

5.2.1 Hydrostatic pressure

The hydrostatic pressure applied to the inner ear via the ossicular chain and stapes footplate during surgery has often been proposed as a cause of postoperative sensorineural hearing loss (e.g. à Wengen et al., 1992; Babighian & Albu, 2009; de Zinis, Cottelli, & Koka, 2010; Hallmo & Mair, 1996; Kylén, Arlinger, Jerlvall, & Harder, 1980; Mair & Laukli, 1986; Økstad, Laukli, & Mair, 1988; Palva et al., 1973; Schuknecht, 1962; Smyth, 1972, 1976, 1977; Urquhart, McIntosh, & Bodenstein, 1992; Vartiainen & Seppa, 1997). Under normal conditions, displacement of the stapes footplate is approximately 3×10^{-9} mm in response to a 1 kHz tone at the threshold of hearing (Schuknecht & Tonndorf, 1960). The forces imparted on the ossicles during direct manipulation are exponentially greater than the forces present

physiologically. At the most extreme level, stapes footplate fenestration may result in depression of the footplate up to one millimetre into the vestibule (Schuknecht & Tonndorf, 1960).

In considering the risk of inner ear trauma from ossicular manipulation, it is not only the amplitude of the movement that is important, but also how fast the movement is executed. Schuknecht and Tonndorf (1960) proposed that acoustic trauma results from stress to the inner ear, where stress describes the force per unit area, and force is equal to mass multiplied by acceleration. As the mass of the organ of Corti is not altered by movement of the stapes, acceleration must be the critical determinant of stress. This theory predicts that a movement of a given amplitude applied to the stapes will produce greater force and therefore stress to the inner ear if that movement is executed over a shorter time period. In other words, the stress on the cochlear partition that occurs during displacement of that partition will be proportional to the acceleration of ossicular movement.

The velocity of the force applied to the ossicles the can also be thought of as the frequency. In the case of middle ear surgery, this frequency is typically low, with palpation of the stapes with just enough force to assess mobility taking approximately half a second; equivalent to a frequency of 1 Hz (Bergin, 2011). Histological investigations of the cochlea following experimental stapes fracture in cats have shown injury localised to a region approximately 8 – 12 mm from the basal turn of the cochlea (Singleton & Schuknecht, 1959). The hurdle in explaining the association between surgical force and lesions to the basal cochlea is that, based on the low-frequency of the input, the basal turn of the cochlea is not where the travelling wave should reach maximum amplitude. Schuknecht and Tonndorf (1960) suggest that although ossicular manipulations occur over long time constants, the elastic limitations of the round window membrane are exceeded by the huge amplitude stimuli, resulting in phase alteration of the travelling bulge and centre-clipping of the waveform. Clipping of the waveform creates a bulge with steeper slopes and thus shorter time constants. The maximum amplitude in the envelope of the resulting travelling wave will therefore be shifted proximally along the basilar membrane. The theory of non-linear distortion provides an attractive explanation for basal cochlear trauma that fits with the current understanding of cochlear mechanics, however at this stage there is no direct evidence for this phenomenon.

Although hydrostatic force is frequently cited as a cause of cochlear injury, there is no conclusive data demonstrating a correlation between ossicular manipulation and hearing loss. This is exemplified by Kylén et al.'s (1980) study, which showed no significant changes to

intraoperative bone-conduction electrocochleography thresholds following ossicular manipulation in 12 tympanoplasty cases, regardless of the duration of manipulation. Central to Kylén et al.'s study is the assumption that the force transmitted to the inner ear is proportional to the duration of manipulation of the ossicular chain. As described above, the amplitude and speed are considered critical in determining the level of stress placed on the inner ear (Schuknecht & Tonndorf, 1960), neither of which was measured here. The authors suggest that longer manipulation times indicate that dissection has been difficult, however it is also possible that slow manipulations limit the pressure transmitted to the inner ear.

Despite the lack of direct evidence of ossicular manipulation as a cause of sensorineural loss, associations between postoperative hearing loss and surgical factors thought to increase the degree of force conveyed to the inner ear have been described. For example, removal of tympanosclerotic plaques from the middle ear during myringoplasty has been associated with poorer hearing outcomes (de Zinis et al., 2010). Further support for a role of ossicular manipulation in hearing loss may exist in the trend for trainee surgeons to produce higher rates of sensorineural loss following stapes surgery than experienced surgeons (Backous, Coker, & Jenkins, 1993; Chandler & Rodriguez-Torro, 1983; Handley & Hicks, 1990; Vital, Konstantinidis, Vital, & Triaridis, 2008; Yung, Oates, & Vowler, 2006). Using a force transducer incorporated into the handle of surgical instruments, Bergin (2011) measured the forces applied to the ossicular chain during middle ear procedures. Testing on temporal bones and in patients indicated that junior staff generally used greater force than more experienced otologists, potentially increasing the risk of cochlear injury.

Minimisation of force trauma to the inner ear has been a key factor in the shift in preference from stapedectomy to the stapedotomy (Sergi et al., 2010; Somers et al., 2006). The reduction in the area of footplate that is removed in stapedotomy is thought to reduce the risk to the cochlea relative to stapedectomy by decreasing mechanical manipulation in the oval window and lessening the forces transmitted to the inner ear (Bailey, Pappas, & Graham, 1983). There is a general consensus that the reduced cochlear trauma in stapedotomy is demonstrated by the improved hearing outcomes compared to stapedectomy, particularly at high-frequencies (e.g. Colletti, Sittoni, & Fiorino, 1988; Cremers, Beusen, & Huygen, 1991; Fisch, 1982; Levy, Shvero, & Hadar, 1990; Marchese, Paludetti, De Corso, & Cianfrone, 2007; McGee, 1981; Quaranta, Besozzi, Fallacara, & Quaranta, 2005; Somers, Govaerts, Marquet, & Offeciers, 1994; Spandow, Soderberg, & Bohlin, 2000). This indirectly supports the case for force trauma as a cause of post-stapedectomy hearing loss. Stapedotomy does not, however,

entirely remove the risk of cochlear injury, and high-frequency hearing losses continue to be reported after these procedures (Gerard et al., 2008; Motta, Ruosi, & Motta, 1996).

The transmission of large forces to the inner ear is a highly plausible explanation for EHF hearing loss following stapes surgery and ossiculoplasty. The highest rates of EHF hearing loss in our series were documented following stapedectomy, which is consistent with the creation of the greatest forces at the stapes footplate during this procedure relative to ossiculoplasty and tympanoplasty. However, this theory fails to account for the relatively high rate of postoperative EHF hearing loss we found following tympanoplasty in the series. In particular, if mechanical force were the primary cause of EHF hearing loss, we would expect that rates of threshold increases would be significantly higher following tympanoplasty relative to ossiculoplasty, which was not the case. Clearly other mechanisms must contribute to the development of EHF hearing, at least in some cases, and particularly after tympanoplasty during which ossicular manipulation is limited compared to other middle ear surgeries.

5.2.2 Noise exposure

Noise generated by the otologic drill during ear surgery has consistently been found to reach potentially harmful levels (Hilmi, McKee, Abel, Spielmann, & Hussain, 2012; Holmquist, Oleander, & Hallen, 1979; Kylén & Arlinger, 1976; Kylén, Stjernvall, & Arlinger, 1977; Spencer & Reid, 1985). For instance, airborne noise levels ranging from 84 to 125 dB SPL have been recorded from close to the site of drilling during mastoidectomy (Stromberg, Yin, Olofsson, & Duan, 2010; Yin, Stromberg, & Duan, 2011). Suction irrigation also contributes significantly to the overall noise levels during middle ear surgery, and the highest overall sound pressure levels in the EAC and mastoid cavity have been measured when drilling is combined with suction irrigation (Parkin, Wood, Wood, & McCandless, 1980; Yin et al., 2011). The spectrum of drill noise transmitted to the cochlea has its energy centred around 2 - 4 kHz (Hilmi et al., 2012; Kylén & Arlinger, 1976; Spencer & Reid, 1985), with airborne sound measureable up to at least 16 kHz (Hilmi et al., 2012).

Vibratory energy produced by drills creates an additional risk of cochlear trauma as it leads to oscillation of the cochlear compartments (Zou, Bretlau, Pyykko, Starck, & Toppila, 2001). As the transcranial attenuation of bone-conducted sound is minimal, it has been proposed that drilling of the temporal bone presents a risk to the contralateral as well as the ipsilateral

cochlea (Kylén & Arlinger, 1976; Man & Winerman, 1985; Zou et al., 2001). Given the absence of other factors that may cause hearing loss in the non-operated ear, such as force trauma, evidence of postoperative hearing loss in contralateral ear would strengthen the argument that noise or vibration are responsible for hearing loss in the operated ear.

While evidence that noise during otologic surgery reaches potentially harmful levels is clear, evidence of a clear link between drill or suction use and postoperative hearing loss is weaker. In one study supporting the role of drilling in the development of hearing loss, de Zinis et al. (2010) reported a significant relationship was between drilling in the EAC and the presence of an increase of greater than 10 dB in the bone-conduction threshold at 4 kHz 6 to 12 months after myringoplasty. Drill use, which was required in 20 of the 134 cases, was associated with an impairment at 4 kHz in 20% of patients, whereas the rate of comparable change was 4% in the group in which drilling was not necessary. While suggestive of a link between drill use and sensorineural hearing loss, the study is limited by the small number of patients who underwent drilling.

There is stronger evidence that temporary threshold shifts may result from noise exposure during otologic surgery. Kylén, Arlinger, and Bergholtz (1977) used intraoperative bone-conduction electrocochleography to demonstrate an immediate threshold shift of 10 – 40 dB HL in nine patients who underwent temporal bone drilling. A significant correlation was found between the degree of threshold shift and the duration of drilling for thresholds at 4 and 8 kHz, but not 2 kHz. The patient with the largest intraoperative threshold shift and the longest drill-time was the only subject with an increase, albeit temporary, in bone-conduction thresholds one week after surgery. Conversely, other studies have failed to find evidence of a temporary or permanent increase in bone-conduction thresholds following mastoid surgery with drilling (Leonetti et al., 2012; Spencer & Reid, 1985; Urquhart et al., 1992).

Studies assessing the effects of drilling during otologic surgery on the contralateral ear have also produced mixed results. Following mastoidectomy, a temporary reduction in contralateral otoacoustic emission amplitude, consistent with impairment of OHC function, was documented in two of twelve patients by da Cruz, Fagan, Atlas, and McNeill (1997), and as a significant mean group change in two other series (Karatas, Miman, Ozturan, Erdem, & Kalcioglu, 2007; Migirov & Wolf, 2009). Migirov and Wolf (2009) found no evidence of contralateral cochlear damage in a group of patients who underwent myringoplasty without drilling, supporting the theory that the damage following mastoidectomy was related to drill use. In contrast, Hallmo and Mair (1996) found no significant increase in mean contralateral

bone-conduction thresholds in the conventional or EHF ranges three months after ear surgeries involving drilling. Reports documenting hearing after prolonged temporal bone drilling during vestibular schwannoma excision have also shown no contralateral hearing loss (Man & Winerman, 1985; Tos, Trojaborg, & Thomsen, 1989), weakening the argument that vibration from the more limited drill use in middle ear surgery is a cause of hearing loss.

Although Hallmo and Mair (1996) found only very limited change in mean EHF bone-conduction thresholds in the operated ear three months after surgery using a high-speed drill, a transient EHF loss cannot be ruled out. Doménech et al. (1989) found that when electrostimulation audiometric thresholds were measured up to 20 kHz following tympanoplasty, nine of 24 patients experienced a hearing loss in the upper limits of their audible frequencies. As drill time is not reported, it is unclear whether a correlation was present between duration of exposure and postoperative hearing loss. This relationship between exposure time and EHF hearing loss was assessed by Hegewald et al. (1989), who also found evidence of a temporary mean threshold shifts in electrostimulation bone-conduction thresholds in the conventional and EHF ranges following 25 mastoidectomies. Drill time was measured in 18 patients and was not significantly correlated with either threshold shift at any frequency or change in highest frequency heard. Therefore, again, any causal link between drill exposure and loss of high-frequency hearing cannot be established.

Following noise exposure, lesions at the extreme base of the cochlea have been found in addition to stimulus frequency-specific lesions (Liberman & Kiang, 1978; Ou, Bohne, & Harding, 2000; Wang, Hirose, & Liberman, 2002). Whereas the tonotopic focus of the stimulus-specific lesion has a clear relationship with the place of maximum basilar membrane vibration amplitude (Cody & Johnstone, 1981; Liberman & Mulroy, 1982), the basal turn of the cochlea is not where the travelling wave should reach maximum amplitude. As described in Section 5.2.1, regarding hydrostatic pressure, a possible explanation for the creation of EHF hearing loss in response to such large stressors is non-linear distortion in the cochlea (Schuknecht & Tonndorf, 1960).

The sound and vibration levels produced during middle ear surgery will be specific to the procedure, the degree of drilling and suctioning required, and the equipment used. The intermittent and often brief nature of noise exposure during surgery is likely to reduce the risk of significant injury (Urquhart et al., 1992), therefore, although acoustic trauma is a reasonable hypothesis for the cause of EHF hearing loss following mastoidectomy, it is unlikely to be the causal factor in tympanoplasty. The use of the drill and the duration of

drilling were, unfortunately, not recorded for the cases presented in Chapter 3, therefore any link between drill use and EHF hearing loss cannot be determined.

5.2.3 Direct drill trauma to the ossicular chain

Strong evidence exists that direct contact of the drill with the ossicular chain can result in a prominent sensorineural hearing loss. Experimentally induced drill injuries to the incus or malleus have consistently produced irreversible cochlear damage (Gjuric, Schneider, Buhr, Wolf, & Wigand, 1997; Helms, 1976; Jiang et al., 2007; Paparella, 1962). Using a guinea pig model, Gjuric et al. (1997) clearly demonstrated a permanent detrimental effect of drill injury to the body of the incus on electrocochleography thresholds. The fifteen animals in which a drill was held to the body of the incus for ten seconds showed an immediate threshold shift of 15 to 70 dB nHL that persisted over the five week follow-up period.

Jiang et al. (2007) demonstrated that ten seconds of drilling on the short process of the incus in five human cadaveric temporal bones produced stapes displacement, as measured using laser Doppler vibrometry (LDV), consistent with equivalent noise levels of 93 – 125 dB SPL. The frequency distribution of the noise varied with drill type, with cutting drills demonstrating increased energy at the higher end of the frequency spectrum. The authors suggest that the greater vibratory energy at higher frequencies, particularly 8 kHz, produced by cutting burrs may be responsible for the increased incidence of high-frequency hearing loss seen clinically following mastoidectomy. In agreement with this theory, histopathologic investigation of the cochleae of cats following contact of a 4 mm cutting burr to the incus or malleus by Paparella (1962) showed injury to the organ of Corti that was most severe in the OHCs in the lower basal turn of the cochlea, which would be expected to correspond to a high-frequency loss. Certainly this evidence suggests direct drill injury to the ossicles can cause high-frequency postoperative hearing loss, however it must be assumed that such drill contact occurs relatively rarely, and that this is not the cause of the widespread isolated EHF hearing loss after middle ear surgery.

5.2.4 Lasers

Lasers are commonly used as an alternative to the microdrill in middle ear surgery. Although most frequently employed during stapedotomy, the applications of lasers during middle ear procedures are extensive. During surgery for COM, concerns regarding cochlear trauma are

minimised with a laser as soft tissue, such as cholesteatoma or granulation tissue, can be safely vaporised from the ossicles, oval window, round window niche, or from a dehiscent facial nerve without using physical contact (Hamilton, 2010; Lesinski, 2010). In stapedotomy, lasers enable the surgeon to dissect the crura and create a precise perforation in the footplate without mechanical contact (Kartush & McGee, 1991). The reduced incidence of inner ear trauma during laser stapedotomy has been demonstrated in several studies that show sensorineural hearing loss and vertigo occur less frequently following stapedotomy performed with a laser compared to surgeries using drills or manual perforators, particularly in the case of revision surgeries (e.g. Albers, Schonfeld, Kandilakis, & Jovanovic, 2013; Lesinski, 1990, 2003; Lesinski & Newrock, 1993; McGee, Diaz-Ordaz, & Kartush, 1993; Moscillo et al., 2006; Motta & Moscillo, 2002; Shabana, Allam, & Pedersen, 1999). Other studies have documented no significant difference in long-term hearing outcomes of stapedotomies performed with lasers and manual perforation or drilling (Brase et al., 2013; Cuda, Murri, Mochi, Solenghi, & Tinelli, 2009; Huber, Linder, & Fisch, 2001; Parrilla, Galli, Fetoni, Rigante, & Paludetti, 2008; Somers et al., 2007).

Even this relatively atraumatic method of operating on the middle ear carries a risk of damage to the inner ear that is unique to the type of laser used. Lasers in current use in otology are categorised as either visible or invisible, depending on their wavelength. Lasers with wavelengths in the visible range are the argon and potassium-titanyl-phosphate (KTP) lasers, and the invisible lasers used are the erbium yttrium aluminium garnet (Er:YAG) and carbon dioxide (CO_2) lasers. The primary risk to the inner ear presented by visible lasers results from the ability of the laser energy to pass through perilymph to reach the deeper tissues where it can be absorbed by the pigmented cells, particularly the stria vascularis, potentially causing irradiation damage (Brase et al., 2013; Silverstein, Bendet, Rosenberg, & Nichols, 1994; Wiet, Kubek, Lemberg, & Byskosh, 1997). The passage of laser energy through the perilymph also raises concerns regarding the elevation of the temperature of the vestibule and thermal injury to the inner ear (Oswal, 2002). Invisible laser wavelengths have near-optimal tissue absorption properties that minimise direct damage to other tissues (Galli, Parrilla, Fiorita, Marchese, & Paludetti, 2005; Parrilla et al., 2008), however, CO_2 lasers do generate heat that may cause thermal damage to the inner ear (Jovanovic, 2005; Jovanovic et al., 1995). The Er:YAG laser creates a unique risk to the inner ear through explosive bone ablation which creates pressure waves of up to 140 – 160 dB (A) in the labyrinth accompanied by a “snapping” sound as the vapour channel created by the laser beam in the

perilymph collapses (Häusler et al., 1999; Hibst, 1992; Huber et al., 2001; Pfalz, Hibst, & Bald, 1995).

Despite these risks to the inner ear, several studies have demonstrated that both visible and invisible lasers can be used effectively in middle ear surgery without causing permanent cochlear damage (Bartels, 1990; DiBartolomeo & Ellis, 1980; Huber et al., 2001; Keck, Burner, & Rettinger, 2005; Keck et al., 2002; McGee et al., 1993; Palva, 1987; Shah et al., 1996; Szyfter, Mielcarek-Kuchta, Mietkiewska-Leszniewska, Mlodkowska, & Laczkowska-Przybylska, 2013; Wiet et al., 1997). Comparisons of outcomes following stapedotomy with CO_2 lasers and with visible lasers have shown a non-significant trend towards less sensorineural loss with CO_2 lasers relative to argon lasers (Buchman, Fucci, Roberson, & De La Cruz, 2000), and no difference in outcomes compared to surgeries performed with KTP lasers (Vincent et al., 2012).

Significant temporary sensorineural hearing loss has, however, been documented immediately after stapedotomy performed with an Er:YAG laser (Arnoldner, Schwab, & Lenarz, 2006; Häusler et al., 1999; Jovanovic, Schonfeld, & Scherer, 2004). In a series of 15 stapedotomies, Häusler et al. (1999) reported that mid- and high-frequency bone-conduction thresholds were elevated by up to 75 dB HL two hours after surgery in the three patients operated on using an Er:YAG laser. Thresholds returned to preoperative levels within six hours. Other groups have shown milder transient sensorineural loss following Er:YAG assisted stapedotomy that may take several days or weeks to recover (Arnoldner et al., 2006; Keck et al., 2002). Transient declines in bone-conduction thresholds, particularly at 4 kHz, within the first two weeks of stapedotomy have also been documented following procedures performed using CO_2 and KTP lasers (Antonelli et al., 1998; Somers et al., 2006; Somers et al., 2007). It seems that trauma to the inner ear resulting in a high-frequency sensorineural loss is not eliminated, and may be caused, by the use of a laser.

In our series of stapes surgeries, all but one of the 44 procedures involved the use of a laser in conjunction with a microdrill. An argon laser was employed in 31 cases and a CO_2 laser in 12 surgeries. Unfortunately, patient numbers at follow-up appointments were too low to detect statistical differences between patients operated on with each type of laser. Certainly, the use of the laser could have contributed to EHF hearing loss in this series, however the lack of a control group who underwent surgery without the use of a laser means it is impossible to determine whether lasers influenced hearing outcomes.

5.2.5 Perilymph aspiration

The aspiration of perilymph from the labyrinth during stapes surgery is widely acknowledged as a significant risk factor for permanent or temporary postoperative sensorineural hearing loss (Bellucci, 1979; Hough, 1966; Ikeda et al., 2011; Somers et al., 1994; Wiet et al., 1993). Inadvertent perilymph aspiration from the vestibule was considered by Bellucci (1979) to be the most predictive factor of postoperative hearing loss at 2 – 8 kHz in a series of 103 stapedectomies. Of 11 cases in which significant perilymph aspiration was documented by Bellucci, nine presented with high-frequency sensorineural hearing loss. Although it is not clear when postoperative assessments were performed or to what extent hearing changed, the majority of patients reportedly showed a gradual, but incomplete, recovery of hearing following surgery.

Using a guinea pig model, Ikeda et al. (2011) measured endocochlear potential changes following different degrees of suctioning at the open oval window. As predicted, indirect perilymph suctioning caused a minor reduction in the endocochlear potential, while direct aspiration of perilymph caused a larger, rapid, reduction in the potential. Continuous recordings for 25 minutes showed that in animals in which indirect suctioning was performed the endocochlear potential recovered almost completely, but no recovery was observed in three of the six animals in which perilymph was directly aspirated. Bellucci (1979) proposed that the loss of perilymph creates considerable pressure waves in the inner ear, potentially damaging the OHCs in the basal turn of the cochlea. However, Ikeda et al. found no evidence of damage to the inner ear on histological inspection of temporal bone sections from animals that demonstrated a clear decrease in the endocochlear potential following perilymph aspiration has shown. Regardless of the mechanism, it is clear from experimental reports that perilymph aspiration has the potential to cause permanent hearing loss, particularly at higher frequencies. No cases of perilymph aspiration were documented in our series, although minor, inadvertent perilymph aspiration cannot be ruled out.

5.2.6 Fistula

A perilymph fistula is a rare complication of middle ear surgery that may result from an inadequate seal at the oval window following stapes surgery or from the opening of any portion of the labyrinth, either during surgery or by erosion from disease (Harrison, Shambaugh, Derlacki, & Clemis, 1967; House, 1967; Jovanovic et al., 2004; Lesinski &

Stein, 1989; Lippy & Schuring, 1984; Palva & Sorri, 1979; Shelton & Sheehy, 1990; Vartiainen, 1992). The most common symptom of a fistula is vertigo (Black et al., 1991; Harrison et al., 1967), and when hearing loss is present it is typically greatest in the low-frequencies and fluctuates (Harrison et al., 1967; Shott & Pensak, 1992). It is therefore unlikely that this is the explanation for isolated postoperative EHF hearing loss in the absence of significant vestibular symptoms.

5.2.7 Endolymphatic hydrops

Any reduction in the perilymph fluid volume, whether as a result of aspiration, or a fistula, will result in perilymphatic pressure being relatively lower than endolymphatic pressure (Beentjes, 1972; Kerth & Allen, 1963). A compensatory increase in endolymph may occur if perilymph loss occurs at a rate faster than it can be replaced; a situation that creates endolymphatic hydrops (Shea, Ge, & Orchik, 1995). Hydrops, occurring secondary to surgical injury that disturbs the pressure balance between endolymph and perilymph, may be a cause of both transient and permanent sensorineural hearing loss following middle ear surgery (Robinson & Kasden, 1977; Shea et al., 1995). Endolymphatic hydrops has a classical combination of symptoms of a fluctuating, often low-frequency, sensorineural hearing loss, episodic vertigo, aural fullness, and tinnitus (Shea et al., 1995). Obviously these symptoms closely follow those that occur with a fistula as the two processes both involve disturbances to the labyrinthine fluid pressures. As noted for fistulae, the symptoms produced by hydrops are inconsistent with isolated EHF hearing loss.

5.2.8 Reparative granuloma

Reparative granuloma formation is a rare complication of stapes surgery, reported to occur in 0.07 to 1.3% of cases (Seicshnaydre, Sismanis, & Hughes, 1994; Tange, Schimanski, van Lange, Grolman, & Zuur, 2002). Granuloma formation may arise during healing of the footplate in reaction to a foreign body, infection, or toxins in the middle ear (Burtner & Goodman, 1974; Dawes, Cameron, Curry, & Rannie, 1973). Clinical presentation varies, however symptoms commonly include a sudden or progressive decline in hearing; typically within six weeks of surgery, persistent disequilibrium or vertigo, tinnitus, hyperacusis, and aural fullness (Kaufman & Schuknecht, 1967; Tange et al., 2002; Tsang, Woo, & Tong,

2006). Audiometry will usually show a mixed hearing loss (Tsang et al., 2006) and we would not expect the effects to be limited to high-frequency hearing sensitivity.

5.2.9 Labyrinthitis

Sensorineural hearing loss and balance disturbance, particularly symptoms that are transient, following middle ear surgery have often been attributed to serous labyrinthitis (Schuknecht, 1962; Somers et al., 2006; Wiet et al., 1993). Labyrinthitis describes an inflammation of the inner ear and serous labyrinthitis specifically refers to inflammation due to the entry of toxins into the labyrinthine fluids, as opposed to frank bacterial or viral infection (McMenomey & Gubbels, 2008). Labyrinthitis may develop in response to entry of bacteria or bacterial toxins, blood, proteolytic enzymes, or foreign bodies into the labyrinth (Robinson & Kasden, 1977), however it may also be sterile and occur as a response of the inner ear to trauma (Meyerhoff, Marple, & Roland, 1996). An additional threat in stapes surgery comes from proteolytic enzymes in an otospongiotic lesion which may be released into the inner ear during manipulation of the stapes footplate (Barbara et al., 2005).

In addition to disease related toxins, potentially ototoxic substances used in surgery have been suggested as a cause of hearing loss. Agents that have been associated with inner ear harm include certain antiseptics (Bicknell, 1971; Packer, Mackendrick, & Solar, 1982), stapedectomy seal materials, such as Gelfoam (Lippy & Schuring, 1984; Rangheard, Marsot-Dupuch, Mark, Meyer, & Tubiana, 2001; Schuknecht & Mendoza, 1981), tissue glues (Kerr & Smyth, 1970), and prosthesis materials (de Bruijn, Tange, & Dreschler, 2001; Massey et al., 2005). The mechanisms by which each material exerts its effects on the inner ear varies, but may include inflammation (Rangheard et al., 2001), reparative granuloma (Kaufman & Schuknecht, 1967), and fistula formation (Lippy & Schuring, 1984).

Toxins or other inflammatory agents may enter the inner ear through an acquired pathway, such as a stapedotomy or fistula, or by diffusion through the round window membrane (Gloddek, Lamm, & Haslov, 1992; Kubo, Anniko, Stenqvist, & Hsu, 1998; McMenomey & Gubbels, 2008). The tonotopic organisation of the cochlea renders high-frequency hearing particularly susceptible to the effects of the spread of toxins, inflammation, or infectious agents (Paparella et al., 1984). Indeed, the effects of inner ear inflammation are reported to manifest clinically as a decrease in hearing above 2 kHz (Shea, 1963), making serous labyrinthitis a very plausible explanation for high-frequency postoperative hearing loss.

5.3 Mechanisms of cochlear damage

While the factors discussed above may be the direct cause of sensorineural hearing loss following middle ear surgery, we must also consider the mechanisms by which stressors such as noise, force, or toxins exert their effects on the cochlea. These mechanisms are often considered the targets for prevention of inner ear damage due to surgical trauma.

5.3.1 Inflammation

The presence of inflammatory cells in the cochlea has been demonstrated following both middle ear infections (Cureoglu et al., 2005) and high intensity noise exposure (Fredelius & Rask-Andersen, 1990; Hirose, Discolo, Keasler, & Ransohoff, 2005; Tornabene, Sato, Pham, Billings, & Keithley, 2006). Evidence suggests that following insult, leukocytes, particularly macrophages, are rapidly recruited to site of trauma in the inner ear (Hirose et al., 2005; Tornabene et al., 2006). Although the inflammatory process plays a critical role in the organism's defence system and contributes to wound healing following trauma (Park & Barbul, 2004), uncontrolled inflammation can rapidly cause permanent and severe structural damage to the delicate inner ear (Ye, Tillein, Hartmann, Gstoettner, & Kiefer, 2007).

The recruitment and migration of leukocytes is mediated by small proteins known as chemokines and cytokines (Keithley, Wang, & Barkdull, 2008; Tornabene et al., 2006). These proteins may themselves cause cochlear damage. In particular, tumour necrosis factor alpha (TNFα), a pro-inflammatory cytokine is produced by cells within the cochlea in response to high-intensity noise and vibration (Fujioka et al., 2006; Zou, Pyykko, Sutinen, & Toppila, 2005). Increased levels of TNFα in the cochlea are associated with apoptosis of several cell types, including hair cells, and are therefore thought to play a role in post-traumatic hearing loss (Cheng, Cunningham, & Rubel, 2005; Dinh et al., 2008; Haake, Dinh, Chen, Eshraghi, & Van De Water, 2009; Zou et al., 2005).

5.3.2 Vascular changes

Contrast enhanced MRI in animals and humans has been used to demonstrate that a key feature of cochlear inflammation is a transient increase in the permeability of blood vessels in stria vascularis associated with the breakdown of the blood-labyrinth barrier (Floc'h et al., 2014; Hegarty, Patel, Fischbein, Jackler, & Lalwani, 2002; Mark et al., 1992; Sone, Mizuno,

Naganawa, & Nakashima, 2009; Sugiura, Naganawa, Teranishi, & Nakashima, 2006). This endothelial-blood/tissue barrier plays an important homeostatic function; maintaining the composition of labyrinthine fluids and limiting the entry of toxic substances into the inner ear (Juhn, Hunter, & Odland, 2001). It is believed that disruption of the blood-labyrinth barrier, and thus disturbance of the ionic balance of the labyrinthine fluids, contributes to the development of cochlear damage and sensorineural hearing loss in response to a wide range of stressors (Juhn et al., 2001).

Vascular sludging and anoxia in the cochlea are also cited as a cause of postoperative sensorineural hearing loss (Robinson & Kasden, 1977; Smyth, 1977), although direct evidence supporting this theory is scarce. Increases in permeability of blood vessels in the stria vascularis in response to high-intensity noise, however, are well recognised (Seki, Miyasaka, Edamatsu, & Watanabe, 2001). Vasospasm of vessels in the zona arcuata of the basilar membrane in response to noise of even a relatively low intensity has also been demonstrated (Lawrence, 1973). Such morphological changes in the vascular supply to the inner ear may cause temporary or permanent functional damage (Smyth, 1977). The basal cochlea may be particularly vulnerable to increases in vascular permeability and ischemia of the inner ear following trauma. The vascular theory of increased basal cochlear susceptibility to trauma maintains that the watershed blood supply to the basal turn of the cochlea renders it more susceptible to damage than the remainder of the cochlea which has a more robust blood supply (Crowe, Guild, & Polvogt, 1934; Schuknecht & Tonndorf, 1960).

5.3.3 Oxidative stress

Another key hypothesis regarding the role of inflammation in cochlear damage concerns its relationship with the production of reactive oxygen species (ROS) and reactive nitrogen species (RNS). ROS and RNS comprise both free radicals, which are highly reactive molecules, and non-radical species that are readily capable of generating free-radicals (Halliwell & Gutteridge, 1999). In health, ROS and RNS serve important cellular regulatory and signalling functions and are maintained at appropriate levels in the cochlea by a system of antioxidants and enzymes (Ciorba, Gasparini, Chicca, Pinamonti, & Martini, 2010; Poirrier, Pincemail, Van Den Ackerveken, Lefebvre, & Malgrange, 2010; Thannickal & Fanburg, 2000). Redox imbalance will occur when the generation of ROS/RNS exceeds the capacity of the defence system to restore homeostasis, either as a result of ROS/RNS

overproduction, inadequate defences, or both (Evans & Halliwell, 1999; Huang et al., 2000; Lefebvre et al., 2002). Oxidative stress resulting from redox imbalance activates signalling pathways that can disrupt cellular structure and trigger cell death via several mechanisms including lipid peroxidation of the cellular membrane (Warner, Sheng, & Batinic-Haberle, 2004), alteration of cell membrane calcium channels (Az-ma, Saeki, & Yuge, 1999), ischemia-reperfusion injury (Miller, Brown, & Schacht, 2003), and ultimately activation of the apoptotic and necrotic cell death pathways (Abi-Hachem, Zine, & Van De Water, 2010; Halliwell & Gutteridge, 1985, 1999; Kopke, Coleman, Liu, Jackson, & Van De Water, 2005; Warner et al., 2004).

The effects of inflammation on the inner ear and those of oxidative stress appear to be inextricably linked (Du et al., 2011). As described above, inflammatory reactions are characterised by the movement of leukocytes to the site of trauma. In addition to the release of enzymatic granules, leukocytes release large amounts of ROS/RNS, which contribute to the damaging effects of inflammatory reactions on the cochlea (Johar et al., 2004). Conversely, oxidative stress induces an inflammatory reaction that further amplifies ROS production (Koppula, Kumar, Kim, & Choi, 2012; Vaziri, 2008).

Environmental stimuli that have been either directly or indirectly (through a reduction in trauma with the application of antioxidants or ROS scavengers) shown to increase ROS production in the cochlea include excessive noise exposure (e.g. Clerici & Yang, 1996; Du et al., 2011; Forge & Van De Water, 2008; Henderson, Bielefeld, Harris, & Hu, 2006; Hirose, Hockenbery, & Rubel, 1997; Kopke et al., 1997; Ohinata, Miller, Altschuler, & Schacht, 2000; Ohlemiller, Wright, & Dugan, 1999; Yamashita, Jiang, Schacht, & Miller, 2004), cisplatin (Campbell, Rybak, Meech, & Hughes, 1996; Kopke et al., 1997; Ravi, Somani, & Rybak, 1995; Rybak, Ravi, & Somani, 1995), aminoglycoside antibiotics, (Forge & Li, 2000; Forge & Schacht, 2000; Hirose et al., 1997; Pirvola et al., 2000; Sha & Schacht, 2000; Ton & Parng, 2005), and cochlear implant electrode insertion trauma (Eshraghi et al., 2007; Jia et al., 2013). We are not aware of any studies that have investigated ROS production in the inner ear following surgical procedures in the middle ear, however given the evidence of the role of oxidative stress in cochlear damage following excessive noise exposure and mechanical trauma from cochlear implant electrode insertion, it seems a reasonable supposition that ROS may play a role in the development of sensorineural hearing loss following middle ear surgeries.

Although direct evidence of a relationship between surgically induced cochlear trauma and ROS production has not yet been found, it has been posited that vascular changes documented following drill injury to the ossicles may be a result of free radical generation (Hashimoto, Seki, Miyasaka, & Watanabe, 2006). Seki et al. (2001) reported that direct drill-induced damage to the ossicles in guinea pigs produced an increase in the permeability across stria vascularis capillaries that increased significantly with duration of drilling. Based on studies demonstrating a relationship between ROS and increased vascular permeability in brain injury (e.g. Hall, Andrus, & Yonkers, 1993; Jesberger & Richardson, 1991), Hashimoto et al. (2006) propose that ROS, specifically hydroxyl radicals, are responsible for the increase in permeability in stria vascularis capillaries following vibration.

It is hypothesised that intrinsic differences in the susceptibility of OHCs to oxidative stress depending on their position in the cochlea is responsible for the pattern of increasing injury from apex to base in response to trauma. Measurements of cellular levels of glutathione, an antioxidant, have shown that concentrations are 25% higher present in apical OHCs compared to basal OHCs (Sha, Taylor, Forge, & Schacht, 2001). Given that cellular antioxidants form a primary level of defence against free radicals, the naturally higher levels of antioxidant production in apical hair cells may effectively reduce damage from ROS produced in response to cochlear trauma (Sha et al., 2001). This hypothesis is supported by a significant increase in OHC survival when basal hair cells are maintained in a solution supplemented with antioxidants (Sha et al., 2001). The implication of these findings is that ROS damage, which can be mitigated by added antioxidants, is a cause of the accelerated cell death observed in vitro in basal OHCs. By extension, the patterns of high-frequency hearing loss and basal cochlear damage documented in response to stressors such as cisplatin, noise, and perhaps force imparted during middle ear surgery, may also be due to an intrinsic susceptibility to ROS that differs among cochlear cell populations (Sha et al., 2001; Song & Schacht, 1996).

5.3.4 Structural damage

Structural damage to cochlear cells, as demonstrated following acoustic trauma (Clark & Pickles, 1996; Liberman & Dodds, 1987; Patterson & Hamernik, 1997), may also contribute to sensorineural hearing loss following middle ear surgery. Animal studies of mild acoustic trauma have produced evidence of potentially reversible splaying of the OHC stereocilia and

damage to tip links (Clark & Pickles, 1996; Liberman & Dodds, 1987). Damage is permanent in cases of severe acoustic trauma and is characterised by kinked or fractured stereocilia, depolymerised actin filaments, and broken tip links between adjacent stereocilia (Liberman & Dodds, 1987). Presumably strong forces exerted on the inner ear through other means, such as hydrostatic pressure from manipulation of the ossicles during surgery, have the potential to cause comparable mechanical damage to the cochlea in the regions of maximal stimulation.

5.3.5 Additional risk factors

The risk of high-frequency hearing loss following middle ear surgery may be in part determined by the tolerance of the individual labyrinth to insult (Smyth, 1977). In particular, there is evidence suggesting there is an increased likelihood of at least transient postoperative hearing loss with increasing age. Bauchet St Martin et al. (2008)'s analysis of hearing 4 to 6 weeks after stapes surgery indicated that the odds of a patient over 40 years of age presenting with an increase in the 4 kHz bone-conduction threshold were approximately four times greater than the odds for patients younger than 40 years. The same calculation for the air-conduction threshold at 8 kHz showed that older patients were over six times more likely to sustain a loss than younger patients. Interestingly, there was no significant difference in the rates of hearing loss between the two groups at the final assessment at least nine months after surgery, suggesting that although older patients may be more susceptible to surgical trauma to the cochlea, they are able to recover from such trauma. Similar observations of poorer postoperative results in the high-frequencies have been documented following stapedectomy in patients older than 40 (à Wengen, 1993; à Wengen et al., 1992; Meyer, 1999), 50 (Langman, Jackler, & Sooy, 1991), and 70 (Lippy, Burkey, Fucci, Schuring, & Rizer, 1996) years of age.

It is unclear whether the correlation between sensorineural hearing loss following stapes surgery and age is due to the increased duration of otosclerotic disease in these patients, or to a greater degree of preoperative sensorineural hearing loss, whether that loss is due to cochlear otosclerosis, presbycusis, or some other factor. From the limited evidence available, it appears that pre-existing sensorineural hearing loss may be the key factor in determining the fragility of the cochlea. Del Bo, Zaghis, and Ambrosetti (1987) found that patients with more than a mild elevation of bone-conduction thresholds preoperatively were more likely to experience sensorineural impairment after stapedectomy, irrespective of age. Del Bo et al.

assumed that increased bone-conduction thresholds preoperatively were indicative of advanced otosclerosis, which resulted in labyrinthine fragility. Although this is a compelling explanation, it is not possible to determine that the elevated bone-conduction thresholds preoperatively were the results of endosteal involvement. Histopathologic investigations of temporal bones with cochlear otosclerosis have shown atrophy of the spiral ligament and stria vascularis in regions adjacent to the otosclerostic foci (Benitez & Schuknecht, 1962; Hildyard, Sando, & Davison, 1972; Wiet, Morgenstein, Zwolan, & Pircon, 1987). Wiet et al. (1993) suggest that spiral ligament atrophy may lead to basilar membrane rupture, rendering the cochlea more fragile during surgery. However, whether otosclerosis with endosteal involvement is responsible for increased cochlear fragility in all older patients with pre-existing sensorineural hearing loss is unknown.

5.4 Hearing loss caused by changes to the middle ear anatomy

It is plausible that the effects of middle ear surgery on high-frequency hearing are the result of an alteration in middle ear transmission characteristics, as opposed to inner ear trauma. Middle ear surgery may alter the physical properties of one or more of the ossicles, TM, or tympanic cavity, which in turn may compromise hearing sensitivity.

5.4.1 Overall sound transmission through the reconstructed middle ear

Surgical alterations to the anatomy of the middle ear may reduce the overall intensity of energy transmitted to the cochlea. Using LDV in a cadaveric human temporal bone, Wysocki, Kwacz, Mrowka, and Skarzynski (2011) demonstrated an approximately five-fold decrease in round window vibration amplitude post-stapedotomy that tended to decrease in magnitude as a function of increasing input frequency (from 0.4 to 10 kHz). There was, however, some increase in vibration amplitude above 4 kHz and round window displacement at 8 kHz was six times higher than the same measurement at 4 kHz. In agreement with Wysocki et al. (2011), Sim, Chatzimichalis, Roosli, Laske, and Huber (2012) found a mean reduction in round window displacement amplitude following stapedotomy in 12 temporal bones at 0.125 – 8 kHz, although no significant differences were found across input frequencies. The results of both studies suggest that stapedotomy decreases perilymph stimulation and therefore round window membrane displacement, presumably by altering the input impedance at the cochlea. The effect of frequency is debatable, although it is clear that sound transmission is reduced to

some degree across all frequencies tested. The reason that hearing outcomes following stapedotomy are typically very good suggests that the clinical importance of these findings may be lower than expected for a five-fold reduction in perilymph stimulation.

A reduction in sound transmission to the inner ear has also been demonstrated following ossiculoplasty. Alian, Majdalawieh, Van Wijhe, Ejnell, and Bance (2012) used LDV to compare sound-evoked round window vibrations in five human temporal bones for prostheses that connected the TM to either the stapes head or the footplate. With both prostheses, round window vibration was significantly reduced compared to the intact ear at 0.5 – 8 kHz, with no significant effect of frequency. Interestingly, umbo velocity in reconstructed ears was found to be equivalent to bones with intact ossicular chains, except for a 5 – 10 dB increase for reconstructed ears at mid-frequencies. This suggests that although the attachment of a prosthesis to the TM is not detrimental to the vibration of the umbo, vibration declines by the point of cochlear stimulation.

Measurements of sound pressure in the vestibule have also been used to demonstrate a decrease in inner ear stimulation in cadaveric temporal bones after ossicular reconstruction (Murugasu, Puria, & Roberson, 2005; Puria, Kunda, Roberson, & Perkins, 2005). Both Murugasu et al. (2005) and Puria et al. (2005) demonstrated that the loss in cochleovestibular pressure when the ossicles were replaced with a prosthesis was greatest at 0.25 to 4 kHz. Between 6 and 10 kHz the magnitude of loss following prosthesis insertion tended to decrease. Overall, these studies demonstrate that overall transmission of acoustic stimuli through a reconstructed ear is reduced relative to a normal ear; however the disadvantage appears to be reduced at higher frequencies.

The main flaw in the mechanical hypothesis for hearing loss following middle ear surgery is that the theory fails to explain why hearing losses are not found in all patients postoperatively. If a middle ear prosthesis is not capable of transmitting acoustic stimuli as effectively as the normal ossicular chain, hearing loss should be seen universally after middle ear surgery, which does not appear to be the case. Certainly the evidence discussed above shows that vibration transmission is, at least in temporal bone models, reduced following replacement of all or part of the ossicular chain, however evidence that this effect is particularly detrimental to high-frequency hearing sensitivity is limited.

5.4.2 Tympanic membrane structure and vibration patterns

The sound-induced motion across the surface of the TM is complex, particularly in response to high-frequency stimuli (e.g. Decraemer, Khanna, & Funnell, 1989; Goode, Ball, Nishihara, & Nakamura, 1996; Khanna & Tonndorf, 1972; Konrádsson et al., 1987; Rosowski et al., 2009; Tonndorf & Khanna, 1972). In response to acoustic stimulation below around 2 kHz, the entire surface of the TM moves approximately in the same phase, with three or fewer displacement maxima (Cheng et al., 2010). At higher frequencies, the complexity of the movement pattern increases significantly, and Cheng et al. (2010) describe TM surface vibration patterns in response to 4 and 8 kHz stimuli as consisting of 4 – 10 local displacement maxima of varying phases distributed across the membrane surface.

As described in Chapter 2, the lamina propria of the TM is composed of a series of radially and circumferentially oriented collagen fibres. It has been proposed that the radial fibres transmit travelling waves that occur across the TM surface in response to high-frequency stimuli, propagating the vibration towards the umbo (O'Connor, Tam, Blevins, & Puria, 2008). If this hypothesis is correct, it could be predicted that disruption of the microanatomy of the lamina propria, and particularly the radial collagen fibres, would affect sound transmission at the high-frequencies. This hypothesis has been supported by demonstrations in temporal bones that when slits in the TM fibres, particularly the radial fibres, are patched with paper, stapes velocity in response to acoustic stimuli is significantly reduced at 4 kHz and up to 8 to 12.5 kHz, despite restoration of the TM pressure gradient (O'Connor et al., 2008; Roosli, Sim, Chatzimichalis, & Huber, 2012). The results of these studies suggest that the integrity of the microanatomy of the TM is particularly critical for high-frequency sound transmission. Patches in the TM lack the complex fibre arrangement of the normal TM and therefore the mechanism by which high-frequency vibration propagates across the membrane will remain disrupted (O'Connor et al., 2008). Persistent disruption of high-frequency TM vibration may be expected to cause a reduction in hearing above 4 kHz.

In contrast to the findings of O'Connor et al. (2008) and Roosli et al. (2012), Aarnisalo et al. (2009) found that although images of TM motion produced using high-speed optoelectronic laser holography showed clear decreases in high-frequency (4 – 8 kHz) sound induced motion of areas backed with cartilage grafts, this did not correspond to a decrease in stapes velocity. Aarnisalo et al. suggest that their findings are consistent with the theory that the TM becomes uncoupled from the ossicular chain in response to stimulation at frequencies above 3 – 4 kHz (Tonndorf & Khanna, 1970, 1971, 1972). This would suggest that alterations in

TM vibration in response to high-frequency stimuli may not be as critical to hearing sensitivity as other studies suggest.

Unfortunately, as the studies described above have been performed in temporal bones, the effect of healing that occurs following tympanoplasty is unknown. Merchant, McKenna, Mehta, Ravicz, and Rosowski (2003) state that the eventual thickness and characteristics of the grafted TM vary depending on the type and thickness of the grafted material and the healing response of the ear. If healing of the grafted area restores the microanatomy more closely to the physiologic condition, this may explain the resolution of many high-frequency hearing losses over the postoperative course.

5.4.3 Effects of changes in ossicular mass and stiffness

The middle ear functions as a complex resonant system, and as such, any alterations to the mass or stiffness of the system's components will shift its resonant frequency. By altering the resonant frequency of the system, an ossicular prosthesis of lower mass should optimise higher frequency transmission, whereas a heavier prosthesis will favour transmission of lower frequencies (Huttenbrink, 2003). Indeed, studies comparing hearing outcomes in stapesplasty using pistons constructed with different materials have demonstrated this trend (de Bruijn, Tange, & Dreschler, 1999; Robinson, 1974), however when other factors are controlled for, such as whether implantation was considered successful or not, the effect of stapes prosthesis mass on hearing appears to be negligible (de Bruijn et al., 1999).

Predictive model analysis also suggests that the impact of an increase in stapes mass on sound transmission is not significant. Rosowski and Merchant (1995)'s mathematical model of middle ear transmission demonstrated that increasing the mass of the stapes from its normal weight of approximately 3 mg to 48 mg had little effect on the air-bone gap. The loss predicted from this large increase in mass was evident only above 1 kHz, and did not exceed 7 dB in amplitude up to the model's upper limit of 10 kHz. It is possible that the effects of an increase in mass are more evident in the EHF range than the conventional range, however we are not aware of any analysis that takes EHFs into account.

Increasing the mass of the incus and malleus may have a greater effect on high-frequency sound transmission than the effect observed for the stapes. Consistent with studies of mass loading intact ossicular chains (Gan, Dyer, Wood, & Dormer, 2001; Gundersen, 1971; Lawrence, 1960), Bance, Morris, and Van Wijhe (2007) found that the addition of mass to a

prosthesis connecting the TM to the stapes head had little impact on stapes vibration velocity in response to low-frequency stimuli, but marked effects at 4 kHz to 8 kHz. The maximum measured decrease in stapes footplate vibration relative to the unloaded prosthesis condition was 10 dB above 4 kHz when the prosthesis was maximally loaded. Similarly, Nishihara and Goode (1994) demonstrated that the addition of mass to an incus prosthesis positioned between the TM and stapes head produced a greater reduction in stapes vibration velocity above 2.5 kHz than below. The results of these studies provide a potential explanation for high-frequency hearing loss following ossiculoplasty, although not stapedectomy.

Bance et al. (2007) noted that while the standard deviation of stapes velocity measurements across temporal bones was relatively small with intact ossicular chains, there was approximately 50 to 100 per cent more variability following ossicular reconstruction. This variation is thought to reflect inconsistencies across specimens in factors that affect prosthesis function, including the tension, angulation, and attachment point. If the alteration of the mass of the middle ear components is responsible for postoperative EHF hearing loss, this variability across ears may provide an explanation for the fact such hearing loss is not observed universally across apparently identical procedures.

In general, the stiffness of an ossicular prosthesis does not appear to have a major effect on sound conduction. Merchant and Rosowski (2010) predict that stiffness will not have a significant influence on the hearing when the stiffness of the prosthesis is greater than that of the impedance at the stapes footplate-cochlea interface. Materials commonly used to construct prostheses generally meet this criterion and are of adequate stiffness that small variations will not affect the hearing outcome following reconstruction (Merchant & Rosowski, 2010). The dominance of the effects of stiffness on low-frequency sound transmission also suggest that should stiffness in fact have some impact on middle ear transmission, this is unlikely to be the cause of any hearing loss in the EHF range.

Although the absolute stiffness does not influence acoustic performance of ossicular prostheses, the tension created by the prosthesis between the TM and the stapes, which is primarily a function of the prosthesis length, has been shown to affect sound transmission (Aritomo & Goode, 1992; Morris, Bance, van Wijhe, Kiefte, & Smith, 2004; Nishihara & Goode, 1994; Vlaming & Feenstra, 1986). For example, Nishihara and Goode (1994) showed that with increasing tension between the TM or malleus and the stapes head or footplate, stapes displacement increased for input frequencies of 3 – 10 kHz, at the expense of transmission below 1.3 kHz. Similar findings of improved high-frequency and reduced low-

frequency transmission with increased prosthesis tension have been reported by Aritomo and Goode (1992) and Bance, Morris, Vanwijhe, Kiefte, and Funnell (2004). If we extrapolate the findings thus far, we would assume that if tension is very low we may find good results in the lower-frequencies of the conventional range but EHF hearing loss after middle ear surgery. As Merchant and Rosowski (2010) point out, as at present there is no reliable, objective, intraoperative test of prosthesis tension, this parameter is difficult to quantify and thus correlate with hearing outcomes.

5.4.4 The impact of alterations of the oval window–stapes footplate interface

A key consideration for the impact of stapedectomy on the conductive mechanism is the degree to which changes at the stapes footplate–oval window interface alter the transmission of sound to the cochlea. In the physiologic state, the stapes has a footplate approximately 3.2 mm^2 in area (Huttenbrink, 2003), sealed in the oval window by the annular ligament. The rigid collagen fibres of the annular ligament are responsible for 90% of the overall impedance of the normal middle ear at low frequencies and therefore determine the amplitude of stapes vibration in response to these low frequencies (Huttenbrink, 2003). In the case of otosclerosis, when surgery is performed to create a mobile interface between the ossicular chain and the inner ear, the cochlear input impedance is reduced from the pathological state and the annular ligament is eliminated at the dominant contributor to the overall middle ear impedance (Merchant et al., 2003).

The volume of cochlear fluid displaced corresponds to the volume velocity of the stapes, which is the product of the area of the footplate and the amplitude of its vibration (Huttenbrink, 2003). Any alteration in stapes footplate area may alter the volume velocity, changing the sound pressure level transmitted to the inner ear. To a large extent, reductions in the area of the footplate are compensated for by an increased velocity of vibration at equivalent sound pressure levels (Huttenbrink, 2003). However, both mathematical models and clinical outcomes suggest that a reduction in the size of the stapes footplate–perilymph interface will have a significant influence of the volume velocity of the stapes (Arnold, Ferekidis, & Hamann, 2007; Rosowski & Merchant, 1995). At present, the most commonly used pistons in stapedotomy have diameters of 0.4 mm and 0.6 mm (Laske, Roosli, Chatzimichalis, Sim, & Huber, 2011), therefore post-stapesplasty, the sound transmitting area

at the oval window will be reduced to 0.12 mm^2 and 0.28 mm^2 with 0.4 and 0.6 mm prostheses, respectively (Huttenbrink, 2003).

An analysis of data pooled from 62 studies reporting postoperative hearing results of stapedotomy with 0.4 mm and 0.6 mm prostheses was performed by Laske et al. (2011) to address the question of the impact of prosthesis diameter on hearing outcome. Significantly better air-conduction thresholds and smaller air-bone gaps were found in the pooled group data for 0.6 mm prostheses compared to the 0.4 mm diameter prosthesis at 0.5, 1, and 2 kHz, and not for 4 kHz. This suggests the detrimental effects of a reduced oval window-footplate/piston interface diameter are dominant for low frequency sound transmission, and thus unlikely to cause EHF hearing loss.

Another parameter than must be taken into account is that the vibrating area at the interface between the footplate or prosthesis and the labyrinth is not limited to the piston, but includes the membrane on which the piston sits (Rosowski & Merchant, 1995). This increases the size of the effective sound transmitting area, as is perhaps best illustrated by the good acoustic outcomes of stapedectomies performed with connective tissue and wire prostheses (Huttenbrink, 2003). Given that fenestra diameters are typically slightly larger than the piston (Fisch, 1982; Smyth & Hassard, 1978), this may be a confounding factor in assessing the results of comparative studies of footplate size as both piston and fenestra diameters will differ between groups. Fucci, Lippy, Schuring, and Rizer (1998) reported no significant difference in hearing outcomes for patients with either 0.4 mm or 0.6 mm pistons inserted into fenestrations of identical size. However, as studies with both piston diameter and fenestra sizes manipulated have also shown no difference in outcomes (Fisch, 1982; Shabana et al., 1999), it is not possible to draw conclusions from this single study.

The membrane covering the oval window is of further interest as, like the grafted TM, an oval window replacement membrane may undergo progressive physical changes over time as the ear heals postoperatively. Antoli-Candela, Gomez-Molinero, and Busturia-Berrade (2009) suggest that these changes may be accompanied by a recovery in hearing over the postoperative period, explaining the higher incidence of high-frequency hearing loss in the early stages of the postoperative course. Thicker replacement membranes from interposed materials such as fat or veins may be beneficial for high-frequency hearing due to the greater efficiency of the resulting seal of the opening to the inner ear (Shambaugh, 1963). Thinner membranes with poorer seals may cause dispersion of high-frequency vibrations due to a ballooning effect on the membrane (Raman, 1983). Again, although such an effect has not

been demonstrated, changes in the oval window membrane could theoretically influence EHF hearing either temporarily or permanently.

5.4.5 Effects of changes to the volume of the middle ear and EAC air spaces

Vibration of the TM and sound transmission through the middle ear is influenced by the impedance of the air space behind the drum (the cavity impedance), which may be either increased or decreased by mastoid surgery (Rosowski & Merchant, 1995). Modelling calculations suggest that whereas increases in the air volume in the middle ear should have a negligible effect on acoustic transmission, an air-space volume that is markedly lower than normal may reduce the transmission of sounds below 2 – 3 kHz by increasing the middle ear impedance (Rosowski & Merchant, 1995). A reduction in the total volume of the middle ear air spaces by a factor of four to 1.5 cm^3 is predicted to result in an air-bone gap of only 2 dB below 1 kHz, whereas a further decrease to 0.5 cm^3 should produce a low-frequency air-bone gap of just under 10 dB HL (Rosowski & Merchant, 1995). These predictions are supported by experimental data showing that the volume of the middle ear spaces can be significantly altered without major adverse effects on acoustic transmission (Gyo, Goode, & Miller, 1986; Whittemore, Merchant, & Rosowski, 1998).

There has been a general consensus across the abovementioned studies that the small effect of the volume of the middle ear air space on sound transmission is restricted to low-frequencies. However, Stepp and Voss (2005) suggest that changes in the volume of the middle ear spaces may have more complex effects on the middle ear impedance for frequencies above 1 kHz. Using measurements of middle ear impedance in three cadaveric ears and predictions from analogue circuit models, Stepp and Voss demonstrated that for frequencies above 1 kHz, alterations of the middle ear spaces can introduce multiple minima and maxima to the impedance at the TM. These effects are complicated and dependent on the specific anatomy of each ear, but do suggest that the impedance at the TM can be altered by as much as 10 dB at high-frequencies in response to changes in the middle-ear air space impedance. Although the importance of these findings for high-frequency hearing thresholds is not clear, they do suggest the effects of changes to the volume of the middle ear air spaces may be more important for high-frequency sound transmission than previously thought.

While the middle ear space created by a CWD mastoidectomy may have only a limited effect on sound transmission, a CWD procedure also creates a large ear space lateral to the TM

where the EAC and the mastoid bowl are connected. Such alterations to the normal anatomy can shift the resonant frequency of the canal and create additional resonances that can influence the sound pressure level at the TM (Goode, Friedrichs, & Falk, 1977; Jang, 2002). Theoretically, mastoid cavity resonances may be generated above 1 – 2 kHz that are sufficiently large to shift hearing thresholds either favourably or unfavourably (Goode et al., 1977; Merchant & Rosowski, 2010). It is possible that some of the high-frequency hearing loss observed following surgery that has altered the EAC anatomy may be due to postoperative changes in canal acoustics, and thus impaired sound conduction.

The volume of the middle ear space is often temporarily reduced and movement of the ossicular chain and TM are restricted immediately following surgery due to packing materials such as gelfoam, which are used in the middle ear cavity and EAC to stabilise grafts, skin flaps, and prostheses (Shen, Teh, Friedland, Eikelboom, & Atlas, 2011; Wiesenthal & Garber, 1999). As expected, Cho et al. (2007) demonstrated that average air-conduction thresholds following tympanoplasty increased immediately after surgery and remained significantly elevated until EAC packing was removed three weeks postoperatively. Less predictably, the average bone-conduction threshold at 2, 3, and 4 kHz across the 17 patients also remained slightly but significantly elevated until after packing was removed. Cho et al. provided support for their theory that the elevation in high-frequency bone-conduction thresholds resulted from a reduction in the external and middle ear contributions to bone-conduction hearing by demonstrating a significant mean increase in the high-frequency average bone-conduction threshold when packing was placed in the EACs of 18 otologically normal volunteers. If high-frequency air-conduction thresholds, and particularly bone-conduction thresholds, can be altered by the presence of middle ear and EAC packing, this could certainly have implications for the interpretation of EHF postoperative hearing losses.

As illustrated by Cho et al.'s (2007) bone-conduction findings, a key issue in interpreting the effects of middle ear pathology or surgery on the inner ear is that bone-conduction threshold measurements are not a pure or exact measurement of the cochlear reserve. Most evidence suggests that the external and middle ear contributions to bone-conduction thresholds are relatively minor (e.g. Stenfelt & Goode, 2005), although this conclusion is applicable only to the conventional frequency range in which most research is performed. Cho et al.'s results are interesting in that they suggest that high-frequency bone-conduction thresholds may be particularly vulnerable to the loss of middle ear contributions to bone-conduction postoperatively.

5.4.6 Residual middle ear secretions or mucosal oedema

In a similar manner to middle ear packing, a temporary increase in the mass of the middle ear system and a reduction in air volume resulting from residual secretions in the middle ear space after myringotomy has been proposed as a mechanism for the transient EHF hearing losses documented following ventilation tube insertion (Mair, Fjermedal, & Laukli, 1989). Although ventilation tube insertion is not included in the present study, the patterns of hearing loss seen after that procedure may provide some clues as to the changes that occur in the middle ear immediately after other procedures. For example, surgery for COM may be expected to have similar effects to ventilation tube insertion in terms of residual secretions or oedema in the tympanic cavity. Results from Mair, Fjermedal, et al.'s (1989) study of hearing in the conventional and EHF ranges following ventilation tube insertion showed that although the air-bone gap at 2 kHz and below typically closed within 24 hours of surgery, threshold "normalisation" in the EHF range did not occur until between two and eight weeks after surgery. On average, thresholds in the EHF range significantly improved by two months after surgery, however in six cases in which thresholds in the operated ear could be compared to a healthy contralateral ear, EHF thresholds recovered to equal levels as the contralateral ear in only two cases. It is unclear if this persistent loss was conductive or sensorineural.

Mair, Fjermedal, et al. (1989) acknowledge that interpretation of their findings is difficult in light of the gaps in the present state of knowledge of middle ear transmission of EHF acoustic stimuli. They propose that retained mucus or mucosal oedema in the epitympanum may increase the mass of the system sufficiently to increase thresholds in the EHF range, while ventilation of the mesotympanum causes an adequate reduction in middle ear stiffness to allow improvement of thresholds in the conventional frequencies. Evidence illustrating a continuing increase in the volume of the middle ear space up to three months after ventilation tube insertion (Tashima, Tanaka, & Saito, 1986) supports the theory of gradual resorption of mucus or its removal via mucociliary mechanisms over the weeks following surgery. This process would be expected to cause a corresponding improvement in EHF hearing thresholds over the months following surgery, as was documented in the present study.

5.4.7 Effects of changes in ossicular chain movement patterns

A healthy, intact ossicular chain is suspended and supported by ligaments and muscles and has two joints that enable the articulated ossicles to glide against each other (Guinan &

Peake, 1967; Willi, Ferrazzini, & Huber, 2002). At frequencies above the resonant frequency, at least the malleus and incus display complex movements is all three dimensions (Decraemer & Khanna, 1994, 1995). Measurements of sound-induced ossicular motion using LDV by Willi et al. (2002) and Decraemer and Khanna (2004) have demonstrated that the relative motion between the malleus and incus increases somewhat in response to frequencies above 2 kHz, and that flexion continues at frequencies as high as 20 kHz. It is this relative flexibility in the rotation axis that is believed to result in slippage in the ossicular chain, which in turn is hypothesised to be at least partially responsible for the increasing inefficiency of the human middle ear transfer function above 1 kHz (Goode, Killion, Nakamura, & Nishihara, 1994; Gyo, Aritomo, & Goode, 1987; Kringlebotn & Gundersen, 1985; Vlaming & Feenstra, 1986).

In opposition to the apparent disadvantage of a flexible ossicular chain for the transmission of high-frequencies is the theory that twisting motion of the ossicular chain actually improves high-frequency sound transmission by significantly reducing the effective inertial mass relative to the absolute mass of the ossicles (Puria & Steele, 2010). Puria and Steele (2010) argue that in larger mammals, including humans, the reduction in the effective inertia of the ossicular chain afforded by the twisting motion of the malleus and incus allows transmission of higher frequency sounds through the middle ear than would not otherwise be possible given the absolute masses of the ossicles. An ossicular replacement prosthesis is typically a rigid, non-jointed implant, and as such does not rotate in the same manner as an unaltered ossicular chain (Guinan & Peake, 1967; Kelly, Prendergast, & Blayney, 2003). As Nishihara and Goode (1994) point out, a prosthesis that exactly matched the weight of an average human male incus would have a higher inertia than the ossicle because of the absence of supporting structures, flexible joints, and rotational movements (Rosowski & Merchant, 1995).

Measurements in human temporal bone specimens and modelling studies have demonstrated that the stapes displays primarily piston-like motion below 1 – 2 kHz, but motion becomes complex and involves multiple modes above this frequency (Decraemer & Khanna, 2004; Hato, Stenfelt, & Goode, 2003; Heiland, Goode, Asai, & Huber, 1999). Measurements of stapes velocity in patients with normal middle ears have shown an increased difference between the magnitude of velocity measured at the posterior crus and the head of the stapes in response to stimuli above 1 kHz (Chien et al., 2009). This increase in the relative velocities

at different points of the stapes at higher frequencies is consistent with the idea of increased movement complexity with increasing frequency, at least up to 6 kHz.

It is clear from the preceding review of the literature that the physiologic motion patterns of the ossicular chain are complex, particularly in response to high-frequency sound inputs. While the precise mechanisms of ossicular motion remain somewhat vague, the importance of these movement patterns for hearing sensitivity is even more poorly understood. Any ossicular prosthesis is likely to disrupt the normal modes of ossicular movement, and therefore could potentially affect hearing. It is plausible that given the increased complexity of ossicular motion at high-frequencies, hearing sensitivity within this higher frequency range may be more prone to disturbance when ossicular motion patterns are altered.

5.5 Summary of the influence of middle ear factors on postoperative high-frequency hearing

The function of the middle ear at higher frequencies remains poorly understood; therefore the effects of altering the physical characteristics of the system on hearing within that frequency range are also unclear. The preceding discussion highlights many factors that could potentially influence EHF hearing thresholds postoperatively, either temporarily or permanently, however the extent to which each of these factors is clinically important in explaining hearing loss is not known. It is important to note that even within the conventional frequency range some of the acoustic and biomechanical consequences of replacing the stapes or other ossicles with prostheses remain obscure, despite far more extensive research into hearing outcomes in this frequency range. It must also be noted that many of the studies discussed above have been performed on temporal bones in which the other parameters of the middle ear are normal. This is often not the case in patients undergoing middle ear surgery, particularly for chronic ear disease. It is unclear to what extent the factors that influence the efficiency of middle ear transmission may interact when more than one element is altered. It is hoped that future research will continue to elucidate the effects of changes in the middle ear anatomy on hearing across the entire range of audible frequencies. Until then, it is evident that potential middle ear transmission changes must be taken into account when evaluating the possible reasons for postoperative hearing loss, even in cases where bone-conduction thresholds are increased.

5.6 Establishing the cause of postoperative hearing loss

There are clearly many potential causes of EHF hearing loss and in many cases multiple factors may contribute to hearing deterioration following middle ear surgery. Based on air-conduction thresholds alone, it is not possible to distinguish between middle and inner ear causes of hearing loss, much less to differentiate between specific middle or inner ear factors that have resulted in hearing loss. Establishing the cause(s) of hearing loss is essential if methods are to be developed to reduce the incidence of such hearing loss.

Chapters 6, 7 and 8 describe research carried out to determine whether EHF hearing loss following middle ear surgery is of inner or middle ear origin. This issue was approached in two ways. The first was to develop a method of assessing bone-conduction thresholds above 4 kHz and use this to measure changes in inner ear function after surgery. Secondly, patients were assessed for changes in vestibular function that indicated that trauma to the inner ear had occurred. As described above, many causes of cochlear hearing loss involve trauma to the entire labyrinth and patients will present with balance dysfunction as well as hearing loss. We therefore hypothesised that evidence of postoperative vestibular disturbance in patients with EHF hearing loss would provide support for the theory that the hearing loss was the result of inner ear injury.

Distinguishing between specific causes of inner ear trauma or changes in middle ear transmission of high-frequency stimuli is beyond the scope of this thesis, however a comparison of outcomes across different types of middle ear surgery can provide some clues as to particular components of procedures or physical changes to the middle ear that are more often associated with hearing loss. These issues are discussed in greater detail in the following chapters.

PART III: ESTABLISHING THE NATURE OF HIGH-FREQUENCY POSTOPERATIVE HEARING LOSS

Chapter 6: Measurement of extended high-frequency bone-conduction thresholds

6.1 High-frequency bone-conduction transducers

Audiometric thresholds can be measured up to at least 16 kHz using air-conduction transducers; however there is no standardised transducer for assessment of the corresponding bone-conduction thresholds above 6 kHz. Consequently, diagnostic information regarding the separate functional status of the cochlea and the conductive mechanism is incomplete in the EHF range. The interpretation of changes in thresholds in terms of determining whether cochlear damage has occurred will therefore remain speculative until a reliable method for assessing cochlear function above 6 kHz is developed.

Bone-conduction transducers for routine use in EHF audiometry will need to provide sufficient output over a frequency range of at least 8 to 16 kHz to allow thresholds to be measured in most cases. Intensity levels adequate for measurement of elevated thresholds must be reached without distortion or airborne sound contaminating measurements. Ideally, this transducer will be comfortable to wear and its physical characteristics should permit reliable and stable placement on the skull. At least three technologies are available that can be used to create bone-conduction transducers that meet these requirements with varying levels of success. The mechanics, reliability, and clinical utility of these technologies are discussed in the following sections.

6.1.1 Electromagnetic bone-conduction transducers

Variable reluctance electromagnetic transducers are most commonly used in clinical audiology. These transducers consist of an armature with a permanent magnet, which is screwed to the top of a plastic casing and suspended above a yoke, with a small air-filled gap separating the two components. An electrical input signal passing through coils of wire wound around the armature generates a dynamic magnetic field that interacts with the static magnetic field of the armature to create a magnetic flux across the gap between the armature and the yoke. The vibration of the mass of the armature created by the magnetic force is propagated to the casing, thus creating the vibratory stimulus that is applied to the skull.

6.1.1.1 Radioear B-71 and B-72 transducers

Recommendations for audiometric bone-conduction vibrators from the International Electrotechnical Commission (IEC) and the American National Standards Institute (ANSI) are that the transducer should have a plane, circular contact tip with an area of 1.75 cm^2 and that it should be coupled to the mastoid process with a force of 5.4 N (IEC 373 (1971); ANSI 3.13 (1987)). Radioear (New Eagle, PA) developed two electromagnetic models that meet these specifications; the B-71 and the B-72. Both are encapsulated in a rectangular plastic casing with a circular protruding portion that is pressed against the skull with the appropriate force level by a steel sprung headband (Radioear model P-3333).

The Radioear B-71 weighs approximately 19.9 g without the headband attached and has a frequency response characterised by three resonant peaks at 0.45, 1.5, and 3.8 kHz, in order of decreasing amplitude (Richards & Frank, 1982). The frequency response curve drops off steeply below 0.25 kHz and above 4 kHz (Dirks & Kamm, 1975; Richards & Frank, 1982), severely limiting output at lower and higher frequencies. The output of the B-71 is also limited by the high levels of total harmonic distortion at low-frequencies (Arlinger, Kylen, & Hellqvist, 1978; Dirks & Kamm, 1975; Dolan & Morris, 1990; Parving & Elberling, 1982).

The poor low-frequency response of the Radioear B-71 is improved upon with the B-72 bone-vibrator, although the output in the high-frequencies is further restricted. The B-72 has an added dynamic mass, which increases its weight to 48 g and lowers the resonant peaks to approximately 0.25, 1.25, and 3.7 kHz (Dirks & Kamm, 1975; Richards & Frank, 1982). Electroacoustic advantages of the increased mass of the B-72 device are higher output levels and reduced harmonic distortion at 0.25 kHz (Dirks & Kamm, 1975). Unfortunately, the downside of the larger size is an increase in the amount of airborne sound leakage, or acoustic radiation, resulting from the vibration of the larger case at higher test frequencies (Bell, Goodsell, & Thornton, 1980; Frank & Crandell, 1986; Frank & Holmes, 1981). The high degree of acoustic radiation suggests that the B-72 is unsuitable for audiometric testing at frequencies of 2 kHz and above (Frank & Crandell, 1986; Frank & Holmes, 1981).

6.1.1.2 Präcitronic KH-70 transducer

A third electromagnetic transducer with a plane circular contact area of approximately 1.75 cm^2 is the Präcitronic KH-70 (Dresden, Germany), which is approximately 2.5 times the length and five times the weight of the B-71. The KH-70 bone vibrator has a frequency

response characterised by one major resonance at 0.2 kHz and a gradual decline in output beyond the resonant frequency up to 14 kHz, above which there is a precipitous drop in the output (Frank & Ragland, 1987; Richter & Frank, 1985). Although the dynamic range becomes more limited as the test frequency approaches 16 kHz, the frequency response of the KH-70 enables it to be used for testing bone-conduction thresholds up to and including 16 kHz (Hallmo, Sundby, & Mair, 1991; Richter & Frank, 1985). The encapsulation of the vibrator mechanism of the transducer in a rubber housing effectively reduces the levels of airborne sound leaking from the bone-conductor, ensuring high-frequency bone-conduction thresholds are not artificially enhanced by acoustic radiation (Frank & Crandell, 1986).

Despite the significant electroacoustic advantages of the KH-70 bone vibrator, its suitability for clinical use is limited by its large, heavy, and cumbersome design, which reportedly makes stable placement on the mastoid without touching the pinna or hair very difficult (Frank & Ragland, 1987; Hallmo & Mair, 1996; Mair & Hallmo, 1994). This is a particular concern when measuring hearing thresholds following middle ear surgery performed via a retroauricular approach. In these situations any bone-conductor must be placed with care to avoid disrupting the wound and causing pain; a task that can be difficult even with a B-71 bone-conduction vibrator. Hallmo and Mair (1996) also note that correct retroauricular placement of the KH-70 was particularly difficult when defects were present in the mastoid cortex postoperatively. They suggest that this issue was the cause of the change in bone-conduction thresholds documented after surgery, rather than any cochlear trauma. Certainly the inability to reliably make this distinction limits the usefulness of the transducer clinically. Despite difficulty with correct placement, evidence suggests that the test-retest reliability of thresholds measured at 0.25 – 16 kHz with the KH-70 transducer is satisfactory for clinical applications, at least with non-surgical patients (Frank & Ragland, 1987; Hallmo et al., 1991).

6.1.1.3 Balanced electromagnetic separation transducer

A recently developed bone-conduction vibrator, the new balanced electromagnetic separation transducer (BEST) offers significantly improved performance at low test-frequencies. Håkansson (2003) reported that a transducer based on the BEST principle offered a good frequency response and low distortion through a design that incorporated a second, opposing air gap to counterbalance static forces. Electroacoustic assessment of a new version of the BEST transducer adapted for serial production, the Radioear B81, confirmed that maximum

test levels can be significantly increased below 1.5 kHz using this technology, compared to the B71 (Jansson, Hakansson, Johannsen, & Tengstrand, 2014). However, the output above 4 kHz is not increased beyond that of the B-71 (Håkansson, 2003; Jansson et al., 2014), therefore it is still not possible to test thresholds in the EHF range using a BEST device.

6.1.2 Piezoelectric bone-conduction transducers

Piezoelectric transducers contain an active element consisting of a plate made of material, most commonly the ceramic lead zirconate titanate, which has piezoelectric properties. When an alternating current, such as a pure-tone, is applied to a plate made of piezoelectric material, the plate will mechanically deform, bending back and forth to create a vibratory signal that oscillates at the input frequency.

The physical dimensions and the mass of the piezoelectric plate will determine the frequency response of a given transducer. For example, given two transducers of similar mass but different lengths, the shorter of the transducers will have the higher resonant frequency (Javel, Grant, & Kroll, 2003). Transducers with low mass will also be characterised by a higher resonant frequency. The ability to construct the transducer to produce a desired frequency response offers the potential to develop bone-conduction transducers with very good output in the EHF range for audiometric testing (Chi et al., 2009).

Early studies using piezoelectric devices for bone-conduction audiometry have illustrated the capability of this technology to produce pure-tone signals at frequencies well above 8 kHz, and even up to 100 kHz (Corso, 1963; Sagalovich & Bednin, 1982). More recently, Gallichan et al. (1998) compared thresholds above 4 kHz elicited by their custom built piezoelectric bone-conduction vibrator to those measured with the Präcitronic KH-70 in normal hearing subjects. The piezoelectric device could be used to reliably measure thresholds at least up to 12 kHz and, unlike the KH-70, produced negligible acoustic radiation. Although few details regarding the transducer are provided, the data does show that piezoelectric technology is a promising area for future development in the area of bone-conduction audiometry. Unfortunately, no piezoelectric audiometric transducers are currently available commercially.

6.1.3 Electric bone-conduction audiometry

The commercially available Audimax 500 (Audimax Co., Hackensack, NJ) audiometer uses transcutaneous electrical stimulation to assess hearing thresholds from 0.5 to 20 kHz (Tonndorf & Kurman, 1984). Electric bone-conduction involves the application of a low radio-frequency signal modulated by the test stimulus to a pair of Mylar-coated electrodes. Typically, one electrode is placed on the mastoid of test ear and the other is positioned on the contralateral mastoid or the arm. The presentation of the stimulus capacitively couples the subject to the electrical circuit and the electrical forces induce vibration of the tissues in the head. These vibrations are thought to be perceived as sound in a similar manner to conventional bone-conduction stimuli (Tonndorf & Kurman, 1984).

Evidence regarding whether electric bone-conduction does indeed stimulate the cochlea in the same manner as conventional vibromechanical bone-conduction testing has been somewhat mixed. In support of the view that electric bone-conduction produces electromechnical stimulation of the cochlea, it has been demonstrated that it is possible to mask the electric signal using airborne noise to produce monaural thresholds at 0.5 – 14 kHz (Löppönen, 1992; Tonndorf & Kurman, 1984). The phenomenon of binaural summation that is known to occur with traditional bone-conduction measurements was also demonstrated with electric bone-conduction by Löppönen (1992). Further objective evidence of a true bone-conduction effect associated with electric signals was provided by Löppönen, Laitakari, and Sorri (1991), who showed that electric bone-conduction signals produced measureable skull vibrations at the precise frequency of the test signal from 0.5 to 20 kHz.

Contrary to vibromechnical bone-conduction and classical theories of bone-conduction hearing (Tonndorf, 1976), signals in the EHF range presented by electric bone-conduction have been found to lateralise to the side of an occluded EAC (Økstad et al., 1988; Tonndorf & Kurman, 1984), suggesting that the modes of cochlear stimulation for electric and conventional vibromechnical bone-conduction may not be identical (Löppönen, Laitakari, et al., 1991; Löppönen & Sorri, 1991; Økstad et al., 1988). Further doubts have been raised by the different configurations of air-conduction and electric bone-conduction signals, with thresholds for electric signals consistently being recorded at lower levels than those for air-conduction above 8 kHz, and at higher levels below 8 kHz (Økstad et al., 1988). It has been suggested that electric bone-conduction stimulation may not be confined to classical bone-conduction pathways, but may involve an additional electrical component (Löppönen,

Laitakari, et al., 1991; Löppönen & Sorri, 1991; Löppönen, Sorri, & Bloigu, 1991; Økstad et al., 1988; Thornton, Bell, & Phillipps, 1989). The relative influence of each pathway may change depending on the test frequency (Löppönen & Sorri, 1991; Økstad et al., 1988).

Differences in threshold changes documented pre- and post-stapes surgery also suggest the electric and vibromechanical methods of bone-conduction testing may not be stimulating the cochlea in exactly the same manner. Following successful stapes surgery, the external and middle ear contributions to bone-conduction hearing are often restored, and an improvement in bone-conduction thresholds at 2 kHz and below will be documented (Linstrom et al., 2001). When thresholds at 0.5 – 8 kHz were measured in 28 patients before and after stapes surgery using both conventional and electric bone-conduction, Laitakari and Lopponen (1994) found that the Carhart effect was present with conventional bone-conduction measures, but absent in electric bone-conduction thresholds. This suggests that auditory sensations evoked by electrostimulation may not include the middle ear contribution present when a vibromechanical transducer is used. However, in a larger study of 138 patients using the same methodology, Löppönen and Laitakari (2001) found that both traditional and electric bone-conduction mean thresholds showed a similar degree of improvement at 1 and 2 kHz after stapes surgery. Whether the mode of cochlear stimulation varies between the two bone-conduction test methods therefore remains unknown.

Test-retest reliability of electric bone-conduction thresholds has been consistently found to be very good and variance is comparable with that obtained with conventional audiometry (Löppönen & Sorri, 1991; Økstad et al., 1988; Thornton et al., 1989). The restrictions on the routine clinical use of electric bone-conduction therefore are not related to the reliability of the method, but uncertainties regarding exactly what is being tested, and the practicalities of using electrodes and a speciality audiometer to test thresholds.

6.1.4 Magnetostrictive bone-conduction transducers

Bone-conduction transducers can also be designed based on the concept of magnetostriction; a process by which a flat plate made of a material with magnetostrictive properties will change shape in the presence of a magnetic field created by an electrical current. Ferromagnetic materials such as nickel, iron, cobalt, and particularly alloys combining iron, terbium, and dysprosium, have varying levels of magnetostrictive properties and can be employed in the production of transducers. In the context of a bone-conduction transducer, a

coil around the flat plate generates a magnetic field when a current is applied that causes the magnetostrictive material to expand and then, when the magnetic field is removed, to contract. Therefore, when an alternating current is applied to the transducer, the rotation of magnetic domains will cause internal strains in the material and the plate will bend back and forth at the frequency of the input, providing an output that can be used for bone-conduction stimulation. As a magnetostrictive transducer can be designed with a low mass, the output can potentially be adequate to allow testing of EHF audiometric bone-conduction thresholds.

6.1.4.1 Experimental magnetostrictive transducers

The use of magnetostrictive technology in a transducer designed to measure audiometric bone-conduction thresholds was first described by Khanna et al. (1976). Using a rod of nickel as the vibrating element with an aluminium disk positioned on the forehead of the listeners, it was demonstrated that the magnetostrictive drive system could be used to produce low-level output from 5 Hz to over 20 kHz. The transducer created by Khanna et al. was designed to have a relatively low resonant frequency of 2.5 kHz which, for nickel, meant the required length of the rod was 110 cm. From a clinical perspective such a large transducer is not at all practical for routine use, although it does demonstrate the wide frequency range of outputs that could be produced using magnetostrictive technology.

An experimental magnetostrictive transducer of a much more practical size was developed and assessed using a rat model by Sakai, Karino, and Kaga (2006). Measurements of the vibratory velocity of the skull performed using laser Doppler vibrometry showed that the output of the magnetostrictive transducer was linear, had minimal harmonic distortion, and was of clinically useable amplitude from 2 to 30 kHz. A comparison to the skull vibratory velocity recorded with stimulation from an electromagnetic Oticon 10452 bone-conductor showed that the high-frequency output of the experimental transducer was far greater than that of the electromagnetic transducer. Bone-conduction auditory brainstem response (ABR) waveforms measured in the rats with the two transducer types were found to be clearer with the magnetostrictive device, and the maximum output level extended above the ABR thresholds in all rats by at least 50 – 60 dB. Although these results are certainly positive in terms of describing the capabilities of a magnetostrictive transducer, data collected with this device in humans is not available, nor is the transducer available commercially.

6.1.4.2 TEAC Filltune HP-F100 and HP-F200 transducers

TEAC has produced two commercially available magnetostrictive bone conduction transducers; the HP-F100 and HP-F200, both of which are intended to be used as headphones for listening to music. Laboratory studies and tests on human listeners evaluating the suitability of the HP-F100 device for use in bone-conduction audiometry by Popelka, Telukuntla, and Puria (2010) suggest that the transducer may also be used to measure hearing thresholds in the EHF range. In their measurements of the vibratory output of the HP-F100 using an auditory research manikin and a laser Doppler vibrometer, Popelka et al. found that the output of the transducer was linear across voltage input levels from -19.5 dB re 1 V p (110 mV p) to -40.5 dB re 1 V p (9.4 mV p). The primary resonant peak was found at approximately 7 kHz, and the output decreased smoothly at a rate of at least 30 dB per octave above this peak, with considerable vibratory output remaining at least up to 16 kHz. Harmonic distortion was less than 3%, and therefore acceptable based on the ANSI standard for audiological transducers (ANSI 3.13 1987).

The contact surface of the TEAC HP-F100 transducer varies markedly from that of the Radioear B-71 bone-vibrator, and is slightly convex, with a diameter of 2.35 cm and an area of approximately 4.34 cm^2. As these physical properties of the TEAC transducer mean that it cannot be calibrated using a standard artificial mastoid, Popelka et al. (2010) estimated the level of 0 dB HL based on threshold measurements in five normal hearing subjects. Measurements of audiometric thresholds at 8 – 16 kHz using the TEAC bone-conduction device and a GSI-61 audiometer were then performed on nine subjects with no conductive pathology, and were compared to air-conduction thresholds recorded in the same frequency range using Sennheiser HDA 200 headphones. The shape of threshold curves recorded with the two transducers corresponded closely, although increased variation across subjects in the size of air-bone gaps was documented above 6 kHz (*SD* = 6.7 dB HL) compared to that for measurements at 6 kHz and below (*SD* = 3.6 dB HL). This slightly increased variability in the EHF range was judged by Popelka et al. to be clinically acceptable.

As noted in relation to electromagnetic bone-conduction vibrators, acoustic radiation directly emitted from the body of the transducer can artificially improve bone-conduction thresholds if it can be detected via the air-conduction pathway. Measurements made using a microphone positioned approximately 1 cm from the entrance to the EAC while the transducer was worn on the zygomatic process indicated that the level of acoustic energy radiating directly from the TEAC transducer was not sufficient to contaminate the bone-conduction threshold

measurement (Popelka et al., 2010). There was no difference in thresholds at 8 – 16 kHz for any of the three subjects depending on whether the radiated sound was allowed to enter the uncovered canal, or whether it was blocked from entering by a circumaural headphone positioned over the pinna, further suggesting that direct acoustic radiation did not significantly influence bone-conduction thresholds. Popelka et al. (2010) reported that blocking the ear canals of two subjects with foam plugs to prevent acoustic radiation from soft tissue vibration also failed to significantly alter bone-conduction thresholds at 8 – 16 kHz compared to the unoccluded state. In sum, Popelka et al.'s assessments of the contribution of non-bone conduction pathways on thresholds measured with the TEAC device is minimal.

Overall, Popelka et al.'s (2010) publication of preliminary data on the TEAC bone-conduction transducer suggest that this magnetostrictive device is capable of generating pure-tone stimuli at least at 8 – 16 kHz that are adequate for accurately measuring audiometric bone-conduction thresholds in this frequency range. An assessment of this transducer in cases of conductive hearing loss is not available in the extant literature; however Popelka et al.'s results do appear to represent an important step towards accurately differentiating between sensorineural and conductive hearing losses in the EHF range.

Based on reports in the literature of the availability of devices, ease of use, and physical dimensions that are appropriate for use on an ear that has recently been operated on, the TEAC magnetostrictive devices seem most appropriate for repeated measures of the high-frequency sensorineural reserve pre- and post-middle ear surgery. There are, however, several characteristics of the TEAC device that do vary from the Radioear devices that meet the ANSI (2010) standards for audiometric testing, and the clinical impact of these will be considered here.

6.2 Modification of the TEAC transducer for use in audiometric testing

6.2.1 Physical characteristics of the TEAC HP-F100 bone-conduction transducer

Given the intended purpose of the TEAC Filltune HP-F100 bone-conduction headphones as a consumer product for listening to music, they are designed to provide bilateral stimulation, with the two transducers separated by a plastic headband (as shown in Figure 36a). The headphones employ a specific amplifier (Figure 36b) powered by three AAA batteries with an external input. This is in contrast to the passive B-71, which is designed to be connected directly to an audiometer. The key difference and thus the concern regarding the physical

properties of the HP-F100 transducer is the way in which the large, convex, contact surface affects the reliability and sensitivity with which audiometric thresholds can be measured using the device.

Figure 36. a. the TEAC HP-F100 transducer shown in its original condition with two earphones connected by a plastic headband, and b. the separate battery-operated amplifier that powers the TEAC transducer.

The static coupling pressure of a bone-conduction vibrator to the skull is defined as the force per unit area, therefore the area of contact between the transducer and the skull will, together with the coupling force, determine the effectiveness of stimulus transmission. Increases in the size of the contact surface of a bone-conduction vibrator have minimal effect on thresholds below 2 kHz, but result in a significant decrease in bone conduction thresholds at 2 kHz and above (Nilo, 1968; Watson, 1938). The potential to increase the dynamic range of the transducer at high-frequencies by using larger contact areas must be balanced against the poorer measurement reliability associated with larger surfaces (Goodhill & Holcomb, 1955). The increased variability in stimulation levels associated with a larger surface area is likely a result of greater difficulty in placing the contact area in the precise same location, as the surface in contact with the head may vary with transducer placement due to the curvature of the skull (Henry & Letowski, 2007). Certainly, the potential for increased measurement variability with the relatively large surface area of the TEAC transducer is of some concern and the issue of skull placement and reliability is considered in detail in Section 6.4.

The application force of a bone-conduction vibrator must be sufficient to overcome the damping effects of the skin on the vibratory signal in order to effectively and reliably stimulate the cochlea. According to von Békésy (1960), for a vibrator with a contact surface of 0.5 cm^2, transmission of vibration through the skin without excessive loss of the signal can be achieved using an application force of 2.5 N. Other groups have reported acceptable transducer performance with similar static force levels of 1.9 N (Harris, Haines, & Myers, 1953; Watson, 1938), and 2.9 N (Goodhill & Holcomb, 1955). The application force provided by the plastic headband of the TEAC transducer is much less than that provided by a standard clinical bone-conductor and does not appear to provide the same consistency in static coupling force across different head sizes. To address this concern and ensure sensitive and reliable measurements could be obtained using the TEAC HP-F100 device, we modified the headset to optimise the transducer set-up for audiometric use. These modifications are detailed below.

6.2.2 Modifications made to the TEAC transducer to enable use in audiometry

Based on the approach taken by Popelka et al. (2010), we attached the TEAC transducer to a Radioear P-3333 headband to ensure that a consistent, adequate, static coupling force could be achieved. This headband is made of chrome plated sprung steel and is designed to bring the transducer in contact with the skull with a specific and consistent force. Used with a B-71 vibrator, the P-3333 headband ensures that stimulation is delivered at a force of approximately 5.4 N. The P-3333 headband has a plastic handle with foam padding on the flat surface at one end, and a steel yoke into which the transducer is designed to clip into. As the TEAC transducer is not designed to fit into the yoke, the headband was modified by removing the yoke and attaching the 6 cm long steel bracket that originally connected the TEAC headphone to its plastic headband directly to the curved steel of the P-3333 headband. The two pieces of steel were attached using three small brass screws, as illustrated below in Figure 37. One screw fastened the transducer bracket to the headband at the end closest to the headphone and two small metal plates connected by two screws held the two steel structures together at the top of the transducer bracket.

Following informal trials, it was decided that with the bracket attached to the headband in the manner described, the angle at which contact surface of the transducer met the skull was not sufficiently controlled. To address this concern, a 12 mm brass screw was inserted through

the plastic casing at the top of the earphone to rest against the steel bracket (Figure 37b). When the headband and transducer were placed on the head, the screw rested against the bracket ensuring that the contact surface was always at the same angle relative to the head.

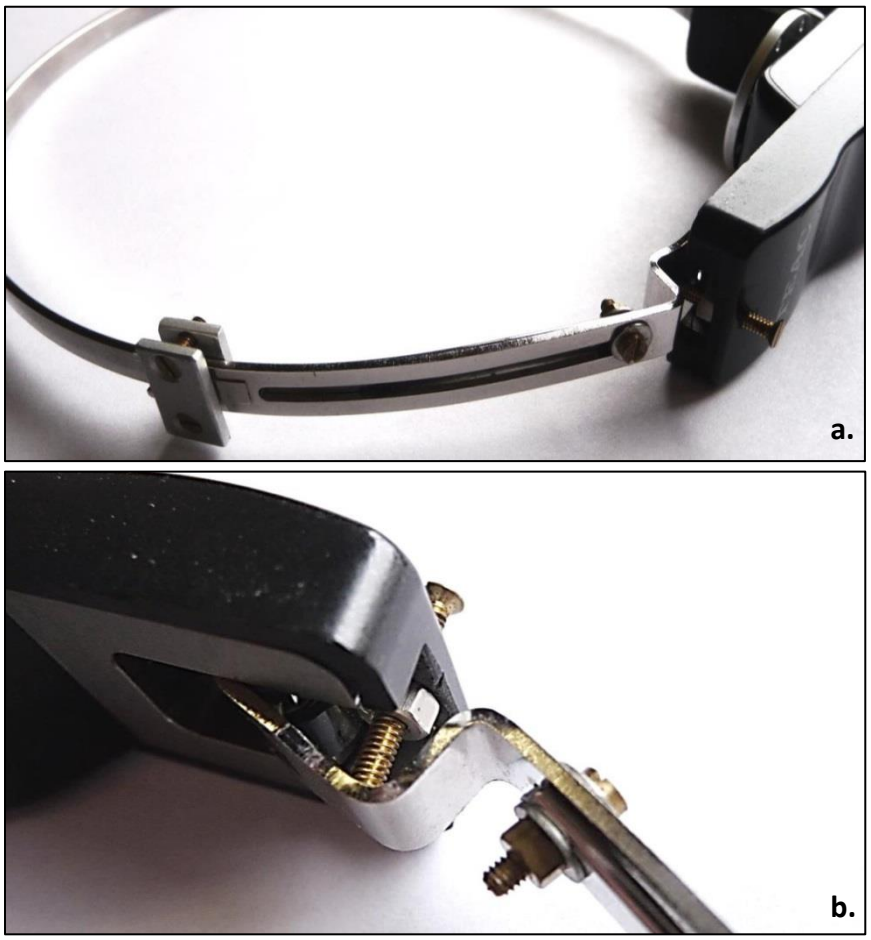

Figure 37. a). The attachment of the P-3333 headband to the TEAC transducer using the bracket of the TEAC transducer, two small metal plates joined by two screws and a third screw at the distal end of the headband. b). shows a close-up view of the screw inserted through the top of the transducer casing to consistently hold the transducer at the correct angle against the head.

Although the static coupling force between the transducer and the skull was not measured directly, we considered that the force was adequate based on assessments of test-retest reliability measures and the ability to obtain thresholds across the EHF range across the majority of listeners assessed with normal hearing or EHF hearing loss. These assessments are described later in this chapter.

With the original headband and both vibrators, the headset weighs 120 grams (g). With the P-3333 headband and a single vibrator, as was used for testing in this study, the transducer weighed 70 g. The separate amplifier added an additional 95 g in weight, however this was placed on a desk next to the listener.

The body of the TEAC transducer is larger than that of the B-71 and is 65 mm in length and 29 mm in width. The dimensions of the transducer attached to the P-3333 headband in its final modified form are shown in Figure 38.

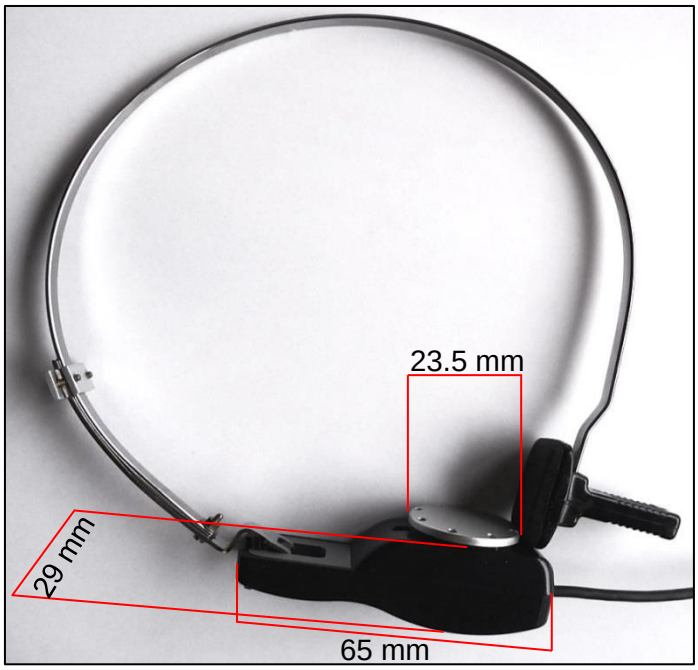

Figure 38. Final transducer and headband set-up showing dimensions of the transducer.

The battery-powered amplifier connected to the TEAC transducer has a rotary dial that controls the output of the bone-vibrator. In this study it was necessary to control the stimulus level using an audiometer to ensure consistency of presentation levels. The dial on the amplifier was therefore fixed using tape to ensure the output was not altered unintentionally. The setting selected was chosen subjectively as the level that provided the maximum volume with no audible distortion at any test frequency.

6.3 Development of a protocol for EHF bone-conduction audiometry

The measurement of reliable auditory thresholds depends on many factors beyond the electroacoustic properties of the transducer. The absolute thresholds recorded will be influenced by test parameters, such as the location at which the transducer is placed on the skull, the force with which it is coupled to the head, the level of ambient noise during testing, and the masking protocol used. Valid threshold measurement also depends on the device being correctly calibrated to ensure that measurements are consistent across a population of listeners and are repeatable when recorded on more than one occasion in the same listener. Based on a review of the literature, practical considerations, and testing on otologically healthy subjects, protocols were developed that we believe are optimal for the purposes of recording reliable, ear-specific bone-conduction thresholds using the TEAC HP-F100 transducer. Once these protocols were established, adult volunteers were tested to obtain the values required to calibrate the device in dB HL and to determine the test-retest reliability associated with thresholds measured with the TEAC transducer. The investigations discussed in the following sections were designed to confirm that the HP-F100 transducer, when used with the testing and calibration protocols developed, could be used to provide a valid and reliable measure of EHF bone-conduction hearing acuity.

6.4 The position of the transducer on the head

The TEAC HP-F100 bone-conduction headphones were designed to be applied to the zygomatic process in front of the external ear, rather than primary locations used for bone-conduction audiometry; the mastoid process or forehead. Given the complexity of vibration patterns of the human skull and the multiple mechanisms that contribute to bone-conduction hearing, the location at which a bone-conduction vibrator is positioned can affect the level at which the stimulus is delivered to the cochlea (Dirks, 1964; Hart & Naunton, 1961; Studebaker, 1962b). Experimental investigations of the effects of bone-vibrator position on audiometric thresholds have focused primarily on the forehead and mastoid locations, although vertex placement has also be suggested (Hood, 1957; Studebaker, 1962b).

Advantages of placing the bone-conduction vibrator in the centre of the forehead are afforded by the relatively flat shape and uniform thickness of the bone, skin, and tissue across listeners in this location compared to the mastoid. The more homogenous surface of the forehead provides some degree of tolerance for changes of up to 4 cm in the precise position of the

transducer (Dirks, 1964; Studebaker, 1962b). In contrast, small changes in the position of the bone-conductor on the mastoid can significantly alter the level of the signal reaching the cochlea (Weston, Gengel, & Hirsh, 1967). Test-retest reliability has been shown to be higher and intersubject variability lower for forehead placement than for mastoid placement of the bone-conductor, consistent with the reduced dependence on specific placement with the forehead position (Hart & Naunton, 1961; Studebaker, 1962b; Weston et al., 1967).

The key advantage of positioning a bone-vibrator on the mastoid rather than the forehead is that the force levels required to reach threshold at the mastoid are lower, therefore the dynamic range is increased (Dirks, Malmquist, & Bower, 1968; Frank, 1982; McBride, Letowski, & Tran, 2008; Richter & Brinkmann, 1981; Weston et al., 1967). The higher sensitivity to bone-conduction stimulation at the side of the head (the mastoid) compared to stimulation at the midline (the forehead) has been attributed to the differential activation of the middle ear inertial component of bone-conduction by the different locations of the bone-conductor. When vibratory stimulation is in the same axis as the inertial movement of the ossicles, as it is with mastoid bone-conductor placement, the contribution of the middle ear to the threshold will be greater than when stimulation is applied perpendicularly to the ossicular motion (Bárány, 1938; Dirks & Malmquist, 1969; Studebaker, 1962b). The result is lower thresholds when the vibrator is placed on the mastoid, but also a greater effect of middle ear pathology on thresholds (Dirks & Malmquist, 1969; Studebaker, 1962b). The validity of bone-conduction audiometry as a measure of the cochlear reserve is therefore considered to be better with the forehead position (Studebaker, 1962b).

Vibratory stimulation delivered to the skull will, in general, produce a lower threshold when it is positioned closer to the cochlea (Eeg-Olofsson, Stenfelt, Tjellstrom, & Granstrom, 2008; Stenfelt, Hakansson, & Tjellstrom, 2000). Despite this, the attenuation provided by the skull is low and a bone-conduction vibrator positioned anywhere on the skull could potentially be used to stimulate an auditory response. McBride et al. (2008) published a comprehensive study comparing thresholds for pure-tone stimuli from 0.25 to 8 kHz presented via an Oticon A20 bone-vibrator positioned at 11 different skull locations. Mean thresholds across 14 normal hearing listeners were lowest when the vibrator was positioned on the condyle (the closest position to the zygomatic process), followed by the jaw angle, mastoid, then vertex. A concern with transducer positions such as the condyle and zygomatic process is that as they are close to the entrance to the EAC, sound leaking from the vibrator could produce an auditory stimulation predominantly via air-conduction. However, McBride et al. found no

significant interaction between transducer position and the presence or absence of white noise, suggesting that direct acoustic radiation did not substantially affect thresholds. The authors conclude that the thresholds measured at any of the skull locations tested can be considered as true bone-conduction data.

Recent evidence suggests the presence of an additional, non-osseous or soft tissue mode of auditory stimulation. Auditory responses, either behavioural or electrophysiological, have been evoked using a standard bone-conduction vibrator applied to various soft tissue sites on the head, neck, and thorax (Adelman, Fraenkel, Kriksunov, & Sohmer, 2012; Adelman & Sohmer, 2013; Ito et al., 2011; Kaufmann, Adelman, & Sohmer, 2012; Sohmer, Freeman, Geal-Dor, Adelman, & Savion, 2000; Watanabe, Bertoli, & Probst, 2008). The mechanism by which vibration applied to soft tissues stimulates the cochlea is not well understood, however it appears that cochlear stimulation is produced without activating classical bone-conduction mechanisms (Kaufmann et al., 2012). Even the so-called osseous sites for positioning a bone-conduction transducer are covered by skin and soft tissue that may be involved in the transmission of vibration to the cochlea. We have noted that the zygomatic process, on which the TEAC transducer is designed to be positioned, is variable across individuals in the thickness of soft tissue coverage and generally has a thicker layer of soft tissue than the mastoid. Based on previous findings of thresholds at sites with increased soft tissue (Adelman et al., 2012), we would expect that thresholds may be higher with the transducer at this site.

The physical properties of the TEAC bone-conduction transducer with its larger, convex contact surface area, and heavier body than the Radioear B-71 bone-vibrator may affect the susceptibility of threshold measurements to slight differences in transducer placement between test sessions. Popelka et al. (2010) concluded that the threshold variability they recorded with the TEAC device on the zygomatic process was small enough that it would not prohibit clinical interpretation of audiometric data. In order to confirm Popelka et al.'s conclusion and to determine whether the zygomatic process was the most appropriate position to place the bone-conductor, we assessed the variability associated with the TEAC transducer for repeated measures made at three different positions on the skull; the forehead, mastoid, and zygomatic process. It was hypothesised that the forehead would provide the best test-retest reliability, with the lowest thresholds recorded at the mastoid.

6.4.1 Method

6.4.1.1 Participants

Five postgraduate students at the University of Canterbury volunteered to participate in this study. All reported no significant history of otologic disease. Participants ranged in age from 23 to 39 years (M = 31.8 years, SD = 6.5) and the group included four females and one male. To meet the inclusion criteria for this study all participants were required to have measureable bone-conduction thresholds from 0.25 to 16 kHz, however no restrictions were placed on the threshold level at any frequency. It was required that participants had no asymmetry of EHF air-conduction thresholds, defined as no difference in thresholds between the left and right ear of greater than 10 dB HL at two or more frequencies. Informed written consent (see Appendix A) was obtained from all subjects prior to their participation, in accordance with ethical approval granted by the University of Canterbury Human Ethics Committee (ref: HEC 2014/127).

6.4.1.2 Equipment

Pure-tone audiometry was carried out with the participant seated in a sound treated booth at the University of Canterbury, which fulfilled the criteria of ISO 8253-1 (2010). Bone-conduction stimuli were presented via TEAC HP-F100 bone-conduction headphones (TEAC, Tokyo, Japan) that had been modified for use in audiometric testing, as described in section 6.2. Sennheiser HDA 200 headphones (Sennheiser electronic GmbH & Co., Wennebostel, Germany) were used to present air-conduction stimuli. A GSI 61 diagnostic audiometer (Grason-Stadler, Eden Prairie, MN), calibrated only for the HDA headphones, was used for generation of continuous pure-tone stimuli at 1/6th octave frequencies from 8 to 16 kHz.

6.4.1.3 Procedure

Prior to audiometric testing, both ears of each participant were examined otoscopically to rule out occlusion of the EACs or abnormalities of the TM that would suggest the presence of a conductive-mechanism pathology. Subjects first underwent air-conduction threshold testing in the EHF range using the GSI 61 audiometer and Sennheiser HDA 200 headphones. The purpose of assessing air-conduction thresholds was to check that hearing was measureable within the limits of the audiometer at all test frequencies.

Both air- and bone-conduction thresholds were measured at frequencies in 1/6th octave steps from 8 to 16 kHz. Threshold seeking was performed in 5 dB steps using the modified Hughson-Westlake technique. Air-conduction thresholds were measured in both ears and for bone-conduction measurements the test ear was selected at random. All measurements were unmasked and bone-conduction thresholds were measured with both ears unoccluded.

Bone-conduction thresholds were measured at three skull locations: the mastoid process, the zygomatic process, and the forehead. The mastoid and zygomatic processes were identified as the most prominent point of the mastoid bone behind the test ear, and of the zygomatic bone in front of the test ear, respectively. Care was taken to ensure that the transducer was not touching the pinna or the hair. The forehead location was defined as the midline of the forehead as close to the centre as could be obtained while maintaining stable transducer placement. In all cases the tester positioned the transducer at the test location just prior to threshold measurement. Thresholds were measured three times at each skull location for each subject, with removal and replacement of the transducer between each set of measurements. The order in which locations were tested was counterbalanced across participants.

Participants were instructed that they would hear a series of tones that could be perceived in either ear and were asked to press the response button whenever they heard the tone, even if the tone was very faint.

6.4.1.4 Data analysis

The mean and standard deviation of the three threshold measurements were calculated at each frequency and skull location for individual participants and as group averages across all subjects. How the variance across repeated threshold measurements differed across sites was the primary parameter of interest. For individual participants standard deviations of 10 dB or greater across the three measurements at any frequency were considered unacceptable. This criterion was based on published data demonstrating that air- and bone-conduction thresholds measured with standard transducers in the conventional range are associated with test-retest variability of plus or minus 10 dB HL (Lemkens et al., 2002). The rate of unacceptable variances was calculated as a percentage of all standard deviation calculations across all subjects. The effect of frequency and position on mean thresholds and standard deviations was assessed using two-way repeated measures ANOVAs with pairwise comparisons. Analyses were performed using IBM SPSS version 21 (SPSS IBM, Armonk, NY).

6.4.2 Results

As is shown in Figure 39, the standard deviation of the three measurements reached the 10 dB criteria for unacceptability in two of the 35 sets of data assessed. Both of these high standard deviations were calculated as 10.41 dB and both occurred for measurements made with the transducer positioned on the zygomatic process in response to 12.5 kHz stimuli. When the number of measurement sets reaching the unacceptable criteria were calculated as a percentage of individual measurement sets at each locations, standard deviations were unacceptable at the zygomatic location in 5.7% of sets. No standard deviations of repeated measurement sets were unacceptable at any frequency for any individual subject at the mastoid and forehead locations.

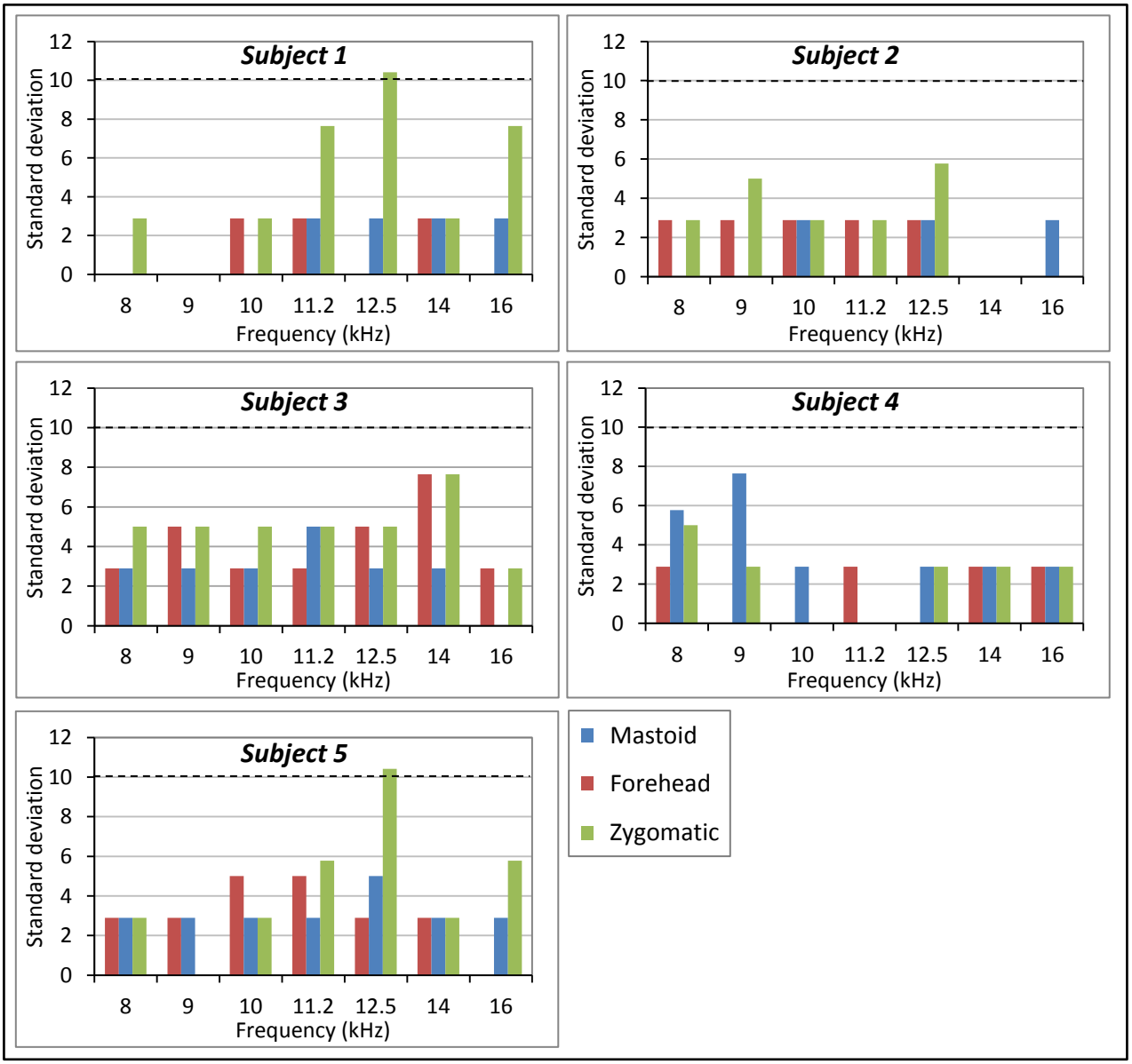

Figure 39. Standard deviation of the three measurements at each location for each subject. The dashed line indicates the standard deviation above which variance was considered to be unacceptable.

Overall, the standard deviations averaged across the five participants (Figure 40), showed that the largest variation across measurements was measured for four of the seven frequencies at the zygomatic process position (8, 11.2, 12.5, and 16 kHz), at one frequency for the forehead position (9 kHz), and was equally largest for both the mastoid and zygomatic process at 10 and 14 kHz. The largest group mean standard deviation noted was 6.90 dB for measurements at 12.5 kHz in the zygomatic location. A two-way repeated measures ANOVA showed no significant effect of position ($F(2, 6) = 2.54$, $p = .16$) or frequency ($F(6, 18) = 5.18$, $p = .58$) on the standard deviation of repeated measurements. There was also no significant interaction evident between position and frequency ($F(12, 36) = 1.83$, $p = .08$).

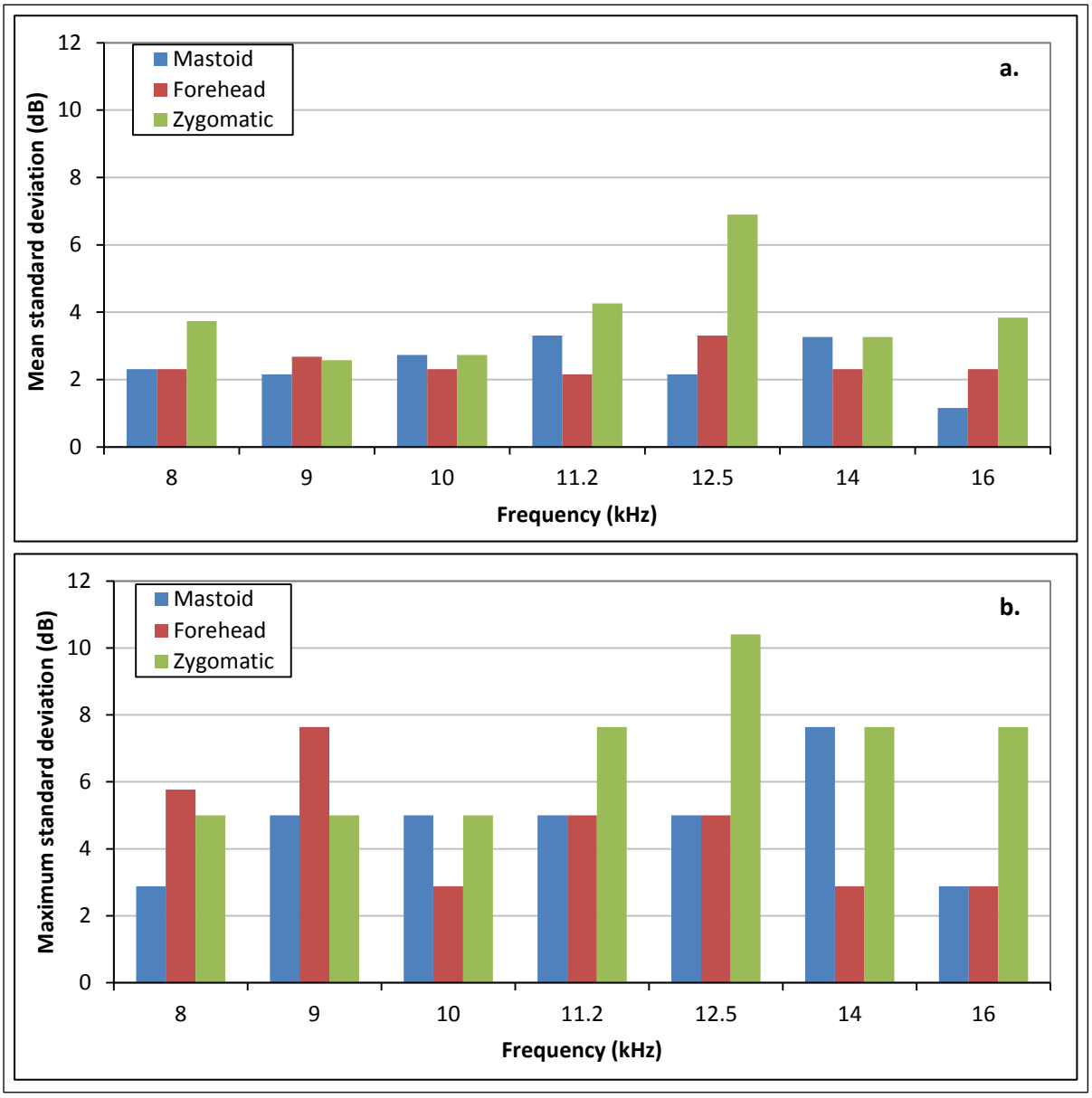

Figure 40. Mean (a) and maximum (b) standard deviations of repeated threshold measurements across subjects for each frequency and transducer position.

Mean thresholds for the three skull locations are shown for each of the five participants in Figure 41. A two-way repeated measures ANOVA examining the effects of frequency and transducer position on mean thresholds showed a significant effect of transducer position on mean threshold ($F(2, 8) = 18.96$, $p = .001$). Estimated marginal means were calculated as 24.62 dB for the mastoid position (standard error *(SE)* = 5.26), 29.95 dB (*SE* = 5.47) for the forehead, and 26.62 dB (*SE* = 5.38) at the zygomatic process. Pairwise comparisons of these marginal means performed using Bonferroni adjustments for multiple comparisons showed that the mean threshold at the mastoid was significantly lower than for the forehead and zygomatic positions ($p = .014$ and .012, respectively). There was no significant difference between mean thresholds for the forehead and zygomatic positions ($p = 1.00$). No significant effect of frequency ($F(6, 24) = 2.03$, $p = .10$) on mean threshold was found, nor was there any evidence of a significant interaction between transducer position and frequency ($F(12, 48) = 1.74$, $p = .09$).

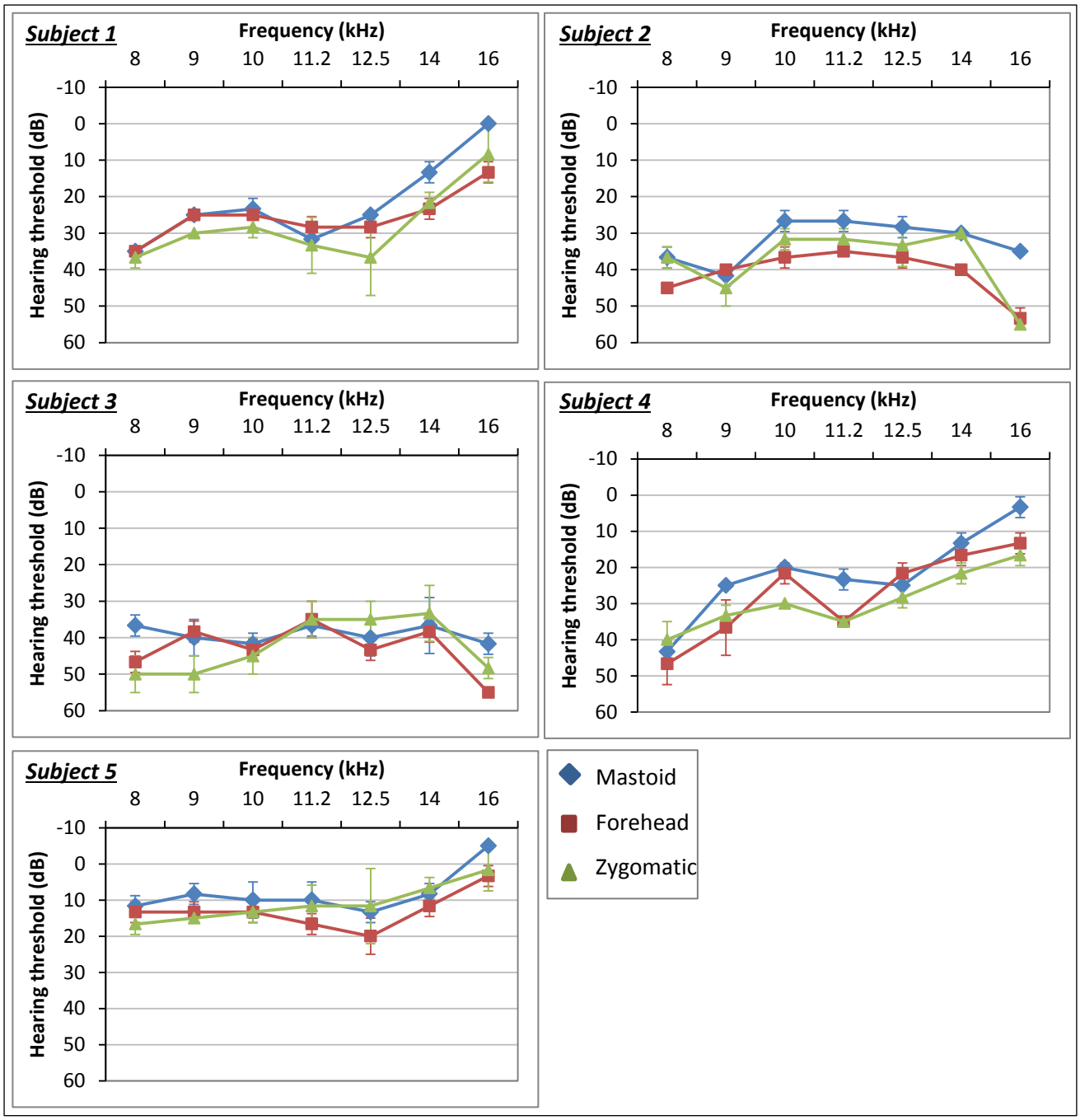

Figure 41. Mean hearing threshold of the three measurements at each location for each subject. Error bars show the standard deviation of the repeated measurements.

6.4.3 Discussion

Overall, the results of this study indicate that in our small group of subjects, intrasubject reliability of repeated threshold measurements made with the TEAC transducer positioned on the zygomatic process were less reliable than measurements made with the transducer on the forehead and mastoid. No significant difference was noted between the variability of measurements made from the forehead and the mastoid. Although the absence of a difference in test-retest variability between the mastoid and forehead positions is in contradiction to previous studies showing intrasubject reliability is superior for the forehead placement (Hart & Naunton, 1961; Studebaker, 1962b; Weston et al., 1967), it is probable that our small sample size and use of a single test session reduced the likelihood of any small differences between the two positions being detected.

The purpose of this study was to identify any significant contraindications, in particular difficulties in obtaining stable transducer placement, or markedly poorer test-retest reliability associated with any of the skull locations. Minor differences in variability between sites were therefore less of a concern. Although the sample size very small, sufficient data was collected to allow us to quickly identify that the zygomatic process placement of the bone-conductor did not provide adequate test-retest reliability according to our 10 dB criterion. This 10 dB criterion was selected to ensure that the test-retest variability associated with the TEAC transducer was not higher than that associated with standard audiometric transducers used for bone-conduction testing (Lemkens et al., 2002).

Given that our overall aim in developing this method of assessing EHF bone-conduction thresholds was to compare repeated measures in individual subjects across time, test-retest reliability was of primary importance. The other parameter of interest was the sensitivity of each location for bone-conductor placement for threshold measurements. The dynamic range for testing and the maximum threshold that can be measured will be determined by the force level required to reach threshold. If greater force is required at threshold, the maximum level that can be tested before the limits of the audiometer and/or transducer are reached will be reduced. It was therefore critical that the site did not present a significant disadvantage in terms of the maximum threshold that could be tested. We found that overall mean thresholds were significantly lower when measured with the transducer positioned at the mastoid than when measured at the forehead or the zygomatic process. This finding is in agreement with previous studies that have found that positioning a bone-vibrator on the mastoid rather than the forehead requires that lower force levels are needed to reach threshold (Dirks et al., 1968;

Frank, 1982; McBride et al., 2008; Richter & Brinkmann, 1981; Weston et al., 1967). Although this effect was statistically significant when the mean threshold across frequencies was considered, we did not consider that the mean difference of approximately 5 dB between positions warranted that precedence be given to this factor over other, more practical, concerns when considering the optimal transducer placement.

Once the zygomatic process was eliminated based on the test-retest reliability data, the remaining two acceptable options for transducer placement were the forehead and mastoid. Other considerations for selecting the bone-conductor position were that it could be reliably placed without patient discomfort even when a wound was present postoperatively. Following consultation with the surgeon performing the majority of surgical procedures for patients recruited into this study, it was decided that, for the purposes of this study, the forehead placement was preferable in postoperative patients who had undergone surgery via a retroauricular approach given the larger size of the TEAC transducer compared to the B-71. We were also mindful of Hallmo and Mair (1996) paper in which it was noted that defects in the mastoid cortex postoperatively appeared to compromise transmission of bone-conduction stimuli to the cochlea. The forehead position eliminated these concerns with little loss of sensitivity. The preliminary data presented here does, however, indicate that the mastoid could be an appropriate location to position the transducer in non-surgical patients.

Following selection of the forehead site for EHF bone-conduction measurements a more detailed study on the test-retest reliability of the transducer in this position was performed in order to calculate the threshold shift that would be considered a significant change when comparing bone-conduction thresholds measured pre- and postoperatively and across postoperative assessments. This was conducted concurrently with the collection of calibration data and is described in Section 6.6.

6.5 Masking of extended high-frequency bone-conduction thresholds

The application on appropriate masking to the non-test ear when performing bone-conduction audiometry is vital as the minimum IAA for bone-conducted stimuli, at least in the conventional frequency range, is negligible, and for clinical purposes is assumed to be 0 dB HL (Hood, 1957). This implies that the threshold for an unmasked bone-conducted stimulus could represent the response of either cochlea, or a binaural response from both cochleae, regardless of the position of the transducer.

We are aware of only one study assessing IAA values for bone-conduction testing above 6 kHz. Hallmo, Sundby, and Mair (1992) determined the IAA associated with signals from 0.25 to 16 kHz presented via a Präcitronic KH-70 by measuring thresholds with the transducer placed on the mastoid of the hearing and then the deaf ears of 22 unilaterally anacusic subjects. For all frequencies tested, minimum IAA values were between -15 and 5 dB HL, therefore the conservative assumption of 0 dB HL minimum IAA used to determine when masking is required in the conventional frequency range also seems to be valid for the EHF range. It is therefore essential that masking noise is always applied to the contralateral ear.

Based on a review of the literature, a masking protocol was developed for use in EHF testing with the TEAC HP-F100 bone-conduction transducer, Sennheiser HDA 200 headphones, and a custom audiometer with an external multi-channel soundcard. These protocols are described in the following sections.

6.5.1 Generation and calibration of narrowband masking noise

Masked EHF bone-conduction testing was performed using a computer-based audiometer comprised of a laptop (HP Compaq nw9440 laptop, Hewlett Packard, Palo Alto, CA) running custom software (written in LabVIEW 2012, National Instruments, Austin, TX) and an external multi-channel soundcard (MOTU Ultralite mk3, Cambridge, MA).

Narrowband masking noise was generated according to ANSI (2010) standards. White noise was geometrically centred at the frequency of the test tone and filtered using 2nd order Butterworth filters (slope of -12 dB per octave). Filtering was performed using the upper and lower corner frequencies shown in Table 16. These values were approximated as the midpoint of the maximum and minimum values for each corner frequency provided in the ANSI (2010) standard using the following formulae:

Masking lower corner frequency = $10^{-0.0625} \cdot F_c = 0.865964 \cdot F_c$

Masking upper corner frequency = $10^{+0.0625} \cdot F_c = 1.154782 \cdot F_c$

Where F_c refers to the centre frequency of the masking noise in Hz.

Table 16. Upper and lower corner frequencies for narrowband masking noise in the EHF range. Corner frequencies are calculated based on the ANSI (2004) recommendations.

Centre frequency (Hz)	Lower corner frequency (Hz)	Upper corner frequency (Hz)
8000	6927.71	9238.26
9000	7793.68	10393.04
10000	8659.64	11547.82
11200	9698.80	12933.56
12500	10824.55	14434.78
14000	12123.50	16166.95
16000	13855.42	18476.51

Calibration of the masking noise in dB HL was required prior to any audiometric testing to allow known and effective masking levels to be presented according to our test protocol.

Prediction of the output sound level in dB HL for a given soundcard output was achieved by comparing the power spectrum of the electrical output from the GSI 61 audiometer to the speaker to the electrical output from the MOTU soundcard for the same stimuli.

Measurements and comparisons were performed for narrowband masking noise with centre frequencies at 1/6th octave frequencies from 8 to 16 kHz. Electrical levels were measured using custom software written in LabVIEW 2012 (National Instruments, Austin, TX) that acquired voltage data in line with the HDA200 headphones using a National Instruments NI USB-6009 data acquisition card (National Instruments, Austin, TX). Twenty averages each consisting of 96000 samples were collected at each frequency at a sampling rate of 192 kHz. The difference between the output levels with each device at the centre frequency of the narrowband noise was used to calculate correction values that allowed conversion of the MOTU output sound level values measured in arbitrary dB units into dB HL.

These levels were calculated according to the following formula:

Maximum level (dB) = *X*+*Y*+*Z*

Where:

X = Attenuation level of masking noise presented using soundcard (dB re: 0 dB atten using soundcard)

Y = Level of masking noise presented using GSI 61 (dB HL)

Z = Raw amplitude difference for soundcard re: GSI 61 = (electrical output to speaker at frequency at *X* dB attenuation level using soundcard) - (electrical output to speaker at frequency at *Y* dB HL presentation level using GSI 61).

The soundcard in 16-bit mode has a theoretical 96 dB dynamic range, so maximum output (i.e. no attenuation) is 96 dB greater than maximum attenuation. Soundcard output at that maximum level gives us the dB HL values shown in the first row of Table 17 below. To obtain the correction values to be applied to thresholds measured with the soundcard, the dB HL value for the unattenuated soundcard output was subtracted from 96 dB to give the equivalent value for maximum attenuation. These values are presented in the second row of Table 17.

The frequency-specific correction values calculated and shown in the second row of Table 17 were then built into the custom software so that the output level shown on the audiometer dial was in units of dB HL.

Table 17. Amplitude values in dB HL values for unattenuated MOTU soundcard narrowband masking noise output and for 0 dB output.

Frequency (kHz)	8	9	10	11.2	12.5	14	16
dB HL for unattenuated MOTU soundcard output	74.7	71.5	73.1	72.9	71.0	65.6	51.5
Correction values to convert MOTU soundcard thresholds to dB HL	21.3	24.5	22.9	23.1	25.0	30.4	44.9

6.5.2 Development of a masking protocol for EHF bone-conduction testing

6.5.2.1 IAA

Based on the data presented by Hallmo et al. (1992), a minimum IAA of 0 dB was assumed for all EHF test frequencies, therefore masking was always applied to the contralateral ear when bone-conduction thresholds were measured.

6.5.2.2 Initial masking level

The initial masking level selected was 30 dB SL relative to the air-conduction threshold in the non-test ear at the test frequency. The decision to add 30 dB to the non-test ear threshold was designed to ensure adequate masking was applied without the need for extended masking procedures in at least most, if not all, subjects. Hallmo et al. (1992) found that minimum masking levels required ranged from 0 to 25 dB across the EHF range, therefore 30 dB SL of masking should be adequate to effectively mask the non-test ear in the majority of subjects. McDermott, Fausti, Henry, and Frey (1990) also found that 30 dB SL of narrowband noise was adequate to effectively mask the non-test ear during EHF bone-conduction testing.

The minimum IAA for air-conduction thresholds measured with Sennheiser HDA 200 headphones in the EHF range is conservatively estimated as 40 dB HL (Brannstrom & Lantz, 2010). Therefore, the risk of overmasking; where the masking stimulus crosses over to the test ear, should be minimal until the level presented to the contralateral ear exceeds the unmasked bone-conduction threshold (or air-conduction threshold in the test ear) by greater than 40 dB HL. In situations in which a masking dilemma occurred, defined as a situation in which the minimum amount of masking required already resulted in overmasking (Hood, 1957), the masking level was applied as prescribed and the concern regarding overmasking was noted on the audiogram. This same procedure was followed if an increase in masking

noise was required that resulted in overmasking. If the prescribed masking level resulted in discomfort to the subject, the level was reduced by 2 – 10 dB until comfort was restored and this deviation from protocol was noted on the audiogram.

6.5.2.3 Masking procedure

Following application of masking noise at the initial level to the non-test ear, the bone-conduction threshold was re-checked. If the threshold increased by more than 10 dB HL, an additional 20 dB HL of masking noise was applied and the threshold was again re-checked. Clearly the application of subsequent masking could result in overmasking. If when checked following subsequent masking the threshold shifted again, it was judged that there was a risk that the shift was caused by overmasking. In this case a plateau masking method was used (Hood, 1957).

Plateau masking involved initially presenting the masking noise at 0 dB SL relative to the air-conduction threshold in the non-test ear and measuring the pure-tone threshold again. A shift in the pure-tone threshold was responded to by increasing the masking noise by 10 dB HL. The level of the pure-tone test tone was increased in 5 dB steps (or 2 dB steps, depending on the pure-tone step size being employed in threshold seeking) until a response was obtained, at which point the masking level was increased by a further 10 dB. Threshold was taken as the intensity at which a response to the pure-tone could be recorded over a 20 dB increase in the level of masking noise.

6.6 Transducer calibration and assessment of test-retest reliability

6.6.1 Methods of transducer calibration

Calibration of audiometric equipment is a critical process to ensure accurate results are obtained that can be compared across time, listeners, and equipment. Ideally, bone-conduction transducers will be objectively calibrated using an artificial mastoid; a device that approximates the mechanical impedance of the human mastoid process. Using an artificial mastoid, the level of vibration (force and acceleration) of a bone-conductor is measured and calibrated to meet standard reference equivalent threshold force levels. The IEC (1998) and ANSI (1987) standards for bone-vibrator calibration in dB HL are based on the Brüel & Kjær type 4930 artificial mastoid (Brüel & Kjær, Nærum, Denmark) and require that the attached transducer has a plane, circular contact surface 1.75 cm^2 in area, and that the transducer is applied to the artificial mastoid and to the skull with a static force of 5.4 N. Transducers that do not meet these requirements will not be loaded onto the artificial mastoid with the specified mechanical impedance and inaccuracies in measurement are likely. The large, convex surface of the TEAC transducer makes it unsuitable for use with a standard artificial mastoid and an alternative approach must be used.

6.6.1.1 Real ear method

The real ear calibration method is based on the comparison of average thresholds for air-conduction and bone-conduction stimuli across a group of listeners with normal hearing or purely sensorineural hearing loss (Hedgecock, 1961; Roach & Carhart, 1956). This method is based on the assumption that, on average, in the absence of conductive pathology, air- and bone-conduction thresholds will be equal (Wilber & Goodhill, 1967). For each subject, air-conduction thresholds are measured using a calibrated system, and then bone-conduction thresholds are measured using the same audiometer. The average difference between air- and bone-conduction thresholds at each frequency should provide the correction factor required to bring the bone-conduction system into correct calibration. The primary concern regarding real ear calibration is that the assumption of the equivalency of air- and bone-conduction thresholds is based on statistics from a large number of listeners, far more than are typically used when this calibration method is employed. The phenomenon of threshold equivalence cannot be expected to occur for individual listeners, or for a small group of listeners tested to obtain calibration data (Studebaker, 1967; Wilber & Goodhill, 1967).

A real ear calibration method was used by Popelka et al. (2010) in their testing of the TEAC HP-F100 transducer. Popelka et al. obtained an initial estimate of audiometric zero by varying the gain control of the TEAC transducer and the audiometer attenuator to reach threshold at each frequency in five normal hearing subjects. The gain control was then fixed and air- and bone-conduction thresholds were measured at 8 to 16 kHz in nine subjects with a range of sensorineural hearing levels. The air-bone gaps are not reported for individual frequencies, however an average negative air-bone gap of 7.2 dB HL across the test frequencies was documented. This is interpreted as suggesting a reduction of 7.2 dB HL in the gain control could be applied to bring the calibration in line with air-conduction values. Alternatively, this deviation from the expected 0 dB HL air-bone gap could be indicative of natural variation across the small group of subjects tested.

6.6.1.2 Loudness balance method

The loudness balance technique has long been used for the transfer of audiometric calibration data between air-conduction transducers, but has been less frequently been used to calibrate bone-conduction transducers (Barry & Vaughan, 1981). The procedure involves alternately presenting a signal via a calibrated air-conduction transducer and an uncalibrated bone-conduction transducer. The level of one of the two signals is adjusted and alternating presentations are repeated until the listener judges the two signals to be equal in loudness. Typically, several listeners are tested multiple times each and results are averaged to calculate correction values for calibration (Beranek, 1949; Miller, Engebretson, & Weston, 1964).

Given that the loudness balance method is based on average data collected from a small group of individuals, it is subject to the same sources of statistical variability as the real ear method (Wilber & Goodhill, 1967). A comparison of the real ear and loudness balance techniques has shown very similar calibration values are produced with the two methods, at least at 0.25 to 2 kHz (Hedgecock, 1961).

6.6.1.3 Phase cancellation method

A signal delivered to the cochlea by a bone-conduction vibrator can be cancelled by a second signal of equal amplitude but opposite phase that reaches the cochlea via either air- or bone-conduction. The phase cancellation method involves the presentation of two tones simultaneously to a listener, one through the bone-conductor being calibrated, and one

through a calibrated transducer. The subject is asked to adjust the phase and intensity of the signal from the bone-conductor until the tones are inaudible. This is the point at which cancellation has been achieved. Using the known intensity and phase of the reference signal, the same properties of the tone presented via the bone-conductor can de deduced and averaged across a number of listeners to calculate calibration values (Dempsey & Levitt, 1990; Kapteyn, Boezeman, & Snel, 1983; Levitt, 1987).

This procedure has been shown to be very precise for amplitude measurements when repeated measurements are made on one listener without removal and replacement of the transducers (Dempsey & Levitt, 1990; Kapteyn et al., 1983). Variability in measurements, particularly of signal phase, across test sessions is substantially greater, however it has still been deemed acceptably low for amplitude measurements to allow use of the method in calibration (Dempsey & Levitt, 1990; Kapteyn et al., 1983). However, Dempsey and Levitt (1990) suggest that accurate measurements cannot be made with untrained listeners and that the practical use of the technique is limited by the requirements for skilled subjects. In addition, the disadvantages of other perceptual methods and measurements averaged across groups of subjects, as discussed above, will also apply to the phase cancellation method.

6.6.1.4 Otoacoustic emission method

Otoacoustic emissions (OAEs), which are largely dependent on active processes in the cochlear hair cells (Kemp, 1978), can be recorded in the EAC in response to air- or bone-conduction stimulation (Purcell, Kunov, & Cleghorn, 1999, 2003). Purcell et al. (1999, 2003) have demonstrated that a bone-conduction transducer can be calibrated using distortion product OAEs (DPOAEs) elicited by the bone-conductor and referenced to responses to stimulation via a calibrated air-conduction transducer. In the majority of ears without significant hearing loss, an emission resulting from the nonlinear processing of the two input signals in the cochlea (f_1 and f_2), can be recorded at the frequency $2f_1 - f_2$ (Probst, Lonsbury-Martin, & Martin, 1991). The magnitude of this emission is dependent on the relative intensities of f_1 and f_2 (Whitehead, Stagner, McCoy, Lonsbury-Martin, & Martin, 1995).

To obtain transducer calibration values using DPOAEs, two sets of emissions are recorded with f_2 set at each of the frequencies requiring calibration. For both sets of data, the f_1 tone is delivered by air-conduction, whereas f_2 is presented first at a known intensity level using the calibrated earphone and then at an unknown magnitude using the bone-conductor. The

amplitude of emissions obtained in response to bone-conduction stimulation at each f_2 frequency can be compared to the amplitude of responses to air-conduction stimulation at a specified sound pressure level and the differences can be used to provide values to calibrate the bone-conductor to produce a response of equal magnitude (Purcell et al., 1999).

This method is appealing in that it is objective, non-invasive, and does not require training of listeners. Theoretically, data from a large number of listeners could be collected and averaged to calibrate a transducer. However, the challenge of obtaining DPOAEs above the noise-floor at low-frequencies limits calibration to 1 kHz and above (Purcell et al., 1999). The reliability of individualised calibrations of a piezoelectric bone-conductor using the OAE method has been shown to be reasonable in most listeners at standard bone-conduction test frequencies (Purcell et al., 1999, 2003). Purcell et al. (1999) did note that calibration data across sessions was more variable at 6 kHz, the highest test frequency, suggesting the accuracy of calibration performed using this method may be reduced at higher test-frequencies.

6.6.1.5 Selection of a calibration technique

Based on the preceding discussion of available methods of transducer calibration, it is clear that all have their limitations. For our purposes it was essential that the technique used was capable of producing reliable calibration values in the EHF range, thus the OAE method was ruled out. The requirement for trained listeners for optimal calibration reliability also led to the exclusion of the phase cancellation method was excluded. The remaining two methods evaluated; the real ear method and the loudness balance method are both subject to the same limitations regarding the use of group averages and perceptual judgements. Despite these weaknesses, given the inability to calibrate the transducer using objective methods, these perceptual techniques represent the most feasible calibration options. Based on the simplicity of the task listeners were required to perform, it was decided that the real ear method would be used to calibrate the TEAC HP-F100 transducer.

6.6.2 Test-retest reliability of bone-conduction thresholds

It is accepted that there is measurement variability inherent to audiometry that cannot be eliminated, but can be minimised through careful adherence to standardised calibration and test procedures. The principle on which much of this thesis is based is that by comparing thresholds measured at different points in the postoperative course, it can be determined

whether a given surgical intervention has altered hearing sensitivity. It is therefore critical to assess the intrasubject variability associated with test procedures to ascertain the level or certainty with which we can distinguish genuine changes in auditory function from threshold changes due to measurement variability over time.

Intersubject variability of bone-conduction thresholds is known to be greater than that for air-conduction thresholds (Coles, Lutman, & Robinson, 1991; Dirks & Swindeman, 1967; Robinson & Shipton, 1982). The majority of this variability is attributed to physiological differences across subjects, such as the thickness of skin and bone (Lemkens et al., 2002; Studebaker, 1962b). Correct and consistent placement of the bone-conduction transducer is essential for reliable thresholds to be measured and errors caused by variations in the coupling of the transducer to the skull are well recognised (Zwislocki et al., 1988). Despite these limitations on threshold repeatability, the intrasubject variability of bone-conduction threshold measurements is generally considered acceptable for clinical purposes (Carhart & Hayes, 1949; Dirks, 1964; Wilber & Goodhill, 1967). Typically, both air- and bone-conduction audiometric thresholds are associated with test-retest variability of plus or minus 10 dB HL (Dirks, 1964; Lemkens et al., 2002; Studebaker, 1962a).

As discussed in Chapter 4, air-conduction thresholds in the EHF range are known to be inherently more variable across listeners than thresholds in the conventional frequency range, although intrasubject variability remains within a clinically acceptable +/- 10 dB HL in this extended range (Schmuziger et al., 2004). Although subject numbers were very limited, the test-retest reliability associated with bone-conduction thresholds measured above 8 kHz with the KH-70 transducer have been shown to be comparable to lower frequency bone-conduction thresholds, varying from 2.2 dB HL to 6.0 dB HL at 8 kHz and above for two listeners tested 16 times over eight days (Hallmo et al., 1991). No such test-retest reliability data is currently available for the TEAC HP-F100 transducer.

6.6.3 Aims

The aims of this phase of the present study were to obtain calibration values for the TEAC HP-F100 transducer using the real ear method and to determine the test-retest reliability of threshold measurements performed using this device. These two components are presented together as the aims were addressed using the same set of data.

6.6.4 Method

6.6.4.1 Participants

The participants in this study were a group of twenty adult volunteers who reported no significant history of middle ear pathology, had normal otoscopic findings and tympanograms, and no significant air-bone gaps in the conventional frequency range. All subjects had measureable air-conduction thresholds from 0.25 to 16 kHz, however no restrictions were placed on the threshold levels that qualified participants for inclusion in this study. The age range of participants was 22 to 43 years (M = 28.1, SD = 6.0), and the group included six males and 14 females. Informed written consent was obtained from all subjects prior to their participation (Appendix A), in accordance with ethical approval granted by the University of Canterbury Human Ethics Committee (ref: HEC 2014/127).

6.6.4.2 Equipment

Tympanometry was performed with a calibrated Madsen OTOflex 100 tympanometer (GN Otometrics, Taastrup, Denmark) using a 226 Hz probe tone and a sweep rate 50 daPa/s. Pure-tone audiometry was carried out with the participant seated in a sound treated booth at the University of Canterbury, which fulfilled the criteria of ISO 8253-1 (2010). A calibrated diagnostic audiometer, the GSI 61 (Grason-Stadler, Eden Prairie, MN), was used for generation and presentation of continuous pure-tone stimuli at frequencies from 0.25 to 8 kHz, and for one set of air-conduction stimuli at 8 to 16 kHz. Air-conduction thresholds at 8 to 16 kHz, were also measured using a custom-built computer-based audiometer (screenshot of user interface shown in Figure 42), as were EHF bone-conduction thresholds. The custom audiometer software was developed using LabVIEW 2012 (National Instruments, Austin, TX). An HP Compaq nw9440 laptop (Hewlett Packard, Palo Alto, CA) was used to run the software and sound stimuli were produced by an external multi-channel sound card (MOTU Ultralite mk3, MOTU, Cambridge, MA) connected to the laptop via USB. Calibration of air-conduction stimuli produced the custom audiometer in dB HL was performed prior to testing. The procedure for calibration is described in section, 6.6.5.4.

In the conventional frequency range, air-conduction stimuli were presented via TDH-39 supra-aural headphones (Telephonics Corporation, Farmingdale, NY), and bone-conduction stimuli were presented using a Radioear B-71 bone-conduction vibrator (Radioear Corporation, New Eagle, PA). Air-conduction stimuli and narrow-band masking noise at 8 to

16 kHz were presented through Sennheiser HDA 200 circumaural headphones (Sennheiser electronic GmbH & Co., Wennebostel, Germany). A set of TEAC HP-F100 bone-conduction headphones (TEAC, Tokyo, Japan) modified as described in Section 6.2 were used for of bone-conduction thresholds in the EHF range.

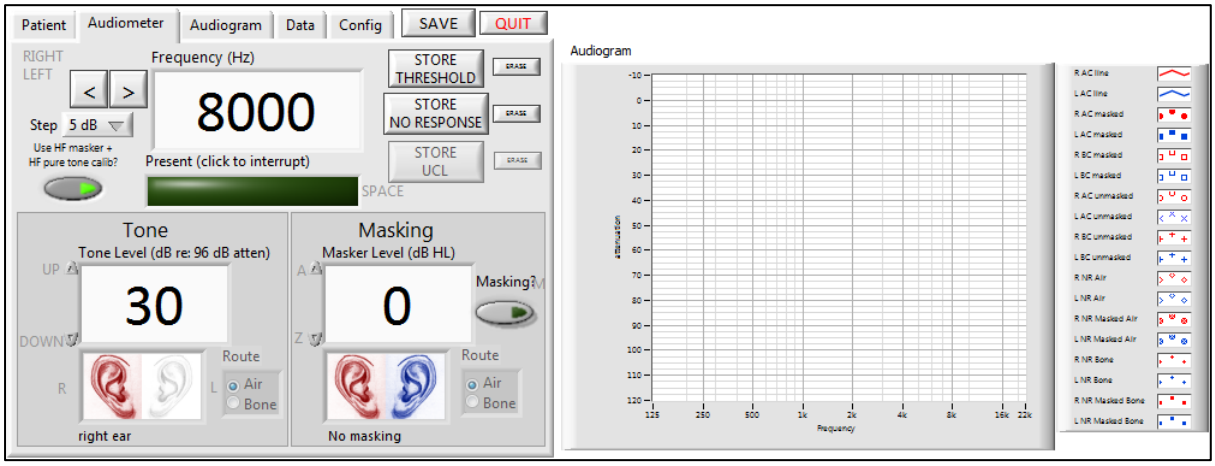

Figure 42. User interface of the Custom UC Audiometer software. Controls are shown on the left side of the screen and the audiogram recorded is shown on the right.

6.6.4.3 Procedure

Both ears of each participant were examined otoscopically to rule out EAC occlusion or abnormalities of the TM. Tympanometry was performed and results were considered normal when the static compensated compliance value fell between 0.30 and 1.49 cc and the compliance value was above -100 daPa.

Air-conduction pure-tone thresholds were first measured at octave frequencies from 0.25 to 8 kHz using the GSI 61 audiometer. Thresholds were determined using the modified Hughson-Westlake technique in 5 dB HL steps. If thresholds exceeded 15 dB HL at any frequency from 0.5 to 4 kHz, masked bone-conduction thresholds were measured for each ear at the frequency in question. Subjects were considered eligible for the study if they had either thresholds of 15 dB HL or lower at 4 kHz and below, or higher thresholds, but an absence of any significant air-bone gaps, defined as a masked bone-conduction threshold that was 15 dB HL or more below the air-conduction threshold.

Eligible subjects underwent air-conduction threshold testing in both ears in the EHF range using the GSI 61 audiometer. Thresholds were measured at 1/6th octave intervals from 8 to 16 kHz. As the EHF range contained the information of greater interest, the step size for

threshold measurement was decreased to 2 dB steps at these frequencies. Thresholds had to be measureable at all test frequencies in both ears for subjects to be included in the study.

EHF air-conduction threshold measurement was repeated for both ears using the custom audiometer and sound card. The transducer and test procedure used was identical to that used for testing with the GSI 61 audiometer. If there was a difference between the ears in air-conduction thresholds measured using the custom audiometer, the better ear was selected for bone-conduction threshold measurement, otherwise the test ear was chosen at random.

The TEAC HP-F100 bone-conduction transducer was positioned by the tester at the midline of the forehead, as close to the centre of the forehead as was possible while maintaining stable placement. Masking was always applied to the contralateral ear via a Sennheiser HDA 200 earphone. Narrowband masking noise calibrated in dB HL as described in Section 6.5.1, was presented at 30 dB above the air-conduction threshold in dB HL in the non-test ear. The test ear remained uncovered for this phase of testing.

Bone-conduction thresholds were measured in 2 dB steps using the custom audiometer and sound card at the same frequencies as those measured for air-conduction testing in the EHF range. Threshold measurements were repeated three times for each subject, with removal and replacement of both transducers between each set of measurements.

6.6.4.4 Data analysis

Air-conduction thresholds measured using the custom audiometer were first converted into dB HL using the correction values provided in Section 6.6.4.5. For each participant these air-conduction thresholds were subtracted from the mean of the three bone-conduction thresholds measured at each test frequency. The average of these differences was calculated across subjects to provide the correction values required to convert the bone-conduction thresholds into dB HL. Frequency-specific correction values were subtracted from each bone-conduction threshold (the mean of the three measurements) to convert the measurement into dB HL. The median, maximum, and minimum differences between air- and bone-conduction thresholds at each frequency were then evaluated to determine the size of the "air-bone gap" that would be used to define a significant conductive hearing loss in future studies.

Repeated bone-conduction measurements were used to determine the test-retest reliability of thresholds measured using the TEAC transducer. The mean and standard deviation of the three threshold measurements were calculated at each frequency for each participant. For

individual participants, standard deviations of 10 dB or greater across the three measurements at any frequency were considered unacceptable and the rate of unacceptable variances was calculated across all subjects. A repeated measures ANOVA was performed to assess for an effect of frequency on the mean standard deviation of the repeated threshold measurements.

Reliability was further assessed by subtracting the minimum threshold of the three measurements at each frequency from the maximum threshold. This value was taken as the "maximum difference" for each subject. The group mean, standard deviation, and maximum of these values were then calculated for each frequency. This set of analyses was designed to ensure that larger differences between two repeated thresholds were not obscured by averaging the three repeated measurements. A second repeated measures ANOVA was performed to assess for an effect of frequency on mean maximum difference values.

Intraclass correlation coefficients (ICCs) were calculated at each frequency for the three sets of thresholds recorded for each subject. Given the single tester, three repeated measure design of the study, a two-way mixed effects ICC model with an absolute agreement definition was used and the ICC for single measures was calculated. According to the recommendations of Cicchetti (1994), ICC values less than .40 were considered to indicate poor test-retest reliability, values between .40 and .59 fair reliability, values between .60 and .74 good reliability, and ICCs between .75 and 1.0 excellent reliability.

Analyses were also performed to determine the standard error of the measurement (SEM) for each test frequency. Where the ICC provides a relative measure of reliability, the SEM provides an absolute index of reliability and better reflects the trial-to-trial noise in the data (Weir, 2005). SEM values were used to define the minimum threshold change needed between separate measures on a subject for the difference in the measures to be considered real for 95% and 98% confidence levels.

All analyses were performed using IBM SPSS version 21 (SPSS IBM, Armonk, NY).

6.6.4.5 Calibration of air-conduction stimuli

Prediction of the output sound level in dB HL for a given soundcard output level was achieved using the same method to that described in Section 6.5.1 above for calibration of narrowband masking noise. In this case, the power spectrum of the electrical output from the GSI 61 audiometer to the speaker was measured for pure-tones at $1/6^{th}$ octave frequencies from 8 to 16 kHz and compared to the electrical output from the soundcard using the same

stimuli to calculate correction values to convert output into dB HL. The apparatus, method, and formula used to calculate these correction values were identical to those described in Section 6.5.1, therefore will not be repeated here. Instead, a worked example is provided showing the calculation of the correction value for 8 kHz:

Maximum level (dB) = $X+Y+Z$

X = pure tone presented at 6 dB attenuation re: 0 dB sound card atten

Y = pure tone presented at 60 dB HL using GSI 61

Z = (electrical output to speaker at masking frequency at 6 dB attenuation using sound card) - (electrical output to speaker at pure-tone frequency at 60 dB HL using GSI 61) = -7.72 – (-32.02) = 24.3 dB

Therefore, maximum level (dB) = 6 + 60 + 24.3 = 90.3 dB HL

To obtain the correction values to be applied to thresholds measured with the soundcard, the dB HL value for the unattenuated sound card output was subtracted from 96 dB to give the equivalent value for maximum attenuation. These values are presented in the second row of Table 18.

Table 18. dB HL values associated with unattenuated sound card output and for 0 dB output

	Frequency (kHz)						
	8	9	10	11.2	12.5	14	16
dB HL for unattenuated sound card output	90.3	84.8	79.3	80.6	76.4	64.6	56.3
Correction values to convert sound card thresholds to dB HL	5.7	11.2	16.7	15.4	19.6	31.4	39.7

The frequency-specific correction values calculated were then subtracted from each air-conduction threshold measured using the sound card to convert the threshold into dB HL.

6.6.5 Results

6.6.5.1 GSI-61 air-conduction thresholds

Mean air-conduction thresholds measured across the entire frequency range of interest; 0.25 – 16 kHz measured using the GSI-61 audiometer are shown in Figure 43. All mean thresholds were below 20 dB HL, although there was a wide range of thresholds documented, particularly in the EHF range, where the standard deviation of the measurements tended to increase with increasing frequency up to a maximum of 18.3 dB for the right ear at 16 kHz.

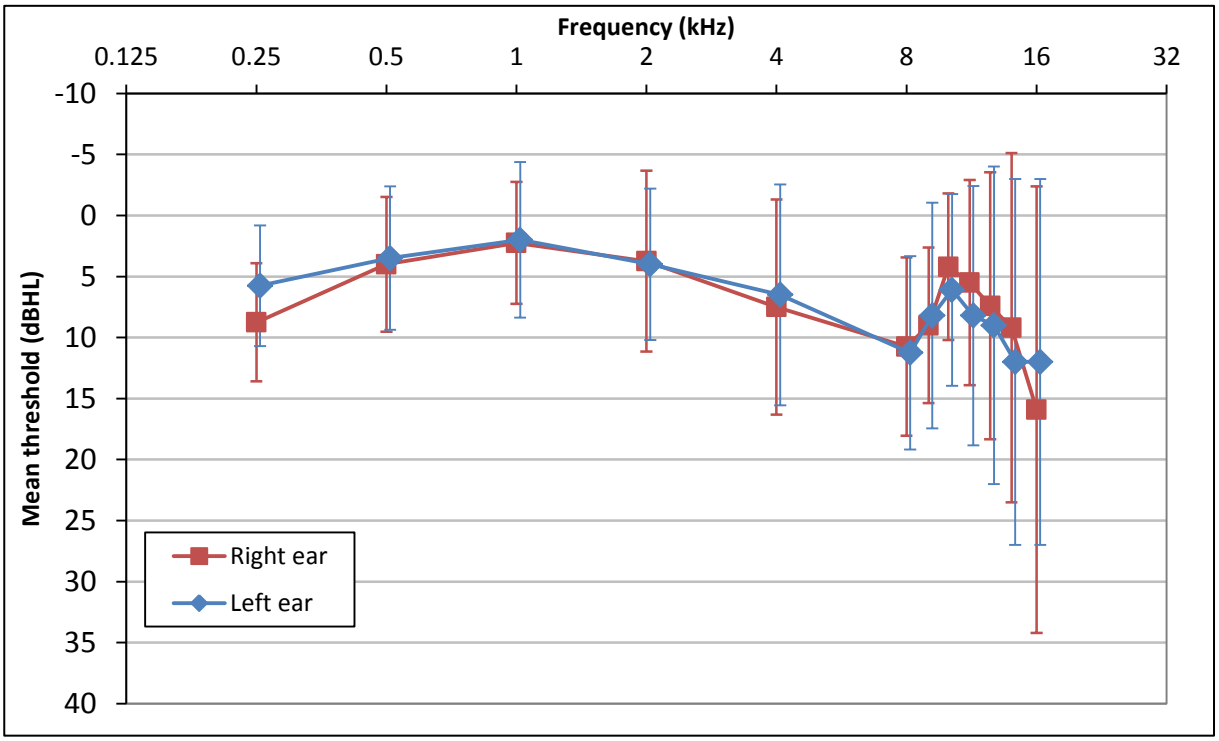

Figure 43. Mean air-conduction thresholds for each ear measured using the GSI-61 audiometer. Error bars show standard deviations.

For the three subjects with thresholds exceeding 15 dB HL at 4 kHz and below, none had an air-bone gap of greater than 10 dB HL. All 20 subjects had Type A tympanograms bilaterally, consistent with normal middle ear function.

6.6.5.2 Soundcard air-conduction thresholds

Air-conduction thresholds measured in arbitrary decibel units with the custom audiometer and MOTU sound card (henceforth referred to as the sound card audiometer) were adjusted using the correction values calculated in Section 6.6.4.5 to specify the thresholds in dB HL.

Air-conduction thresholds in dB HL measured with the sound card audiometer were then compared to air-conduction thresholds in the same units measured with the GSI audiometer to assess the accuracy of calibration. The mean difference between measurements (shown in Figure 44) averaged across both ears was within +/- 5 dB at all frequencies except for 14 kHz, at which the GSI 61 thresholds were higher, on average, by 5.3 dB. Maximum differences in the positive and negative direction between the thresholds were also calculated for each frequency. The greatest variation from zero was documented at 14 kHz, where the maximum variance between air-conduction thresholds measured with the two sets of equipment was 13.4 dB. The range of values was greatest at 16 kHz, extending from +12.3 to -9.7. Although the range of values was reasonably large, most subjects showed differences between thresholds measured with the two audiometers that were close to the mean values reported.

Based on these calculations, the calibration of the sound card audiometer for air-conduction testing in dB HL was considered sufficiently accurate to proceed with bone-conduction calibration based on these values.

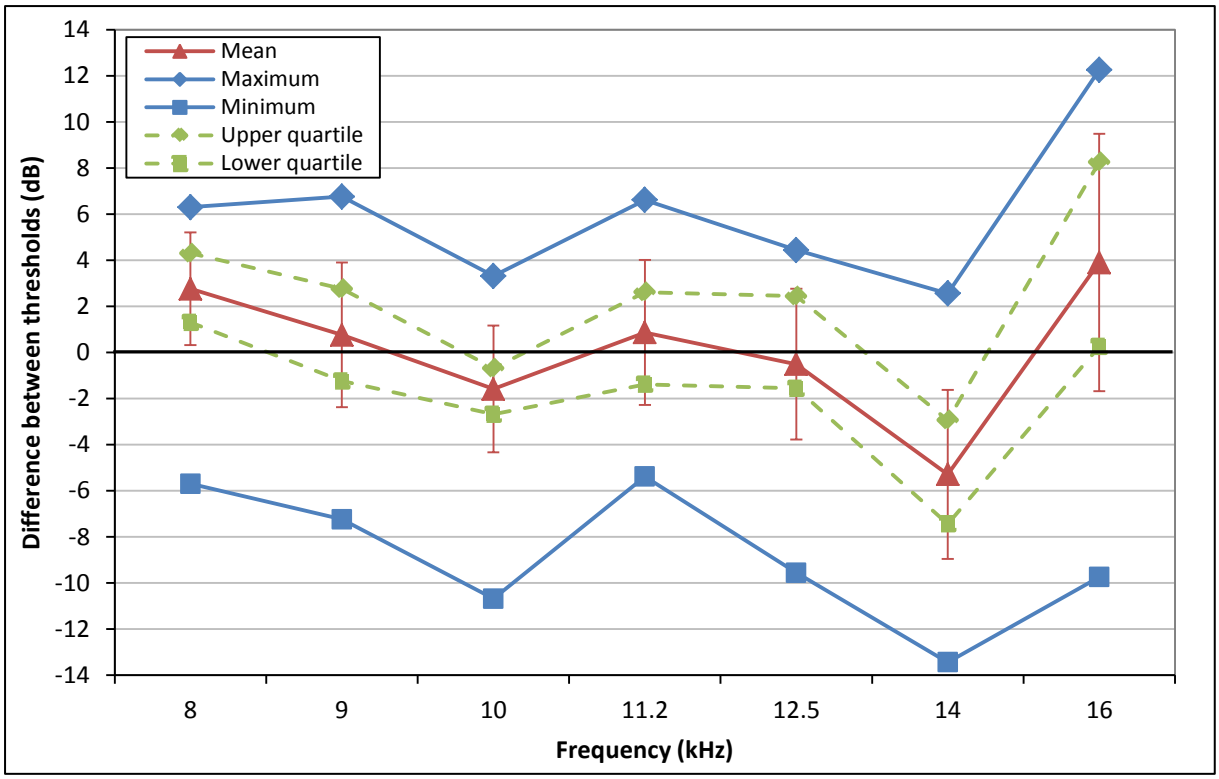

Figure 44. Mean, maximum, and minimum difference between thresholds measured in dB HL using the GSI-61 audiometer and thresholds measured using the sound card audiometer and corrected into dB HL units. Markers connected by dashed lines show upper and lower quartile values for the data set. Positive values indicate that the corrected values were higher and negative values indicate that thresholds measured with the GSI-61 were higher. Error bars show standard deviation.

6.6.5.3 Correction values to convert bone-conduction thresholds to dB HL

Correction values to specify sound card bone-conduction thresholds in dB HL were established by calculating the mean difference between air-conduction thresholds in dB HL measured using the sound card audiometer and bone-conduction thresholds measured using the TEAC HP-F100 and the same audiometer. A single bone-conduction threshold was calculated at each frequency for each subject by averaging the three threshold measurements. Mean differences and the standard deviation of the differences between air- and bone-conduction thresholds at each frequency are shown in Table 19

Table 19. Differences between uncalibrated sound card EHF bone-conduction thresholds and air-conduction thresholds in dB HL.

Frequency (kHz)	8	9	10	11.2	12.5	14	16
Mean	22.8	28.2	34.4	33.5	39.0	49.3	48.1
Standard deviation	5.2	3.6	5.8	5.4	5.3	7.4	8.6

The correction values calculated above were subtracted from the bone-conduction values to convert the thresholds into dB HL. Given that the method of calibration, mean bone-conduction thresholds in dB HL matched mean air-conduction thresholds in dB HL, ranging from 2.8 dB HL at 10 kHz to 16.8 dB HL at 16 kHz.

6.6.5.4 Definition of a significant air-bone gap

To determine the magnitude of difference between air- and bone-conduction thresholds that would be defined as a significant air-bone gap, the bone-conduction values specified in dB HL for each subject were subtracted from the air-conduction thresholds in dB HL. The mean difference was 0 dB at all frequencies due to the application of the correction factors based on the mean difference between air- and bone-conduction thresholds to the bone-conduction thresholds. As shown in Figure 45, the median values were close to 0 dB HL (range = 1.03 to -1.10) for all frequencies.

For 75% of subjects, the air-bone gap was below 7 dB HL across all frequencies with little difference across frequencies. There was a trend towards larger maximum air-bone gaps at higher frequencies, particularly at 14 and 16 kHz where the maximum air-bone gaps were 14.6 and 13.7 dB HL, respectively. The lowest maximum air-bone-gap, 5.63 dB HL, was recorded at 9 kHz. Minimum (negative) air-bone gaps and lower quartile values are also presented in Figure 45, although these were of limited importance when determining the size of the air-bone gap that would be defined as significant.

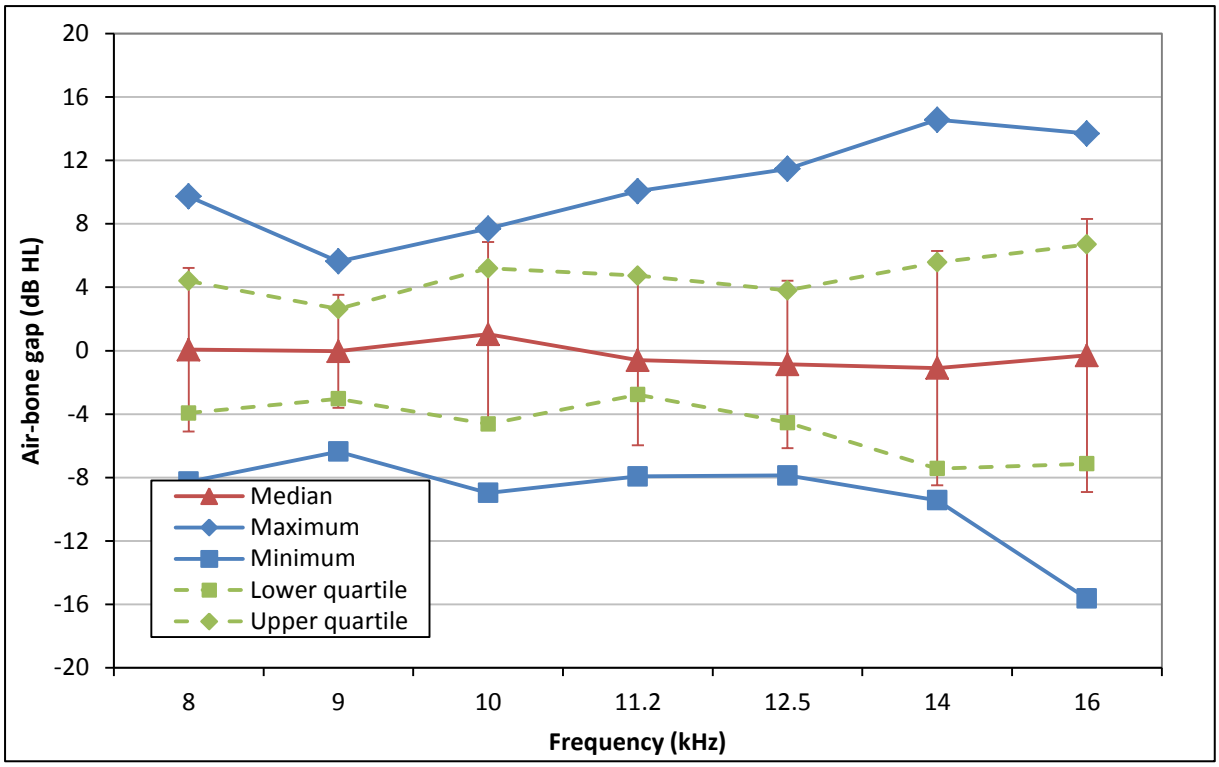

Figure 45. Median, maximum, and minimum differences between air-conduction values in dB HL and bone-conduction values in dB HL. Upper and lower quartile values are displayed using dashed lines. Positive values indicate that the bone-conduction threshold is lower (better) than the air-conduction threshold and negative values indicate that the bone-conduction threshold is higher (poorer) than the air-conduction threshold.

6.6.5.5 Test-retest reliability

The mean standard deviation of the repeated measures across subjects was between 1 and 2 dB for all test frequencies (Figure 46). A one-way repeated measures ANOVA performed using Greenhouse-Geisser corrections showed no significant effect of frequency on the standard deviation of repeated measurements ($F(3.87, 73.44) = 0.45$, $p = .76$).

As is shown by the maximum values in Figure 46, the standard deviation of the three measurements did not reach the 10 dB criteria for unacceptability for any subject. The highest maximum standard deviation recorded was 5.0 dB at 11.2 kHz.

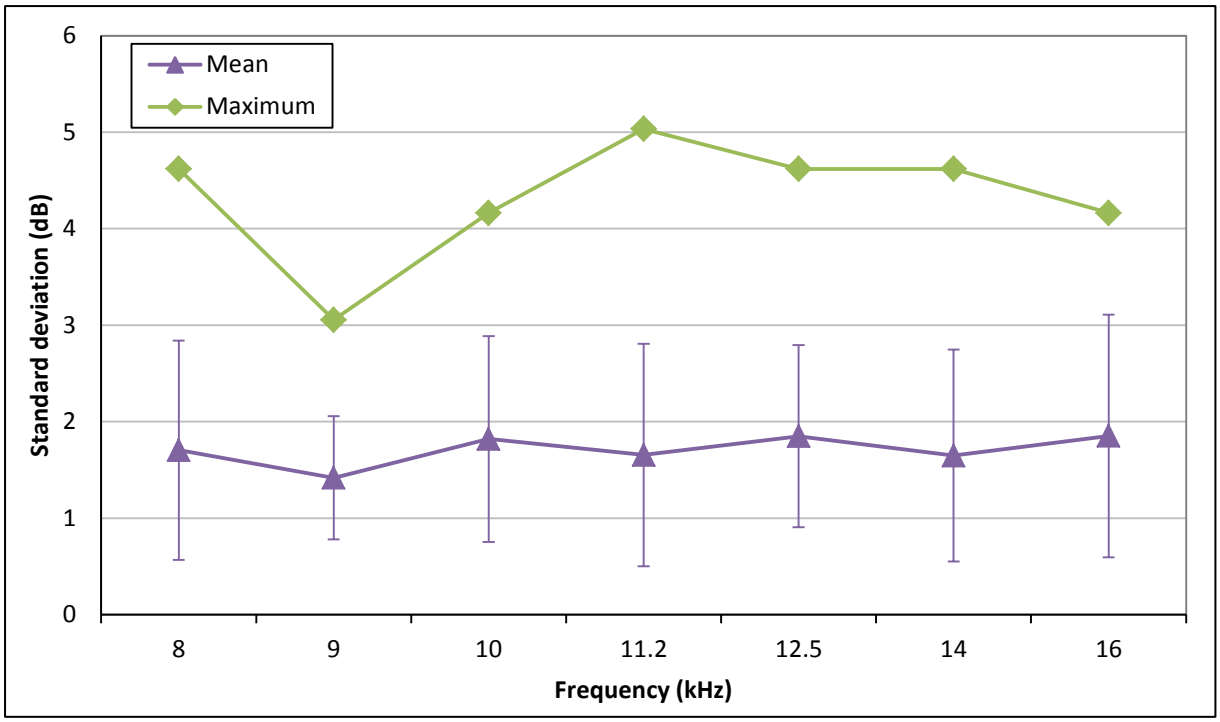

Figure 46. Mean and maximum standard deviation of three repeated measures at each frequency across subjects. Error bars represent that standard deviation of the data used to calculate the mean.

The maximum difference in thresholds recorded for each subject at each frequency was calculated as the difference between the highest and the lowest thresholds recorded from the three measurements. Figure 47 shows the maximum difference identified for any subject and the mean difference between highest and lowest thresholds across subjects for each frequency. Mean differences were close to 3 dB for all frequencies, with the minimum of 2.6 dB recorded at 9 kHz and the 3.4 maximum difference recorded at 10, 12.5, and 16 kHz. A one-way repeated measures ANOVA showed no significant effect of frequency on the mean difference between highest and lowest measurements ($F(6, 114) = 0.44$, $p = .85$).

Maximum differences between two thresholds recorded at the same frequency for any individual subject ranged from 6 dB at 9 kHz ($n = 1$) to 10 dB at 11.2 kHz ($n = 1$). At all other frequencies the maximum difference was 8 dB.

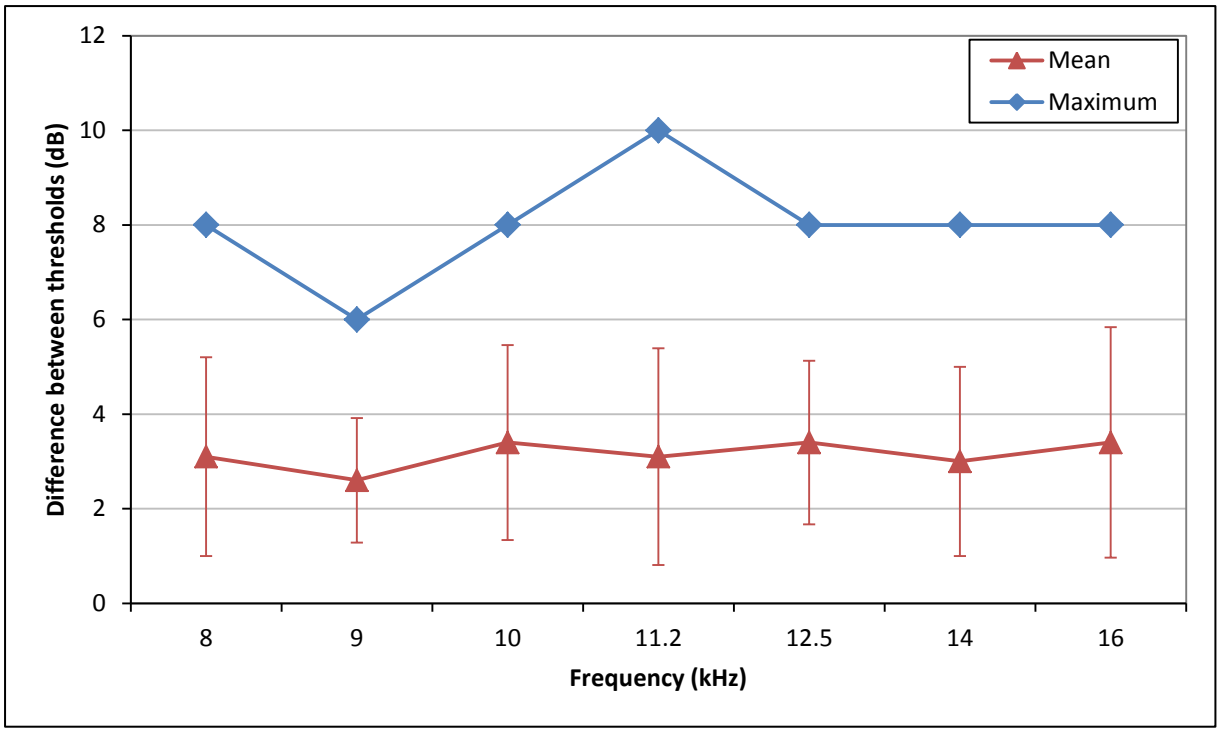

Figure 47. Mean and maximum difference between highest and lowest thresholds of the three repeated measures. Error bars represent that standard deviation of the data used to calculate the mean.

Statistics performed to summarise reliability at each frequency are shown in Table 20. Evaluations of ICCs calculated from the repeated threshold data for each frequency were consistent with excellent test-retest reliability at all frequencies, according to the criteria recommended by Cicchetti (1994). As shown in Table 20, the lowest ICC was calculated for 8 kHz (ICC = .81), whereas the highest was recorded for 16 kHz stimuli (ICC = .98). Similarly, SEM values, used to provide an absolute index of reliability, ranged from 1.53 dB at 9 kHz to a maximum of 2.17 dB at 16 kHz.

Confidence intervals were constructed based on the SEM and were used to calculate minimal differences needed to be considered real at the 95% and 98% levels of confidence. Minimal differences required at the 95% level ranged from +/- 4.23 dB at 9 kHz to +/- 6.00 dB at 16 kHz. When more conservative 98% criteria were applied, the difference between two scores required for a significant change increased to +/- 5.03 at 9 kHz to +/- 7.14 dB at 16 kHz.

Table 20. Summary statistics illustrating test-retest reliability at each frequency.

Frequency (kHz)	SD	ICC	SEM	95% CI	98% CI	95% MD	98% MD
8	4.58	0.81	2.01	3.94	4.68	5.57	6.62
9	6.51	0.95	1.53	2.99	3.55	4.23	5.03
10	6.85	0.91	2.07	4.05	4.82	5.73	6.81
11.2	7.51	0.93	1.97	3.87	4.60	5.47	6.50
12.5	9.14	0.95	2.02	3.96	4.71	5.61	6.66
14	12.01	0.97	1.94	3.80	4.51	5.37	6.38
16	15.32	0.98	2.17	4.25	5.05	6.00	7.14

SD = standard deviation, ICC = intraclass correlation coefficient, SEM = standard error of measurement, CI = confidence interval, MD = minimal difference

6.6.5.6 Criteria for defining a significant threshold shift

As stated above, maximum standard deviations for repeated measures at all frequencies were between 3.1 and 5.0 dB and all 95% MD scores were calculated at 6.0 dB or below. Based on these statistics, the appropriate criteria used to define a significant change in a bone-conduction threshold would be an increase or decrease in threshold of at least 6 dB. However, when we examined the maximum difference between thresholds based on the highest and lowest measurements recorded at each frequency for each subject, the need for more conservative criteria was suggested. The maximum difference scores reached 8 dB for one participant at 10, 12.5, and 14, for two participants at 8 and 16 kHz, and reached 10 dB for one participant at 11.2 kHz. Minimal difference calculations performed at the 98% confidence level resulted in significant change criteria of between 6.5 and 7.14 dB at all frequencies except 9 kHz, where the MD was 5.03 dB. Given these values, 8 dB would be the most appropriate criteria across frequencies to capture a significant threshold change in the majority of cases.

6.6.6 Discussion

6.6.6.1 Bone-conduction transducer calibration

The initial step in obtaining correction values to convert bone-conduction thresholds into dB HL was the conversion of air-conduction thresholds measured with the MOTU audiometer into dB HL. Popelka et al. (2010) performed their calibration of the HP-F100 using the GSI-61 for both air- and bone-conduction measurements. No concerns regarding this audiometer were noted by Popelka et al., however our measurements (reported in Chapter 4) showing spurious noise at higher frequencies in the output from this audiometer led to our decision to develop an alternative audiometer for use in EHF audiometry and calibration. Although the GSI 61 was used as a reference to calibrate the air-conduction output of the sound card audiometer, the use of objective measures of the peak amplitude of the pure-tone of interest eliminated this noise from influencing correction factors.

The range of the differences found between air-conduction thresholds measured with the sound card audiometer in dB HL and those measured with the GSI 61 increased at the highest test frequencies, which may be a result of this unwanted noise affecting the level at which GSI 61 thresholds were measured. The output of the sound card audiometer contained no such noise, and therefore can be considered to provide a more frequency-specific test of hearing sensitivity. Alternatively, the greater overall intrasubject and intersubject variability of threshold measurements at these highest frequencies may be the cause of the increased standard deviations of the difference between the two sets of air-conduction thresholds at 14 and 16 kHz (Schmuziger et al., 2004). Regardless, the deviation between the two sets of measurements following application of the correction factors was judged small enough that the air-conduction calibration was considered valid.

Our method of bone-conduction transducer calibration was based on two key assumptions. The first was that in the absence of evidence of a conductive hearing loss at 0.5 – 4 kHz and with no otoscopic or tympanometric evidence of middle ear dysfunction, there will be no conductive loss in the EHF range. Essentially, we are proposing that there is no such thing as an isolated EHF conductive hearing loss. We are not aware of any evidence that contradicts this assumption, however given the limits of current knowledge regarding middle ear function in the EHF range, this remains unconfirmed.

The second major assumption underpinning our bone-conduction calibration method is that, on average, in the absence of a conductive hearing loss, EHF bone-conduction thresholds will

be equal to air-conduction thresholds. This assumption is based on evidence of air- and bone-conduction threshold equivalency in the conventional frequency range. It is, however, critical to note that whereas on average listeners with normal hearing or purely sensorineural hearing loss will not exhibit air-bone gaps, in individual listeners an air-bone gap will be greater or less than zero more often than air- and bone conduction thresholds will be equal (Margolis, 2008; Studebaker, 1967). Margolis (2008) suggested that the air-bone gap could be modelled as a difference between two normally distributed variables. Based on estimates of the standard deviations of 5 and 7 dB for air-conduction thresholds and bone-conduction thresholds, respectively, Margolis calculated that the standard deviation of the distribution of air-bone differences will be 8.6 dB. This estimate leads to the prediction that air-bone gaps of 10 dB in either the positive or negative direction will occur for 23% of measurements in listeners with normal middle ear function. This variation in air-bone gaps is an unavoidable issue in audiometry, regardless of the transducer calibration method. Of course, the additional assumption here is that the relationship between air- and bone-conduction thresholds in the EHF range is comparable to that observed in the conventional frequency range.

Due to the calibration method selected, mean EHF bone-conduction thresholds in dB HL were equal to mean air-conduction thresholds in dB HL measured using the same audiometer. Of greater interest is the variation in the difference between air- and bone-conduction thresholds across the group of 20 participants. The standard deviations ranged from 3.56 dB at 9 kHz to 8.61 dB at 16 kHz which, when compared to the analyses provided by Margolis (2008), is comparable to what would be expected in the conventional frequency range with threshold seeking step sizes of 5 dB.

6.6.6.2 Definition of a "significant" air-bone gap

The magnitude of the air-bone gap that would be considered "significant" when using the bone-conductor and audiometer for threshold measurement in the future was defined based on the upper quartile and maximum air-bone gap values recorded. Across all subjects maximum air-bone gaps ranged from 5.6 dB HL at 9 kHz to 14.6 at 14 kHz. In order to simplify the test protocol and maintain consistency across frequencies, the maximum value across all frequencies was taken at the maximum "normal" positive air-bone gap. Differences exceeding this amount in listeners tested in the future will be considered to be significant air-bone gaps, indicative of a conductive component to the hearing loss. Therefore, 15 dB HL

when testing in 5 dB HL steps and 16 dB HL when testing in 2 dB HL steps was defined as the minimum air-bone gap required for significance. While these criteria are relatively conservative given that 75% of participants demonstrated an air-bone gap of less than 7 dB at each test frequency, we believe that given the limitations of the calibration method used, as discussed below, a conservative approach is appropriate.

6.6.6.3 Test-retest reliability

Based on the evaluation of several reliability measures, the test-retest reliability associated with threshold measurements made using the TEAC HP-F100 transducer was found to be very good across the EHF range. Maximum standard deviations across the three repeated measurements were between 3.1 and 5.0 dB across all test frequencies and all 95% minimal difference values were 6.0 dB or below. When evaluated against published reports of test-retest reliability associated with bone-conduction thresholds measured in the conventional frequency range (Dirks, 1964; Studebaker, 1962b), and in the EHF range (Hallmo et al., 1991), our results are comparable. Of particular interest is the comparison to Hallmo et al.'s reported test-retest reliability associated with bone-conduction thresholds measured with the KH-70 transducer in the EHFs. Although only two subjects were tested, validity was improved by repeating measurements 16 times over eight days. Standard deviations were reported that varied from 2.2 dB HL to 6.0 dB HL, and therefore were close to those found in the present study in the same frequency range.

Although removal and replacement of the transducer between sets of measurements was used to improve the validity of the test-retest variability estimate, test-retest reliability would be expected to be poorer if test sessions were separated further over time, something that was not done in the present study. In consideration of this limitation, more conservative criteria were selected for determining the magnitude of threshold change that would be defined as significant. Individual maximum difference scores reached a maximum of 8 dB for one participant at 10, 12.5, and 14, for two participants at 8 and 16 kHz, and reached 10 dB for one participant at 11.2 kHz. Based on these values and testing in 2 dB steps, 8 dB would be the most appropriate criteria across frequencies to capture a significant threshold change in the majority of cases. However, in the interests of selecting a more conservative criterion, primarily due to the limited subject numbers in this study and the expectation that variability would be greater when test sessions were separated by longer periods of time, a criterion of

10 dB or greater for all frequencies was selected for testing in both 2 and 5 dB steps. Applied to our data, this criterion would give a 5% false positive rate when the lowest and highest thresholds from each set of three for each participant are compared. It is also important to again note that threshold changes at each test frequency are independent (Atherley & Dingwall-Fordyce, 1963), and the probability that threshold changes of 10 dB or greater will occur in the same direction at more than one frequency due to normal variability is low. Greater certainty can therefore be attached to significant threshold changes at multiple frequencies.

6.6.6.4 Conclusions

As noted in Section 6.6.1.1, the real-ear method of transducer calibration is constrained by the normal variability that is apparent across listeners. Ideally, a very large group of subjects would have been tested to provide transducer calibration and test-retest reliability data. This is a particular constraint in the calibration phase of this study, as the high inter- and intra-subject variability in the relationship between air- and bone-conduction thresholds can produce inaccurate correction factors when small groups of subjects are tested (Wilber & Goodhill, 1967). Unfortunately, time considerations made testing a larger group impractical. As noted above, in acknowledgement of the limitations imposed by the relatively small subject numbers, we have selected more conservative criteria to define a significant air-bone gap and a significant threshold change than the data collected suggests is required. Despite this significant limitation our evaluations of variation in air-bone gaps and test-retest reliability indicate that the calibration is valid and that the reliability of repeated measurements performed with the TEAC HP-F100 device is clinically acceptable.

6.7 Non-osseous contributions to bone-conduction thresholds

As noted in Section 6.1, the degree to which thresholds measured with a given transducer are influenced by airborne sound is an important consideration. Airborne sound can be produced in response to bone-conduction stimulation either through acoustic energy leaking directly from the transducer, or from vibration of the cartilaginous walls of the canal (Stenfelt, Wild, et al., 2003). Both mechanisms of acoustic radiation result in cochlear stimulation via the air-conduction pathway. This is a concern clinically when airborne sound is of sufficient intensity to be perceived at a lower level than the true bone-conduction threshold. Acoustic radiation is typically minimal at low- and mid-frequencies, however at 4 kHz, and presumably higher frequencies, it can result in anomalous air-bone gaps (Frank & Crandell, 1986; Frank & Holmes, 1981; Matos, Valle, Dias, Santos, & Leite, 2010).

Direct acoustic radiation is dependent on the properties of the transducer, for example, the KH-70 device has a rubber housing that minimises acoustic radiation (Frank & Crandell, 1986). The TEAC devices do not offer any such protection. Popelka et al. (2010) performed measurements of acoustic radiation from the TEAC HP-F100 using a probe tube microphone positioned close to the EAC on three listeners and a research manikin wearing the transducer on the zygomatic process. Airborne sound radiated from the transducer was a minimum of 15 dB HL below the 45 or 65 dB HL bone-conducted test signal at each frequency from 0.125 to 16 kHz. In this previous study, airborne sound was measured only at a single presentation level at each frequency and analysed only in a one-third octave band centred at the test frequency. The presence of airborne sound at frequencies other than the test frequency is therefore unknown. This is an important consideration, given that in many cases listeners present with a sloping audiometric configuration, particularly in the EHF range.

The contribution of direct acoustic radiation to thresholds can be minimised by occluding the EAC during bone-conduction testing (Bell et al., 1980; Frank & Crandell, 1986; Frank & Holmes, 1981; Shipton, John, & Robinson, 1980). Indeed, Popelka et al. (2010) confirmed that airborne sound did not contribute to bone-conduction thresholds in three listeners by showing that thresholds did not shift when any airborne sound was blocked from entering the EAC by a circumaural earphone positioned over the pinna. However, an additional risk of airborne sound generated by the EAC affecting thresholds is introduced by the occlusion of the EAC. As discussed in Chapter 2, the external ear contributes to bone-conduction hearing through the vibration of the cartilaginous walls of the lateral part of the EAC, which set up a sound pressure that is transmitted to the cochlea via the air-conduction route. When the ear is

occluded, acoustic energy that would leak out of the patent EAC is trapped and travels to the inner ear, decreasing the measured threshold. The degree of threshold improvement resulting from EAC occlusion is typically negligible for frequencies above 1 kHz (Brinkmann & Richter, 1980; Dean & Martin, 2000; Elpern & Naunton, 1963; Kelley & Reger, 1937; Sullivan, Gotlieb, & Hodges, 1947; Tsai, Ostroff, Korman, & Chen, 2005; Watson & Gales, 1943). Although the effects of occluding the ears on bone-conduction thresholds in the EHF range have infrequently been measured, the available data suggests that there is no significant effect of occlusion on thresholds in this range (Hallmo et al., 1991; Popelka et al., 2010; Thornton et al., 1989). In the case of the TEAC bone-conduction transducer, a significant effect on EHF thresholds from airborne sound generated by soft tissue vibration was ruled out by Popelka et al. (2010) by comparing thresholds recorded with canals open and with foam earplugs inserted bilaterally to prevent EAC tissue vibration in two subjects.

In contrast to data demonstrating the absence of an occlusion effect in the EHF range, evidence suggests that occluding one canal causes EHF tones to lateralise to the occluded side, consistent with an increase in sound pressure in that EAC (Hallmo et al., 1991; Økstad et al., 1988; Tonndorf & Kurman, 1984). Hallmo et al. (1991) reported that with the KH-70 bone-conductor positioned on the forehead and one ear occluded with a finger, many listeners could lateralise EHF tones to the occluded ear, and at 16 kHz lateralisation was reported in 8 of 16 ears. It is interesting that in the absence of a measureable occlusion effect at least some high-frequency sound pressure must be trapped in the occluded EAC to enable lateralisation. Further investigation is required to explain this effect.

6.7.1 Aims and hypotheses

In order to confirm Popelka et al.'s (2010) finding that the contribution of non-bone conduction pathways to EHF thresholds measured with the TEAC device is negligible, we used both objective and behavioural measurements to investigate the level of airborne sound radiated from the bone-conductor and the effect of this sound on thresholds. The first aim of this phase of the study was to objectively measure airborne sound levels at the level of the EAC when EHF stimuli were presented to the TEAC transducer worn on the forehead. In an extension of the measurements performed by Popelka et al., recordings were made for pure-tone stimuli across a range of presentation levels, and airborne sound was analysed in one-third octave bands extending above and below the test frequency.

Our second goal was to replicate Popelka et al.'s (2010) comparison of thresholds with canals open and occluded in a larger number of subjects. This is of importance given the small number of subjects tested by Popelka et al. and that output levels from the transducers tested may vary given the absence of calibration standards. The study was designed to separate the effects of preventing the cartilaginous tissues of the ear canal vibrating and thus transmitting sound to the inner ear, and of covering the EAC to prevent sound radiating from the transducer from entering. The separation of these two effects was accomplished by assessing thresholds with both foam plugs and a circumaural earphone as the occluding devices. We hypothesised that if acoustic radiation is not a concern when the bone-conductor is positioned on the zygomatic process, it should be even less of an issue when the transducer is placed on the forehead; a site which reduces the level of airborne sound from the transducer that reaches the EAC (Margolis, 2008).

6.7.2 Method

6.7.2.1 Participants

Ten of the subjects who participated in the calibration phase of this study had a further set of bone-conduction thresholds measured with one of two occluding devices in place to provide the data for this component of the study. The ten subjects were randomly divided into two equal groups so that each occluding device was used with five participants. One of these participants was also employed to sit with the TEAC transducer positioned on his head so that objective measurements could be made. The age range of the participants was 22 to 43 years (M = 26.5, SD = 6.4), and the group included two males and eight females.

6.7.2.2 Equipment

6.7.2.2.1 Objective measurements

Two microphones were used to measure the airborne sound radiating from the TEAC bone-conduction transducer. On the left side, a Brüel & Kjær 4189 ½ inch microphone (Brüel & Kjær, Nærum, Denmark), and on the right side, a G.R.A.S. 40HF low-noise measurement system which has a 1 inch microphone (G.R.A.S., Holte, Denmark). According to the manufacturers specifications, the Brüel & Kjær (B & K) ½ inch microphone has a frequency range of 6.3 Hz to 20 kHz and a dynamic range of 14.6 – 146 dB(A), whereas the G.R.A.S. 1 inch microphone has a smaller frequency range of 6 Hz to 12.5 kHz, but a lower limit on the dynamic range of -2 dB(A), extending up to 110 dB(A). Used together, the two microphones enabled us to make very sensitive measurements across a wide frequency range. Adjustable height stands were used to hold the microphones at ear level. The microphones were connected to a Brüel & Kjær PULSE multi-analyser system Type 3560-C laptop running Brüel & Kjær PULSE LabShop software (Brüel & Kjær, Nærum, Denmark).

The pure-tone stimuli were presented using the modified TEAC HP-F100 bone-conduction transducer (TEAC, Tokyo, Japan) and sound card audiometer.

Measurements were made with the adult volunteer seated on a chair in the centre of a sound treated, double-walled booth. Stimulus presentation and recording equipment was positioned outside the booth and cables were run through a small gap underneath the door.

6.7.2.2.2 Threshold measurements

The apparatus used for the measurement of occluded versus unoccluded thresholds was identical to that described for EHF bone-conduction threshold measurement in Section 7.4.4.2 aside from the addition of occluding devices. Two occluding devices were used to assess the contribution of non-bone-conduction pathways: E·A·R TaperFit foam earplugs (3M, Maplewood, MN) and the Sennheiser HDA 200 circumaural headphones.

6.7.2.3 Procedure

6.7.2.3.1 Objective measurements

The bone-conduction transducer was positioned with the contact surface at the centre of the forehead, on the midline. The height of the microphone stands was adjusted and each microphone was positioned 1 cm from the entrance to the participant's ear EAC. The participant was asked to sit as still and quiet as possible during recordings.

Continuous pure-tone stimuli at audiometric test frequencies from 8 – 16 kHz were presented in 5 dB HL steps from 0 dB HL to the maximum output of the audiometer. Tones were presented for 2 seconds with a 1 second interval between presentations.

Sound levels were measured in one-third octave bands centred on frequencies from 31.5 Hz to 20 kHz using a fast time weighting (τ = 125 ms). Discrete samples of sound levels were recorded with a time between samples of 0.01s. Data was exported from the PULSE LabShop software into Microsoft Excel (2010) (Microsoft, Redmond, WA) for analysis.

6.7.2.3.2 Threshold measurements

A fourth set of EHF bone conduction thresholds were measured during the same test session as calibration threshold measurement in the ten subjects. As for the previous measurements, the bone-conductor was positioned on the forehead and a Sennheiser HDA 200 earphone was positioned over the non-test ear. To ensure that the only parameter altered between the occluded and unoccluded measurements was the presence of the occluding device, the bone-conductor and the circumaural earphone covering the non-test ear were not moved from the positions used for the set of unoccluded threshold measurements to which they were compared. In five subjects the remaining HDA 200 earphone was positioned over the test ear. In the other five subjects the test ear was occluded using an E·A·R foam plug. The plug was

inserted so that the lateral edge was flush with the tragus. EHF bone-conduction thresholds were measured at 8 – 16 kHz using the same protocol as for the three sets of bone-conduction measurements previously described. The order in which occluded and unoccluded threshold measurement sets were performed was counterbalanced across participants.

6.7.2.4 Data analysis

The maximum amplitude of airborne sound was calculated for each analysis frequency band for each stimulus presentation level. These values were extracted from the data recorded using each of the two microphones and converted from dB SPL into dB HL using reference thresholds for binaural free-field listening (frontal incidence) as specified by the ISO (2005).

To determine whether there was an effect of occluding the test ear with the foam plug or circumaural earphone, thresholds measured with each occluding device in place were compared at each frequency to the set of unoccluded thresholds measured with the transducer in exactly the same location. Two factors must be considered when the test ear is occluded; the possibility of an increase in energy generated by the vibration of the EAC walls being transmitted to the inner ear, which would result in threshold decrease, and that acoustic radiation from the body of the transducer is prevented from reaching the inner ear, which potentially increases thresholds. The comparison of thresholds measured with each type of occluding device to unoccluded thresholds is important to distinguish between the two effects. Both occluding devices should prevent airborne sound leaking from the transducer lowering bone-conduction thresholds, whereas only the foam plug should prevent sound pressure being generated by vibration of the soft tissue of the canal and transmitted to the cochlea via the air-conduction route. The effects of occlusion itself, type of occluding device, and frequency on bone-conduction thresholds were assessed by performing a three-way mixed design ANOVA. Two separate repeated-measures ANOVAs, one for each type of occluding device, were also performed to assess for an effect of occlusion on thresholds. Analyses were performed using IBM SPSS version 21 (SPSS IBM, Armonk, NY).

6.7.3 Results

6.7.3.1 Direct acoustic radiation

Figures 48 to 51 show the airborne sound levels recorded when pure-tone stimuli were presented to the TEAC bone-conductor at 1/6th octave frequencies from 8 to 16 kHz. At all frequencies assessed, the level of airborne sound increased approximately linearly (≈1 dB/dB) with the presentation level of the stimulus. No airborne sound was detected above the measurement noise floor for noise bands below 5 kHz for any test frequency, therefore data is presented only for one-third octave bands with centre frequencies of 5 kHz to 16 kHz.

The differences in the characteristics of the two microphones used are evident in the measurements at all frequencies. In particular, the lower noise floor of the G.R.A.S. 1 inch microphone results in a greater ability to demonstrate the presence of acoustic radiation at lower stimulus presentation levels than is possible with the B & K ½ inch microphone.

When pure-tone stimuli were presented at 8 and 10 kHz airborne sound exceeded 0 dB HL at presentation levels of 25 dB HL and above and was highest in the noise band centred at the test frequency (Figures 48a and b and 49a and b). When measured using the B & K microphone, airborne sound present in the one-third octave band centred at the test frequency was a minimum of 18 dB and 17 dB lower than the stimulus presentation level for 8 kHz and 10 kHz, respectively. The same measurements performed using the G.R.A.S. microphone showed airborne sound levels at least 23 dB below the test tone for an 8 kHz signal and 25 dB below for a 10 kHz signal. As is evident from Figure 49 and 50, airborne sound was present at frequencies both higher and lower than the test tones. For 8 kHz the greatest off-frequency energy was present in the noise band centred at 6.3 kHz, where energy was at least 31 dB below the stimulus presentation level. When the stimulus was a 10 kHz signal, airborne sound was present as almost equal levels in the noise bands centred at 8 and 12.5 kHz and was always at least 34 dB HL lower than the test tone.

The 9 kHz pure-tone stimulus produced airborne sound that was maximal in the two noise bands centred either side of the test frequency; 8 and 10 kHz (Figure 48c and d) and exceeded 0 dB HL with test tone presentations at 30 dB HL and above. The level of airborne sound in the one-third octave band centred at 8 kHz was a minimum of 28 dB lower than the bone-conducted signal when measured using the B & K microphone and 25 dB lower than the presentation level measured with the G.R.A.S. microphone. Similar levels were recorded in the 10 kHz noise band, with airborne sound reaching a maximum of 25 dB below the test

tone presentation level for the B & K microphone and 26 dB below for the G.R.A.S. microphone. Energy was at least 20 dB lower again in other frequency bands.

Airborne sound levels measured during the presentation of 11.2 kHz (Figure 49c and d) and 12.5 kHz test tones (Figure 50a and b) were similar to those at the three lower frequencies and was measureable above 0 dB HL at presentation levels of approximately 30 dB HL and higher for both stimulus frequencies. When measured using the B & K microphone, acoustic radiation generated during presentation of the 11.2 kHz stimulus was at least 30 dB lower than the presentation level at 10 kHz, and at least 24 dB lower in the noise band centred at 12.5 kHz. For the same stimulus, using the G.R.A.S. microphone, acoustic radiation was at least 38 dB lower than the presentation level at 10 kHz, and at least 37 dB lower in the noise band centred at 12.5 kHz. Acoustic radiation above the level of the noise floor was minimal in other frequency bands. For the 12.5 kHz tone, airborne sound was at least 21 dB (B & K microphone) to 22 dB (G.R.A.S. microphone) below the presentation level of the test tone in the noise band centred at 12.5 kHz. Airborne sound in the 10 and 16 kHz noise bands remained at least 34 dB below the stimulus presentation level.

Measurements of airborne noise when a pure-tone of 14 kHz was presented to the bone-conductor were of the greatest concern. As shown in Figure 50c and d, airborne sound exceeded the noise floor in the 12.5 and 16 kHz noise bands from the 5 dB HL presentation level. Acoustic radiation was maximal in the 12.5 kHz noise band and was within 6 dB of the presentation level at its maximum when measured with the G.R.A.S. microphone and within 2 dB of the presentation level when measured with the B & K microphone. Airborne sound was markedly lower in the 16 kHz noise band and was a minimum of 34 dB below the bone-conduction presentation level with the G.R.A.S. microphone and 30 dB with the B & K microphone. The concern here is that the level of sound exactly at the 14 kHz test frequency is likely to be higher than that in the one-third band centred at 12.5 kHz, and could therefore exceed the level of the test tone.

Airborne sound was also measureable in the recording noise band centred at 20 kHz when the 14 kHz stimulus was presented at 20 dB HL and above. At its maximum, airborne sound in the 20 kHz band exceeded the noise floor by 19.2 dB SPL when measured using the G.R.A.S microphone at 40 dB HL presentation level. These values were not converted into dB HL due to the absence of ISO (2005) reference levels for this frequency.

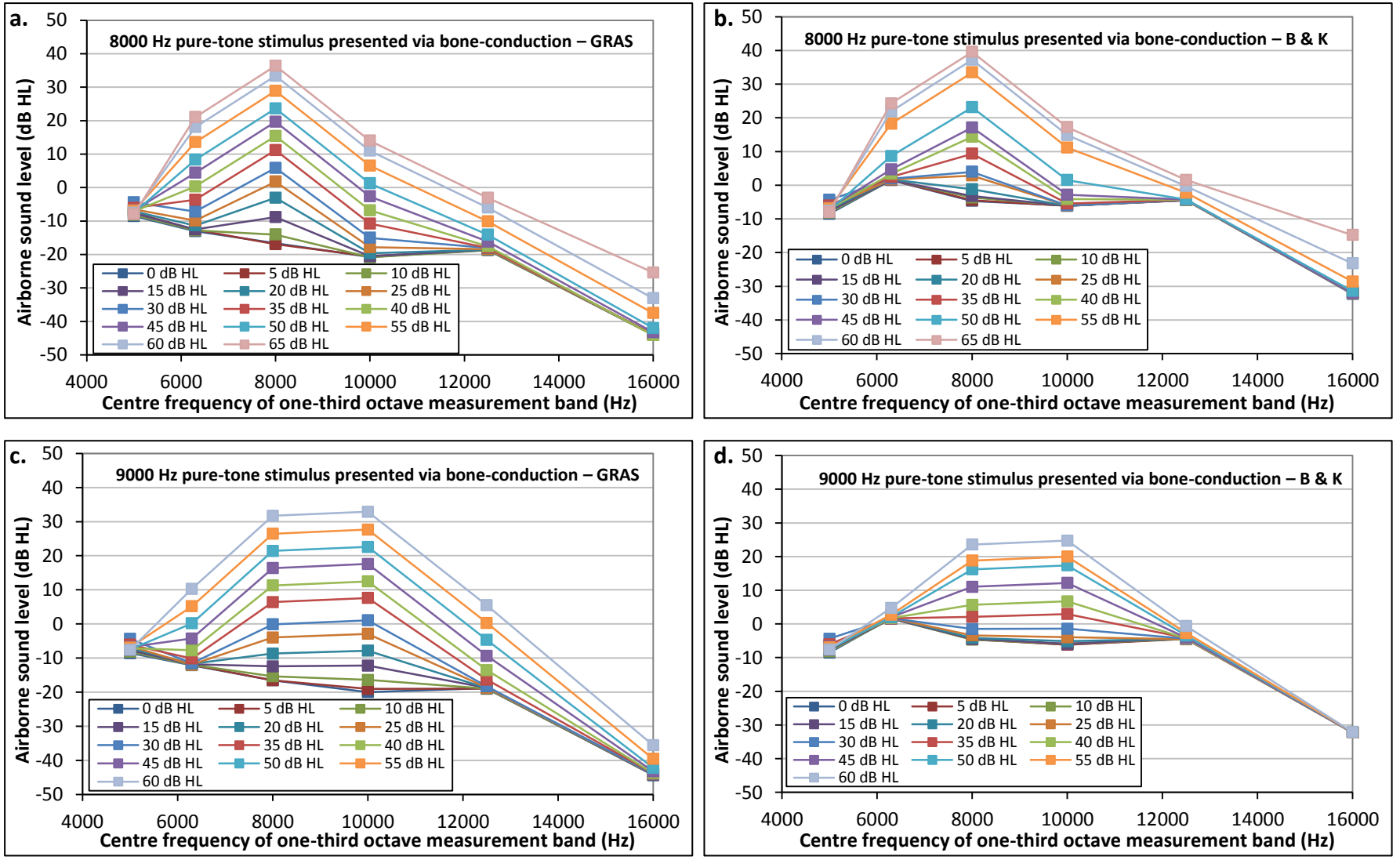

Figure 48. Airborne sound in one-third octave bands with centre frequencies from 5 to 16 kHz measured with GRAS (a and c) and B&K (b and d) microphones during the presentation of 8 kHz (a and b) and 9 kHz (c and d) pure-tones to the TEAC bone-conduction transducer.

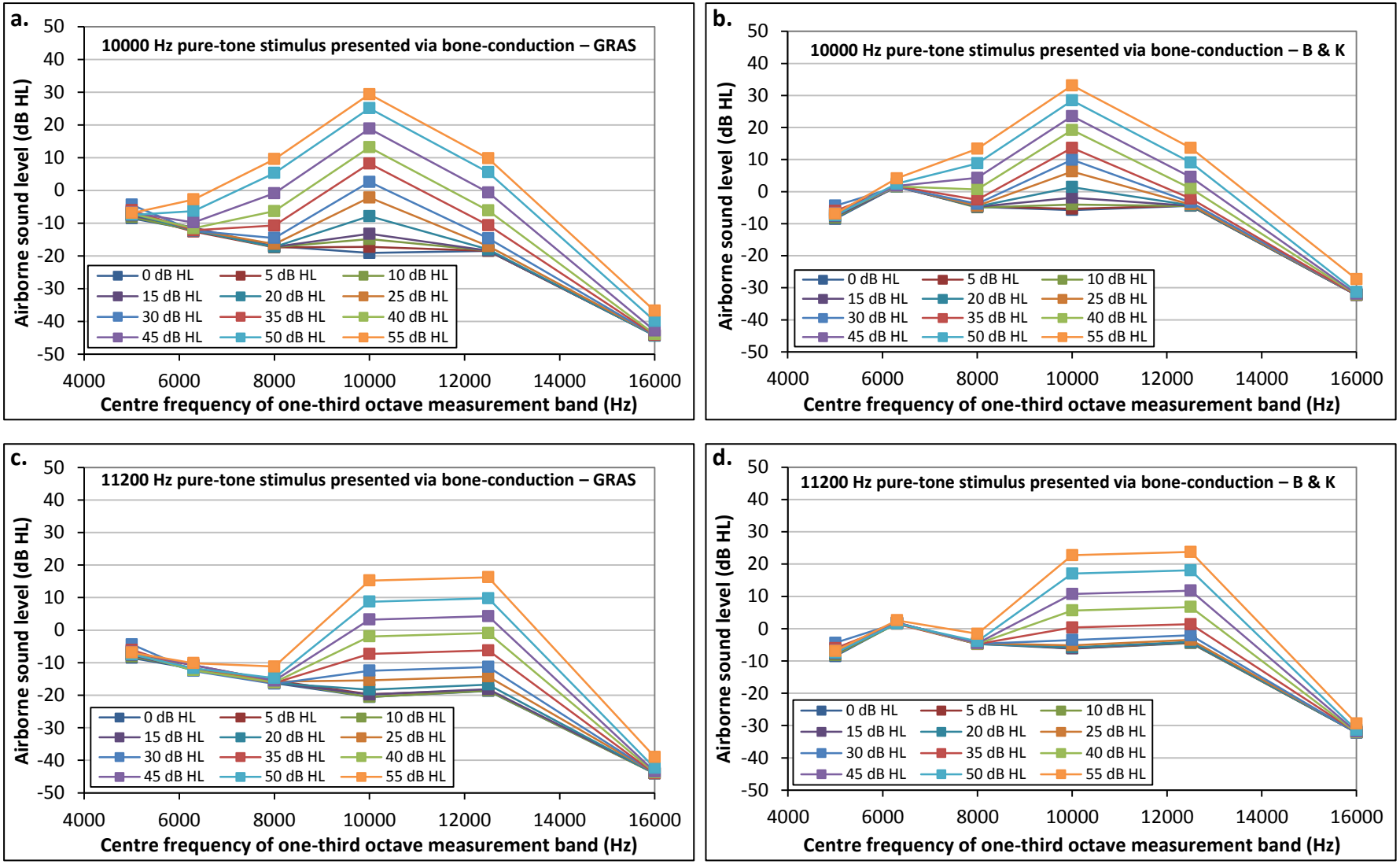

Figure 49. Airborne sound in one-third octave bands with centre frequencies from 5 to 16 kHz measured with GRAS (a and c) and B&K (b and d) microphones during the presentation of 10 kHz (a and b) and 11.2 kHz (c and d) pure-tones to the TEAC bone-conduction transducer.

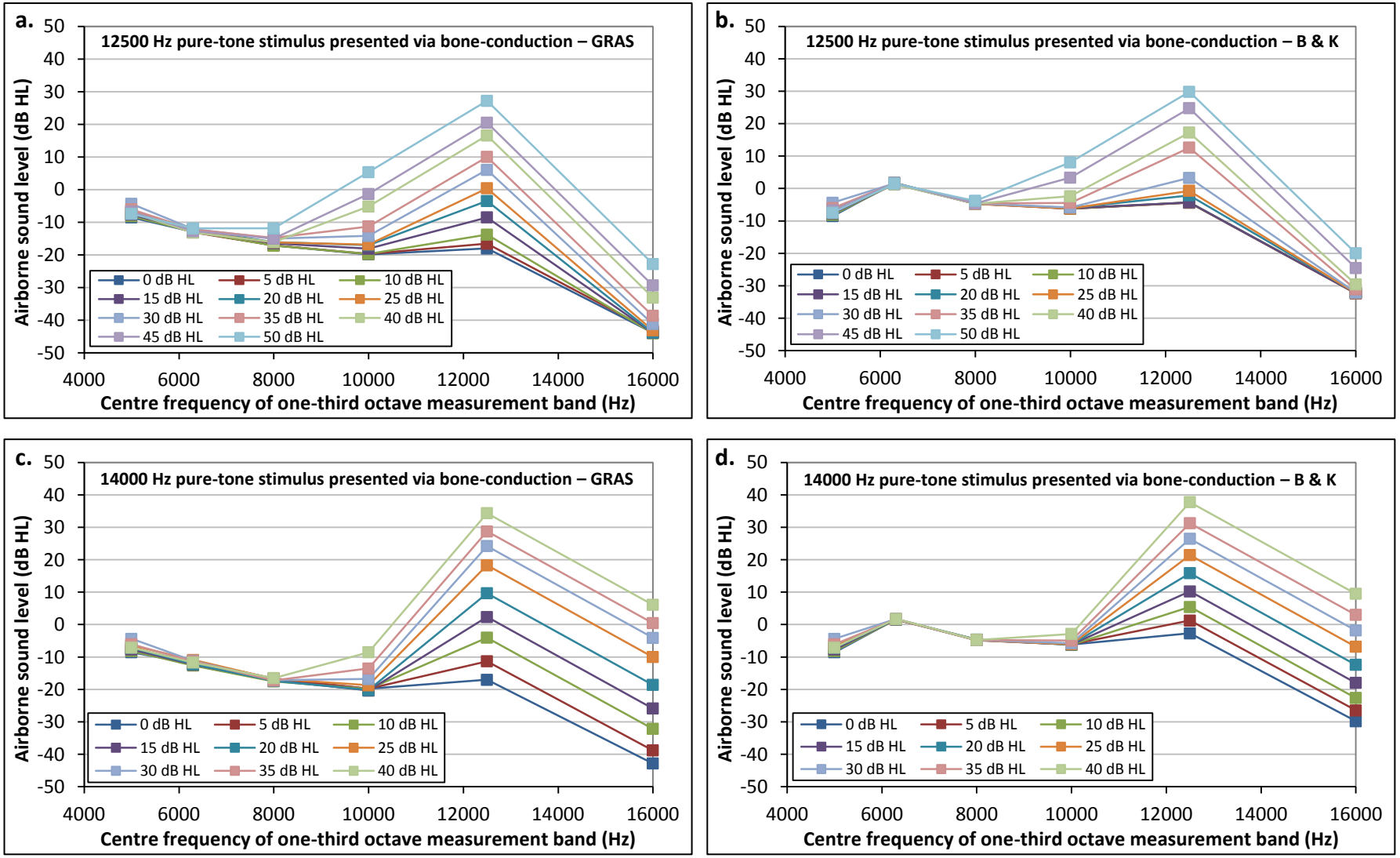

Figure 50. Airborne sound in one-third octave bands with centre frequencies from 5 to 16 kHz measured with GRAS (a and c) and B&K (b and d) microphones during the presentation of 12.5 kHz (a and b) and 14 kHz (c and d) pure-tones to the TEAC bone-conduction transducer.

Airborne sound generated by the bone-conductor in response to the presentation of a 16 kHz pure-tone was present only in bands centred at 12.5 kHz and above (Figure 51) and always remained below 0 dB HL. Acoustic radiation was a minimum of 36 dB below the presentation level measured with either microphone in the 16 kHz noise band, and at least 33 dB (B & K microphone) and 36 dB (G.R.A.S. microphone) below the presentation level in the noise band centred at 12.5 kHz. Airborne sound was also measureable at presentation levels of 20 dB HL and above in the band centred at 20 kHz. At its maximum, airborne sound in the 20 kHz band exceeded the noise floor of the G.R.A.S microphone by only 8.7 dB SPL, and reached 7.2 dB SPL.

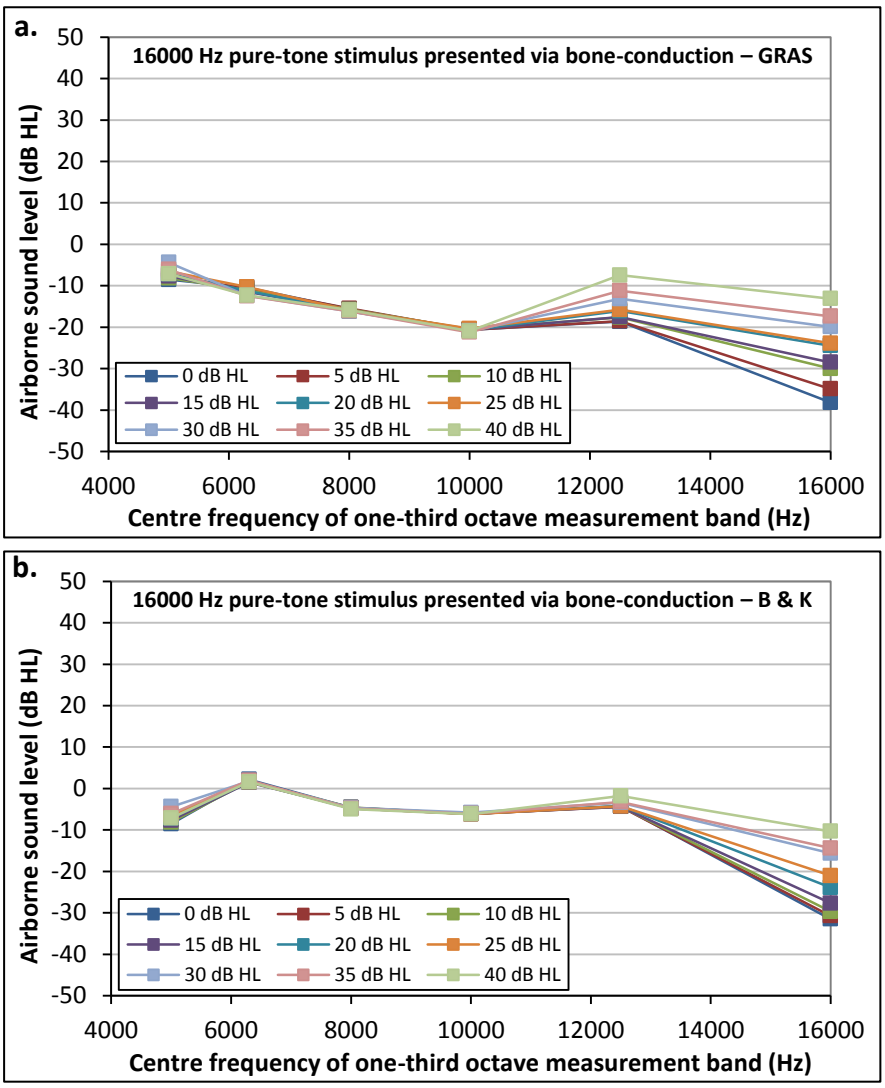

Figure 51. Airborne sound in one-third octave bands with centre frequencies from 5 to 16 kHz measured with GRAS (a) and B&K (b) microphones during the presentation of a 16 kHz pure-tone to the TEAC bone-conduction transducer.

6.7.3.2 Occluded versus unoccluded thresholds

As shown in Figure 52, occluding the test ear with a circumaural earphone produced a small mean increase in the bone-conduction threshold at all frequencies except 16 kHz, at which the mean change was 0 dB (*SD* = 2.4 dB). The greatest threshold increase compared to the unoccluded condition was found at 9 kHz (*M* = 3.2 dB, *SD* = 2.3 dB) where four of the five subjects tested demonstrated a threshold increase. Mean unoccluded-occluded threshold differences at all other frequencies were less than 2 dB. When we defined a significant change as greater than two threshold-seeking steps (+/- 4 dB), only one participant showed significant change in threshold with occlusion; an increase of 6 dB at 9 kHz.

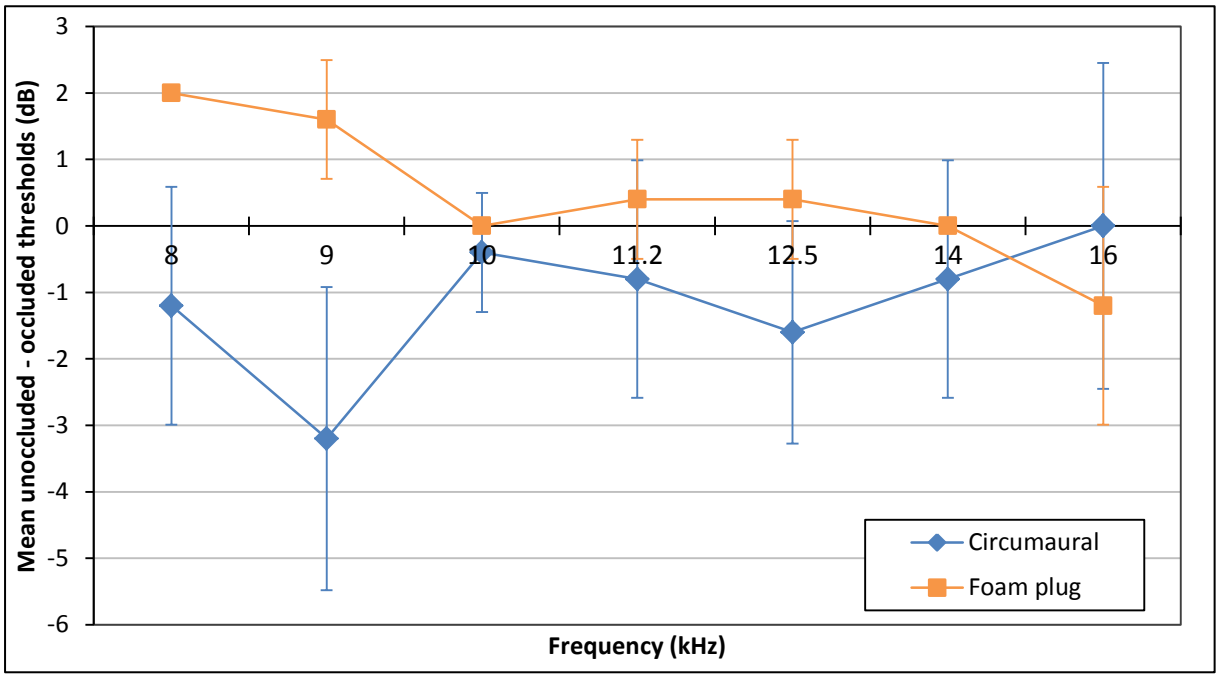

Figure 52. Difference between thresholds measured with the test ear unoccluded and occluded. Positive values indicate a decrease (improvement) in the threshold and negative values indicate an increase (worsening) of the threshold when the ear was occluded. Error bars show standard deviation.

When the foam plug was used to occlude the test ear, a mean threshold increase was documented at 16 kHz only (*M* = 1.2 dB, *SD* = 1.8 dB), while mean threshold decreases with occlusion were found at 8, 9, 11.2, and 12.5 dB. The greatest mean decrease recorded was 2 dB (*SD* = 0 dB) at 8 kHz. No unoccluded-occluded differences exceeded +/- 2 dB for any subject at any frequency.

A three-way mixed factor ANOVA was performed with two within subjects variables; test frequency and occlusion state (open vs. occluded), and one between subjects variable; type of occluding device. The analysis showed no significant difference between occluded and unoccluded thresholds ($F(1, 8) = 3.07$, $p = .12$). There was however a significant interaction between occlusion and type of occluding device ($F(1, 8) = 6.90$, $p = .03$), indicating that although occlusion with either device does not produce a significant change from thresholds measured with the ear open, the effect does vary depending on whether a foam plug or a circumaural earphone are used. This is evident from the pattern of results shown in Figure 52, which illustrates, particularly at 8 and 9 kHz, that occluding the ear with a circumaural earphone resulted in a mean worsening of thresholds, whereas occlusion with a foam plug resulted in improved mean thresholds.

Mean thresholds varied significantly with test frequency ($F(6, 48) = 21.00$, $p < .001$), however the effect of frequency was not found to differ depending on whether or not the test ear was occluded ($F(2.97, 23.76) = 0.93$, $p = .44$). It is interesting to note that the effect of occlusion was significantly greater at lower frequencies, whereas at 14 kHz, the frequency at which we had concerns regarding acoustic radiation based on the airborne sound measurements, threshold changes with occlusion were minimal.

In view of the significant interaction found between occlusion and occluding device, two separate two-way repeated measures ANOVAs were performed; one for each occluding device group. For both analyses the two within-subjects variables were occlusion and frequency. Neither ANOVA showed a significant effect of occlusion ($F(1, 4) = 7.62$, $p = .051$ and $F(1, 4) = 0.52$, $p = .51$, for the circumaural earphone and the foam plug, respectively). There was a significant effect of frequency on thresholds for both the circumaural ($F(6, 24) = 11.97$, $p = < .001$) and foam plug ($F(6, 24) = 9.93$, $p = < .001$) groups, but no significant interaction between occlusion and frequency for either group (circumaural: $F(6, 24) = 1.78$, $p = .15$; foam plug: $F(6, 24) = .60$, $p = .73$), consistent with the overall effect of frequency found when data from both groups were included.

6.7.4 Discussion

Objective measurements of acoustic radiation generated by the TEAC HP-F100 transducer showed that for stimuli presented at 8 – 12.5 kHz and at 16 kHz, airborne sound levels are well below the level of the bone-conducted stimulus. This suggests that acoustic radiation will not result in underestimation of the bone-conduction threshold at these frequencies. Airborne sound in each one-third octave frequency band was a minimum of 17 dB below the presentation level of the stimulus across all of these test frequencies and increased approximately linearly with stimulus intensity. These findings are in agreement with Popelka et al. (2010), who found that the minimum difference between the bone-conduction presentation level and the level of acoustic radiation at the test frequency was 15 dB HL for a 4 kHz pure-tone presented at 65 dB HL.

Airborne sound generated by the presentation of a 14 kHz stimulus to the TEAC transducer, however, was of a level that could potentially contaminate bone-conduction threshold measurements. Based on airborne sound levels recorded using the B & K microphone, airborne sound reached a level only 2 dB below the presentation level of the 14 kHz stimulus. The maximum level of acoustic radiation was present in the one-third octave band centred at 12.5 kHz, raising the possibility that if we had recorded airborne sound at discrete frequencies, rather than in one-third octave bands, we may have recorded an even higher level of airborne sound at 14 kHz. This is considered a limitation of the methodology of the present study. Given that many hearing losses are sloping, airborne sound at 12.5 kHz could exceed the threshold at that frequency causing the listener to respond before the 14 kHz threshold is reached.

Why we found results suggesting problematic airborne sound at 14 kHz and Popelka et al. (2010) did not, is unclear. One strong possibility is that as the B & K type 4176 ½ inch microphone used by Popelka et al. has a frequency range of 6.5 Hz to 12.5 kHz, it was less sensitive to the high frequency airborne sound at 14 kHz than the measurement equipment used in the present study. However, our G.R.A.S microphone had the same reported frequency range, albeit with a greater dynamic range, as the B & K type 4176, and still produced data showing high-frequency airborne noise that was only slightly lower than our wider frequency range B & K microphone. Another potential reason for the differences between the two studies is that differences or errors in the real-ear calibration used in each case may have meant stimuli were presented at different levels in each study. As Popelka et al. positioned the transducer on the zygomatic process much closer to the EAC, the

apparently increased effect of acoustic radiation found in our study where the transducer was positioned on the forehead, contradicts our hypothesis that the level of airborne sound in our study should be lower than that previously reported.

A key difference between the methodology in the present study and that employed by Popelka et al. (2010) was that we recorded airborne sound in one-third octave bands centred at frequencies from 31.5 Hz to 20 kHz, rather than only the band centred at the test frequency. This method was designed to determine whether output at non-test frequencies indicated the presence of distortion, and whether airborne sound at other frequencies could be sufficient to influence the measured threshold. At all frequencies our measurements showed the presence of low-level airborne sound at frequencies above and below the test frequency. With the exception of the results for 14 kHz, acoustic radiation was not of a level likely to influence thresholds by being detected by air-conduction at other frequencies before the stimulus is detected by bone-conduction at the test frequency. The results do, however, indicate some degree of distortion in the output of the TEAC transducer, which limits the dynamic range by spreading output across frequencies. Popelka et al. conducted electroacoustic assessments of the TEAC transducer and demonstrated that distortion produced by the transducer was less than 3%, which was considered clinically acceptable.

Whereas objective measurements suggested that airborne sound generated by the TEAC transducer during production of a 14 kHz pure-tone could potentially shift the bone-conduction threshold, we found no significant difference between the thresholds measured at any frequency with the ears occluded and unoccluded. If direct acoustic radiation from the transducer is contributing to thresholds, we would expect thresholds to increase when the airborne sound energy is blocked from entering the EAC using either the circumaural earphone or the foam plug. The present results showed no significant change in thresholds with either occluding device. A small, non-significant mean increase in thresholds was documented when the circumaural earphone was used, however the finding that the foam plug resulted in improved thresholds suggests that the trend towards increased thresholds was not a consequence of precluding acoustic radiation from reaching the inner ear. Overall, these results suggest that acoustic radiation did not contribute significantly to thresholds.

Although occlusion of the canal is an effective method of preventing acoustic radiation generated by the transducer from reaching the cochlea, occlusion may also cause the sound pressure set-up by the vibration of the cartilaginous walls of the EAC to be transmitted to the cochlea, potentially improving thresholds (Brinkmann & Richter, 1980; Elpern & Naunton,

1963; Kelley & Reger, 1937; Sullivan et al., 1947; Tsai et al., 2005; Watson & Gales, 1943). The foam plug, but not the circumaural earphone, used in the present study should prevent vibration of the EAC walls by pressing against them, ensuring an increase in sound pressure to the inner ear would not result from occlusion. We therefore predicted that if cochlear stimulation in the EHF range includes a contribution from the vibration of the cartilaginous canal walls transmitted via air-conduction, thresholds with the foam plug would worsen beyond those measured with the circumaural headphone. Under the same assumption, we would expect that thresholds would improve when the ear was occluded with an earphone relative to those measured with the ear unoccluded. Our results contradict these hypotheses. Occlusion with the foam plug resulted in a non-significant improvement in thresholds compared to those measured unoccluded, whereas occlusion with the earphone corresponded to a slight worsening of thresholds. This effect suggests there is no significant increase in EHF acoustic energy transmitted to the cochlea when the ear is occluded and therefore sound pressure set up by canal wall vibration does not significantly influence unoccluded EHF thresholds. Again, these results are in agreement with those of Popelka et al. (2010).

Although overall we found no significant effect of occlusion on thresholds at any frequency, there was a significant interaction between occlusion and occluding device. Using an earplug resulted in improved thresholds at most frequencies, whereas the circumaural earphone resulted in a worsening in thresholds at most frequencies. While this interaction indicates opposite effects on thresholds produced by occluding the ear with each of the devices, overall the results still show that neither device produced a significant change in thresholds compared with those measured with the test ear unoccluded. It seems likely that the unexpectedly divergent effects of the two occluding devices used were the result of small subject numbers employed and normal test-retest variation between the measurements.

While the behavioural measures may indicate that the level of airborne sound, including that produced in response to a 14 kHz test tone, is not sufficient to contaminate bone-conduction thresholds in our participants, this may not necessarily be the case for all listeners. In listeners with a more precipitous decline in hearing with increasing frequency, airborne sound at lower frequencies would be more likely to be detected by air-conduction before the true bone-conduction threshold is reached at the test frequency. Given this risk and the evidence that occluding the ears does not have a detrimental effect on thresholds, we concluded that both ears should be occluded during future testing to minimise any chance of acoustic radiation being transmitted through the EACs during bone-conduction testing.

6.8 Summary

The aims of the studies presented in this chapter were to confirm that the TEAC HP-F100 transducer was suitable for assessment of EHF bone-conduction thresholds; to develop the optimal protocol for bone-conduction threshold using the TEAC transducer; and to assess the reliability associated with audiometric thresholds measured with this device.

We first established that measurement reliability with the transducer positioned on the zygomatic process was inadequate. With preliminary data indicating that reliability was acceptable with the transducer in both the mastoid and forehead positions, it was decided based on practical considerations regarding the use of the transducer postoperatively, that the most suitable location to position the transducer was the forehead. Masking protocols were then developed and calibration of narrowband masking noise using the custom audiometer was performed so that ear-specific correction values could be measured to calibrate the bone-conductor in dB HL.

Calibration of the HP-F100 transducer was performed using the real ear method under the assumption that in the absence of a conductive hearing loss air- and bone-conduction thresholds will, on average, be equal. The initial step in this procedure was to convert air-conduction thresholds measured with the sound card audiometer using correction values calculated using comparisons of objective measures of audiometer output from the calibrated GSI 61 audiometer and the sound card audiometer. Twenty participants then underwent three sets of bone-conduction threshold measurements in the EHF range to determine the average difference between air- and bone-conduction thresholds and calculate frequency-specific correction values that could be applied to bone-conduction thresholds to specify them in dB HL. Given the mean, maximum, and minimum differences between the air- and bone-conduction thresholds in dB HL in this population without conductive hearing loss, the criterion for a significant air-bone gap to be used in future studies was conservatively defined as when a single air-conduction threshold exceeded the bone-conduction threshold at the same frequency by at least 16 dB HL.

The variation across the three sets of thresholds measured during the calibration phase of this study was assessed to determine the test-retest variability of thresholds measured with the TEAC transducer. Intrasubject reliability was found to be very good at all frequencies and was comparable with previously published data for bone-conduction thresholds in both the conventional frequency and EHF ranges. Due to the limitations of this study protocol in that

test-retest reliability was determined by comparing measurements made in a single test session in a reasonably small group of listeners, more conservative criteria than the data suggested were required were adopted and the degree of threshold change at a single frequency that will be taken as significant was set at 10 dB HL or greater.

The final stage of this study was the examination of the contribution of non-osseous pathways, specifically acoustic radiation directly from the transducer and from vibration of the cartilaginous walls of the EAC, to bone-conduction thresholds. Objective measurements of airborne sound generated by the transducer were performed, as were assessments of changes in thresholds using two types occluding devices in ten participants. Laboratory measurements showed levels of airborne sound that were potentially disruptive to frequency specific and bone-conduction specific testing at 14 kHz only. However, behavioural testing revealed no significant difference between occluded and unoccluded thresholds, suggesting that airborne sound resulting from application of the bone-conduction stimulus was not sufficient to alter thresholds in our participants at any frequency. Overall, these results indicate that thresholds measured with the HP-F100 device provide a valid indication of bone-conduction hearing sensitivity; nevertheless due to the concerns arising from objective acoustic radiation measures, we concluded that thresholds should, in future, be measured with both ears occluded to prevent airborne sound reaching the cochlea.

In summary, in this chapter we determined that valid and reliable bone-conduction thresholds could be measured using the HP-F100 transducer. The protocol developed will be applied to listeners who potentially have a conductive hearing loss in the EHFs in the following chapter and the implications of the results for the reliability and protocol issues introduced in this chapter will be discussed.

Chapter 7: Distinguishing between conductive and sensorineural EHF hearing loss following middle ear surgery

7.1 The nature of EHF hearing loss following middle ear surgery

As demonstrated in the study presented in Chapter 3, hearing loss in the EHF range that persists well beyond the period over which conventional frequency thresholds have recovered occurs in approximately half of patients following stapes surgery and in a slightly lower percentage of patients after tympanoplasty. Additionally, transient EHF hearing loss occurs in the early postoperative period in a significant number of patients who have undergone ossiculoplasty. Our data shows that EHF hearing loss is more severe and more prevalent shortly after surgery, and that complete recovery in some patients and partial recovery in others occurs by around three months after surgery. As has been emphasised, the key piece of data regarding postoperative EHF hearing loss that has not yet been adequately described is changes in bone-conduction thresholds relative to air-conduction thresholds. Specifically, it is not clear whether bone-conduction thresholds are elevated after surgery along with air-conduction thresholds, indicating that the hearing loss is sensorineural, or whether bone-conduction thresholds are maintained at preoperative levels while air-conduction thresholds increase, consistent with a conductive hearing loss. It is necessary to make this distinction to clarify whether surgery is traumatic to the cochlea, or whether EHF hearing loss is a result of changes in the physical properties of the middle ear structures, and thus middle ear transmission characteristics.

The limited literature regarding EHF bone-conduction threshold changes following reconstructive middle ear surgery was reviewed in detail in Chapter 3. To summarise, deterioration of EHF electrostimulation thresholds has been reported following stapedectomy (Doménech & Carulla, 1988) and tympanoplasty (Doménech et al., 1989). The clinical importance of these postoperative changes in electrostimulation thresholds measured using the Audimax 500 high-frequency audiometer is unclear given that the method of cochlear stimulation differs from traditional bone-conduction measurements. Assuming that electrostimulation provides a valid estimate of cochlear function, despite the stimulation pathway most likely not being identical to that for a mechanical bone-conductor (Löppönen, Laitakari, et al., 1991; Löppönen & Sorri, 1991; Økstad et al., 1988), both Doménech and Carulla (1988) and Doménech et al.'s (1989) studies do demonstrate that inner ear function

can be at least temporarily impaired following middle ear surgery performed to reconstruct the conductive mechanism. Doménech and Carulla demonstrated a "moderate" hearing loss at 6 – 19 kHz in 20 of 24 patients a few days after stapedectomy, and a lowering of the highest frequency at which a hearing threshold was measureable in 16 patients. Whether this apparently sensorineural loss persisted beyond the initial postoperative period is unknown. Similarly, Doménech et al. (1989) demonstrated a measurable EHF hearing loss in nine of 24 patients following tympanoplasty, however, again whether this hearing loss was permanent is not clear as the timing of follow-up assessments was not stated. Aside from the absence of data beyond the initial postoperative period in these studies, the key concerns regarding these previous investigations is the absence of masking to ensure the response measured is that of the operated ear, and the lack of corresponding air-conduction measurements made to confirm the EHF threshold shift.

Myringoplasty is the only surgery for which data describing both EHF air- and bone-conduction changes postoperatively has been published. Mair and Hallmo (1994) demonstrated that although mean air-conduction thresholds across the 22 patients were elevated at 6 to 18 kHz after surgery, mean bone-conduction thresholds at the same frequencies measured using the Präcitronic KH70 electromagnetic high-frequency bone-conductor did not change significantly from preoperative levels. This data, collected an average of 4.5 months after surgery, suggests that the mean hearing loss remaining at this stage after surgery was conductive. What we cannot tell from this data is whether hearing was initially poorer in the early postoperative period, as occurred in our series, and whether this initial loss may have been the result of a recoverable (at least on average) injury to the cochlea. In addition, cases of EHF sensorineural loss in Mair and Hallmo's series may also have been obscured by the use of group mean data to evaluate outcomes.

As discussed in Chapter 3, it is possible that early EHF hearing loss and persistent postoperative EHF hearing loss are the result of two different mechanisms. For instance, the early depression of the 4 kHz bone-conduction threshold may be indicative of some degree of trauma to the inner ear that recovers in the majority of patients. Potentially, a similar phenomenon occurs in the EHF range, with early sensorineural loss, and perhaps persistent conductive hearing loss resulting from permanent changes to the physical properties of the middle ear transmission pathway. If this scenario was correct, it may be that Mair and Hallmo (1994) study detected the persistent conductive hearing loss 4.5 months after myringoplasty,

but that the assessment protocol was not sensitive to transient sensorineural hearing loss in the early postoperative period.

Alternatively, while the conclusion of Mair and Hallmo (1994) that postoperative EHF hearing loss is conductive may be correct in the case of myringoplasty, long-term EHF hearing loss after stapedectomy, which we hypothesise is associated with a greater risk of cochlear harm, may be due to permanent damage to the inner ear. In order to resolve these questions EHF bone-conduction and air-conduction threshold measurements are required both in the days following surgery and later in the postoperative period once healing has been allowed to take place. The magnetostrictive bone-conduction transducer described, tested, and adapted for audiometric testing in the previous chapter provides an opportunity to test bone-conduction thresholds in the EHF range and compare these to air-conduction thresholds so that the site of lesion can be established.

7.1.1 Aims and hypotheses

This chapter describes a small pilot study designed to demonstrate both the potential of the bone-conduction technology described in Chapter 6 to measure audiometric thresholds in cases on conductive hearing loss and to begin to collect data regarding the nature of postoperative hearing loss. As the data presented in Chapter 3 shows, if hearing loss occurs following middle ear surgery, any recovery that occurs generally takes place by three months after surgery. For this reason, the postoperative testing in this study was performed one week, one month, and three months after surgery. We elected to include only patients undergoing primary procedures in this study, to exclude any effects of previous ear surgery on EHF hearing thresholds pre- or postoperatively.

Based on the knowledge that air-bone gaps in the conventional frequency range take time to close after surgery, we hypothesised that some degree of conductive loss may also be present in the EHF range in the early postoperative period. However, given the high rate of elevation of the 4 kHz bone-conduction threshold following middle ear surgery, particularly stapedectomy, and the potential mechanisms for cochlear injury involved during the procedures included in the study, we also expected that EHF bone-conduction thresholds would be depressed in the days following surgery. Persistent hearing loss was expected to be more frequently purely sensorineural, as many of the factors that cause conductive hearing

loss, at least at lower frequencies, would have resolved by the time thresholds were tested three months after surgery.

Another important aspect of this study was to further test the bone-conductor in a true clinical setting. Testing of the non-operated ear provided us with a more realistic estimate of test-retest reliability across a normal clinical time frame, albeit in only a few participants. We also had the opportunity to test the masking protocol in patients with conductive hearing losses and potentially asymmetrical bone-conduction thresholds. Overall, this study allowed us to determine whether the bone-conductor, which appeared a reliable and valid tool in controlled testing in participants without conductive hearing loss, was suitable for repeated testing in a clinical situation.

7.2 Method

7.2.1 Participants

This prospective pilot study was conducted in association with the Department of Otolaryngology Head and Neck Surgery, Christchurch Hospital, and one otologist working in the private sector in Christchurch. Patients scheduled to undergo primary middle ear surgery under general anaesthetic at Christchurch Hospital or St Georges Hospital were considered for eligibility by their surgeon based on the following inclusion criteria:

a) 16 years of age or older

b) Scheduled to undergo primary stapedectomy/stapedotomy, ossiculoplasty, or tympanoplasty

c) An average preoperative bone-conduction threshold of 50 dB HL or less at 0.5, 1, and 2 kHz

d) Measureable air-conduction thresholds up to at least 10 kHz bilaterally

e) No other known disorders which might affect the auditory or vestibular system

f) Available for postoperative assessments

Patients meeting the eligibility criteria were given an information sheet regarding the study (see Appendix A) at the time of their preadmission assessment and invited to participate either by the surgeon or another researcher. Written consent (see Appendix A) was obtained from all patients who agreed to participate in accordance with ethical approval (Southern Health and Disability Ethics Committee, ethics reference number URB/09/07/029/AM01). Demographic information collected at the preoperative assessment included age, sex, history of previous otologic surgery, proposed surgery, and otologic symptoms.

Four patients satisfied the inclusion criteria and agreed to participate in this study. Participants ranged in age from 22 to 67 years (M = 41.6 years, SD = 16.5) and the group included three females and one male.

7.2.2 Equipment

Audiometric testing was carried out in sound treated rooms at the University of Canterbury or Christchurch Public Hospital, which fulfilled the criteria of ISO 8253-1 (2010).

Pure-tone audiometry in the conventional frequency range (0.25 – 8 kHz) was performed using a calibrated diagnostic audiometer, the GSI 61 (Grason-Stadler, Eden Prairie, MN). Air-conduction stimuli in this frequency range were presented via ER-3A insert earphones (Etymotic Research Inc., Elk Grove Village, IL) whenever possible, or using TDH-39 supra-aural headphones (Telephonics Corporation, Farmingdal, NY) if the EAC was not adequately clear of wax, discharge, blood, or other matter. Bone-conduction stimuli from 0.5 – 4 kHz were presented using a Radioear B-71 (Radioear Corporation, New Eagle, PA) bone-conduction vibrator positioned on the mastoid.

Air-conduction stimuli in the EHF range were presented via Sennheiser HDA 200 circumaural headphones (Sennheiser electronic GmbH & Co., Wennebostel, Germany) using the GSI 61 audiometer. Bone-conduction stimuli in the EHF range were presented through TEAC HP-F100 bone-conduction headphones (TEAC, Tokyo, Japan) that had been modified for use in audiometric testing, as described in Chapter 6. EHF narrowband masking noise was presented using the Sennheiser HDA 200 headphones. EHF bone-conduction threshold measurement was performed using the custom audiometer software used for transducer calibration in Chapter 6. This software was written using LabVIEW 2012 (National Instruments, Austin, TX) and run through an HP Compaq nw9440 laptop (Hewlett Packard, Palo Alto, CA). Sound stimuli were produced by an external multi-channel sound card (MOTU, Cambridge, MA) connected to the laptop via USB.

7.2.3 Procedure

7.2.3.1 General procedure

All participants underwent a preoperative assessment no more than one month before their scheduled surgery. This assessment included otoscopy, and bilateral air- and bone-conduction audiometry in both the conventional frequency and EHF ranges. Detailed descriptions of the protocols used for each procedure are provided below. We aimed to repeat the full preoperative examination battery at approximately 1 - 2 weeks, 1 month, and 3 months postoperatively. The exact timing of postoperative testing was dependent on when follow-up appointments with otolaryngologists were scheduled.

Participants were instructed that they would hear a series of tones that could be perceived in either ear and were asked to press the response button whenever they heard the tone, even if

the tone was very faint. “No response” was recorded when the participant did not respond to a tone presented at the limits of the audiometer for the frequency and ear being tested.

7.2.3.2 Conventional frequency pure-tone audiometry

Following otoscopic assessment to assess for occlusion of the EAC, pure-tone audiometry was performed using the appropriate air-conduction transducer. Thresholds for continuous pure-tone stimuli in dB HL were measured in 5 dB steps using the modified Hughson-Westlake technique (Carhart & Jerger, 1959). In the conventional frequency range, air-conduction thresholds in each ear were measured at octave frequencies from 0.25 to 8 kHz, and at 3 kHz. Narrowband masking noise was applied to the contralateral ear via the selected air-conduction transducer when the difference between the air-conduction threshold in the test ear and the air- or bone-conduction threshold non-test ear exceeded the minimum IAA values published by Yacullo (1996) for the relevant test frequency and transducer. Bone-conduction thresholds were measured at 0.5, 1, 2, 3, and 4 kHz with the B-71 transducer positioned on the mastoid. Contralateral masking was always applied during bone-conduction testing using narrowband masking noise and a step masking method (Yacullo, 1996).

7.2.3.3 EHF pure-tone audiometry

In the EHF range, air-conduction thresholds were measured at $1/6^{th}$ octave frequencies from 9 to 16 kHz. Threshold seeking was performed in 5 dB steps using the modified Hughson-Westlake technique. The IAA in the EHF range was conservatively estimated as 40 dB. Contralateral narrowband masking noise was applied to the non-test ear when the threshold in the test ear exceeded that in the non-test ear by 40 dB or more.

Bone-conduction thresholds were measured with the TEAC transducer positioned at the midline of the forehead as close to the centre as could be obtained while maintaining stable transducer placement. Narrowband masking was always presented to the non-test ear at 30 dB HL above the air-conduction threshold for the contralateral ear. Both ears were covered with the Sennheiser HDA 200 headphones throughout testing and the bone-conductor and headphones were not shifted between testing each ear. At least twice during testing of each ear, participants were asked which ear they heard the tone in to check for lateralisation. EHF bone-conduction thresholds were converted into dB HL using the correction values provided in Chapter 6.

7.2.4 Data analysis

Due to the small number of participants in this pilot study, audiometric changes were analysed using a case study approach. At each postoperative assessment, audiometric thresholds were subtracted from preoperative measurements and the change in threshold was calculated. Negative changes indicated a loss in hearing and positive changes indicated an improvement in hearing. Where thresholds were recorded as no response at the limits of the audiometer, the threshold was taken as 5 dB above the maximum output level at that frequency for the purpose of calculations.

7.3 Results

7.3.1 Case A

This 43 year old female underwent left stapedectomy via a transcanal approach, indicated by a clinical diagnosis of bilateral otosclerosis. Left stapedial fixation was confirmed intraoperatively and a stapedotomy was performed using an argon laser. A SMart 0.6 mm nitinol piston was inserted and crimped to the incus. No intraoperative or postoperative complications were documented.

Pre- and postoperative audiograms for Patient A are presented in Figure 53. The preoperative audiogram (Figure 53a) illustrates the moderate to moderately-severe mixed hearing loss in the operated (left) ear, with measureable air- and bone-conduction thresholds up to 16 kHz. A significant improvement of 10 – 45 dB in air-conduction thresholds in the operated ear at 4 kHz and below was documented at all postoperative assessments from 1 week onwards (Figures 53 and 54). Improvement in thresholds in this frequency range was complete by 1 month after surgery. Bone-conduction thresholds at 0.5 kHz remained within +/- 5 dB of the preoperative threshold at all assessments, and at 1 and 2 kHz gradually improved postoperatively to gain 20 and 15 dB respectively by the 3 month assessment. At 4 kHz, the bone-conduction threshold initially increased by 10 dB 1 week after surgery, recovering to 5 dB above the preoperative threshold at the 1 and 3 months assessments.

At 8 kHz and above, all air- and bone-conduction thresholds initially increased following surgery. Air-conduction thresholds could no longer be measured at 14 or 16 kHz, and a bone-conduction threshold could not be recorded at 16 kHz. Changes in bone-conduction thresholds were equal to, or slightly less than air-conduction threshold changes at most frequencies. The largest recordable change was recorded at 12.5 kHz, where the increase in the air-conduction threshold was 25 dB, and the bone-conduction threshold was 20 dB. This is consistent with a predominantly sensorineural hearing loss in the EHF range, with some evidence of a smaller conductive component.

The EHF hearing loss partially recovered by 1 month after surgery, and air-conduction thresholds at 8 – 11.2 kHz and below were 5 – 15 dB better than preoperative thresholds 1 and 3 months after surgery. Air-conduction thresholds remained unmeasurable at 16 kHz at all postoperative assessments, and were elevated at 12.5 kHz and 14 kHz 1 month after surgery, and at 14 kHz 3 months postoperatively. Bone-conduction thresholds did not show the same degree of recovery as air-conduction thresholds at 8 kHz and above. Thresholds

were persistently above the audiometer limits at 16 kHz, consistent with threshold elevation of at least 15 dB. Thresholds also remained elevated by 15 dB at 8 and 12.5 kHz, 1 month after surgery, and at 8, 11.2, and 12 kHz, 3 months after surgery. This suggests a persistent inner ear injury. It should be noted that although some improvement in air-conduction thresholds was recorded, a conductive component to the EHF hearing loss remained at 10 kHz and above 3 months after surgery.

No changes of greater than 10 dB were recorded for any air- or bone-conduction threshold in the non-operated ear at any assessment.

Although contralateral masking noise was below prescribed levels during bone-conduction testing at 14 and 16 kHz bilaterally, the patient always correctly identified the test ear when asked which ear tone the stimulus was heard.

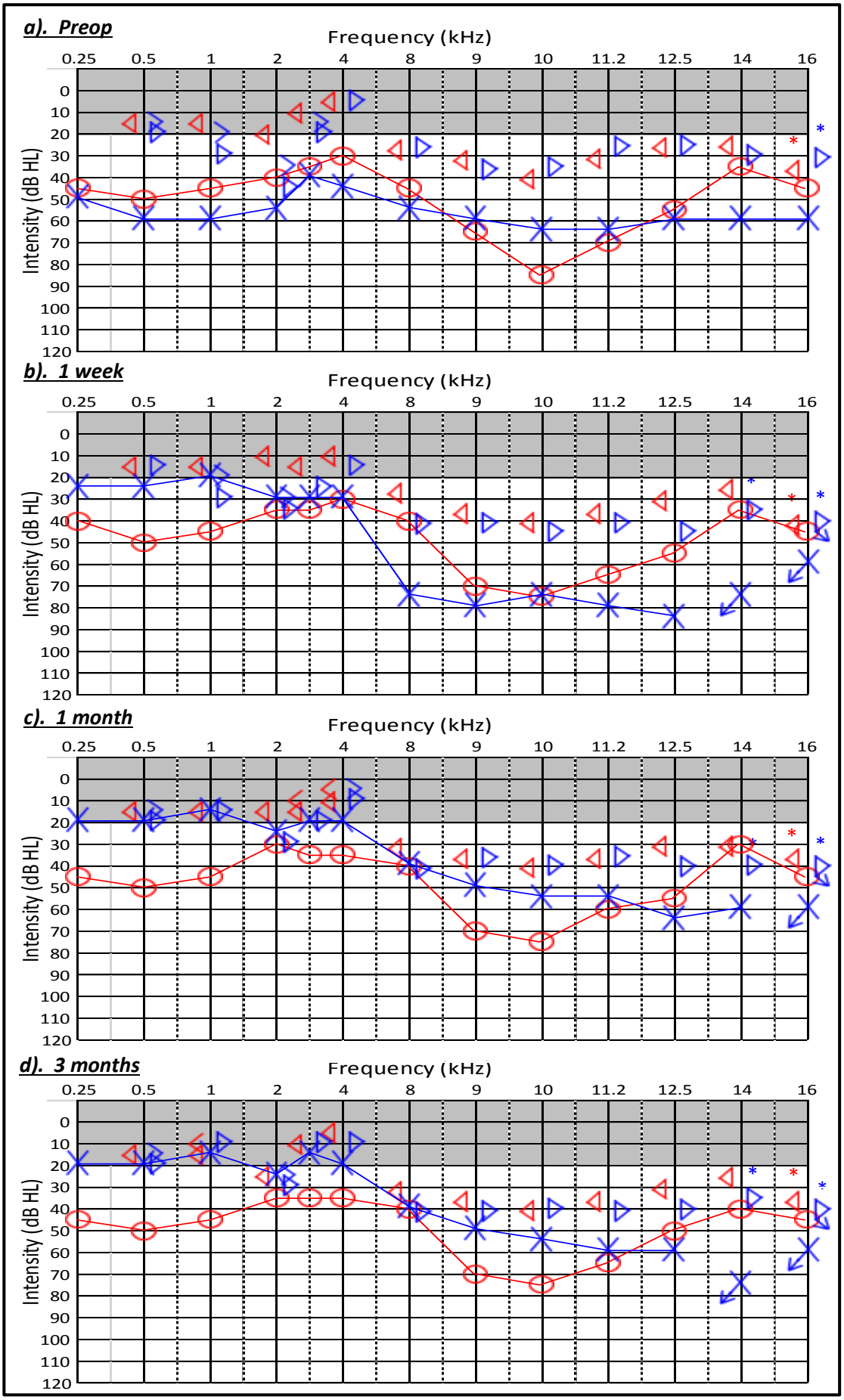

Figure 53. Audiograms recorded from Patient A before surgery was performed on the left ear (a), 1 week after surgery (b), 1 month after surgery (c), and 3 months after surgery (d). Asterisks indicate cases of potentially insufficient masking noise.

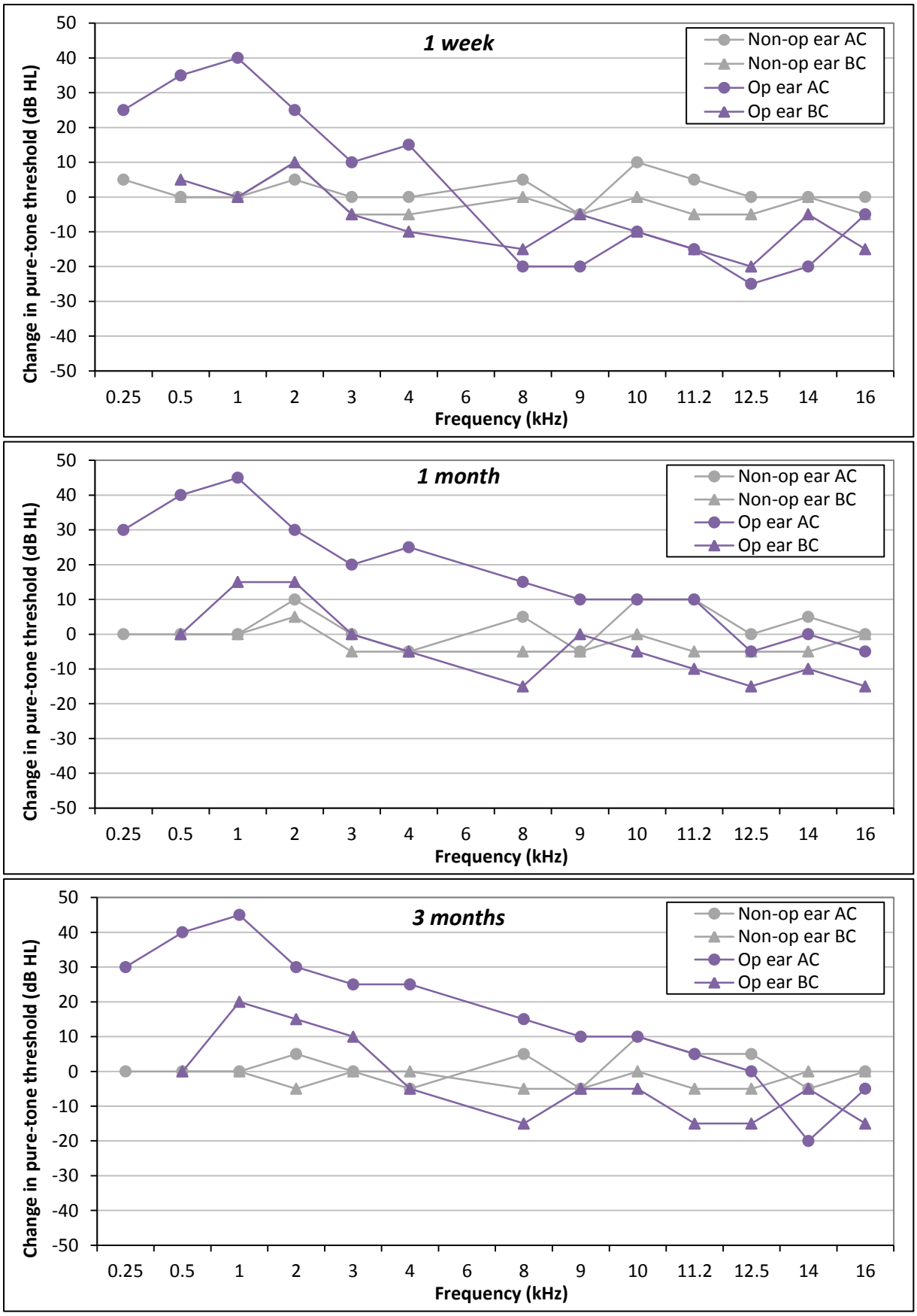

Figure 54. Changes in air- (AC) and bone-conduction (BC) pure-tone thresholds from preoperative levels in Case A. Results are provided for the 1 week (top panel), 1 month (middle panel), and 3 month (bottom panel) postoperative assessments.

7.3.2 Case B

Patient B was a 67 year old female with a steadily progressive bilateral mixed hearing loss and a clinical diagnosis of otosclerosis. It was decided to proceed with left stapedectomy using a transcanal approach.

Intraoperatively, a fixed stapes with thin footplate and an anterior focus of otosclerosis was identified. A 0.7mm stapedotomy was made with a combination of a CO_2 laser, a straight needle and a hand drill. A 0.6 x 4.75mm SMart 360deg prosthesis was then placed into the vestibule and connected to the long process of the incus using the laser. No intraoperative or postoperative complications were documented.

As shown in Figure 55a, the preoperative audiogram in the operated (left) ear showed a moderate to moderately-severe mixed hearing loss in the conventional frequency range, with measureable air- and bone-conduction thresholds up to 10 kHz. Air-conduction thresholds at 0.25 – 4 kHz gradually improved over the three postoperative assessments and 3 months after surgery were 10 to 25 dB better than preoperative thresholds (Figures 55 and 56). Bone-conduction thresholds at 0.5, 3, and 4 kHz deteriorated by 5 dB and the first postoperative assessment. Three months postoperatively, bone-conduction thresholds at 1 and 2 kHz recovered to 15 and 10 dB better than preoperative thresholds, respectively, and only the 4 kHz bone-conduction threshold remained elevated by 5 dB.

At the first postoperative assessment, the air- and bone-conduction thresholds at 10 kHz exceeded the limits of the audiometer, indicating a sensorineural loss of at least 10 dB at this frequency (Figure 55). This loss persisted across all postoperative assessments. The 8 kHz air-conduction threshold and the 9 kHz air-conduction threshold were elevated by 10 dB and 5 dB, respectively, at the first two postoperative assessments, but returned to preoperative levels 3 months after surgery (Figure 55). It appears that bone-conduction thresholds at these frequencies did not shift after surgery, however the patient reported that all EHF bone-conduction stimuli lateralised to the non-operated ear. This indicated some change from the preoperative assessment, at which tones at 8, 9, and 10 kHz were reportedly heard in the operated ear during bone-conduction testing. As shown in Figure 55, insufficient masking noise levels were available for testing at these frequencies, limiting the interpretation of these results.

No changes of greater than 10 dB were recorded for any air- or bone-conduction threshold in the non-operated ear at any assessment.

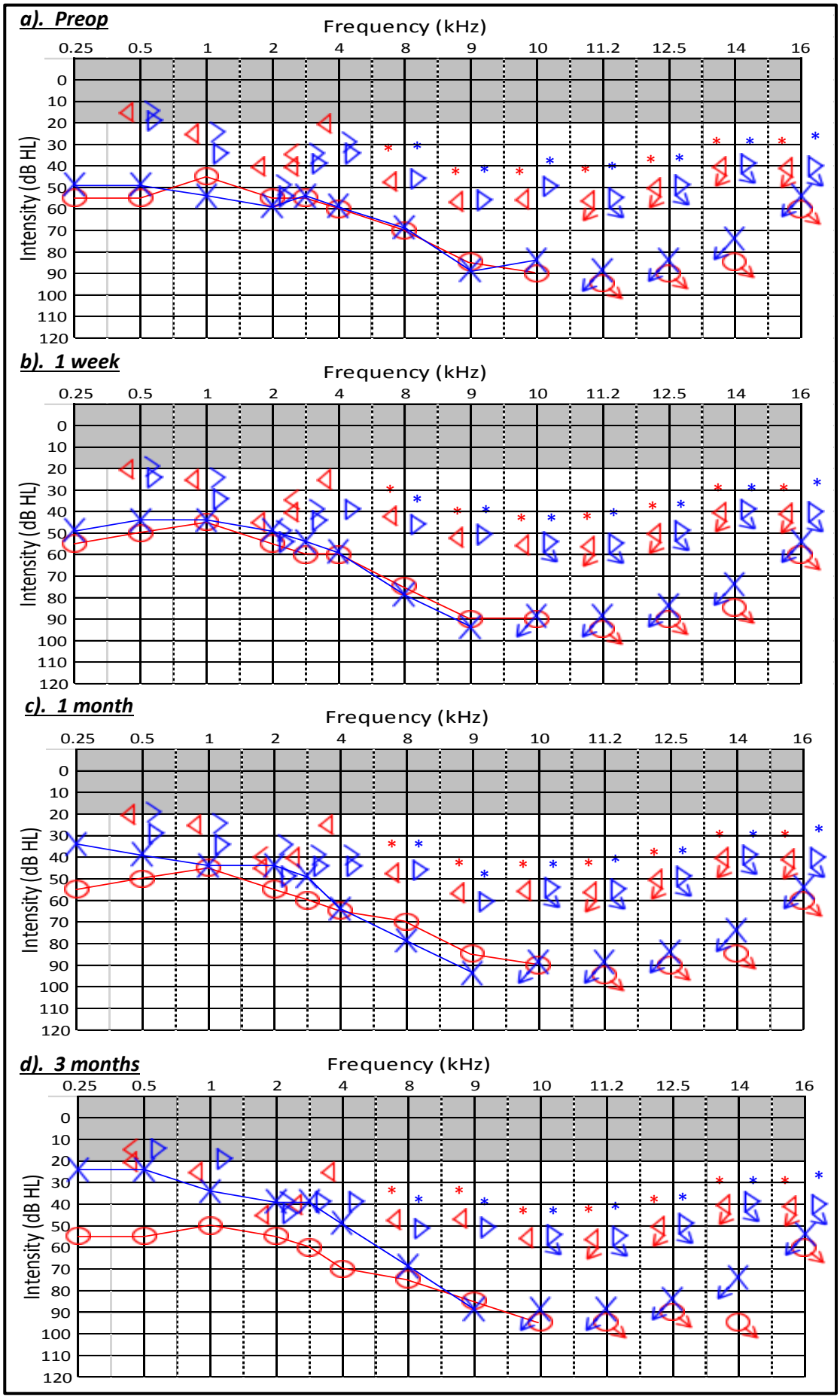

Figure 55. Audiograms recorded from Patient B before surgery on the left ear (a), 1 week after surgery (b), 1 month after surgery (c), and 3 months after surgery (d). Asterisks indicate cases of potentially insufficient masking noise.

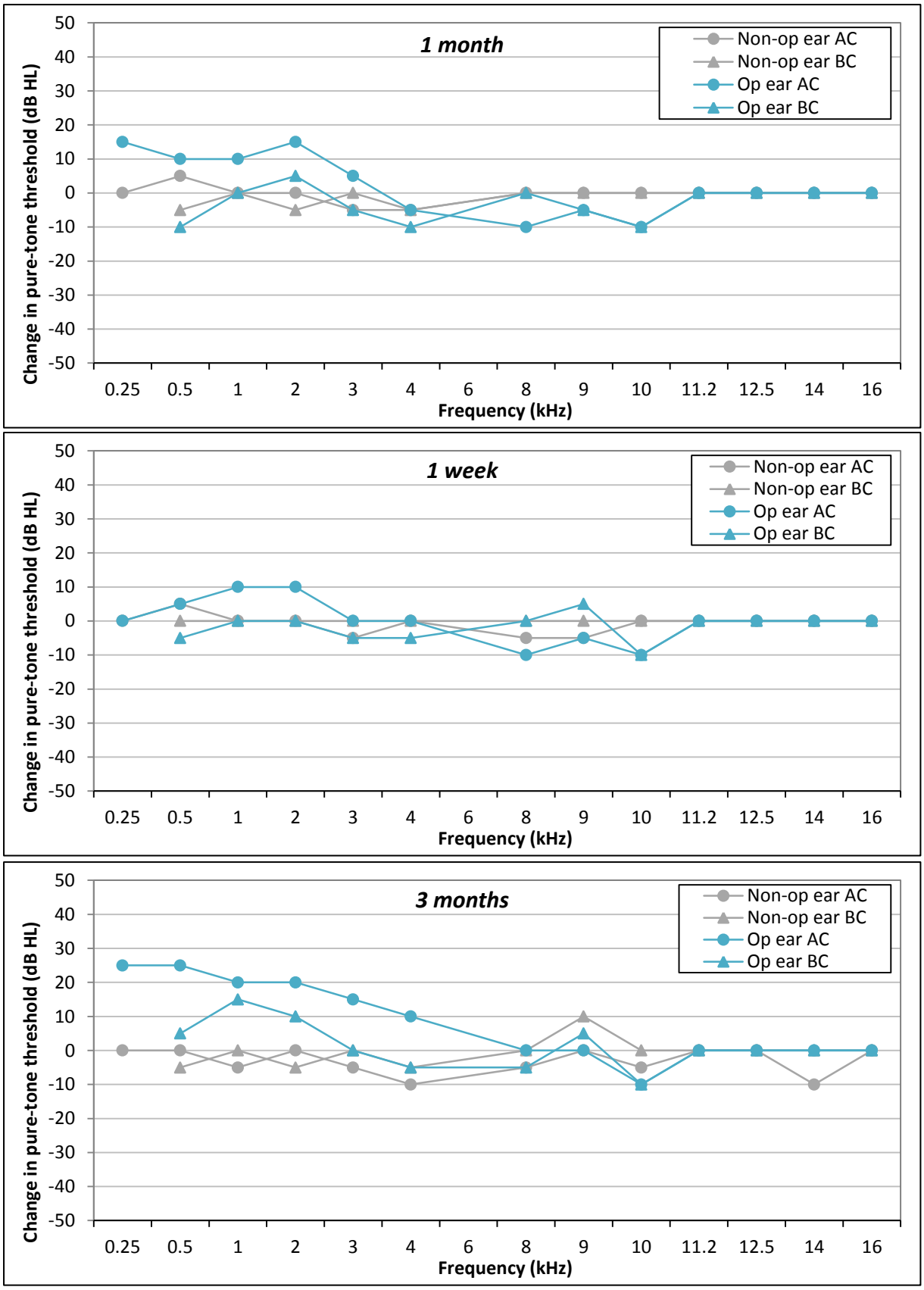

Figure 56. Changes in air- (AC) and bone-conduction (BC) pure-tone thresholds from preoperative levels in Case B. Results are provided for the 1 week (top panel), 1 month (middle panel), and 3 month (bottom panel) postoperative assessments.

7.3.3 Case C

Surgery in this 33 year old male was indicated by a clinical diagnosis bilateral otosclerosis. Transcanal stapedectomy was performed in the left ear, in which hearing was subjectively poorer. A fixed stapes footplate was confirmed intraoperatively and a partial stapedectomy was performed using an argon laser. A tragal perichondrium graft was placed over the oval window following removal of the posterior half of the footplate. A Robinson bucket prosthesis was then placed over the graft and attached to the incus. No postoperative complications were reported.

The preoperative audiogram (Figure 57a), showed a moderate rising to mild conductive loss in the left ear, with air- and bone-conduction thresholds measureable up to 16 kHz. One week after surgery, air-conduction thresholds at 0.5 – 1 kHz improved, whereas thresholds deteriorated at 3 kHz and above (Figures 57 and 58). At this first assessment, deterioration of bone-conduction thresholds of 10 dB was recorded at 0.5 and 4 kHz, and 15 dB at 3 kHz. Gradual, continued improvement occurred in the conventional frequency range, and at 3 months all thresholds at 4 kHz and below were better than those recorded preoperatively. At the 1 and 3 month assessments bone-conduction thresholds at 1 and 2 kHz improved by 10 – 20 dB, and no other shifts of greater than 5 dB were recorded.

The increase in air-conduction thresholds at the first postoperative assessment was largest at 4 – 9 kHz, where thresholds were elevated by 40 dB. The threshold at 16 kHz could no longer be measured at any postoperative assessments. Some recovery of high-frequency air-conduction thresholds occurred by 1 month after surgery, although this was limited to frequencies below 9 kHz. Much greater improvement was recorded at the 3 month assessment, and threshold increases relative to preoperative levels exceeded 10 dB only at 9 kHz (15 dB) and 14 kHz (25 dB). Smaller threshold increases remained at 10 and 12.5 kHz. EHF bone-conduction thresholds indicated that the increase in air-conduction thresholds was partly the result of cochlear injury. Threshold increases of 5 to 15 dB were recorded at all EHF bone-conduction test frequencies at all postoperative assessments, with the exception of a 0 dB change at 10 kHz 1 week after surgery. Bone-conduction thresholds could not be recorded from the operated ear at 14 and 16 kHz at the first two postoperative assessments, or at 16 kHz only at the 3 month assessment.

EHF bone-conduction thresholds did not show the same pattern of recovery over time as air-conduction thresholds, and the level of threshold elevation remained similar across

postoperative assessments. This implies there was a conductive component to the EHF hearing loss that improved over the postoperative course, as well as a sensorineural component that did not recover.

In the non-operated ear no bone-conduction thresholds shifted by more than 10 dB. Three instances in which the air-conduction threshold shifted by +/-15 dB were, however, noted at 1 kHz and 4 kHz 1 week after surgery and at 9 kHz 3 months after surgery.

Although contralateral masking noise was below prescribed levels during postoperative bone-conduction testing at 14 and 16 kHz in the left ear, and at 14 kHz at 3 months in the right ear, the patient always correctly identified the test ear when asked which ear the stimulus was heard.

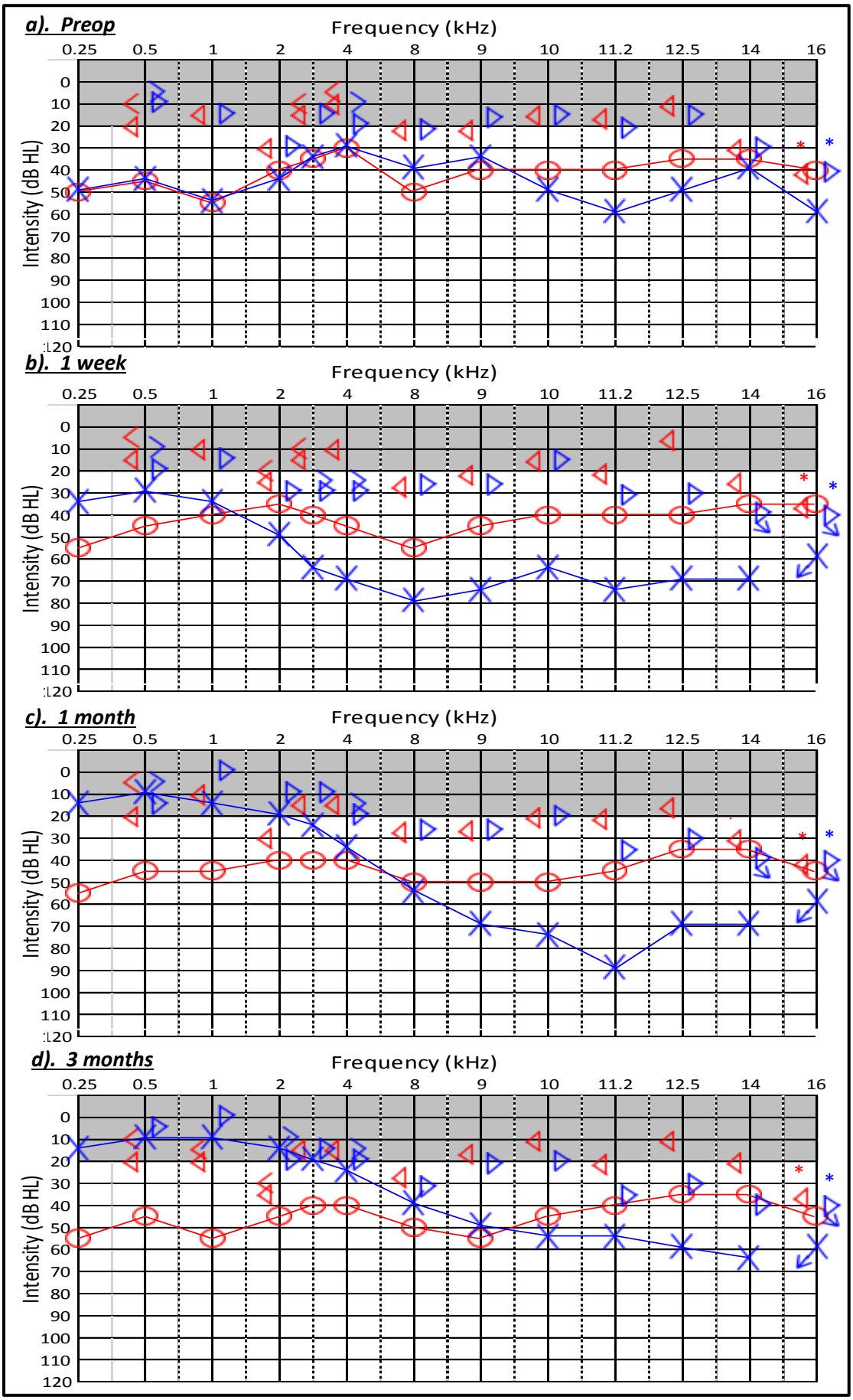

Figure 57. Audiograms recorded from Patient C before surgery was performed on the left ear (a), 1 week after surgery (b), 1 month after surgery (c), and 3 months after surgery (d). Asterisks indicate cases of potentially insufficient masking noise.

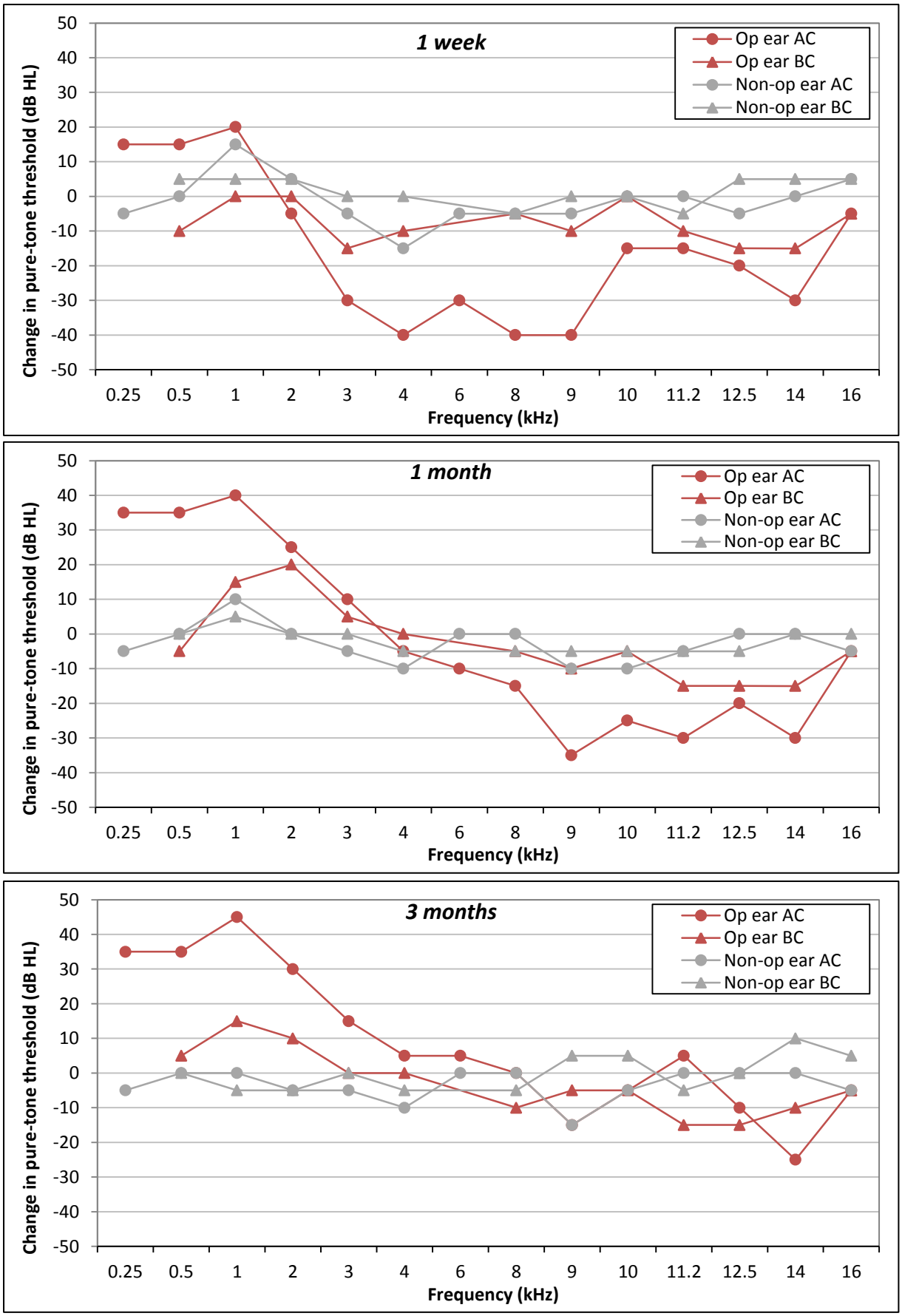

Figure 58. Changes in air- (AC) and bone-conduction (BC) pure-tone thresholds from preoperative levels in Case C. Results are provided for the 1 week (top panel), 1 month (middle panel), and 3 month (bottom panel) postoperative assessments.

7.3.4 Case D

This case involved a 22 year old female scheduled for right middle ear surgery, the type to be decided based on intraoperative findings, to correct a long-term conductive hearing loss. Preoperative air-conduction thresholds were measureable up to 16 kHz bilaterally (Figure 59 a). EHF bone-conduction testing indicated that the bilateral hearing loss was primarily conductive in both the conventional frequency and EHF ranges. Preoperative bone-conduction thresholds could not be recorded at 16 kHz before the limits of the audiometer were reached.

Surgery was performed using a transcanal approach. Intraoperatively, the ossicular chain was found to be dysmorphic. The incus and malleus were mobile, but the mobility of the stapes was reduced. The incudostapedial joint was rotated approximately 90 degrees from the normal position. A tiny anterior superior TM perforation was also identified. Perilymph welled up around the stapes footplate upon stapedial manipulation, although no obvious hole was found. The stapes was therefore not manipulated further to avoid perilymph leakage. The TM perforation was repaired using a tragal graft of cartilage and perichondrium. The incudostapedial joint was divided and the incus removed. A 2.5 mm PORP was placed between the malleus and the stapes superstructure. No postoperative complications were documented.

As shown in Figures 59 and 60, changes in hearing 1 week and 3 months after surgery were limited at all frequencies. Patient 1 did not attend the postoperative assessment scheduled 1 month after surgery. At the 1 week postoperative assessment (Figure 59b and 60a), the only threshold with a shift of greater than 10 dB was an increase in the 8 kHz air-conduction threshold of 15 dB HL. The bone-conduction threshold at the same frequency decreased (improved) by 5 dB, creating an increase in the air-bone gap at this frequency. Three months postoperatively, air-conduction thresholds improved relative to preoperative levels by 10 dB at 3, 8, 10, 11.2, and 12.5 kHz, and by 25 dB at 4 kHz. Bone-conduction thresholds did not improve at any frequency, but increased by 10 dB and 1 and 9 kHz. The air-conduction threshold at 16 kHz also increased by 10 dB. The overall result was a small reduction in the air-bone-gap at most frequencies at 3 kHz and above, with no significant deterioration in bone-conduction thresholds. In the non-operated ear, changes in air- and bone-conduction thresholds were within +/- 5 dB at all frequencies at both postoperative assessments.

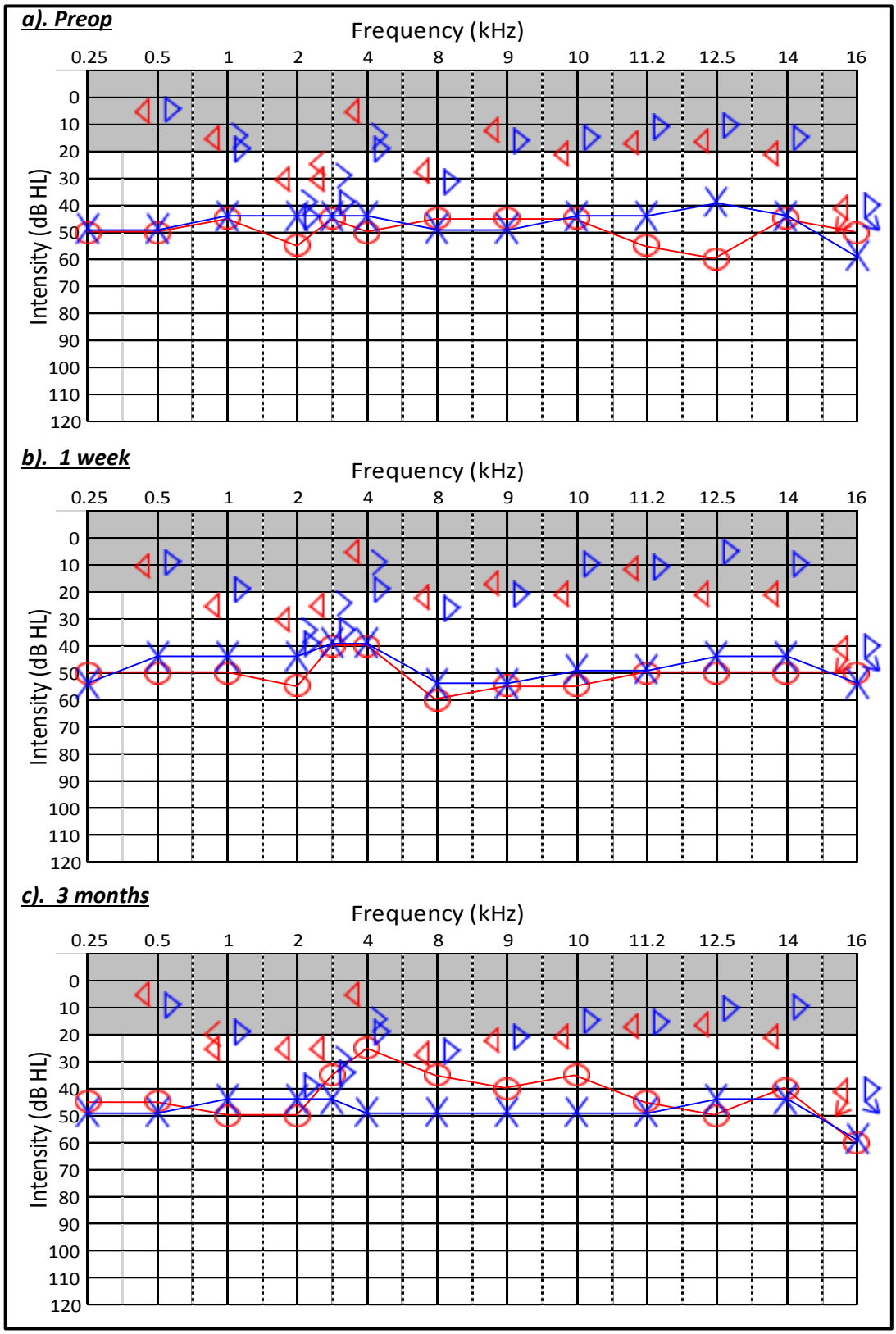

Figure 59. Audiograms recorded from Patient D before ossiculoplasty was performed on the right ear (a), 1 week after surgery (b), and 3 months after surgery (c).

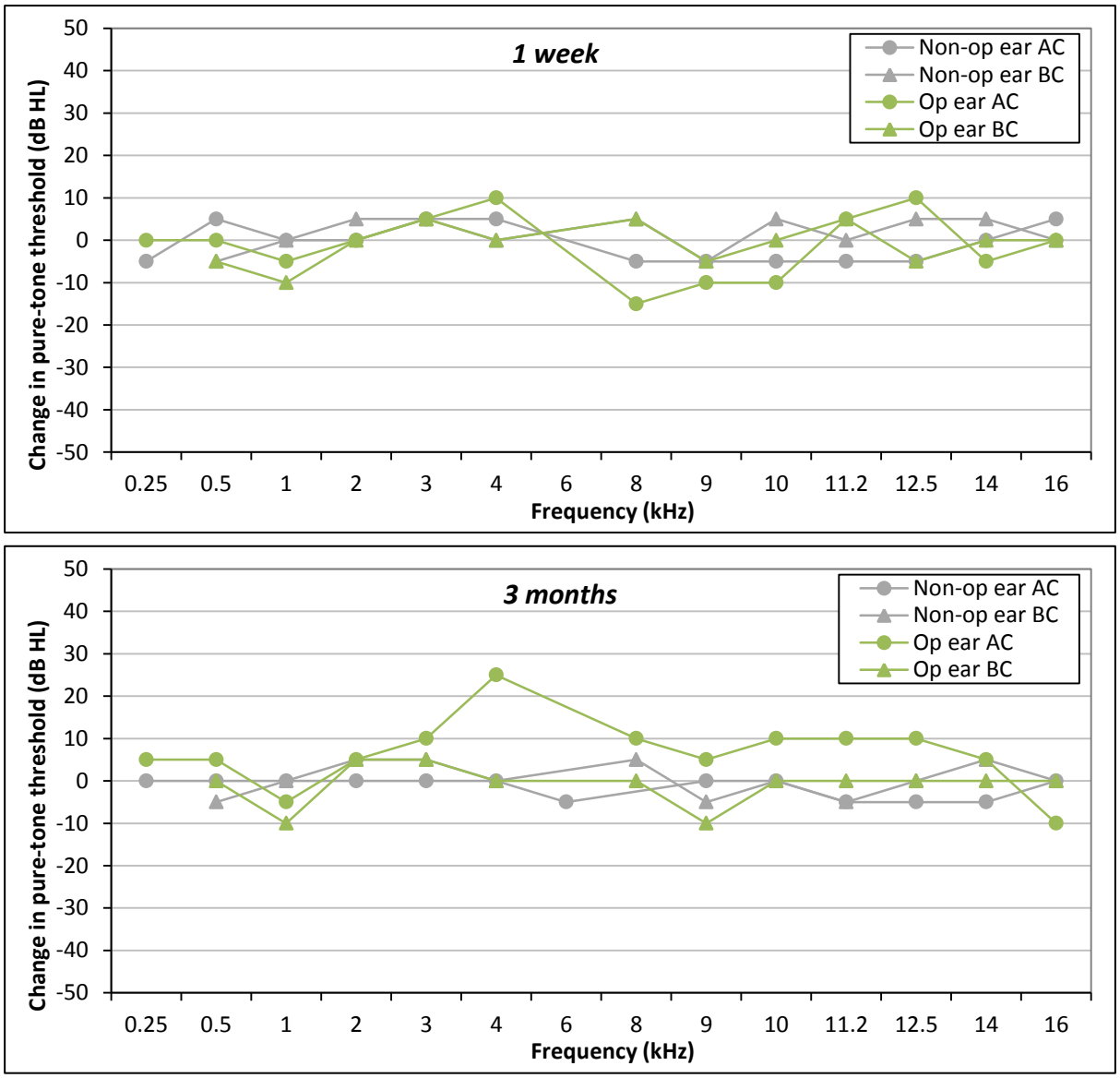

Figure 60. Changes in air- (AC) and bone-conduction (BC) pure-tone thresholds from preoperative levels in Case D. Results are provided for the 1 week (top panel) and 3 month (bottom panel) postoperative assessments.

7.3.5 Summary

Across the four cases presented, a clear postoperative EHF hearing loss in the presence of a good hearing outcome in the conventional frequency range was demonstrated in two cases; A and C. In both of these cases, the initial postoperative EHF hearing loss included both conductive and sensorineural components. In Case A, the hearing loss was predominantly sensorineural, with a smaller conductive component, while in Case C, the greater proportion of the initial increase in thresholds, particularly in the lower EHF range, was conductive. The majority of the postoperative increase in the EHF air-bone gap recovered by 3 months after surgery in both cases, however the sensorineural component in these two cases persisted until at least three months after surgery.

In Case B, the extent of preoperative hearing loss largely prohibited any significant changes in EHF thresholds being recorded. An increase of at least 10 dB in both air- and bone-conduction thresholds in the operated ear at all postoperative assessments does however suggest some inner ear damage occurred during surgery. A loss of subjective lateralisation of the tone to the operated ear may also be indicative of cochlear injury. This case also highlights the limitations of EHF bone-conduction audiometry in patients with significantly elevated EHF air-conduction thresholds.

Case D showed no significant EHF threshold increases after surgery (tympanoplasty with ossiculoplasty). Some minor improvement of air-conduction thresholds at 8 to 12.5 kHz 3 months after surgery suggested that preoperative EHF conductive hearing loss can be improved to some extent with partial reconstruction of the conductive mechanism. This is noteworthy given the lack of improvement at lower frequencies.

7.4 Discussion

The study presented in Chapter 3 and previous reports in the literature have demonstrated that deterioration of EHF air-conduction thresholds frequently occurs following middle ear surgery (Mair & Laukli, 1986; Tange & Dreschler, 1990). There is, however, a distinct lack of reliable data in the literature documenting changes high-frequency bone-conduction thresholds specific to the operated ear. As discussed in Chapter 5, there are many potential causes of postoperative EHF hearing loss, both conductive and sensorineural, and EHF bone-conduction measurements are required to distinguish between middle ear and cochlear causes of EHF hearing loss. This pilot study was designed to confirm that the TEAC HP-F100 bone-conduction transducer could be used to determine whether changes in EHF air-conduction thresholds after middle ear surgery corresponded to changes in bone-conduction thresholds in the same frequency range. The present study is the first to describe the evolution of EHF bone-conduction thresholds, and thus the nature of hearing loss, over the postoperative recovery period following stapedectomy and ossiculoplasty.

Overall, in agreement with the hypothesis, this small series provided evidence that early postoperative EHF hearing loss is, in at least some cases, comprised of both conductive and sensorineural components. These components appear to behave differently over the postoperative course, with at least partial recovery of the conductive portion and persistence of the smaller sensorineural element.

7.4.1 Nature of EHF hearing loss across the postoperative period

Across the four case studies presented, two clearly demonstrated a loss of EHF hearing acuity after stapes surgery. In both of these cases, the patients presented with a relatively small initial increase in both EHF air- and bone-conduction thresholds one week after surgery, indicative of the development of a sensorineural hearing loss. An increase in the magnitude of the EHF air-bone gap at the first postoperative assessment indicated a conductive element to the hearing loss was also present. In Case A, the early hearing loss was primarily sensorineural with a smaller conductive component, whereas in Case C, the larger component of the early hearing loss was conductive. Gradual, although in the case of Patient C, incomplete, recovery of EHF air-conduction thresholds to preoperative levels or better was documented in both of these patients by three months after surgery. Recovery of EHF bone-conduction thresholds was, however, limited in both patients. These results suggest that, in

these cases, the conductive EHF hearing loss resulting from stapedectomy involved a predominantly temporary disruption to the function of the conductive mechanism, together with a more persistent injury to the basal cochlea.

Although in Case B the extent of preoperative hearing loss largely prevented significant changes in EHF thresholds from being recorded, a continuing increase of at least 10 dB in both air- and bone-conduction thresholds at 10 kHz does provide some evidence of iatrogenic inner ear damage in this case as well. The limitations imposed by the maximum masking output in this case meant that it was not possible to confirm whether the initial elevation of air-conduction thresholds at 8 and 9 kHz was due to an additional conductive component to the hearing loss, or whether the loss at these frequencies was also sensorineural.

As the conductive and sensorineural elements of the EHF hearing loss must have different causes, their likely origins will be addressed separately.

7.4.2 Conductive postoperative EHF hearing loss

In the two cases in which a conductive component to the postoperative EHF hearing loss was definitively identified, the increase in the air-bone gap was greatest when assessed one week after surgery, and the majority of the conductive loss resolved by three months after surgery. The absence of a significant increase in the air-bone gap at the three month postoperative assessment (compared to that present before surgery) contrasts with the results of the one previous study published by Mair and Hallmo (1994), which reported both air- and bone-conduction changes in the EHF range from a single postoperative assessment performed an average of 4.5 months after myringoplasty. Based on an average increase in EHF air-conduction thresholds in the presence of stable bone-conduction thresholds, Mair and Hallmo concluded that EHF hearing loss present 4.5 months after myringoplasty was, on average, of a conductive nature. The conflict between these previous findings of a persistent conductive loss and our findings indicating that initial conductive loss mostly resolved in the weeks following surgery may be related to the different types of surgeries investigated. The more conservative explanation, however, is that our small sample lacked the ability to detect the cases of long-term conductive EHF hearing loss identified as an average across a group of 22 patients by Mair and Hallmo.

As the early conductive hearing loss identified recovers over the weeks following surgery, the most likely causes are directly related to surgery in the tympanic cavity. Specifically, sound

transmission is likely to be impaired by factors such as oedema, transudates, and microhaemorrhage, as well as the presence of packing material in the middle ear and EAC (Robinson & Kasden, 1977). The detrimental effect of packing material on both high-frequency air and, to a lesser extent, bone-conduction thresholds in the conventional frequency range has been demonstrated in post-tympanoplasty patients and in otologically normal volunteers by Cho et al. (2007). In the EHF range, a study of changes in air-conduction thresholds following ventilation tube insertion by Mair, Fjermedal, et al. (1989) showed that recovery of preoperatively elevated thresholds did not occur until two to eight weeks after surgery, despite closure of the air-bone gap at 2 kHz and below within 24 hours of the procedure. The authors suggest that retained mucus or mucosal oedema in the epitympanum may increase the mass of the middle ear system and thus EHF thresholds. Any middle ear surgery may be expected to have similar effects if secretions or oedema remain in the tympanic cavity postoperatively and certainly this phenomenon would explain the initial elevation of EHF thresholds with recovery over the weeks following surgery.

Despite improvement, EHF air-conduction thresholds in Mair, Pederson, & Laukli's (1989) study did not recover to levels equivalent to the healthy contralateral ear in several patients, suggesting a more enduring impairment than effusion or oedema. A possible explanation for this persistent hearing loss is that a change to the normal structure of the TM disrupted the transmission of high-frequency vibration to the stapes footplate. The disruption of the normal fibre structure of the TM may also explain the contrast between the present findings, showing that postoperative EHF conductive loss mostly resolves by three months after surgery, and those of Mair and Hallmo (1994), which suggest that significant conductive postoperative EHF hearing loss remained several months after myringoplasty. Experimental evidence gained from studies in temporal bones suggests that high-frequency sound transmission may be particularly inhibited by disruption of the microanatomy of the TM, therefore this is certainly a plausible explanation for EHF conductive hearing loss following myringoplasty (O'Connor et al., 2008; Roosli et al., 2012). Presumably, any effect of surgery on the TM depends on factors such as the grafting material, the size and location of the perforation and the TM graft. This may be the reason that no significant increases in EHF hearing thresholds were recorded after tympanoplasty was performed in conjunction with ossiculoplasty in Case D in this study. Of course, in Case D the otologic dysfunction was the result of more than only a TM perforation, and this case may therefore not be directly comparable to the myringoplasty outcomes evaluated by Mair and Hallmo.

In the case of stapes surgery, persistent conductive hearing loss may be related to the changes in the mass, stiffness, or motion characteristics of the ossicular chain, or to the change in the impedance or area of the stapes footplate – oval window interface. While evidence of any effect of a change in the mass of the stapes on sound transmission is weak (de Bruijn et al., 1999), both mathematical models and clinical studies suggest that a reduction in the size of the stapes footplate–perilymph interface can significantly reduce the volume velocity of the stapes (Arnold et al., 2007; Rosowski & Merchant, 1995). In addition, after surgery the normally efficient seal of the footplate in the oval window is replaced by a piston placed in the centre of an interposed graft between the middle ear and the labyrinth. The replacement membrane is unlikely to act in the same manner as a normal oval window, and in particular, thinner membranes with poorer seals may cause dispersion of high-frequency vibrations, reducing their transmission to the cochlea (Raman, 1983). An oval window replacement membrane may undergo progressive physical changes over time as the ear heals postoperatively, which may be accompanied by a recovery in hearing over the postoperative period (Antoli-Candela et al., 2009). If healing improves transmission of high-frequency sound to the cochlea, this could contribute to the reduction in the conductive EHF hearing loss over time in Cases A and C.

Although significant long-term EHF conductive loss was not documented in this very small series, this does not rule out the development of such hearing loss as a result of alteration of the mass, stiffness, and motion characteristics of the middle ear structures in other patients. Bance et al. (2007) noted that there was approximately 50 to 100 per cent more variability in stapes velocity measurements following ossicular reconstruction that in unaltered temporal bones, suggesting prostheses do not behave identically in all ears. This variability across ears suggests that the cause of hearing loss will not be identical in all cases and provides an explanation for the fact EHF hearing loss is not observed after all surgeries. Given the increasing complexity of ossicular motion and TM vibration patterns at high-frequencies (Cheng et al., 2010; Decraemer & Khanna, 2004; Hato et al., 2003), certainly, we would expect that in some ears, permanent changes to the properties of the ossicular chain and other middle ear structures will have a long-term impact on the transmission characteristics of the middle ear.

7.4.3 Reduction of the EHF air-bone gap postoperatively

Preoperatively, EHF hearing loss was purely conductive or had a significant conductive component in all four cases. The assumption here is that bone-conduction transducer calibration was accurate. In Cases A, B, and C, the stapes footplate was found to be fixed in the oval window. This increased cochlear input impedance appears to affect transmission of stimuli across the audiometric frequency range reasonably equally in Case A and C. In Case B, the extent of preoperative sensorineural loss prohibits accurate identification of the conductive component of the hearing loss. Intraoperative notes in Case D documented a dysmorphic ossicular chain with a footplate of reduced mobility, an abnormally positioned incudostapedial joint, and a tiny TM perforation. Again, cochlear input impedance would be expected to be reduced, and abnormalities in the motion of the ossicular chain that influenced the efficiency of the conductive mechanism are also likely to have been present. Overall, these findings confirm that the status of the middle ear can have a significant impact on EHF hearing.

In the four cases in this series, only two presented with small postoperative reductions in EHF air-conduction thresholds. In case A, the air-bone gap at 8 to 11.2 kHz at the final assessment was also smaller than that preoperatively, although in this case this was partially because of a small increase in bone-conduction thresholds, together with some improvement in air-conduction thresholds compared to before surgery. In Case D, three months after tympanoplasty with ossiculoplasty, a small reduction of approximately 10 dB was documented in the air-bone-gap at 3 kHz to 12.5 kHz, with no significant deterioration in bone-conduction thresholds. In these cases, as well as in Case C, a significant conductive component to the EHF hearing loss remained 3 months after surgery. In all of these cases, it may have been reasonable to expect that by mobilising the ossicular chain, middle ear transmission, while not normal, would have become more similar to that in the healthy ear, and the air-bone gap at all frequencies would have been significantly reduced after surgery. The relatively small improvement in only two patients suggests that this is not the case. This data highlight the limits of our knowledge regarding the transmission of EHF stimuli through the middle ear and the way in which this is affected by the physical properties of the diseased or reconstructed ear. As EHF audiometry appears to show persistent abnormalities in middle ear transmission even when the low-frequency air-bone gap has been closed, testing in this frequency range may be useful in the design of prostheses to more closely mimic the normal function of the ossicular chain.

7.4.4 Sensorineural postoperative EHF hearing loss

To the best of our knowledge, a deterioration of EHF bone-conduction thresholds measured with the TEAC transducer can be interpreted as evidence that iatrogenic cochlear injury has occurred. This assumption is not without limitations given the lack of data available documenting the contributions of the external and middle ear to bone-conduction hearing at high-frequencies. However, most evidence suggests that the external and middle ear contributions to high-frequency bone-conduction thresholds, at least within the conventional frequency range, are relatively minor (e.g. Stenfelt, 2006; Stenfelt, Wild, et al., 2003). Based on this assumption, in three of the four cases in this series, the elevation of both air- and bone conduction EHF thresholds and/or the loss of measureable thresholds after stapedectomy was considered indicative of sensorineural hearing loss.

Postoperative EHF sensorineural hearing loss has previously been documented following middle ear surgery using electrostimulation audiometry (Doménech & Carulla, 1988; Doménech et al., 1989; Hegewald et al., 1989). However, none of these previous studies have documented cochlear hearing loss that persists three months after surgery, or confirmed that the hearing loss is confined to the operated ear by masking audiometric thresholds. Doménech and Carulla (1988) demonstrated an increase in unmasked electrostimulation thresholds at 6 – 19 kHz when hearing was assessed a few days after stapedectomy, however no subsequent testing was carried out to confirm whether hearing recovered. Hegewald et al. (1989), on the other hand, found that a mean increase in unmasked threshold shifts 48 hours following 25 mastoidectomies recovered, on average, by one month after surgery, although a decrease in the highest audible frequency persisted. Unfortunately, only mean results are presented by Hegewald et al., therefore it is not clear whether some patients retained a significant EHF hearing loss while others recovered. The present protocol highlights the variability in hearing outcomes in even a small series, which could be obscured when only mean results are presented.

As discussed in Chapter 5, many reasons have been proposed for the development of sensorineural hearing loss after middle ear surgery. One strong possibility in the case of both stapedectomy and ossiculoplasty is that cochlear injury results from transmission of large mechanical forces to the inner ear through direct manipulation of the ossicular chain. Although there is currently no conclusive data demonstrating a link between the application of force to the ossicles and sensorineural hearing loss, hydrostatic force is frequently proposed as a cause of cochlear injury (e.g. à Wengen et al., 1992; Babighian & Albu, 2009;

de Zinis et al., 2010; Hallmo & Mair, 1996; Kylén et al., 1980; Mair & Laukli, 1986; Økstad et al., 1988; Palva et al., 1973; Schuknecht, 1962; Smyth, 1972, 1976, 1977; Urquhart et al., 1992; Vartiainen & Seppa, 1997). Certainly, given that the forces involved in actions such as palpation of the ossicles to check mobility, or perforation of the stapes footplate, are exponentially greater than those present physiologically (Schuknecht & Tonndorf, 1960), this is a plausible explanation that warrants further research.

Another possibility is that cochlear injury results from the presence of high, potentially damaging, noise levels that have been consistently documented during otologic surgery (Hilmi et al., 2012; Holmquist et al., 1979; Kylén & Arlinger, 1976; Kylén, Stjernvall, et al., 1977; Spencer & Reid, 1985; Yin et al., 2011). Again, there is little evidence to support this theory and, in particular, a lack of studies using EHF audiometry to investigate the link between surgical noise exposure of postoperative hearing loss. Hegewald et al. (1989) found no significant correlation between duration of drilling during 18 mastoidectomies and changes in either the response threshold to electrostimulation audiometry or the highest audible frequency. Although a small, significant mean increase of 1.4 dB at 8 – 16 kHz was found in the operated ear three months following ear surgery involving the use of a high-speed drill by Hallmo and Mair (1996), the authors suggest that this change was a result of difficulties with the placement of the rather large KH-70 transducer on the mastoid following otologic surgery, rather than a true hearing loss. As noise levels were not monitored during the surgeries included in this series, nor was drill time measured, it is not possible to link the observed EHF hearing loss with exposure to noise or vibration.

Clearly, there are many other possible causes for the cochlear hearing loss described in this study. All surgeries involved the use of an argon or CO_2 laser for various stages of the procedure, which minimises mechanical manipulation of the stapes and is therefore expected to reduce the transmission of force to the labyrinth, but laser use may also have been a cause of cochlear trauma. When used to perforate the stapes footplate, the argon laser creates a risk of irradiation damage to pigmented cells and thermal injury to the tissues if the inner ear, as the laser energy passes through the perilymph (Brase et al., 2013; Oswal, 2002; Silverstein et al., 1994; Wiet et al., 1997). CO_2 lasers also generate heat that may cause thermal damage to the cochlea (Jovanovic, 2005; Jovanovic et al., 1995). Despite these risks, several studies have demonstrated that both lasers can be used in stapedectomy/stapedotomy without causing permanent cochlear damage (e.g. Albers et al., 2013; Buchman et al., 2000; Forton, Wuyts, Delsupehe, Verfaillie, & Loncke, 2009; Hodgson & Wilson, 1991; Rauch & Bartley, 1992;

Raut & Halik, 2005; Szyfter et al., 2013). These previous studies do not exclude the possibility that laser energy could cause more subtle inner ear damage that presents as an increase limited to EHF thresholds. This presents one of many surgical variables that EHF audiometry could be used to investigate more closely.

7.4.5 Performance of the TEAC transducer

This study is the first to demonstrate the use of the TEAC HP-F100 to measure ear-specific thresholds in listeners with conductive loss and the first to use the transducer to monitor changes in thresholds over time. In general, the TEAC transducer was used successfully to measure ear-specific changes in bone-conduction sensitivity up to 16 kHz. Testing did, however, raise some methodological issues that warrant consideration.

As with any bone-conduction transducer, the dynamic range and maximum output of the TEAC device limits its use in patients with significant hearing loss. The maximum output of the bone-conduction transducer and the MOTU sound card audiometer varied with frequency, from 65 dB HL at 8 kHz to 40 dB HL at 16 kHz. These limits enabled thresholds to be measured at most frequencies in three of the cases, although the dynamic range was often not sufficient to enable bone-conduction thresholds measurement at 16 kHz after surgery. Additionally, in Case B thresholds at 11.2 kHz and above could not be measured for either ear preoperatively, or at 10 kHz or above in the operated ear postoperatively. This illustrates the significant limitations of both air- and bone-conduction EHF audiometry in monitoring changes in auditory responses in patients, most often older adults, with pre-existing hearing loss. This issue is not specific to the TEAC transducer, but nor does this transducer provide improved performance over other systems.

Based on the series of repeated bone-conduction measurements in 20 volunteers without a conductive hearing loss presented in Chapter 6, 10 dB was selected as the criterion for a significant change in EHF bone-conduction thresholds. Of the 78 postoperative EHF bone-conduction thresholds measured in non-operated ears, thresholds changes of 10 dB were recorded three times. This criterion therefore creates a false positive rate of 3.8%. If the criterion of 10 dB or more at two or more adjacent frequencies is used, no false positives were recorded in non-operated ears. Based on these results, we propose that a 15 dB threshold change at a single frequency, or 10 dB at two or more adjacent frequencies is a more appropriate, conservative significance criterion when testing in 5 dB steps.

7.4.6 Limitations of the study

A greater clinical challenge than the dynamic range of the bone-conductor was the limited level of masking noise that could be presented by the sound card audiometer. This led to an inability to present an adequate level of masking to the non-test ear when contralateral thresholds were also elevated. As the contralateral ear was affected by middle ear disease in all four cases, this proved to be a significant issue on several occasions. In an attempt to verify that masking was sufficient, patients were asked for subjective reports on tone lateralisation at least twice during each test session. This provided evidence that the intended test ear was being stimulated in most cases, the exception being Case B, in which the shift in the lateralisation of all EHF audible bone-conduction stimuli to the non-operated ear after surgery indicated some change in inner ear function from the preoperative assessment, despite the inability to measure ear-specific thresholds. Insufficient masking levels significantly restricted our ability to accurately determine the effect of surgery on bone-conduction thresholds in this case, and would presumably be an issue in many patients with preoperative EHF hearing loss, particularly older adults.

Clearly the small number of participants is the greatest limitation of this pilot study. Valuable information has been obtained regarding the ability to monitor EHF bone-conduction thresholds using the TEAC HP-F100 transducer and preliminary data suggesting that EHF hearing loss following stapedectomy is comprised of both conductive and sensorineural components in at least some cases, has been collected. The essential next step is to collect data in a much larger group of patients undergoing stapedectomy, as well as other middle ear surgical procedures. The limitations of EHF bone-conduction measurements in patients with significant preoperative sensorineural hearing loss in this study indicates that recruitment should favour patients with very good preoperative EHF bone-conduction thresholds to maximise the likelihood that cochlear injury can be detected.

It is possible that thresholds continued to change three months after surgery. Indeed, in a few cases reported in Chapter 3, EHF thresholds improved up to 12 months postoperatively. Given that EHF bone-conduction thresholds have not previously been closely monitored after middle ear surgery, it is unknown whether bone-conduction thresholds could perhaps take longer to recover than air-conduction thresholds. Ideally, were it not for time restrictions, audiometry would have been repeated six and 12 months after surgery.

7.4.7 Directions for future research

Future research will address the limitations noted above, testing many more patients in order to draw conclusions about the cause of postoperative EHF hearing loss. The present results indicate that the TEAC transducer is an appropriate tool to gather this data.

The other major issue left unaddressed by this study is the cause of EHF hearing loss, either conductive or sensorineural. The present results indicate that both may occur, but they do not address how or why they occur. Future studies would benefit from comparing EHF hearing outcomes across different types of middle ear surgery, or surgeries performed using different methods or tools, to obtain information as to particular components of procedures or physical changes to the middle ear that are more often associated with hearing loss. Distinguishing between specific causes of inner ear trauma or changes in middle ear transmission of high-frequency stimuli is necessary to develop targeted methods of preventing hearing loss in the future by minimising traumatic aspects of surgery and preventing any unavoidable trauma from causing permanent cochlear damage. Given that the data presented in Chapter 3 indicates that EHF hearing loss occurs frequently after surgery, questions regarding the cause may be able to be addressed in a reasonably small number of patients.

More rapid deterioration of air- and bone-conduction thresholds within the conventional frequency range has been reported in the ten years following stapedectomy than in control patients (Vartiainen, Virtaniemi, Kemppainen, & Karjalainen, 1993). Sperling et al. (2013) suggest that this could be related to surgical trauma to the cochlea that is not evident in standard bone-conduction thresholds measured several months after surgery. If EHF bone-conduction thresholds provide a more sensitive indicator that cochlear trauma has occurred, it may be that hearing is more likely to deteriorate in the years following surgery in patients with EHF hearing loss than in those without. A longitudinal study comparing long-term hearing outcomes in patients with and without EHF hearing loss following middle ear surgery would certainly be of interest in determining whether threshold increases are indicative of increased fragility of the cochlea. The risk of high-frequency hearing loss following middle ear surgery may be in part determined by the tolerance of the individual labyrinth to insult (Smyth, 1977), therefore long-term studies should also take into account the effects of age and pre-existing sensorineural hearing loss on early and late EHF hearing outcomes.

7.4.8 Conclusions

This pilot study provides clear evidence that early postoperative EHF hearing loss following stapedectomy may be composed of both conductive and sensorineural elements. Two case studies are presented that show at least partial recovery of air-conduction thresholds over the weeks following surgery, with persistence of elevation of EHF bone-conduction thresholds until at least three months after surgery. Importantly, this study also shows that the TEAC HP-F100 transducer can reliably be used to monitor changes in EHF hearing acuity over repeated assessments in listeners with conductive hearing loss. Future studies will benefit from this technology in larger series of patients to clarify the nature of postoperative EHF hearing loss after stapedectomy, ossiculoplasty, and tympanoplasty.

PART IV: CHANGES IN VESTIBULAR FUNCTION FOLLOWING MIDDLE EAR SURGERY

Chapter 8: Balance disturbance following middle ear surgery

8.1 The characteristics and assessment of postoperative vestibular dysfunction

8.1.1 Evidence of balance disturbance following middle ear surgery

Surgically induced trauma to the inner ear may manifest as vestibular dysfunction, either in addition to, or independently from sensorineural hearing loss. Unlike sensorineural loss, which is considered a serious complication of middle ear surgery, patients are typically advised preoperatively that minor dizziness or imbalance, particularly with head movement, is common in the week following surgery (Athanasiadis-Sismanis, 2010). Symptoms of vestibular disturbance following stapes surgery are reported in 12% to 82% of patients, depending on the timing and criteria used to assess symptoms (Aantaa & Virolainen, 1979; Birch & Elbrond, 1985; Causse et al., 1988; Koizuka, Sakagami, Doi, Takeda, & Matsunaga, 1995; Kujala, Aalto, & Hirvonen, 2005, 2010; Özmen et al., 2009; Silverstein, Rosenberg, & Jones, 1989; Stapleton, Mills, & Tham, 2008; Woldag, Meister, & Kosling, 1995). Vestibular symptoms are documented less frequently following tympanoplasty, ossiculoplasty, and mastoidectomy and have been reported in the literature to occur in approximately 0.4 to 1.5% of cases (Kos, Castrillon, Montandon, & Guyot, 2004; Zheng, Guyot, & Montandon, 1996).

Vestibular dysfunction may present with a range of signs and symptoms. For example, Kujala et al. (2010) reported a rate of vestibular symptoms of 52% among 21 patients immediately following hearing improvement surgery with opening of the oval window. Symptoms included rotatory vertigo, a floating or tilting sensation, and unspecific dizziness. Nausea and, less commonly, vomiting, accompanied balance symptoms in several cases. Patients also often present with nystagmus indicative of a change in peripheral vestibular function following surgery, frequently in the absence of subjective balance disturbance (Hirvonen & Aalto, 2013; Kujala et al., 2010).

Symptoms of balance disturbance are most evident in the first week following middle ear surgery, and in most cases patients will recover to normal levels on objective measures of vestibular function within the first postoperative month (Kujala, Aalto, Ramsay, & Hirvonen, 2007; Molony & Marais, 1996; Özmen et al., 2009). However, a small percentage of patients have been found to experience persistent or recurrent vestibular dysfunction after surgery, potentially suggesting more severe trauma to the inner ear has occurred (Oberascher,

Albegger, Gruber, & Baselides, 1992; Plath, Lenart, Matschke, & Kruppa, 1992). The duration of vestibular dysfunction tends to increase with increased severity of symptoms, as illustrated in a series of 33 stapedotomy procedures by Özmen et al. (2009). Immediately following surgery, 82% of patients reported subjective complaints of vestibular disturbance, of which 46% of cases were moderate or severe. The duration of symptoms ranged from an average of two days for mild vertigo to 6.8 days for disabling vertigo. Although the majority of patients were asymptomatic one week after surgery, a significant vestibular deficit could be detected using computerised dynamic posturography in 66% of patients. Repeated testing one month after surgery showed vestibular function had improved to preoperative levels in 73% of patients.

8.1.2 Potential causes of postoperative balance dysfunction

Mechanisms proposed to explain the development of vestibular dysfunction following middle ear surgery include changes in intralabyrinthine pressure; compression of the membranous labyrinth by the stapes piston; serous labyrinthitis; pneumolabyrinth; changes in enzyme processes and blood supply in the labyrinth; compressive forces transmitted to the labyrinth during fenestration or ossicular manipulation; mechanical injury to the otolithic organs; perilymphatic fistula; aspiration of perilymph with collapse of the membranous labyrinth; or disruption or collapse of the saccule or utricle by direct laser energy (Causse et al., 1988; Causse, Causse, Wiet, & Yoo, 1983; Causse et al., 1989; Handzel & McKenna, 2010; Koizuka et al., 1995; Lundy, 2009; Meurman & Aantaa, 1966; Schuknecht, 1993). Many of these mechanisms are hypothesised to cause operative trauma to the cochlea in addition to the vestibular end organs. For instance, labyrinthitis is posited as a mechanism by which both balance and hearing can be disturbed following middle ear surgery (Haynes & Wittkopf, 2010). We may therefore expect rates of postoperative sensorineural hearing loss to be higher in patients who present with significant balance disturbance postoperatively and vice versa.

Although balance disturbance is most common immediately after surgery, symptoms can present at any stage postoperatively. Delayed onset vertigo or imbalance is documented in less than 2% of cases and is likely to have a different pathophysiological mechanism than balance problems presenting immediately after surgery (Hammerschlag, Fishman, & Scheer, 1998). Grayeli, Sterkers, and Toupet (2009) point out that in some cases, delayed-onset vestibular dysfunction will be unrelated to the surgery. In their series of 73 patients with

reported balance dysfunction and a clinical history of otosclerosis, 45 of which had undergone stapes surgery, Grayeli et al. found that few cases presented with signs and symptoms suggestive of surgical trauma. Other cases were believed to be more likely to represent a coincidence between otosclerosis or stapes surgery and vestibular dysfunction. Indeed, even imbalance presenting directly after surgery may not be directly related to trauma to the inner ear, as patients often report dizziness, nausea, and vomiting following surgical procedures unrelated to the ear (Chung, Un, & Su, 1996; Raeder, Gupta, & Pedersen, 1997; Watcha & White, 1992).

Brief episodes of immediate or delayed vertigo associated with head movement following stapes surgery have also been attributed to benign paroxysmal positional vertigo (BPPV), although there is some debate regarding whether this is a direct consequence of surgery (Atacan, Sennaroglu, Genc, & Kaya, 2001; Hughes & Proctor, 1997; Korres & Balatsouras, 2004). Atacan et al. (2001) reported characteristic signs and symptoms of BPPV only on the operated side in four of 63 patients, eight to 348 months after stapedectomy, but no evidence of BPPV in 63 control subjects. In all cases there was no history of preoperative dizziness or vertigo. In contrast, Grayeli et al. (2009) concluded that BPPV in patients with otosclerosis was unrelated to surgery, based on their findings that BPPV was not more frequent in 45 patients with otosclerosis treated surgically than in 28 patients treated nonoperatively. Proponents of the theory that surgery directly causes BPPV hypothesise that surgical trauma to the otolithic organs facilitates detachment of the otoliths, which then move into the SCCs (Hughes & Proctor, 1997). It is further theorised that a co-existing mechanism related to the temporary fragility of the patient's otolithic organs contributes to postoperative BPPV development (Magliulo et al., 2005).

8.1.2.1 Vulnerability of the otolithic organs

Although some researchers have demonstrated a mild change in SCC function following middle ear surgery (Hirvonen & Aalto, 2013; Kujala et al., 2010), it is widely accepted that in most cases the saccule and utricle will be the most vulnerable vestibular end organs during surgery. This conclusion is based on the close anatomical relationship between the otolithic organs and the medial surface of the stapes footplate demonstrated in examinations of human temporal bone specimens (Backous, Minor, Aboujaoude, & Nager, 1999; Pauw, Pollak, & Fisch, 1991; Wang, Chi, & Dai, 2005). Whether the saccule or utricle is closer to the

footplate, and therefore more at risk during surgery, is less certain, and reports vary depending on the point of the footplate from which the measurement is made. Examinations of archival temporal bone sections from 130 patients with no history of otologic disease by Backous et al. (1999), showed that the shortest mean distance between the undersurface of the stapes footplate and the utricle was 0.58 mm at the posterior third of the footplate, whereas there was a greater minimum distance of 1.31 mm between the stapes and the saccule. These results support those of Pauw et al. (1991), who reported that the minimum distance between the footplate and the vestibular end organs was shorter for the utricle, with a minimal distance of 0.58 mm from the posterior border of the footplate to the organ, compared to the saccule, for which a minimum distance from the footplate of 0.76 mm at the anterior border of the stapedial footplate was measured. Greater separation between the stapes and the otolithic organs, particularly the utricle, was documented by Wang et al. (2005), who reported that the mean shortest distance from the stapes footplate to the saccule and the utricle in five human temporal bones was 1.10 mm and 1.67 mm, respectively.

Given their measurements, Pauw et al. (1991) suggested that a piston 0.4 mm in diameter could be introduced relatively safely into the vestibule to a depth of 0.5 mm. However, Causse, Causse, and Parahy (1985) noted that in 2% of patients the saccule and utricle are closer to the footplate; suggesting that some patients may be more prone to otolithic organ damage when the piston protrudes into the vestibule slightly more than is ideal. Further otolithic vulnerability in otosclerotic ears is suggested by distension and increased fragility of the saccule (Igarashi, O Uchi, Isago, & Wright, 1983; Yoon, Paparella, & Schachern, 1990). Conflicting with this theory, no significant differences in the proximity of the stapes footplate to the otolithic organs were noted between measurements in the 10 healthy and 11 otosclerotic temporal bones examined by Pauw et al.

Another factor to consider is the presence of membranous connections between the stapes footplate and the utricle. Backous et al. (1999) found that in 26% of their apparently otologically healthy temporal bone specimens, membranous connections were present between the utricle and footplate. Connections frequently occurred between the posterior and/or central portion of the footplate and the utricle, but were never found between the saccule and the footplate. The presence of connections between the utricle and the stapes footplate may increase the likelihood that this organ will be injured when the stapes is manipulated or fenestrated.

Whereas some proposed mechanisms of operative trauma will be expected to affect the entire labyrinth, others, such as mechanical trauma from stapes manipulation or laser energy, and compression of the membranous labyrinth by the prosthesis, are more specific to the saccule and/or utricle. The theory that vertigo following stapes surgery is the result of stimulation of the otolithic organs by the prosthesis is supported by evidence that modification of the shape of the prosthesis tip is associated with a reduction in the incidence of vertigo. Wang et al. (2005) retrospectively examined the rate of postoperative vertigo in 174 patients who underwent stapes surgery using Fisch's original prosthesis and 108 patients who had Fisch's modified prosthesis inserted, which has a tip with a 45 degree slope facing towards the saccule. Among patients with the original prosthesis, vertigo was documented in 45%, whereas in patients who had the modified prosthesis the rate of vertigo was significantly lower at 15%. Wang et al. hypothesise that vertigo following stapes surgery may occur secondary to inflation of the otolithic organs to restore fluid pressure balance following leakage of perilymph through a small fenestra in the footplate. When the otolithic organs expand, it is more likely that the prosthesis could mechanically stimulate the organs and induce vertigo. The authors suggest that the sloped modification to the usually rounded tip of Fisch's prosthesis reduces the likelihood that the prosthesis will compress the saccule when it becomes inflated. Vertigo would be expected to cease only when the fenestra heals and seals around the shaft of the prosthesis, presumably within the first week after surgery.

Notable developments in stapes surgery include the introduction of lasers as a tool to perforate the stapes footplate, which theoretically reduces the risk to the inner ear by minimising manipulation of the footplate. However, as discussed in Chapter 5, lasers present unique risks to the inner ear (Coker, Ator, Jenkins, & Neblett, 1986; Häusler et al., 1996; Jovanovic, Anft, Schonfeld, Berghaus, & Scherer, 1999; Jovanovic et al., 1998). In a review of the extant literature comparing complications of stapes surgery performed with laser fenestration and conventional fenestration, Wegner et al. (2014) found no evidence that either technique was superior with regard to the rate of immediate postoperative vertigo. However, Lundy (2009) found evidence of very small ruptures of the wall of the saccule and/or utricle in a histological investigation of the temporal bones of six cats immediately following direct discharge of a CO_2 or KTP laser into the vestibule. No differences were found between specimens exposed to each type of laser energy. In six animals that underwent the same trauma, but then had the oval window sealed until sacrifice three months later, there was no evidence of utricular or saccular membrane or neuroepithelial injury, nor had there been any

clinical indicators of vestibular dysfunction immediately after insult. These results suggest that trauma to the vestibular end organs from lasers may recover within the first three months of surgery, consistent with most reports of postoperative vestibular symptoms.

8.1.3 Assessment of vestibular function

Investigation of changes in postoperative function of the otolithic organs in humans relies on objective clinical tests. At present, otolithic function can be assessed clinically using subjective visual horizontal and vertical alignment tests (SVH and SVV respectively), or VEMPs. As described in Chapter 2, SVV and SVH tests assess the function of primarily the utricle by measuring the angle between perceived vertical or horizontal and true (gravitational) vertical or horizontal (Kingma, 2006). In an investigation into the effects of stapes surgery on otolithic function, Tribukait and Bergenius (1998) measured the SVH by way of asking 12 patients to horizontally align a luminous line in darkness in the upright body position prior to, a few days after, and 4 - 8 weeks after stapes surgery. SVH was normal for all patients preoperatively, but at the first assessment after surgery, the SVH was tilted away from the operated side (M = -4.02° +/-2.53°). This finding is the opposite of what is usually found in cases of an acute unilateral loss of vestibular function, where patients tend to demonstrate a tilt of the SVV or SVH towards the lesioned side of around 10 to 20 degrees (Bohmer & Rickenmann, 1995; Curthoys et al., 1991; Gomez Garcia & Jauregui-Renaud, 2003; Tribukait et al., 1998; Vibert et al., 1999). Tribukait and Bergenius suggest the postoperative tilt of the SVH away from the operated side is consistent with an increase in the resting activity of the utricular afferents following surgery. Although the mechanism is uncertain, a possibility is surgical irritation of the utricle, or mechanical stimulation of the otolithic organs by the piston (Singbartl, Basta, Seidl, Ernst, & Todt, 2006).

While assessments of SVH provide unique and important information regarding how stapes surgery affects the otolithic organs, the usefulness of SVH and SVV is limited beyond the acute stage of vestibular trauma due to the effects of vestibular compensation. When Tribukait and Bergenius (1998) reassessed SVH 4 – 8 weeks after surgery, the mean result was not significantly different from that recorded preoperatively, and was pathologic in only one patient. The assumption that compensation has occurred is based on documentation of the recovery of SVH to close to pre-insult levels following deafferentation or permanent damage to the vestibular nerve (Pinar et al., 2005; Tabak et al., 1997; Tribukait et al., 1998; Vibert &

Häusler, 2000). In cases of deafferentation it is known that recovery to the normal anatomical state cannot have occurred, whereas in the case of middle ear surgery we cannot be sure if the return of the SVH to preoperative levels is due to central compensation or to recovery of the otolithic organs from trauma. For this reason, the utility of SVV and SVH tests to diagnose otolithic abnormalities is limited beyond the acute postoperative period.

A more effective method of assessing otolithic function later in the postoperative course is the measurement of VEMPs. The specific vestibular end organ and neural reflex pathway tested when assessing VEMPs varies depending of the stimulus used and the muscle from which the response is measured. A review of the principles underlying VEMP elicitation and interpretation is therefore provided here before studies of VEMPs measured before and after middle ear surgery are discussed.

8.1.3.1 VEMPs

VEMPs are responses of the otolithic organs to brief, high-intensity acoustic or vibratory stimuli that can be measured as a change in surface electromyographic activity from the sternocleidomastoid muscles (SCM) (cVEMPs), or from the extraocular muscles beneath the eyes (oVEMPs) (Murofushi & Kaga, 2009b). Evidence that VEMPs are indeed vestibular and not auditory responses comes from documentation that responses are preserved in cases of profound hearing loss, but are absent in patients who have intact hearing, but have lost vestibular function bilaterally (Iwasaki et al., 2008; Rosengren et al., 2005). VEMPs can also be recorded in patients with a loss of facial nerve function, confirming that the response is not a blink reflex (Huang, Yang, & Young, 2012).

cVEMPs are responses of the vestibulocollic reflex pathway and can be recorded using electrodes placed over the tonically contracted SCM muscles. The short latency biphasic responses consist of an initial positive (inhibitory) peak at approximately 13 ms (p13), followed by a negative peak at approximately 23 ms (n23) (Colebatch & Halmagyi, 1992; Colebatch et al., 1994; Rosengren, Welgampola, & Colebatch, 2010). cVEMPs are uncrossed responses, therefore in cases of unilateral vestibular loss, the cVEMP in response to air-conducted stimuli will be reduced or absent when recorded from the ipsilateral SCM (Halmagyi, Yavor, & Colebatch, 1995). In response to bone-conduction stimuli applied at the midline skull, normal p13-n23 cVEMPs will be recorded in the SCM ipsilateral to the healthy

labyrinth, and as an inverted (negative-positive) potential will be recorded from the SCM on the same side as the dysfunctional vestibular end organs (Halmagyi et al., 1995).

The oVEMP, produced by the vestibulo-ocular reflex pathway, is characterised by an initial negative (excitatory) component at a latency of approximately 10 ms; n10, which is the primary component of interest (Iwasaki et al., 2007; Iwasaki et al., 2008; Rosengren et al., 2005; Todd, Rosengren, Aw, & Colebatch, 2007). Predominantly a crossed response, the oVEMP can be evoked by either air- or bone-conducted stimuli and recorded using surface electrodes positioned over the extraocular muscles (Chihara, Iwasaki, Ushio, & Murofushi, 2007; Iwasaki et al., 2007). In cases of unilateral vestibular loss, the n10 response recorded from the eye contralateral to the lesion to be reduced or absent, regardless of whether the stimulus is delivered by air- or bone-conduction (Curthoys, Iwasaki, et al., 2011; Govender, Rosengren, & Colebatch, 2011; Iwasaki et al., 2007; Iwasaki et al., 2008; Shin et al., 2012).

8.1.3.1.1 VEMPs in response to bone-conduction stimuli

The probability of VEMPs to air-conducted stimuli being present in cases of middle ear pathology is related to the magnitude of the air-bone gap and responses are likely to be absent in patients with an air-bone gap of greater than 20 dB HL (Halmagyi et al., 1995; Trivelli, D'Ascanio, Pappacena, Greco, & Salvinelli, 2010). Bone-conduction stimuli can be used to overcome the reduction in energy reaching the vestibular apparatus that occurs for air-conducted stimuli in cases of conductive hearing loss.

Bone-conduction stimuli applied to the midline of the skull, for example at Fz, will produce linear acceleration that is symmetrical at both mastoids (Iwasaki et al., 2008), and thus in healthy subjects equal responses from each labyrinth should be measureable from the relevant contralateral eye (Iwasaki et al., 2008) or ipsilateral SCMs (Brantberg, Tribukait, & Fransson, 2003; Welgampola, Rosengren, Halmagyi, & Colebatch, 2003). As many balance concerns are the result of asymmetric function from the two vestibular labyrinths (Curthoys, 2012), a key goal in most objective vestibular tests, including VEMPs, is to compare the levels of function in the corresponding organs of the two labyrinths. In order for a reliable functional comparison to be made, equal stimuli must be presented to both labyrinths under equal recording conditions. oVEMP testing using a vibratory stimulus applied to the midline facilitates comparisons between the two labyrinths, as the stimulus reaching each side and the tonic muscle activity at each active electrode is assumed to be comparable without requiring

the corrections for muscle activity level necessary when recording from the SCMs (Manzari, Burgess, & Curthoys, 2010; Nguyen, Welgampola, & Carey, 2010).

Vibratory bone-conduction stimuli are most effective at evoking VEMPs when delivered using a light tap from a tendon hammer or using a mini-shaker, such as the B&K 4810 vibrator (Brantberg et al., 2003; Iwasaki et al., 2007; Iwasaki et al., 2008). Wahat and Patuzzi (2012) demonstrated that VEMPs could also be reliably elicited using a finger tap to the skull as the vibratory stimulus. An advantage of this technique is that stimulus strength can be varied to produce an input-output function relating stimulus strength to response amplitude.

8.1.3.1.2 Underlying physiology of VEMPs

There has been much discussion in the literature as to the specific otolithic organ that mediates each type of VEMP. Vestibular neuritis provides a useful model that can be used to identify the vestibular afferents associated with each VEMP type, as the disease can affect either the superior or the inferior portion of the vestibular nerve independently. The superior division of the vestibular nerve is comprised primarily of afferents from the utricle, with a smaller contribution from the hook region of the saccule, whereas the majority of the saccular afferents course through the inferior vestibular nerve (Curthoys, Burgess, et al., 2011). Studies of patients with superior vestibular neuritis have demonstrated that oVEMPs to both air- and bone-conducted stimuli are typically diminished beneath the eye contralateral to the lesion, whereas cVEMPs to air-conduction stimuli remain intact (Curthoys, 2012; Govender et al., 2011; Iwasaki et al., 2009; Lin & Young, 2011; Manzari, Tedesco, Burgess, & Curthoys, 2010; Shin et al., 2012). These results suggest that oVEMPs primarily reflect the function of the superior vestibular nerve, and therefore the utricle (Rosengren & Kingma, 2013). Although the superior vestibular nerve also contains some contributions from the saccule, the large asymmetries documented in VEMPs likely reflect the greater contribution from the utricle to the response (Rosengren & Kingma, 2013). The presence of air-conduction cVEMPs in superior vestibular neuritis and their absence in inferior vestibular neuritis suggests a primarily saccular origin for these potentials (Curthoys, 2012; Curthoys, Iwasaki, et al., 2011; Iwasaki et al., 2009; Manzari, Tedesco, et al., 2010; Shin et al., 2012).

The origin of vibration-evoked cVEMPs is less certain. Curthoys (2012) reported that stimulation at the forehead with 500 Hz tone bursts produces normal cVEMPs in patients with superior vestibular neuritis, consistent with a saccular and inferior vestibular nerve

origin of the response. However, there is some evidence that cVEMPs in response to tap stimuli applied to either the forehead or to the contralateral mastoid may be abnormal in patients with superior vestibular neuritis, suggesting that the superior vestibular nerve least partially contributes to these responses (Brantberg et al., 2003; Govender et al., 2011). Rosengren and Kingma (2013) suggest that given the strength of the utrico-collic projections (Uchino & Kushiro, 2011), a utricular contribution to cVEMPs would not be unexpected.

While it is clear that the SCM generates cVEMP response, the precise extraocular muscle involved in the oVEMP is less obvious. The strength of the oVEMP response is modulated by the direction of the subject's gaze, and increases in amplitude have been consistently shown when gaze is increased upwards from horizontal (Chihara et al., 2007; Govender, Rosengren, & Colebatch, 2009; Iwasaki et al., 2008; Rosengren et al., 2010; Todd et al., 2007; Welgampola, Migliaccio, Myrie, Minor, & Carey, 2009). When gaze is directed upwards, the most superficial extraocular muscle is the inferior oblique, which is brought close to the skin directly underneath the active electrode (Huang et al., 2012; Iwasaki et al., 2008). Recordings of responses from single motor units of the inferior oblique and inferior rectus extraocular muscles during simultaneous recording of oVEMP potentials confirm that the n10 potential is produced by increased activity of the inferior oblique (Weber et al., 2012).

8.1.3.1.3 VEMP response parameters

VEMP waveforms may be analysed with regards to the latency, amplitude, threshold, and asymmetry ratio of the peaks. When elicited by a bone-conduction stimulus applied at the midline and recorded from the extraocular muscles, the n10 potential will be similar beneath both eyes in healthy subjects (Iwasaki et al., 2007). An asymmetry in the amplitude of responses recorded from beneath each eye will therefore by a diagnostic indicator for abnormal unilateral labyrinthine function. Manzari, Burgess, et al. (2010) reported that the oVEMP asymmetry ratio had a diagnostic accuracy of 94% in separating healthy subjects and those with superior vestibular neuritis.

Although VEMP asymmetry ratios in healthy subjects have been consistently shown to be significantly lower than in patients with unilateral vestibular dysfunction, there is some degree of overlap between the two populations (Iwasaki et al., 2009; Iwasaki et al., 2008; Manzari, Burgess, et al., 2010; Nagai et al., 2014; Valko, Hegemann, Weber, Straumann, & Bockisch, 2011). The average asymmetry ratio for vibratory (B&K mini-shaker 4810) evoked

oVEMPs was reported by Iwasaki et al. (2008) to range from 0.5% to 34.1% across their 67 healthy subjects, with an average asymmetry ratio of 11.7% (*SD* = 8.3). Other studies reporting oVEMP asymmetry ratio to mini-shaker forehead stimulation in healthy subjects have documented mean asymmetry ratios of 15.5 +/- 11% (Valko et al., 2011), 21.7 +/- 14% (Nagai et al., 2014), and 7.4 +/- 4.5% (Manzari, Burgess, et al., 2010). In comparison, patients with unilateral vestibular losses have been found to have mean n10 oVEMP asymmetry ratios using the same stimuli of 66.2 +/- 24% (Valko et al., 2011), 67.0 +/- 16.7% (Iwasaki et al., 2009); 75.0 +/- 16.3% (Iwasaki et al., 2008), and 62.2 +/-13.8% (Manzari, Burgess, et al., 2010). In a study of 109 patients with unilateral inner ear diseases, Nagai et al. (2014) demonstrated that abnormally high oVEMP asymmetry ratios are specific to dysfunction of the otolithic organs or vestibular nerve and are not a general characteristic of vestibular disturbance. Nagai et al. reported that the average bone-conduction oVEMP asymmetry ratio in 22 patients with vestibular neuritis was 65.0% (*SD* = 29.6), whereas in 65 cases of sudden sensorineural hearing loss and 22 of Ménière's disease, the average asymmetry ratios were not significantly different to those in normal subjects, with average ratios of 21.2% (*SD* = 23.7) and 19.0% (*SD* = 14.6), respectively.

A decline in amplitude and an increase in latency of VEMPs with increasing age has been well documented for both air- and bone-conduction evoked cVEMPs (Brantberg, Granath, & Schart, 2007; Nguyen et al., 2010; Rosengren, Govender, & Colebatch, 2011; Su, Huang, Young, & Cheng, 2004; Welgampola & Colebatch, 2001; Zapala & Brey, 2004), and oVEMPs (Iwasaki et al., 2008; Kantner & Gurkov, 2012; Nguyen et al., 2010; Rosengren et al., 2011; Tseng, Chou, & Young, 2010). The age-related changes in VEMPs are believed to be associated with degenerative changes of the vestibular system that occur with age (Bergstrom, 1973a, 1973b; Merchant & Rosowski, 2010; Velazquez-Villasenor et al., 2000). An advantage of using the VEMP asymmetry ratio to detect unilateral vestibular dysfunction is that age has not been found to have an effect on this parameter (Iwasaki et al., 2008; Kantner & Gurkov, 2012; Nguyen et al., 2010; Tseng et al., 2010).

8.1.3.2 VEMPs pre- and post-middle ear surgery

8.1.3.2.1 VEMPs in cases of conductive hearing loss

Given that middle ear dysfunction reduces the energy transferred to the inner ear, it is not surprising that VEMPs in response to air-conducted stimuli are frequently absent in ears with

conductive hearing loss (Wang & Lee, 2007; Wang, Liu, Yu, Wu, & Lee, 2009; Yang & Young, 2003). While bone-conduction stimuli may provide adequate stimulation to elicit VEMPs when conductive hearing loss is present, VEMPs in response to vibratory stimulation may also be abnormal in cases of COM or otosclerosis (Chang, Cheng, & Young, 2014; Yang & Young, 2007).

Chang et al. (2014) reported that in patients with COM, VEMPs in response to bone-conducted vibration applied at the midline were absent or abnormal in amplitude or latency in 62% of 117 ears when oVEMPs were tested and 65% of ears for cVEMPs. The finding of abnormal VEMPs was significantly correlated with the bone-conduction hearing threshold in the affected ear, implying that the pathophysiological mechanism, proposed to be the entry of toxins or pathogens from the middle ear through the round window, disturbed the function of both the vestibular and hearing portions of the inner ear (Chang et al., 2014; Seo et al., 2008). cVEMPs elicited by bone-conduction were found to be significantly more likely to be absent or reduced in the diseased ear of patients with unilateral COM who reported symptoms of vertigo or dizziness compared to those who report no such symptoms (Seo et al., 2008).

In otosclerotic ears, the rate of recordable cVEMPs to bone-conduction stimuli has been shown to be reduced relative to healthy ears, particularly in cases of advanced hearing loss (Singbartl et al., 2006; Yang & Young, 2007). However, Winters et al. (2013) found no significant difference in the response rate or characteristics of bone-conduction oVEMPs between healthy and otosclerotic ears. Given that when evoked by bone-conduction stimuli the cVEMP is thought to be produced primarily by the saccule and the oVEMP by the utricle (Curthoys, 2012), it is possible that the divergence in results indicates a predilection for otosclerosis to impair saccular over utricular function. Histological assessments of the vestibular end organs in otosclerosis, however, show that changes are no more apparent in the saccule than the utricle (Sando, Hemenway, Miller, & Black, 1974). The reason for any difference in responses from the two organs preoperatively therefore remains uncertain.

8.1.3.2.2 Postoperative VEMPs

Despite the relatively high rate of postoperative vertigo reported post-middle ear surgery and the hypothesis that trauma to the saccular and/or utricle may be the cause of these symptoms, little evidence is available that shows a postoperative loss of VEMPs. A factor in this may be that many studies of postoperative VEMPs assess responses several weeks or months after

surgery, at which time most cases of temporary balance dysfunction have resolved. However, it is also surprising is that although air-conducted VEMPs, which are thought to be absent preoperatively due to a reduction in energy reaching the inner ear, often fail to reappear after successful surgery to repair the conductive mechanism (Stapleton et al., 2008; Trivelli et al., 2010). Stapleton et al. (2008) reported that air-conduction evoked cVEMPs remained absent at least six months following successful stapes surgery in 65 of 70 ears tested. Although sacculo-collic responses were absent, only 27 of these 65 patients reported postoperative balance disturbance, and in only eight cases did this persist beyond 48 hours after surgery. In contrast, all five patients who had present cVEMPs after surgery reported balance symptoms which lasted between one and twelve months postoperatively.

In agreement with Stapleton et al. (2008), continued abnormalities in postoperative air-conduction VEMPs were reported by Wang et al. (2009) following tympanoplasty with or without mastoidectomy. Despite the improvement in the overall VEMP response rate from 42% to 67% of the 24 patients and a mean reduction in the 500 Hz pure-tone air-bone gap, Wang et al. found that p13 latencies remained significantly longer three months postoperatively in patients who underwent surgery compared to control subjects. These findings may imply that the relationship between VEMP responses and middle ear pathology is more complicated than a straightforward delay of acoustic energy transfer to the otolithic organs. It is possible either that the preoperative absence of air-conducted VEMPs is genuinely related to vestibular dysfunction, or that operative trauma to the otolithic organs prevents the reappearance of VEMPs despite adequate acoustic stimulation.

In order to clarify the effects of stapes surgery on cVEMPs, Trivelli et al. (2010) assessed responses to both air- and bone-conduction stimuli preoperatively and one, six and twelve months post-stapedotomy in 41 patients. A reappearance of cVEMPs elicited by air-conducted stimuli was documented in only three cases, despite successful closure of the mean air-bone gap to within 10 dB HL in all 42 ears. Including the nine ears in which cVEMPs had been recordable before surgery and were retained after surgery, the total postoperative air-conduction VEMP response rate was 26%. Preoperatively, cVEMPs from the otosclerotic ear could be elicited by bone-conduction stimuli presented via a B-71 bone vibrator positioned on the mastoid in 16 cases. Following successful surgery, bone-conduction cVEMPs became absent in one of these 16 ears, and were unaffected in the remaining 41 cases. No correlation was found between the five cases of vertigo and the elicitability of air- or bone-conducted cVEMPs. Pre- and postoperative average bone-conduction hearing thresholds were

significantly lower in patients with recordable bone-conduction VEMPs in comparison to those with absent bone-conducted VEMPs, suggestive of an inner ear impairment that reduces both auditory and vestibular function. It appears that in the majority of cases this impairment is present preoperatively, although it cannot be determined from the results reported whether vestibular function worsened, as reflected by an increased asymmetry ratio to bone-conducted stimuli postoperatively, or whether the degree of impairment evident preoperatively remained static.

In opposition to Trivelli et al. (2010) results, Singbartl et al. (2006) found no significant correlation between bone-conduction hearing thresholds preoperatively and the presence of bone-conduction evoked cVEMPs in their 23 patients. In Singbartl et al.'s series, bone-conducted cVEMPs reappeared in the operated ear three to six weeks after stapedotomy in three cases and responses did not disappear in any cases following surgery. The reappearance of bone-conducted cVEMPs without any cases of loss of cVEMPs, and despite reports of balance disturbance, presents an interesting situation. One would expect that if postoperative balance symptoms were due to saccular trauma, cVEMPs would be lost after surgery. This does not appear to be the case, although the possibility of utricular damage cannot be excluded. The reappearance of bone-conducted cVEMPs that were absent preoperatively has been suggested to be due to increased mechanical stimulation of the saccule by the piston, or a postsurgical decline in radial vibration energy dispersion (Huttenbrink, 2003; Singbartl et al., 2006).

Postoperative changes in utricular function were assessed using vibration-evoked oVEMPs following stapes surgery by Winters et al. (2013). oVEMPs in eleven patients were measured preoperatively and between eight weeks and 1.5 years after stapes surgery in response to 250 and 500 Hz tone bursts presented to the forehead using a B&K type 4810 mini-shaker. Responses were present in all patients both pre- and postoperatively and the authors note that although the amplitude of the biphasic waveform appeared slightly smaller after surgery, no significant changes were documented in mean oVEMP amplitude, latency, or threshold following successful surgery. Despite no mean change in amplitude, in two of the patients, the oVEMPs at 250 Hz disappeared postoperatively and in two other patients, the response amplitudes increased for both the 250 Hz and 500 Hz stimuli. Although on average there was no effect, whether these individual findings may have clinical significance is unclear.

Given that the patient group in Winters et al. (2013) study reported only mild vestibular symptoms, it is probable that the absence of changes in oVEMPs postoperatively indicates

that no long-term trauma to the utricle occurred. It is also possible that bone-conduction oVEMP measurement was not a sensitive enough test to detect any subtle changes in postoperative utricular function. In order to clarify this issue, assessments of oVEMPs earlier in the postoperative period when vestibular symptoms are present are required, as are assessments of patients both with and without subjective balance disturbance at the time of testing.

8.1.4 Aims and hypotheses

The primary aim of the present study was to determine whether middle ear surgical procedures alter otolithic function, as assessed using tap-evoked oVEMPs. Changes in VEMP parameters compared to preoperative measures would implicate the utricle in postoperative vestibular symptoms. In particular, we aimed to address a gap in the literature examining oVEMPs in the early postoperative period to determine whether abnormal VEMPs are more common when measured in the early period when subjective symptoms of vestibular dysfunction are present. We also sought to monitor oVEMPs over the first year postoperatively to determine whether any changes immediately after surgery were the result of transient or permanent damage to the inner ear. Based on knowledge of the close relationship between the utricle and the stapes footplate, it was hypothesised that utricular function would be at least temporarily altered following surgery involving manipulation of the ossicles. In line with documented recovery of symptoms of imbalance, we predicted that the damage to the vestibular system would be temporary in the majority of cases.

The second goal of this study was to determine whether any relationship was present between the postoperative EHF hearing loss described in Chapter 3 and changes in oVEMPs. This issue was addressed by comparing changes in oVEMPs in patients with and without clear losses of EHF hearing sensitivity. It was hypothesised that if significant EHF hearing loss resulted from trauma to the inner ear, the vestibular system, and thus VEMPs, may also be adversely affected. Conversely, if EHF hearing loss was conductive in nature, VEMPs in response to bone-conduction stimuli would be less likely to be affected.

8.2 Method

8.2.1 Participants

This prospective study was conducted concurrently with the investigation of changes in EHF hearing thresholds following middle ear surgery. The same group of participants were tested for both studies and the inclusion criteria and recruitment method were therefore identical to that detailed in Chapter 3. Briefly, patients were invited by their surgeon to participate in the study if they were at least 16 years of age; scheduled to undergo either primary or revision stapes surgery, tympanoplasty, or ossiculoplasty; had an average preoperative bone-conduction threshold of 50 dB HL or less at 0.5, 1, and 2 kHz; had no other known disorders of the auditory or vestibular system; and were available for repeat postoperative assessments.

Written consent (see Appendix A) was obtained from all patients in accordance with the ethical approval obtained for this phase of the study from the University of Canterbury and the Health and Disability Ethics Committee (Upper South B Ethics Committee, ethics reference number URB/09/07/029). Demographic information collected included age, sex, previous otologic surgery, proposed surgery, and otologic symptoms.

Ninety-six participants who underwent 107 middle ear surgical procedures satisfied the inclusion criteria and were enrolled in this study. Forty-five of the surgeries performed were stapedectomies or stapedotomies, 33 were tympanoplasties, and 30 ossiculoplasties. Where participants underwent both tympanoplasty and ossiculoplasty during a single surgery, the surgery was categorised as an ossiculoplasty to reflect that the ossicles were manipulated.

8.2.2 Equipment

Tap-evoked oVEMPs were measured using equipment and proprietary software (TapVEMP v1.0) developed by Dr Robert Patuzzi of the University of Western Australia. The equipment consisted of a signal processing box connected to a laptop computer (model nw9440, HP Compaq, Hewlett-Packard, Palo Alto, CA) running TapVEMP v1.0 waveform acquisition software in LabVIEW 8.2 (National Instruments, Austin, TX) (Figure 61). The signal processing box contained a National Instruments USB-6215 data acquisition card (National Instruments, Austin, TX) and a custom-made multi-channel amplifier.

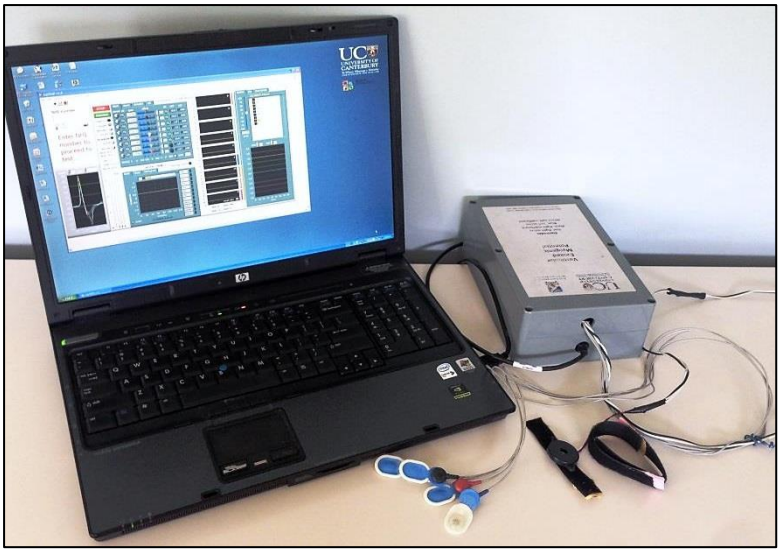

Figure 61. The Tap-evoked oVEMP equipment set-up, consisting of a laptop running TapVEMP v1.0 software, a signal processing box, piezoelectric transducer, electrodes, and electrode leads.

The laptop was run off batteries for reasons of participant safety and to reduce contamination of the recordings by 50 Hz mains power. Self-adhesive electrodes (Ambu Blue Sensor N, Ambu, Copenhagen, Denmark) were used to measure the response and were attached to the signal processing device via electrode leads. A piezoelectric transducer (Kingstate KPEG827, Tamshui, Taiwan), also coupled to the data acquisition card through the amplifier, was used to measure the strength of the finger tap and to provide a trigger pulse to the software averaging the oVEMP responses.

The system was calibrated to calculate the acceleration vectors of the tap stimuli using values derived from measurements made using a pre-calibrated tri-axis accelerometer (Dimension Engineering DE-ACCM3D, Akron, OH). Acceleration was measured with the accelerometer mounted on the mastoid of a representative subject while finger-taps were delivered to the nasion. The peak acceleration in the plane normal to the mastoid surface was used for calibration, as this value peaked within 5 ms of the tap stimulus onset, and was therefore considered the most likely trigger for the n10 peak of the oVEMP response. To provide calibration values, the peak voltage output from the piezoelectric transducer was related to the peak magnitude of acceleration using a regression formula.

The regression formulae relating equivalent peak acceleration were

Equivalent peak acceleration (G) = 0.0042 x [Bracket number] – 0.0014

Equivalent peak acceleration (ms-2) = 0.0408 x [Bracket number] – 0.0139

Based on these peak acceleration values, ten brackets were created into which the responses were sorted based on stimulus magnitude. The equivalent peak acceleration was used as the minimum stimulus acceleration required for the response to be allocated to a given bracket.

8.2.3 Procedure

Otolithic function was assessed pre- and postoperatively using tap-evoked oVEMPs. The initial postoperative assessment was performed within 24 hours of surgery and included VEMPs and a brief interview regarding subjective symptoms of balance disturbance. We aimed to repeat testing approximately 1 - 2 weeks, 1 month, 3 months, 6 months and 1 year postoperatively. The exact timing of postoperative testing was dependent on when follow-up appointments with otolaryngologists were scheduled. If a follow-up appointment was missed, data collection was resumed at the next scheduled postoperative assessment.

Testing was performed with the participant seated upright, either on a chair, or in bed. To reduce the effects of electrical interference on the recordings, testing was performed as far away as was practical from other electronic equipment and non-essential mains-powered devices were switched off. Participants were asked to remove glasses if worn and the skin below each eye and extending down to the upper cheeks was prepared for electrode placement by gently rubbing with an abrasive tape (Red Dot Trace Prep, 3M, St. Paul, MN). One self-adhesive electrode was positioned below the centre of the eye on the inferior orbital rim of each lower eyelid (active electrodes), with the two reference electrodes placed on the cheeks; one approximately 15 – 30 mm below each active electrode (Figure 62a). Care was taken to ensure symmetrical placement of electrodes below each eye.

Participants were asked to maintain their gaze in the maximal upward and medial position in order to increase the degree of underlying inferior oblique stretch and maximise the amplitude of the recordable response (Govender et al., 2009).

The piezoelectric transducer was attached to the dorsal aspect of the middle finger proximal phalynx of the tester's dominant hand using a strip of hook and loop fastening tape. The tapping finger was held with the proximal interphalangeal joint flexed to 90 degrees, and the distal interphalangeal and metacarpophalangeal joints extended to align the transducer perpendicular to the direction of the tap (Figure 62b). Taps were directed orthogonal to the nasion; defined as the midpoint of the nasofrontal suture. Tap strength of was varied in order

to produce an input-output function relating response amplitude to tap intensity. Taps were delivered at a rate of approximately 0.5 Hz.

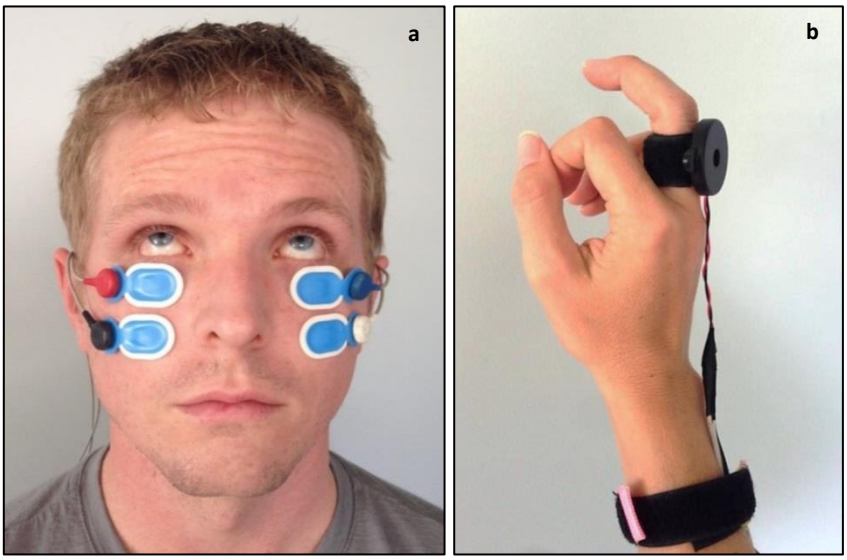

Figure 62. a). Position of active and reference electrodes for oVEMP recordings and b). the piezoelectric transducer secured on the tester's middle finger, which is shown in the tapping position.

Each tap generated a trigger pulse that was sent from the piezoelectric electric transducer to the signal processing box. Electrical activity was amplified by a factor of 1000, filtered in the software to a bandwidth of 10 Hz – 600 Hz using a second-order filter, and averaged over a 100 ms window using a sampling rate of 5 Hz. Prior to averaging, waveforms were sorted into nine bins according to the strength of the tap/trigger signal. This process was designed to improve the signal-to-noise ratio and to produce the input-output function. The TapVEMP software displayed the strength of each tap and the averaged waveform, providing immediate visual feedback regarding the strength and uniformity of tap stimuli and the number of stimuli delivered at each intensity (Figure 63). Testing was continued until stimulus intensity brackets 2 - 8 contained at least 10 and ideally 20 to 30 traces; a number considered adequate to provide a valid averaged waveform for each bracket.

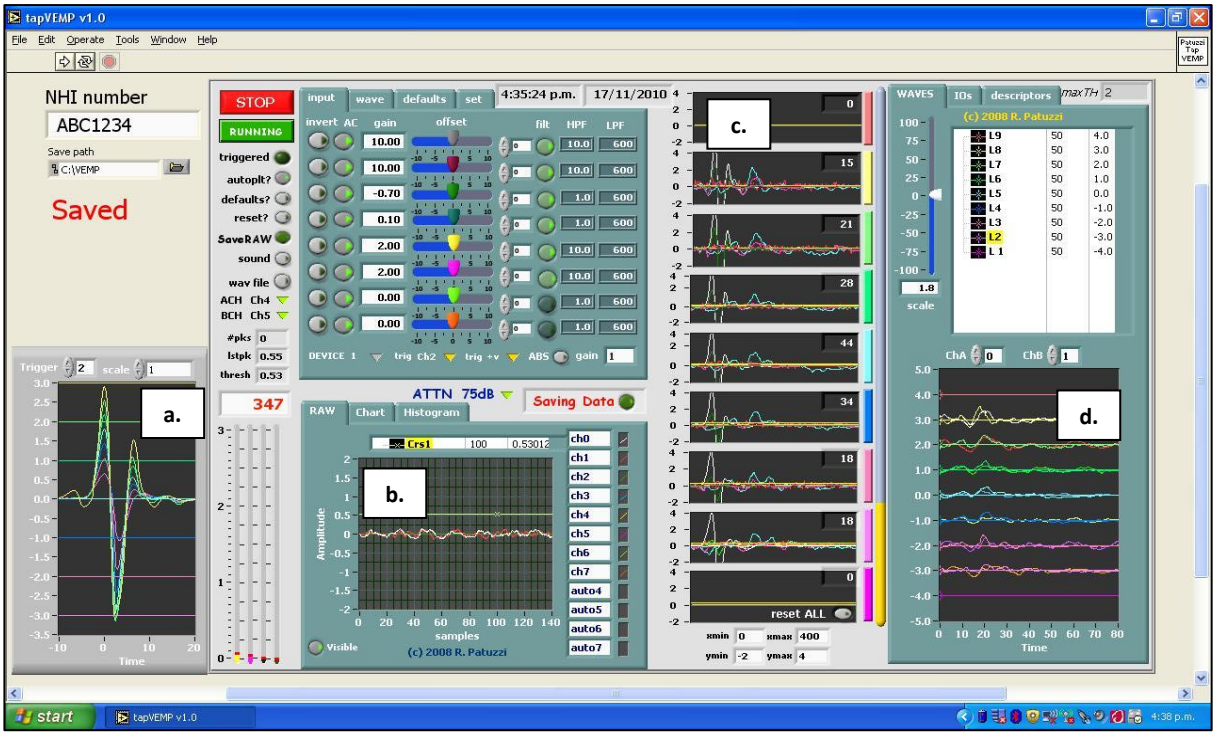

Figure 63. Screenshot of the TapVEMP v1.0 software. Highlighted are: a. the averaged waveform of the trigger pulse for each intensity bracket; b. ongoing electrical activity; c. raw traces and number of taps sorted from lowest intensity at the bottom, to highest intensity at the top; d. Averaged traces recorded for each side at each level.

Data were saved with a participant identifier code and the time and date of the test session, and were imported into a Microsoft Excel spreadsheet.

8.2.4 Data analysis

Analysis of VEMP data was performed separately for each surgery. Data was not included where recordings were not clear enough to distinguish between an absent response and a response obscured by artefact and/or interference. All data reported was therefore obtained in cases where oVEMPs were present and peaks in the waveform could be identified.

8.2.4.1 n10 amplitude and latency

The first negative peak of the averaged waveform in each tap intensity bracket was identified as n10. Peak-picking was performed using a formula to detect the maximum amplitude of the waveform within a 5 – 15 ms post-stimulus analysis window. The selected n10 was confirmed by visual inspection of the waveform to ensure it was repeatable and not artefact; as illustrated by the peak within the analysis window in Trace 8 shown in Figure 64b. The

amplitude of n10 for each tap intensity bracket was taken as the average peak amplitude of the waveform in microvolts (μV) (Figure 64). The average latency of the n10 in each intensity bracket was measured from the time of stimulus onset in milliseconds (ms) (Figure 64a).

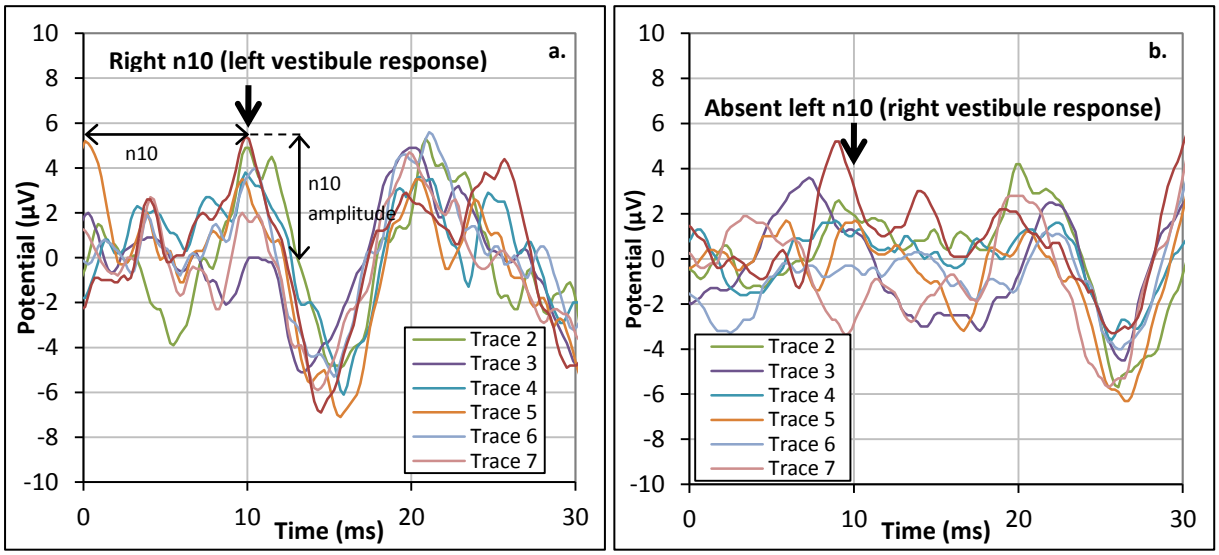

Figure 64. Tap-evoked oVEMP waveforms recorded from the right (a) and left (b) eyes of a participant whose right vestibular nerve could not be preserved during vestibular schwannoma removal. The response from the right eye shows a clear and repeatable n10 across tap intensities. The measurements of n10 latency and amplitude of the n10 for trace 8 are shown on panel a. In panel b, no repeatable negative deflection around 10 ms was present, consistent with right vestibular dysfunction.

To obtain a single amplitude and latency value across stimulus intensities, average n10 amplitudes and latencies were calculated across intensity brackets 3 to 7. An adequate number of traces were seldom recorded in brackets 1 and 9 to produce reliable averaged waveforms at these extreme stimulus intensities. The decision was made to exclude brackets 2 and 8 as it was frequently found too few traces could be obtained to cancel out interference or artefact in these brackets.

The effects of test ear (operated vs. non-operated) and assessment time bracket on mean n10 amplitudes and latencies were assessed using mixed factor ANOVAs. Post-hoc pairwise comparisons with Bonferroni corrections were also employed to determine whether a significant difference between ears was present in any individual assessment bracket and if mean values differed between any pairs of brackets. These analyses were performed on mean

data in each bracket and on the mean change in amplitude and latency compared to the preoperative value in each assessment bracket.

Further analyses were performed on the range and distribution of changes in amplitude and latency across assessment brackets. The percentage of patients with a change falling into one of a range of bins based on the size of change was calculated. The size and distribution of bins was specific to the data being examined. Comparisons in the distribution of patients in each bin were performed across brackets using Fisher's exact tests with the Freeman-Halton extension.

8.2.4.2 Asymmetry ratio

The amplitude of n10 was analysed as an absolute value for each side and as a ratio showing the relative amplitude of responses from each side. The asymmetry ratio was calculated using the formula:

$$100 \text{ x } \frac{\text{Operated ear amplitude} - \text{Nonoperated ear amplitude}}{\text{Operated ear amplitude} + \text{Nonoperated ear amplitude}}$$

Asymmetry ratios were multiplied by a factor of +1 if the right ear was operated on and -1 if the left was the operated ear. Positive asymmetry ratios therefore reflected a stronger response from the non-operated ear relative to the operated ear and negative responses indicated that the response of the operated ear was stronger than the non-operated ear.

Mixed model analyses with pairwise comparisons were performed to assess for any significant change in asymmetry ratio over assessment brackets. Changes in the distribution of asymmetry ratios across patients at each assessment were evaluated using Fisher's exact tests with the Freeman-Halton extension. Again, tests were performed for mean absolute asymmetry ratios and for the mean change in asymmetry ratio in each bracket.

8.2.4.3 Slope of the input-output function

Input-output functions were created to assess the relationship between the n10 amplitude for intensity brackets 3 – 7 for each eye to the tap stimulus intensity (Figure 65). The slope of the function was calculated for the amplitude of both the operated and on-operated sides.

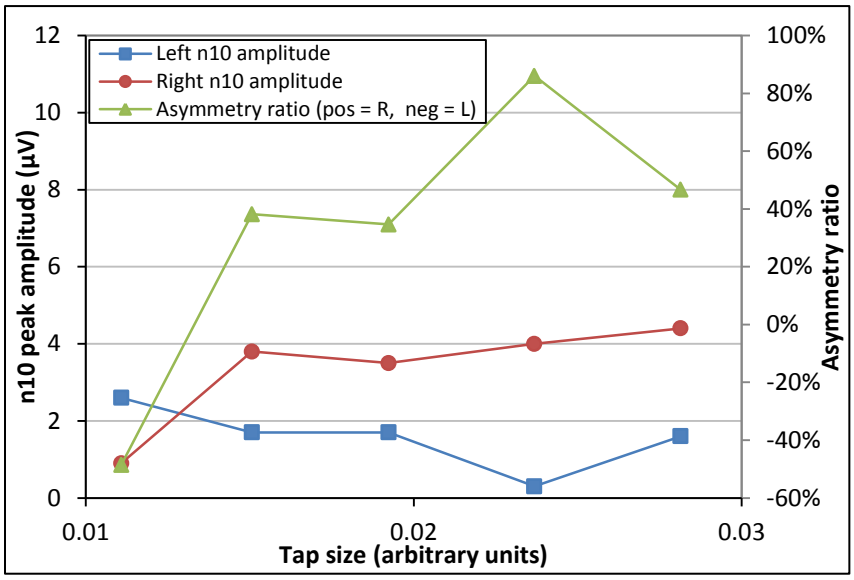

Figure 65. Input-output functions relating the n10 amplitude from each eye and the asymmetry ratio to the tap intensity. Data is taken from the waveforms shown in Figure 64.

Mean slope and mean change in slope relative to before surgery were compared between ears and assessment brackets using mixed factor ANOVAs and Fisher's exact tests in the same way described above for amplitude and latency measurements.

8.2.4.3 Patient reported symptoms of balance dysfunction

Patient reports of any balance disturbance, including, but not limited to; dizziness, vertigo, unsteadiness, and light-headedness, were recorded at each assessment. oVEMPs recorded from patients with pronounced or prolonged balance symptoms were analysed individually and presented as case studies.

8.2.4.4 Relationship between postoperative EHF hearing loss and oVEMPs

8.2.4.4.1 Audiometric changes in patients with vestibular symptoms

In the patients who reported significant symptoms of balance disturbance, audiograms were examined in detail along with oVEMP measurements. Changes in hearing across the entire test frequency range were described qualitatively in each case.

8.2.4.4.2 oVEMPs in patients with and without postoperative EHF hearing loss

The first postoperative audiogram (performed at 1 week) was examined in all patients for whom pre- and postoperative VEMPs were recorded to identify cases of "significant" EHF hearing loss. A significant loss was defined as losing measureable thresholds at three or more EHF test frequencies at which thresholds could be measured before surgery. oVEMPs in this group of patients were compared to those in patients with no loss of measureable EHF thresholds, or with a gain in measureable thresholds at the first postoperative assessment.

The change in the mean oVEMP asymmetry ratio relative to that recorded before surgery was compared between the two groups at each postoperative assessment using a mixed factor ANOVA with post-hoc pairwise comparisons.

The significance criterion for all statistical tests described in this chapter was $p > .05$. All statistical assessments were performed using IBM SPSS version 22 (2013, IBM Corp., Armonk, NY).

8.3 Results

8.3.1 Patient characteristics

Of the 96 patients recruited, 65 had VEMPs that were tested and present preoperatively and at one or more postoperative assessments. Of the 31 patients for whom VEMP data is not presented, eight were not available for any postoperative testing, two declined to participate in VEMP testing, and in the remaining 21 reliable VEMP waveforms could not be obtained. In the majority of cases this was due to equipment failure or electrical interference that could not be eliminated. The 65 patients with VEMP data suitable for analysis underwent 72 middle ear procedures; 38 of which were stapedectomies, 19 ossiculoplasties, and 15 tympanoplasties. Of these procedures, 38 were primary surgeries, 25 were revisions, and 10 were the second step of planned two-stage procedures. Thirty participants were male and 35 were female, with a mean age at the time of surgery of 46.0 years (*SD* = 13.5, range = 17.3 – 70.1 years). Forty-two operations were performed on the right ear and 30 on the left ear. Participant characteristics are presented according to surgery type in Table 21. Given the small number of ears in each group when data was sorted according to whether the surgery was a primary or revision procedure, analyses were not performed to assess the effect of this factor.

The number of participants assessed differed in each follow-up bracket as some patients were not available for postoperative testing and in others reliable results could not be obtained at all postoperative assessments (as shown in Tables 21, 22, and 23). All available VEMP data for a given participant was included regardless of whether all postoperative assessments were completed, as long as at least one set of postoperative data was recorded.

Table 21. Patient characteristics according to surgery type.

Surgery	Ears *n*	Procedures *n*	Procedure type			Mean age (years) *(SD)*	Sex		Ear	
			Primary	Revision	Second stage		*M*	*F*	*R*	*L*
Stapedectomy	33	38	26	12	-	48.7 (*12.4*)	13	25	18	20
Ossiculoplasty	18	19	4	5	10	42.0 (*11.9*)	13	6	14	5
Tympanoplasty	14	15	8	7	-	44.2 (*17.4*)	10	5	10	5
Total	65	72	38	25	10	46.0 *(13.5)*	36	36	42	30

8.3.2 VEMPs pre- and post-stapedectomy

Between 19 and 23 of the 38 ears with oVEMPs that were elicited prior to stapes surgery had oVEMPs that could be recorded at each of the six scheduled postoperative assessments. The mean latency, amplitude, and asymmetry ratios of the n10 peak of the response across the patients tested at each assessment are presented in Table 22.

Table 22. Summary of pre- and postoperative VEMP n10 characteristics in patients undergoing stapedectomy.

		Approximate time since surgery					
	Preop	1 day	1 week	1 month	3 months	6 months	12 months
n	38	23	26	29	19	26	23
Amplitude – Operated ear (µV)							
Mean *(SD)*	6.4 *(3.5)*	8.1 *(5.2)*	8.2 *(4.7)*	6.3 *(3.4)*	6.6 *(3.8)*	8.6 *(4.7)*	7.6 *(3.9)*
Range	1.2 – 17.1	2.4 – 22.5	2.3 – 24.2	0.8 – 13.3	0.7 – 14.6	0.6 – 19.0	1.5 – 18.7
Amplitude – Non-operated ear (µV)							
Mean *(SD)*	8.2 *(4.8)*	8.9 *(5.8)*	7.3 *(4.4)*	6.7 *(3.2)*	7.3 *(3.3)*	9.2 *(5.1)*	8.2 *(3.5)*
Range	1.4 – 20.6	1.5 – 26.0	2.6 – 23.0	1.0 – 14.0	2.0 – 13.3	2.1 – 22.7	1.9 – 18.9
Asymmetry ratio (%)							
Mean *(SD)*	9 *(23)*	4 *(32)*	-5 *(22)*	3 *(22)*	9 *(23)*	5 *(17)*	6 *(16)*
Range	-39 – 67	-76 – 58	-50 – 46	-45 – 42	-23 – 69	-27 – 55	-14 – 48
Latency – Operated ear (ms)							
Mean *(SD)*	10.5 *(0.7)*	10.7 *(0.8)*	10.8 *(0.7)*	10.8 *(0.7)*	10.7 *(0.5)*	10.5 *(0.5)*	10.7 *(0.5)*
Range	9.1 – 12.6	9.6 – 12.5	9.2 – 12.4	9.8 – 12.4	8.1 – 11.6	9.1 – 11.3	9.8 – 11.7
Latency – Non-operated ear (ms)							
Mean *(SD)*	10.5 *(0.6)*	10.5 *(0.7)*	10.7 *(0.6)*	10.5 *(0.5)*	10.7 *(0.5)*	10.5 *(0.5)*	10.6 *(0.4)*
Range	9.5 – 11.8	9.3 – 12.3	9.1 – 12.0	9.6 – 11.3	8.3 – 11.6	9.5 – 11.5	9.7 – 11.5

8.3.2.1 n10 amplitude

As shown in Table 22, the mean amplitude of the n10 response associated with the operated ear was lower than that from the non-operated ear both preoperatively and at all postoperative assessments, except that one week after surgery. The difference between ears was greatest before surgery and tended to decrease postoperatively. There was no statistically significant difference in mean n10 amplitude between ears either overall ($F(1, 36) = 0.78$, $p = .38$), or in any assessment bracket. No significant change in mean response amplitude was found across assessment brackets ($F(4.04, 145.41) = 2.24$, $p = .07$) and the mean amplitude in any individual bracket did not differ significantly from the mean in any other bracket.

While the mean difference in amplitude between the operated and non-operated ears was not significant, the mean change in n10 amplitude relative to preoperative levels did differ significantly between ears ($F(1, 32) = 6.47$, $p = .02$). Averaged across all assessment brackets, the mean n10 amplitude in the operated ear increased 1.0 µV and the amplitude in the non-operated ear decreased by 1.0 µV. This resulted in a reduction in the magnitude of the preoperative (non-significant) n10 amplitude difference between ears. Post-hoc pairwise comparisons showed that the difference in amplitude change between ears was significant only at the 1 week postoperative assessment ($p = .006$), at which point the average change from preoperative n10 amplitude was -1.7 µV for the non-operated ear and 1.5 µV for the operated ear (Figure 66). It must be noted that this significant difference at 1 week resulted from a mean change (in different directions) in both ears, not only the ear that underwent surgery. No statistically significant effect of assessment time on mean change was detected ($F(3.71, 118.79) = 1.56$, $p = .19$).

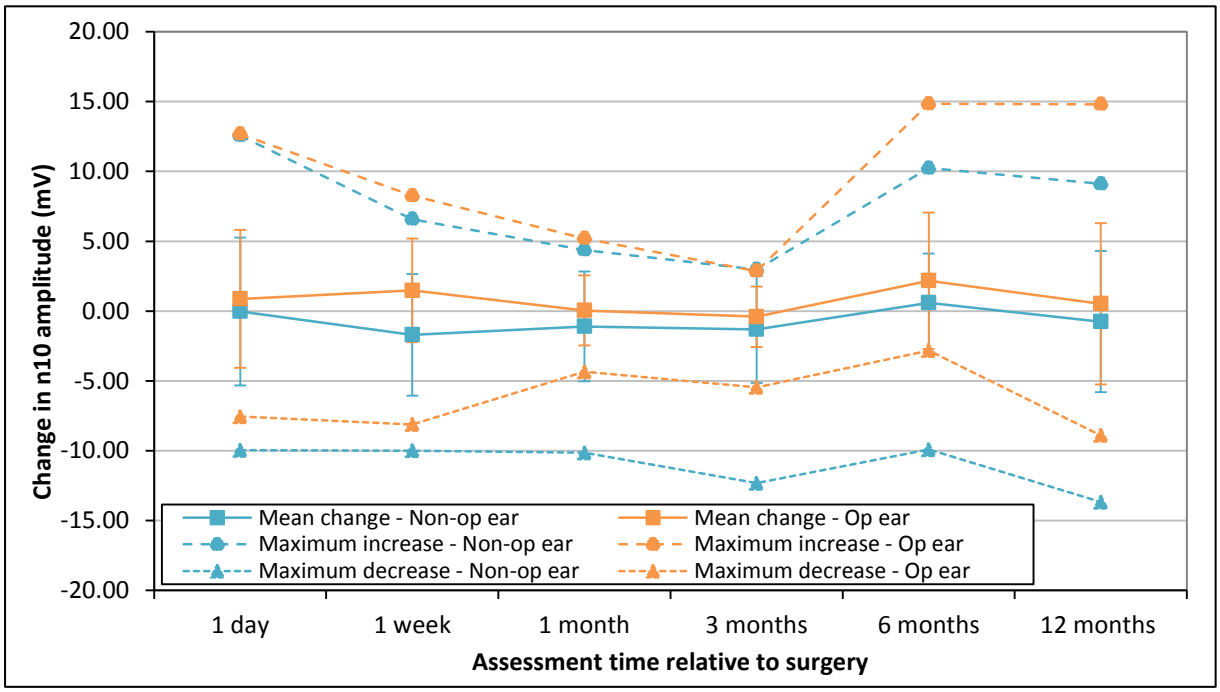

Figure 66. Change in n10 amplitude in each ear relative to the preoperative values across post-stapedectomy assessments.

Amplitude changes in both ears were always within +/-15 µV of the preoperative n10 amplitude. The distribution of positive and negative amplitude changes in each ear was examined by calculating the percentage of patients at each assessment who presented with a change in amplitude of -15 to -5 µV, -4 to 5 µV and 6 to 15 µ (Figure 67). Consistent with

the mean data, there was a trend for more non-operated than operated ears to present with a decreased n10 amplitude at most assessments, although differences are small. Assessment of the percentage of patients in each change bracket using a Fisher's exact test with Freeman-Halton extension showed no significant differences between ears in any assessment bracket.

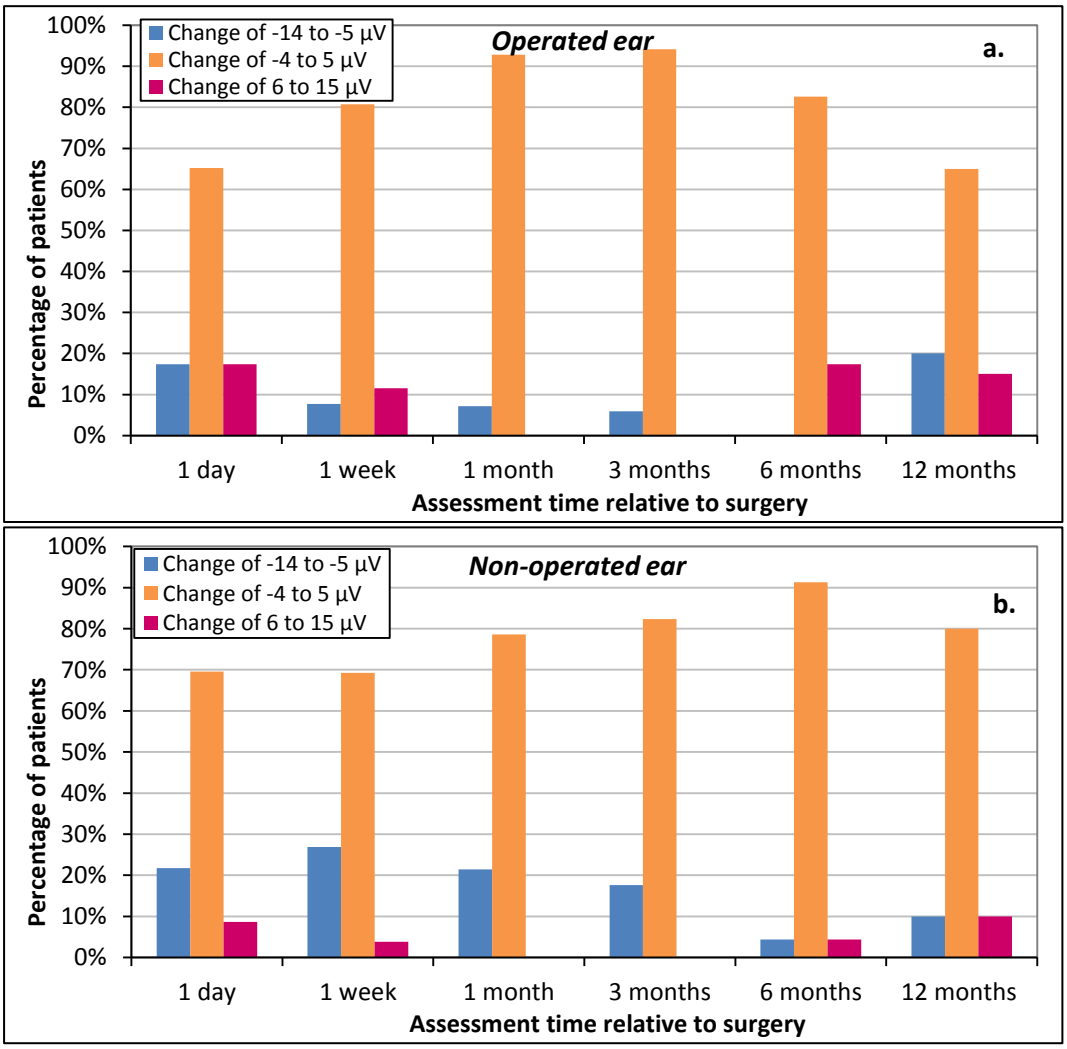

Figure 67. Degree of change in n10 amplitude relative to the preoperative values across post-stapedectomy assessments the (a) operated and (b) non-operated ears.

8.3.2.2 Asymmetry ratio

The mean asymmetry ratio was 9% preoperatively and remained close to zero throughout the postoperative course (Table 23). The difference in mean asymmetry ratio across assessments or between pairs of brackets was not significant ($F(6, 51) = 1.25$, $p = .30$).

With the exception of the 3 month assessment, at which the mean change was 0%, all mean changes in the asymmetry ratio were in the negative direction (Figure 68). The decrease in

the asymmetry ratio was a result of the small decrease in the mean response of the non-operated ear that occurred concurrently with a small increase in the mean response of the operated ear. The difference in the mean change in asymmetry ratio across postoperative assessments was not statistically significant ($F(5, 51 = 1.04$, $p = .41$), nor did the change in any bracket differ significantly from any other bracket. As shown in Figure 68, the range of asymmetry ratio changes was considerable, with particularly large shifts found in the negative direction.

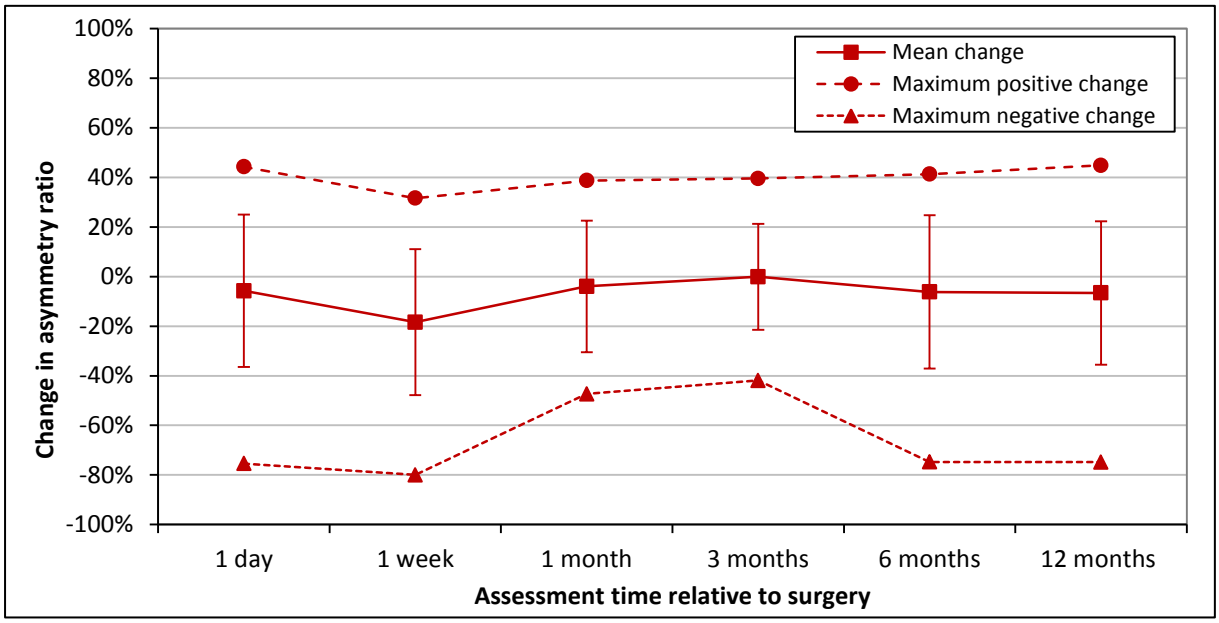

Figure 68. Change in n10 amplitude asymmetry ratios after stapedectomy. Positive changes reflect an increase in the response of the non-operated ear relative to the operated ear, and negative changes reflect an increase in the response amplitude from the operated ear relative to the non-operated ear.

The greatest decreases in asymmetry ratio were recorded at the first two postoperative assessments (Figure 68). Despite the higher percentage of large negative shifts 1 day and 1 week after surgery, no significant differences in the distribution of patients across brackets of 25% from -100% to +100% were detected between any postoperative assessments using Fisher's exact tests with the Freeman-Halton extension.

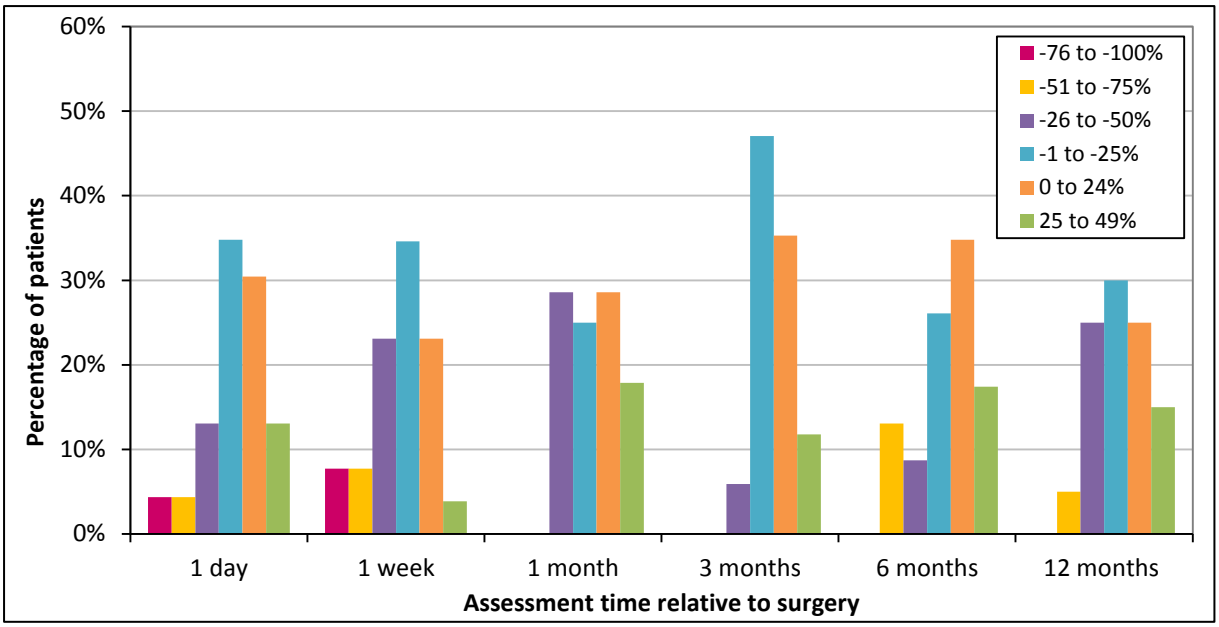

Figure 69. Percentage of stapedectomy patients at each postoperative assessment with changes in asymmetry ratios of different sizes. Patients are sorted into brackets of 25% from -100% to 49% according to the size of the asymmetry ratio change compared to the preoperative measurement.

8.3.2.3 n10 latency

The mean latency of n10 varied minimally in both the operated and non-operated ears following stapedectomy (Table 23). The mean latency was slightly longer in the operated ear than in the non-operated ear at the first three postoperative assessments, however no statistically significant difference was found between ears at any assessment ($F(1, 34) = 2.28$, $p = .14$) and no differences were present between mean latencies across assessments ($F(4.51, 153.36) = 2.02$ $p = .09$).

The mean postoperative change in latency also did not vary significantly between operated and non-operated ears ($F(1, 32) = 1.49$, $p = 0.23$) (Figure 70). The range of change values recorded was greatest at the 1 day postoperative assessment, however there was no significant effect of assessment bracket on mean latency change ($F(5, 155) = 1.78$, $p = .12$) and no significant interaction between test ear and assessment time ($F(5, 155) = 0.64$, $p = .67$).

The effect of surgery on n10 latency was further assessed by comparing the percentage of operated and non-operated ears with latency changes of -1.1 to -2 ms, 0.1 to 1 ms, 0 to 0.9 ms, and 1 to 1.9 ms (data not shown). No trends for any differences in the distribution of changes were noted between ears and Fisher's exact tests with Freeman-Halton extensions for 2x4 tables confirmed there was no significant difference in the proportion of patients in each group between ears at any postoperative assessment.

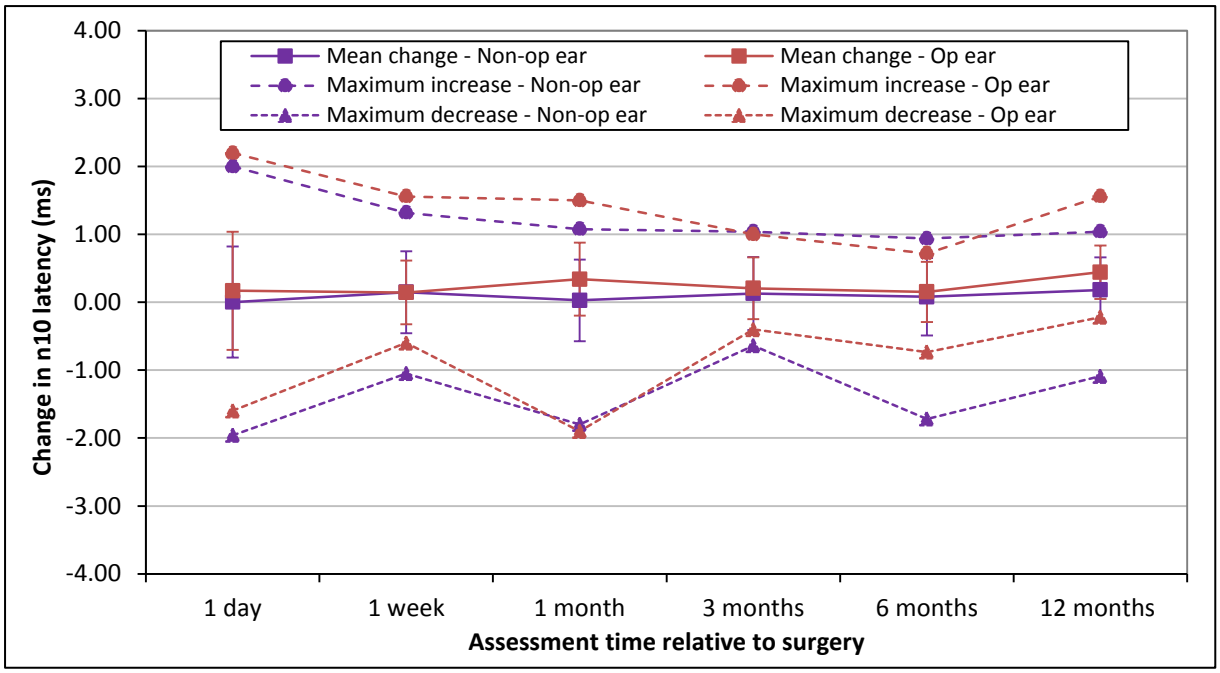

Figure 70. Change in n10 latency relative to the preoperative values across post-stapedectomy assessments.

8.3.2.4 Slope of the input-output function

As expected, the mean slope of input-output function for absolute n10 amplitude was positive for both ears at all assessments (Figure 71). There were however, several patients with negative slopes at each assessment, which is inconsistent with the expected increase in n10 amplitude with increasing tap intensity. A mixed factor ANOVA showed no significant difference in the slope of the input-output function for n10 amplitude between the operated and non-operated ears ($F(1,36) = 0.48$, $p = .49$), no significant effect of assessment bracket on slope ($F(4.08, 146.84) = 1.46$, $p = .22$), and no significant interaction between test ear and assessment bracket ($F(4.08, 146.84) = 0.66$, $p = .63$). The mean post-stapedectomy change in the slope of the input-output function was minimal and not significant for either ear ($F(1, 32) = 0.06$, $p = .81$) in any assessment bracket.

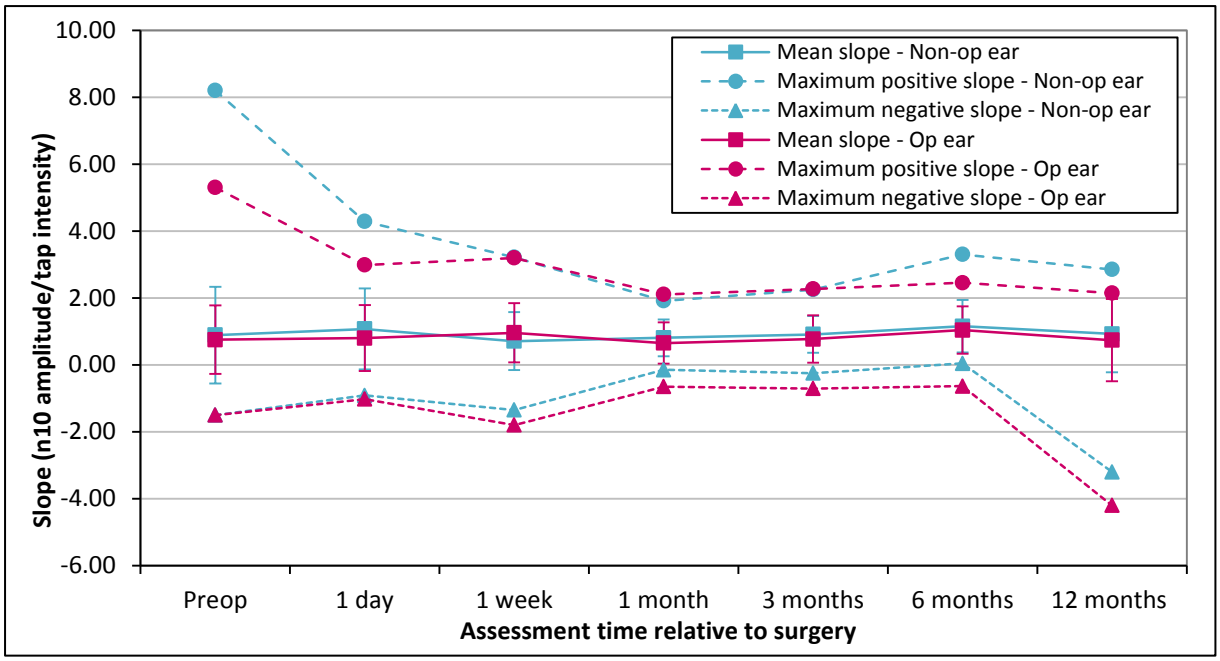

Figure 71. Slope of the input-output function relating tap strength to n10 amplitude from each ear across assessments performed in stapedectomy patients.

8.3.3 VEMPs pre- and post-ossiculoplasty

Prior to primary, revision, or second-stage ossiculoplasty, 19 patients were available for VEMP testing and had responses that could be elicited without excessive electrical or myogenic interference in the recordings. Between 13 and 16 of these patients had VEMPs recorded in each postoperative follow-up bracket. Group mean n10 characteristics from the pre- and postoperative assessments in provided in Table 23.

Table 23. Summary of pre- and postoperative VEMP n10 characteristics in patients undergoing ossiculoplasty.

	Approximate time since surgery						
	Preop	1 day	1 week	1 month	3 months	6 months	12 months
n	19	16	13	14	15	16	13
Amplitude – Operated ear (µV)							
Mean *(SD)*	8.4 *(5.4)*	8.9 *(4.3)*	8.2 *(4.3)*	7.7 *(2.8)*	8.1 *(3.5)*	6.9 *(2.7)*	8.1 *(2.9)*
Range	2.6 – 20.4	2.4 – 20.8	0.7 – 16.9	4.0 – 13.1	3.7 – 15.4	2.6 – 13.0	3.1 – 12.6
Amplitude – Non-operated ear (µV)							
Mean *(SD)*	6.3 *(3.0)*	8.5 *(3.8)*	7.9 *(4.5)*	8.6 *(3.6)*	7.3 *(3.2)*	8.1 *(2.8)*	8.5 *(2.1)*
Range	1.2 – 13.4	2.1 – 15.5	1.7 – 18.4	3.3 – 16.6	2.1 – 13.8	3.8 – 13.8	4.7 – 12.5
Asymmetry ratio (%)							
Mean *(SD)*	-10 *(27)*	-2 *(26)*	-1 *(22)*	6 *(17)*	-5 *(20)*	8 *(22)*	5 *(21)*
Range	-66 – 34	-44 – 47	-31 – 42	-25 – 31	-41 – 32	-34 – 45	-24 – 47
Latency – Operated ear (ms)							
Mean *(SD)*	10.4 *(0.9)*	10.5 *(1.1)*	10.2 *(0.8)*	10.4 *(0.7)*	10.7 *(1.0)*	10.5 *(0.5)*	10.4 *(0.5)*
Range	8.4 – 12.9	9.2 – 13.7	9.1 – 11.7	8.5 – 12.4	8.1 – 13.7	9.5 – 11.3	9.5 – 11.1
Latency – Non-operated ear (ms)							
Mean *(SD)*	10.5 *(1.1)*	10.6 *(1.1)*	10.4 *(1.2)*	10.4 *(0.9)*	10.9 *(1.0)*	10.6 *(0.8)*	10.3 *(0.4)*
Range	8.4 – 12.9	9.4 – 13.6	8.6 – 12.8	8.8 – 12.8	8.3 – 13.5	9.3 – 13.1	9.5 – 10.1

8.3.3.1 n10 amplitude

Mean n10 amplitude did not differ significantly between the operated and non-operated ears across assessments ($F(1, 24) = 0.04$, $p = .85$), or in any individual assessment bracket. Comparison of mean amplitude across assessment brackets showed no significant effect of assessment time ($F(6, 144) = 0.72$, $p = .64$) and pairwise comparisons showed no significant differences between means recorded at any two assessments.

Mean, maximum, and minimum changes in n10 amplitude across the ossiculoplasty group are presented in Figure 72. It is evident that, similar to post-stapedectomy patients, a wide range of amplitude changes were recorded, however these changes were not larger in either the negative or positive direction. Across all ossiculoplasty patients, the mean change in n10 amplitude was not significantly influenced by test ear ($F(1, 12) = 2.05$, $p = .18$) and no interaction was present between test ear and assessment bracket ($F(5, 60) = 0.85$, $p = .52$). In agreement with the mean absolute amplitude data, no significant difference across assessment bracket was present ($F(5, 60) = 0.55$, $p = .74$) and the mean change in any bracket did not differ significantly from that in any other bracket.

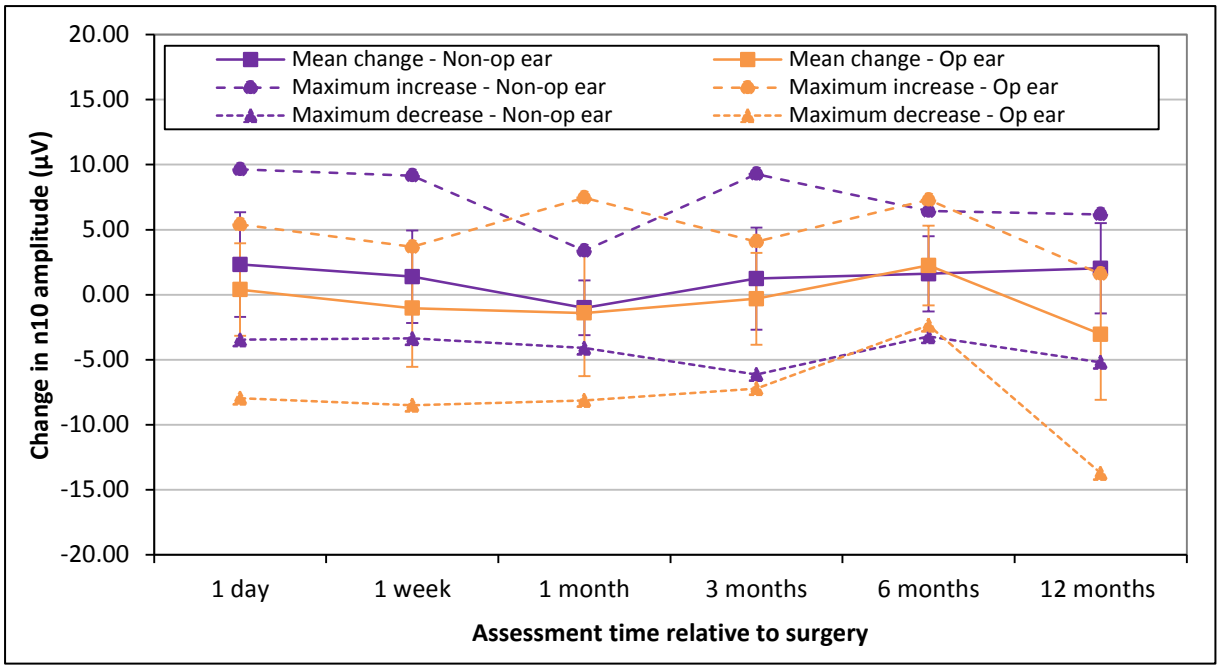

Figure 72. Change in n10 amplitude relative to the preoperative values across post-ossiculoplasty assessments.

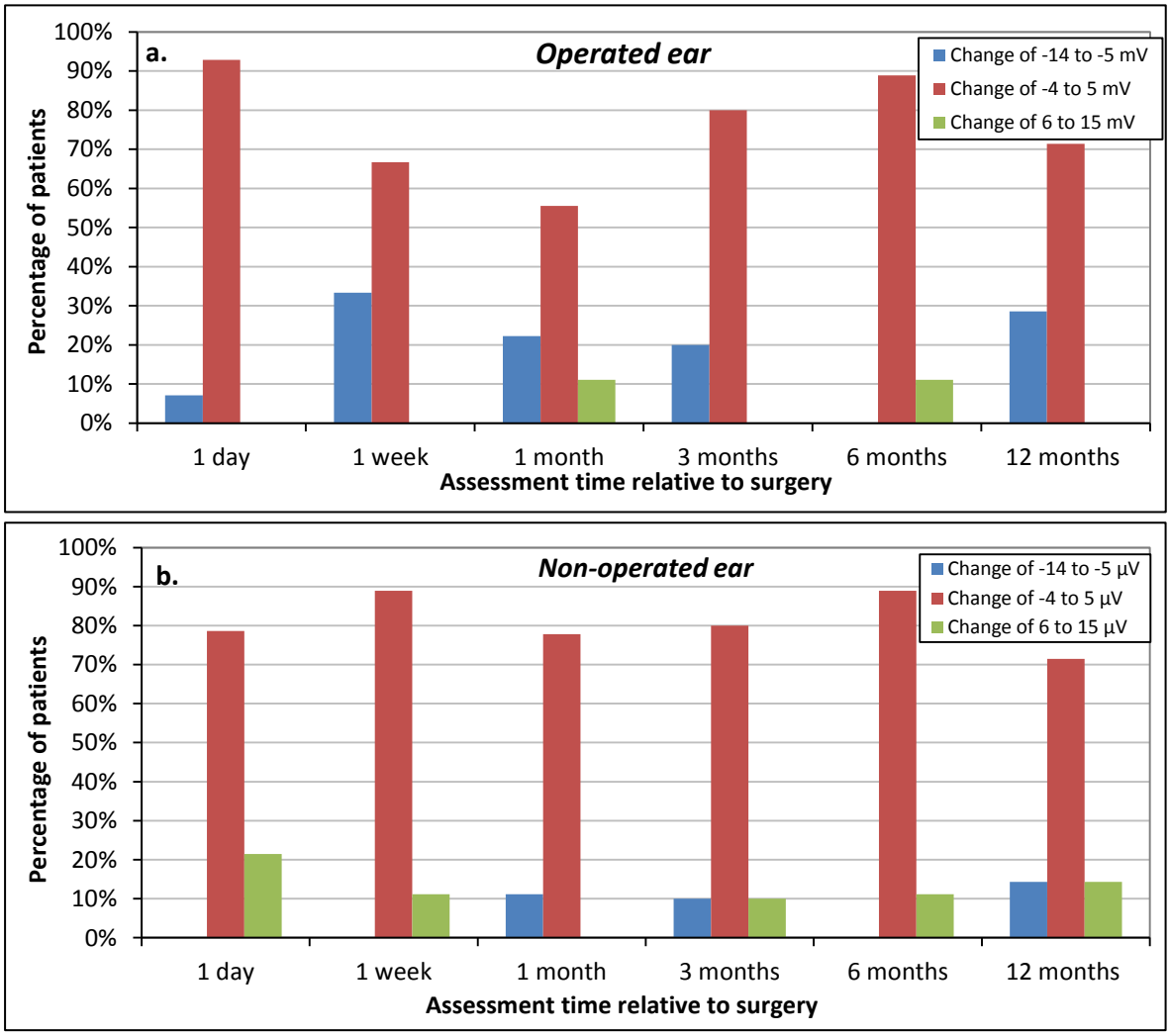

Figure 73. Degree of change in n10 amplitude relative to the preoperative values across post-ossiculoplasty assessments the operated (panel a) and non-operated (panel b) ears.

The distribution of n10 amplitude changes of -15 to -5 µV, -4 to 5 µV and 6 to 15 µV for each ear is shown in Figure 73. The difference in the percentage of patients in each bracket was not statistically significant between ears in any assessment bracket when results were assessed using 2x3 Fisher's exact tests with Freeman-Halton extensions.

8.3.3.2 Asymmetry ratio

At -10%, the mean preoperative asymmetry ratio was lower than that recorded at any follow-up after ossiculoplasty. The range of mean asymmetry ratios the postoperative course was small, and all mean postoperative asymmetry ratios were between -5% and 8% (Table 23). A mixed model analysis confirmed that there was no significant effect of assessment bracket on mean asymmetry ratio ($F(6, 23) = 1.27$, $p = .31$) and pairwise comparisons showed no significant difference in mean ratios between any pair of assessment brackets.

Across the postoperative period, mean changes in the asymmetry ratio were relative small and steady, with the exception of the 12 month assessment, where the mean change in asymmetry ratio increased to 28% from -6% at 6 months (Figure 73). No patients presented with a negative shift relative to the preoperative asymmetry ratio at this final assessment. Mixed model analysis showed no effect of assessment bracket on the mean change in asymmetry ratio ($F(6, 16) = 2.21$, $p = .10$).

The percentage of patients with changes in asymmetry ratios falling in each of six brackets from -100% to +100%, is presented in Figure 74. Again, the contrast between the high rate negative shifts at 6 months and of positive shifts at 12 months is evident. It is also apparent that the range of changes documented was greater in the early postoperative brackets, particularly 1 day after surgery. Significant differences in the distribution of patients across brackets of change magnitude were present only in the comparison of assessments at 6 months and 12 months ($p = .004$) when assessment brackets were compared using Fisher's exact tests with the Freeman-Halton extension.

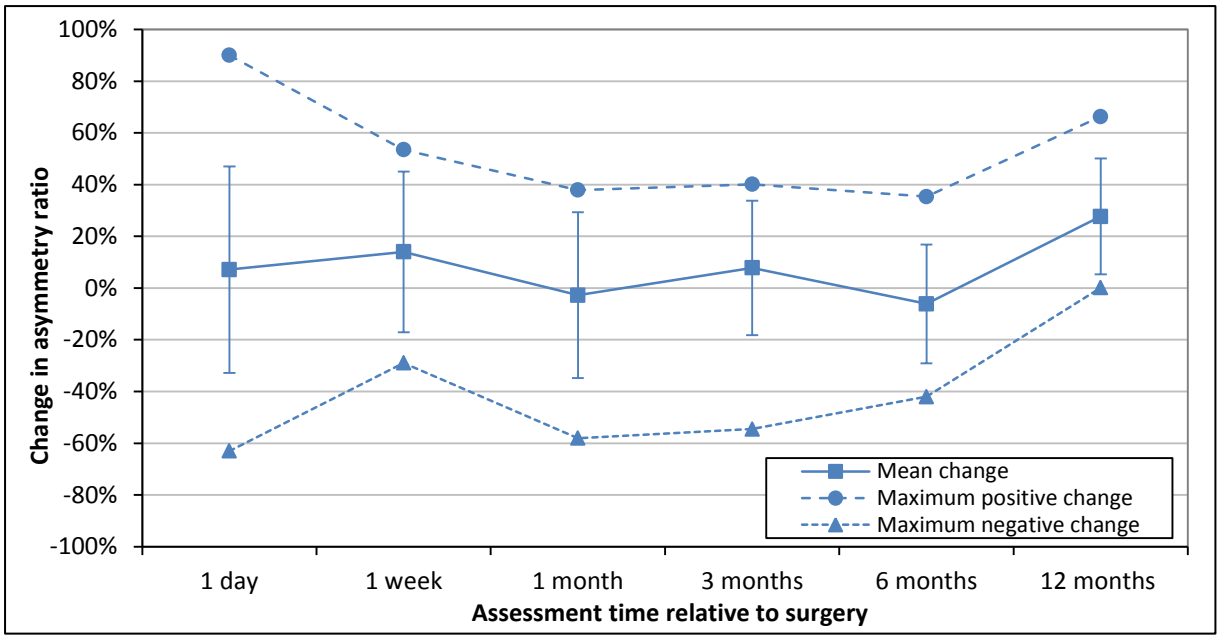

Figure 74. Change in n10 amplitude asymmetry ratios relative to preoperative measurements in patients undergoing ossiculoplasty. Positive changes reflect an increase in the response of the non-operated ear relative to the operated ear, and negative changes reflect an increase in the amplitude of the response of the operated ear relative to the non-operated ear.

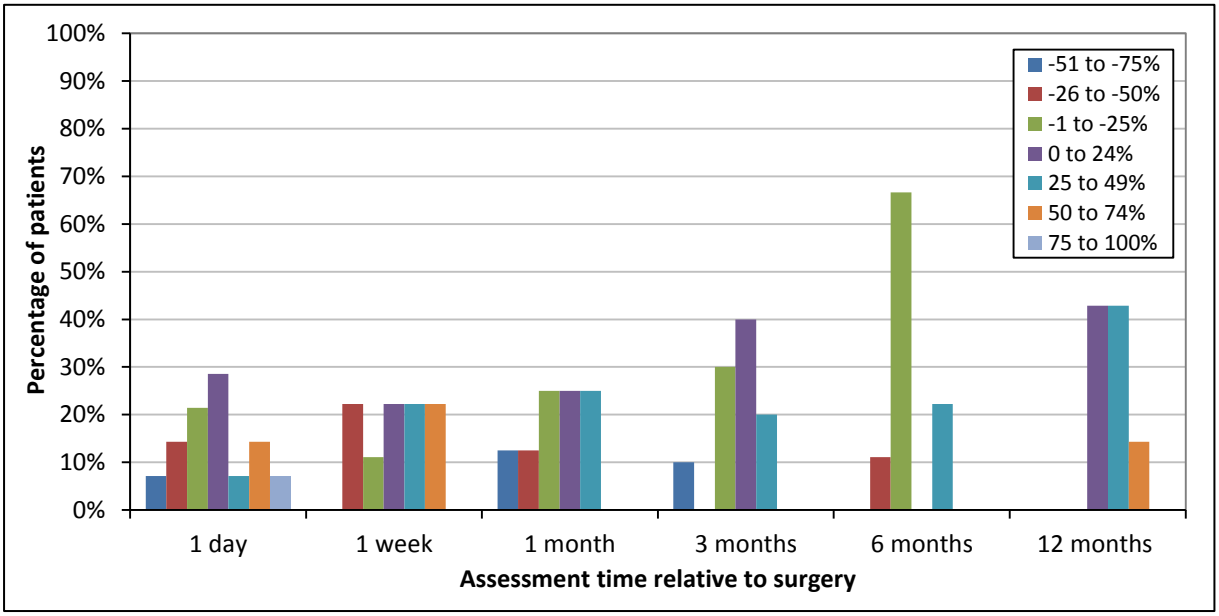

Figure 75. Percentage of ossiculoplasty patients at each postoperative assessment with changes in asymmetry ratios of different sizes. Patients are sorted into brackets of 25% from -50% to 100% according to the size of the asymmetry ratio change compared to the preoperative measurement.

8.3.3.3 n10 latency

Across all assessments, the latency of n10 varied from 8.3 to 13.6 ms in the non-operated ear and 8.1 to 13.7 ms in the operated ear (Table 23). Results were similar to those following stapedectomy in that very little variation in latencies was documented across assessments.

The assessment of mean latency over all assessments showed no significant main effect of ear ($F(1, 24) = .06$, $p = 0.81$), no significant main effect of assessment bracket ($F(4.25, 101.93) = 1.18$, $p = .32$), and no significant interaction between ear and assessment bracket ($F(4.25, 101.93) = 0.15$, $p = .99$).

A comparable lack of significant effects of surgery on n10 latency was documented in the analyses of mean changes in latency compared to preoperative recordings (Figure 76). Again, changes were similar in magnitude in the positive and negative directions, with the exception of the 6 month assessment at which the maximum increase was approximately half the maximum decrease. This effect occurred for both the operated on non-operated ears, and results at 12 months returned to levels similar to those at assessments prior to six months. Overall, there was no significant difference in mean latency change between the ears ($F(1, 12) = 0.14$, $p = .72$), no significant difference across assessments ($F(5, 60) = 0.80$, $p = .56$), and no significant interaction between the two variables ($F(5, 60) = 0.10$, $p = .99$).

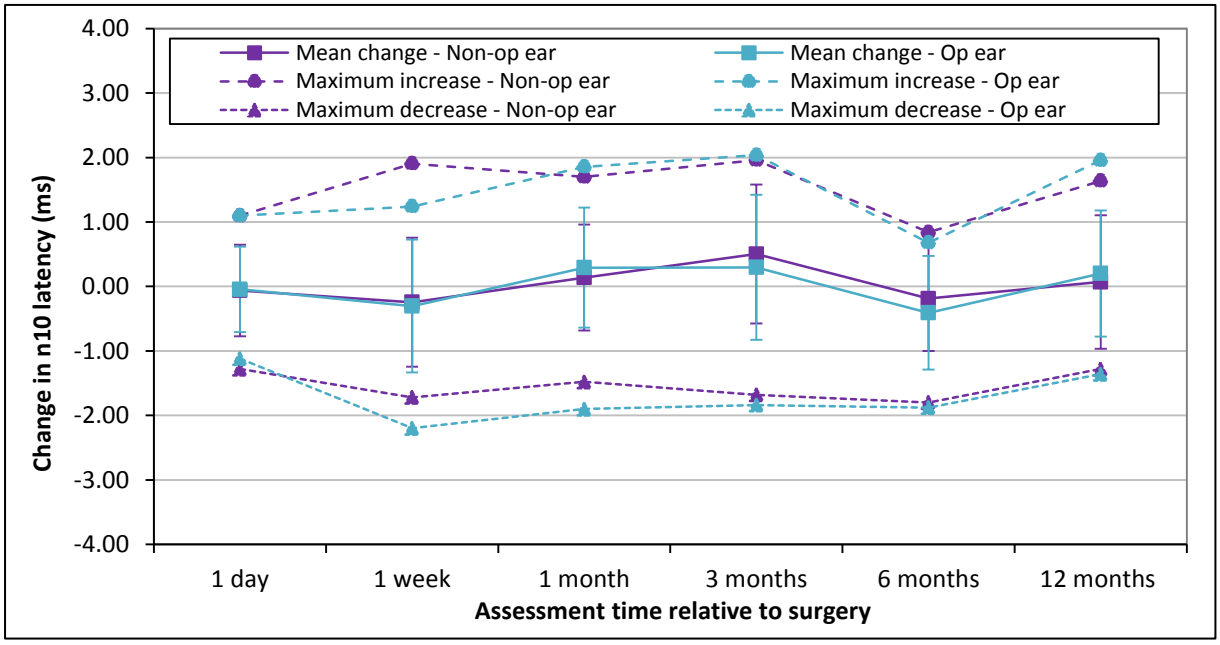

Figure 76. Change in n10 latency relative to the preoperative values across post-ossiculoplasty assessments.

A comparison of percentage of operated and non-operated ears with latency changes of -2.1 to -3ms, -1.1 to -2 ms, 0.1 to 1 ms, 0 to 0.9 ms, and 1 to 1.9 ms (data not shown) showed only minimal differences in the distribution of changes between ears. Fisher's exact tests with Freeman-Halton extensions confirmed there was no significant difference in the proportion of patients in each group between ears at any postoperative assessment.

8.3.3.4 Slope of the input-output function

The mean slope of the input-output function relating tap intensity to n10 amplitude was very similar for ossiculoplasty patients and stapedectomy patients, with mean values for both ears pre- and post-ossiculoplasty remaining close to 1 (Figure 77). Less variability in slope was recorded for ossiculoplasty patients than for stapedectomy patients, and fewer cases of negative slopes were documented. A mixed factor ANOVA confirmed that there was no significant difference in the slope of the input-output function for the n10 amplitude between the operated and non-operated ears ($F(1,24) = 0.10$, $p = .75$), no significant effect of assessment bracket on slope ($F(3.67, 87.97) = 1.31$, $p = .27$), and no significant interaction between test ear and assessment bracket ($F(3.67, 87.97) = 0.91$, $p = .46$).

Following ossiculoplasty, the mean change in the slope of the input-output function was slightly more positive in the non-operated ear compared to the operated ear, although changes were small overall, and no significant difference was present between ears ($F(1, 12) = 1.41$, $p = .26$) or across assessment brackets ($F(2.23, 26.76) = 1.68$, $p = .20$).

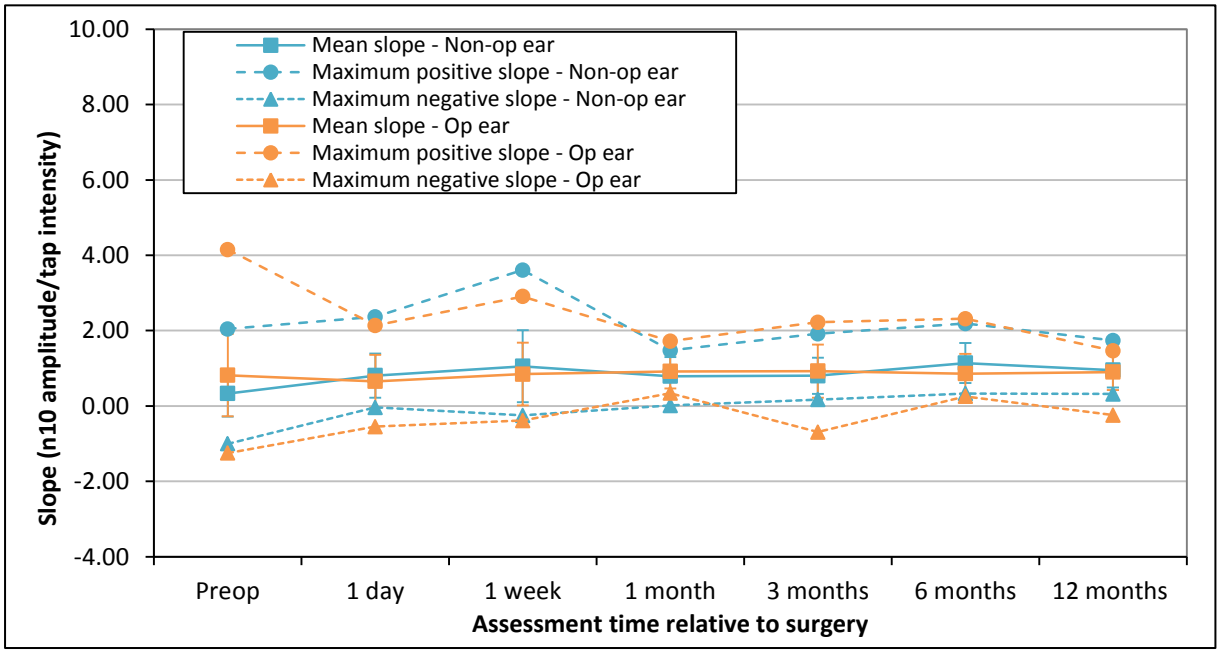

Figure 77. Slope of the input-output function relating tap strength to n10 amplitude from each ear across assessments in ossiculoplasty cases.

8.3.4 VEMPs pre- and post-tympanoplasty

Analysis of changes in VEMPs following tympanoplasty was limited by the small number of participants with responses that could be measured preoperatively and the failure of a high number of those patients to return for all postoperative testing. In particular, at postoperative day 1, data could only be obtained for five of the 15 patients with preoperative results (Table 24). Despite these limitations, statistical analyses were performed as for stapedectomy and ossiculoplasty to determine if any clear changes in VEMP parameters were present.

Table 24. Summary of pre- and postoperative VEMP n10 characteristics in patients undergoing tympanoplasty.

		Approximate time since surgery					
	Preop	1 day	1 week	1 month	3 months	6 months	12 months
n	15	5	8	13	12	9	10
Amplitude – Operated ear (µV)							
Mean *(SD)*	7.8 *(3.0)*	6.9 *(3.1)*	7.9 *(4.9)*	9.1 *(3.5)*	8.6 *(4.2)*	8.9 *(3.0)*	9.7 *(4.0)*
Range	2.1 – 13.8	1.3 – 10.3	2.1 – 18.7	4.2 – 16.5	2.1 – 16.5	4.7 – 15.2	3.7 – 15.3
Amplitude – Non-operated ear (µV)							
Mean *(SD)*	7.8 *(3.6)*	8.1 *(5.8)*	6.0 *(3.4)*	7.6 *(3.5)*	8.5 *(5.2)*	7.4 *(3.9)*	8.7 *(4.6)*
Range	2.4 – 13.8	2.7 – 18.7	1.8 – 11.3	1.9 – 13.5	0.6 – 22.0	2.1 – 15.5	2.5 – 17.8
Asymmetry ratio (%)							
Mean *(SD)*	-3 *(28)*	7 *(25)*	-14 *(24)*	-10 *(27)*	-5 *(22)*	-14 *(21)*	-7 *(18)*
Range	-47 – 56	-27 – 39	-56 – 28	-51 – 52	-53 – 40	-54 – 5	-35 – 15
Latency – Operated ear (ms)							
Mean *(SD)*	10.1 *(1.0)*	10.7 *(0.7)*	10.9 *(0.9)*	10.4 *(0.8)*	10.7 *(0.4)*	10.4 *(0.6)*	10.6 *(0.6)*
Range	8.0 – 11.9	9.5 – 11.7	9.6 – 12.6	9.0 – 12.4	8.1 – 11.7	9.5 – 11.1	9.7 – 11.7
Latency – Non-operated ear (ms)							
Mean *(SD)*	10.0 *(0.9)*	10.2 *(0.8)*	10.5 *(0.5)*	10.4 *(0.6)*	10.4 *(0.8)*	10.8 *(0.8)*	10.8 *(0.7)*
Range	8.0 – 11.1	9.3 – 11.4	9.7 – 11.2	9.0 – 11.5	8.3 – 11.1	9.5 – 12.4	9.6 – 11.6

8.3.4.1 n10 amplitude

No significant difference in mean n10 amplitude between the operated on non-operated ears was present overall ($F(1, 8) = 1.10$, $p = .33$), or in any individual assessment bracket. As was noted for stapedectomy and ossiculoplasty, the range of amplitudes recorded at each assessment was large, but similar for both ears (Table 24). Mean amplitude across both ears did not differ significantly across all assessments ($F(6, 48) = 0.89$, $p = .51$) and no significant interaction was present between ear and assessment bracket ($F(6, 48) = 0.37$, $p = .89$).

Although mean absolute n10 amplitude did not change over time, the difference between preoperative and postoperative amplitude did change significantly across the postoperative course ($F(5, 20) = 3.18$, $p = .03$). Pairwise comparisons, however, found no significant differences in amplitude change between any two assessment brackets. The pattern of increasing amplitude change with increasing time is evident for both the operated and non-operated ears in Figure 78. Comparison of the mean amplitude change between the operated and non-operated sides revealed no significant differences ($F(1, 4) = 0.99$, $p = .38$) and there was no significant interaction between test ear and assessment bracket ($F(5, 20) = 0.21$, $p = .96$). Given that the pattern of amplitude increase was present for both ears, it is likely due to factors unrelated to the surgery itself.

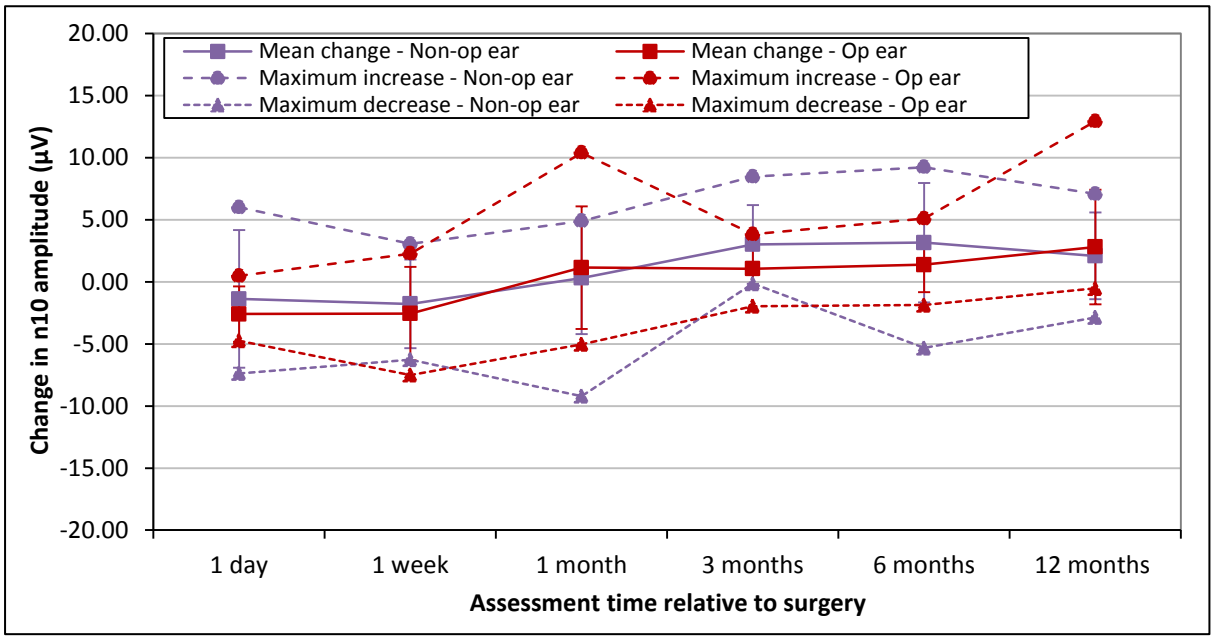

Figure 78. Change in n10 amplitude relative to the preoperative values following tympanoplasty.

Despite the absence of differences between the ears in mean amplitude change, differences were present in the percentage of patients with changes in each bracket of -15 to -5 µV, -4 to 5 µV and 6 to 15 µV (Figure 79). At 1 week and 1 month, 6 to 15 µV increases in n10 amplitude were noted in 17% of operated ears, but no non-operated ears. At later assessments this pattern reversed and amplitude increases of 6 to 15 µV were recorded in 25% and 50% of non-operated ears at 3 and 6 months, respectively, whereas all operated ears maintained an amplitude within 5 µV of the preoperative value. This difference in the percentage of patients in each change bracket was significant between ears only at the 6 month assessment ($p = .03$). That the greater changes were recorded in the non-operated rather than the operated ear highlights the variability inherent in the measurements that is unrelated to surgery.

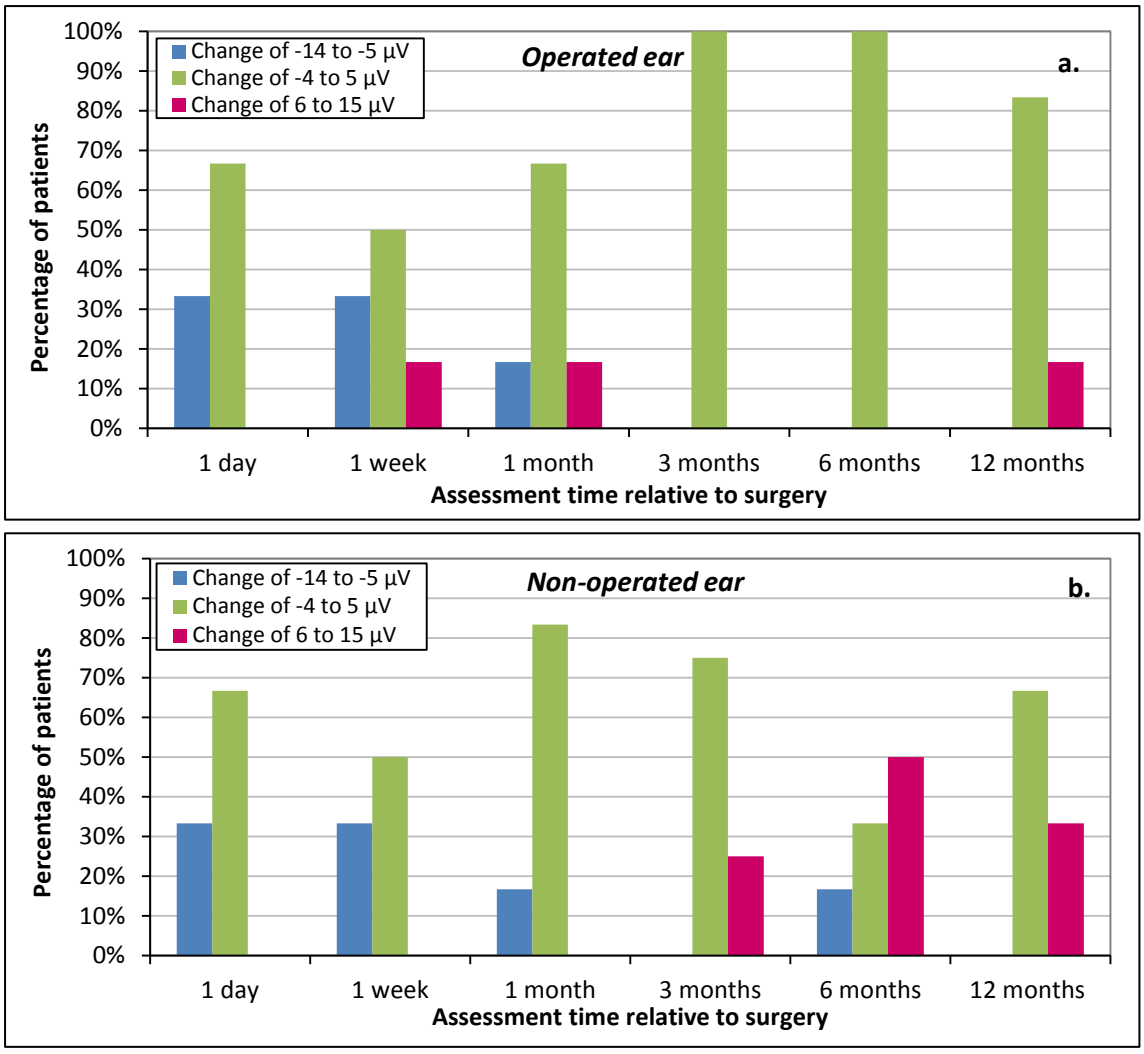

Figure 79. Degree of change in n10 amplitude relative to the preoperative values across post-tympanoplasty assessments the operated (panel a) and non-operated (panel b) ears.

8.3.4.2 Asymmetry ratio

With the exception of the mean asymmetry ratio of 7% recorded 1 day after surgery, all mean asymmetry ratios pre- and post-tympanoplasty were negative, and did not exceed -14% (Table 24). This is consistent with a slightly stronger response from the operated ear relative to the non-operated ear. The absence of a statistically significant main effect of assessment bracket on mean asymmetry ratio ($F(6, 13) = .59$, $p = .73$), or any significant differences between individual pairs of brackets, indicates that the positive mean asymmetry ratio recorded at day 1 was not significantly higher than the asymmetry ratios recorded in later brackets. As noted above, few patients were seen for postoperative testing on postoperative day 1, which may have resulted in the higher asymmetry ratio than that seen in other brackets that included patients that had consistently more negative asymmetry ratios.

The mean change in the asymmetry ratio postoperatively was smallest at the first three postoperative assessments and increased to a maximum positive change of 16% at 3 months and a maximum negative change of 11% at 12 months (Figure 80). A mixed model analysis showed no main effect of assessment bracket on the mean change in asymmetry ratio ($F(5, 6) = .16$, $p = .97$), and pairwise comparisons showed that the mean change was not significantly different between any pair of brackets.

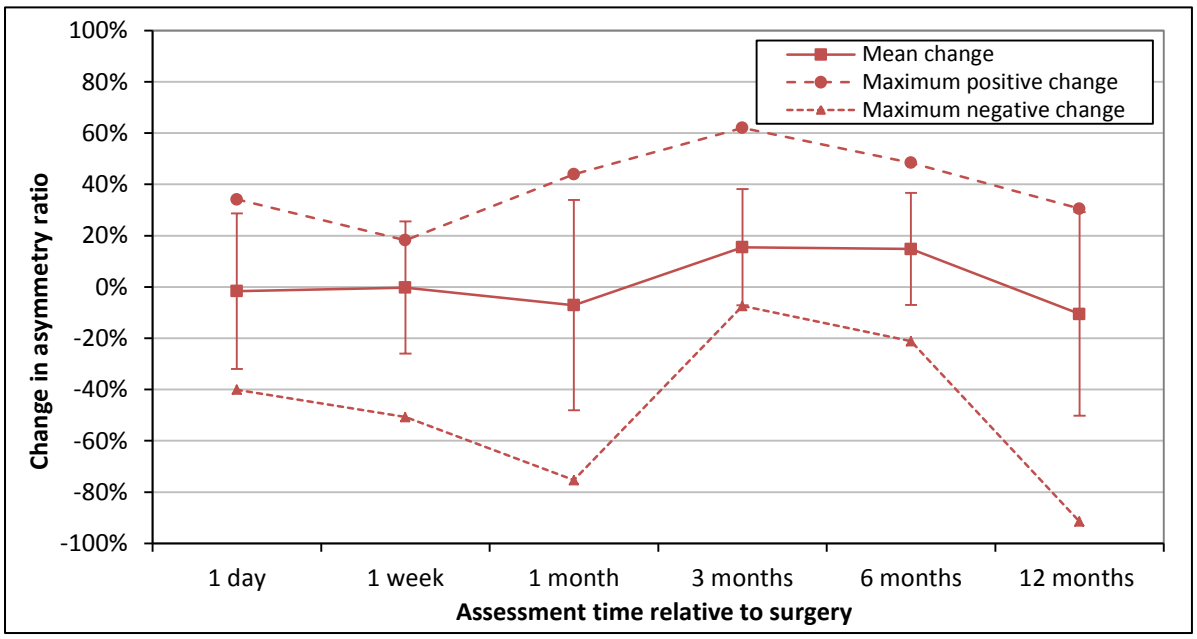

Figure 80. Change in n10 amplitude asymmetry ratios relative to preoperative measurements in patients undergoing tympanoplasty. Positive changes reflect an increase in the response of the non-operated ear relative to the operated ear, and negative changes reflect an increase in the amplitude of the response of the operated ear relative to the non-operated ear.

It is evident from both Figures 80 and 81, that the range of changes in asymmetry ratio recorded across patients was wide and the distribution of changes varied across assessment brackets. At all assessments except 1 day, the most common change in asymmetry ratio was an increase of 0 – 24%, consistent with a decrease in operated ear response strength relative to the contralateral ear. Negative changes were larger than positive changes at most assessments, particularly the changes of -75% and -92% recorded for the same patient at 1 and 12 months (data was not available at other assessments for this participant), who reported no significant balance disturbance. No statistically significant differences in the distribution of patients across brackets of change magnitude were present.

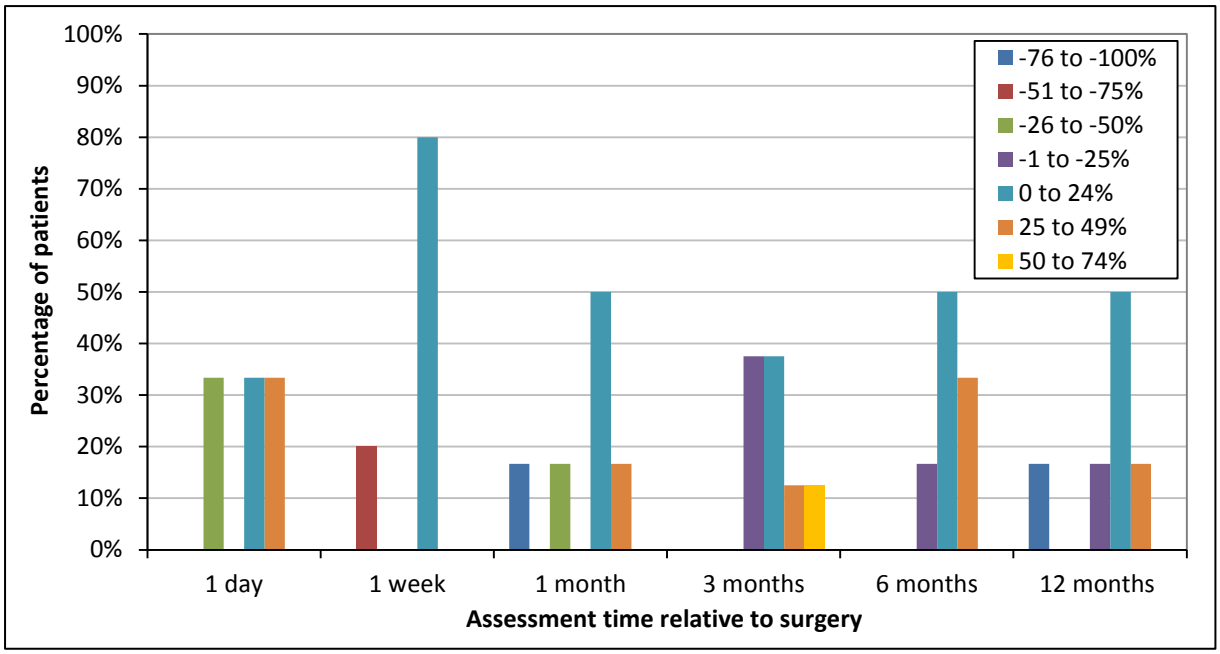

Figure 81. Percentage of tympanoplasty patients at each postoperative assessment with changes in asymmetry ratios of different sizes. Patients are sorted into brackets of 25% from -50% to 100% according to the size of the asymmetry ratio change compared to the preoperative measurement.

8.3.4.3 n10 latency

As with stapedectomy and ossiculoplasty, minimal variation was observed in the mean n10 latencies of the operated or non-operated ears across VEMP assessments (Table 24). No significant difference was present in mean latency between ears ($F(1, 8) = 0.20$, $p = .67$) and no effect of assessment bracket on mean latency was evident ($F(6, 48) = 0.92$, $p = .49$). The lack of a significant interaction between ear and assessment bracket ($F(6, 48) = 0.61$, $p = .72$) and pairwise comparisons between ears in each bracket confirmed that no differences in latency were present between the ears preoperatively or at any postoperative assessment.

Of the five patients tested on postoperative day 1, all demonstrated an increase in mean n10 latency of between 1 and 2.3 ms in both ears. At all subsequent assessments, at which more patients were tested, a range of latency increases and decreases were recorded, with an overall mean prolongation in both the operated and non-operated ears (Figure 82). A mixed design ANOVA showed a significant effect of assessment bracket ($F(5, 20) = 5.44$, $p = .002$), however, post-hoc comparisons showed no significant difference between means in any pair of assessments. No significant difference in latency change was present between the operated and non-operated ears ($F(1, 4) = 0.20$, $p = .68$) and no significant interaction between ear and assessment bracket was calculated ($F(5, 20) = 0.58$, $p = .72$).

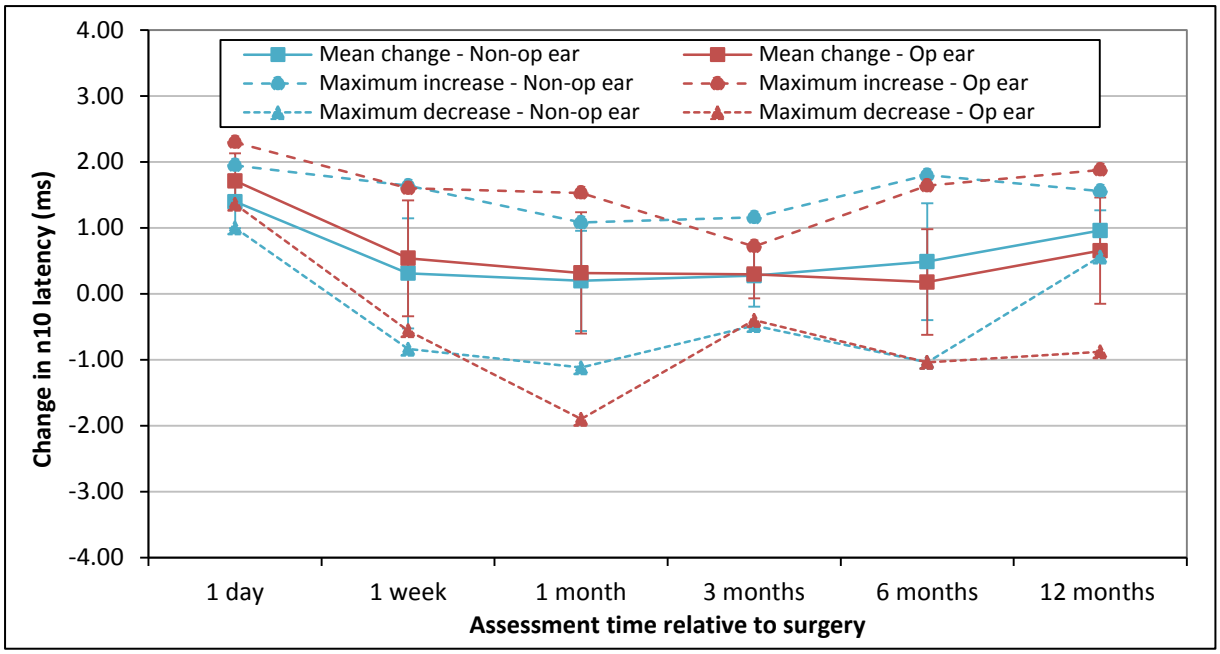

Figure 82. Change in n10 latency relative to the preoperative values across post-tympanoplasty assessments.

A comparison of the percentage of operated and non-operated ears with latency changes of -1.1 to -2 ms, 0.1 to 1 ms, 0 to 0.9 ms, 1 to 1.9 ms, and 2 to 2.9 ms (data not shown) showed that the distribution of sizes of latency changes between ears was very similar. Fisher's exact tests with Freeman-Halton extensions confirmed that there was no significant difference in the proportion of patients in each bracket of latency change between ears at any assessment.

8.3.4.4 Slope of the input-output function

The mean slope of the input-output function relating tap intensity to n10 amplitude was between 0.69 and 1.33 across all assessments for both ears (Figure 83). No significant differences in means across assessments was found ($F(6, 48) = 0.25$, $p = .96$). The range of slopes recorded was smaller than that for stapedectomy and tympanoplasty patients, and the comparative difference in the scale of the y-axis of Figure 82 should be noted. No significant difference in the mean slope was found when operated and non-operated ears were compared ($F(1, 8) = 0.93$, $p = .36$), and the relationship between ears was not affected by assessment time ($F(6, 48) = 0.25$, $p = .96$). In agreement with the results from other surgeries, the mean post-tympanoplasty change in the slope of the input-output function was not significant for either ear ($F(1, 4) = 1.13$, $p = .35$) in any assessment bracket.

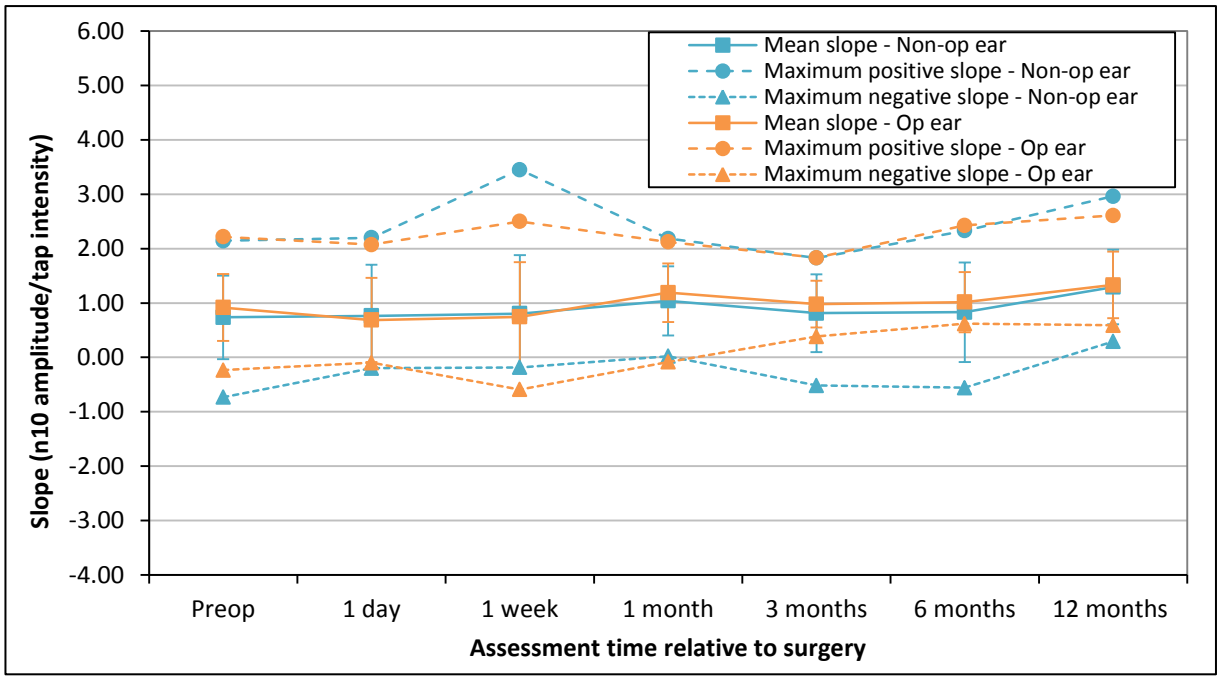

Figure 83. Slope of the input-output function relating tap strength to n10 amplitude from each ear across assessments performed in tympanoplasty patients.

8.3.5 Subjective patient reports of balance disturbance

Patients were asked at all assessments whether they had experienced any symptoms of balance disturbance, such as vertigo, dizziness, unsteadiness, or difficulty walking. This informal questioning was designed to identify patients with significant symptoms indicating disruption to vestibular function. Only two patients presented with clear symptoms of vestibular dysfunction. These cases are described in detail.

8.3.5.1 Case study: Patient 1

Patient 1 was a 43 year old female undergoing left stapes surgery. The patient had not had previous otologic surgery and reported no prior history of balance disturbance. Surgery was indicated due to bilateral, moderate to moderately-severe mixed conductive hearing loss, clinically diagnosed as otosclerosis. Surgery was performed on the poorer hearing ear.

During surgery, the surgeon noted that the stapes footplate was thickened and fixed in the oval window, with a mobile incus and malleus. The anterior and posterior crura of the stapes were divided using an argon laser and, unfortunately, the footplate was mobilised during this procedure. This necessitated that a total stapedectomy was performed using a 4 mm Robinson prosthesis inserted over a tragal perichondrial graft.

The patient reported dizziness and vertigo immediately upon waking from the anaesthesia. She experienced persistent, but gradually reducing, vertigo with nausea and vomiting for approximately two weeks after surgery. During the first week she required assistance to walk and experienced some unsteadiness, which persisted for around six weeks after surgery. From the time of the assessment 3 months after surgery until the final follow-up at 12 months, Patient 1 presented with brief episodic vertigo and nystagmus upon rapid head movement; symptoms consistent with BPPV. During this time she was treated using canalith repositioning manoeuvres, which reduced, but did not eliminate, her symptoms.

VEMP waveforms and n10 parameters recorded preoperatively and postoperatively are presented in Figure 84 and Table 25. The patient was not available for vestibular testing at the 3 month assessment. Overall, it is evident that the patient had robust oVEMPs bilaterally, and that these changed very little over the postoperative course. A small increase in the n10 latency from the operated ear was documented after surgery, however, this was no more variable across all assessments than the latency in the non-operated ear. The asymmetry ratio was within +/-18% across all assessments, except for 1 month, at which it was recorded as 27%, consistent with a stronger response from the non-operated ear relative to the operated ear. Given that a trend for a decreased operative ear response was not consistently documented across brackets and that this change did not correspond to any change in symptoms, it is unclear whether this represents a genuine change in vestibular function, or the result of recording error, such as incorrect electrode placement or inconsistent gaze during recordings. A higher positive asymmetry ratio was also recorded in the subsequent 6 month bracket, possibly indicating a genuine decrease in the response from the operated ear. The asymmetry ratio reverted to a negative value (-18%) at 12 months.

Overall, the results in this case suggest that the footplate mobilisation resulting in severe vertigo did not cause a measureable change in the utricular response immediately after surgery.

Table 25. Summary of pre- and postoperative VEMP n10 characteristics in participant 1.

	Approximate time since surgery					
	Preop	1 day	1 week	1 month	6 months	12 months
Amplitude – Operated ear (μV)	6.6	6.8	11.3	5.7	6.9	11.7
Amplitude – Non-operated ear (μV)	7.6	6.7	11.6	9.9	9.8	8.1
Asymmetry ratio (%)	7	-1	1	27	17	-18
Latency – Operated ear (ms)	10.3	10.2	10.8	10.8	10.7	10.7
Latency – Non-operated ear (ms)	10.8	10.9	10.9	10.3	10.3	1.3

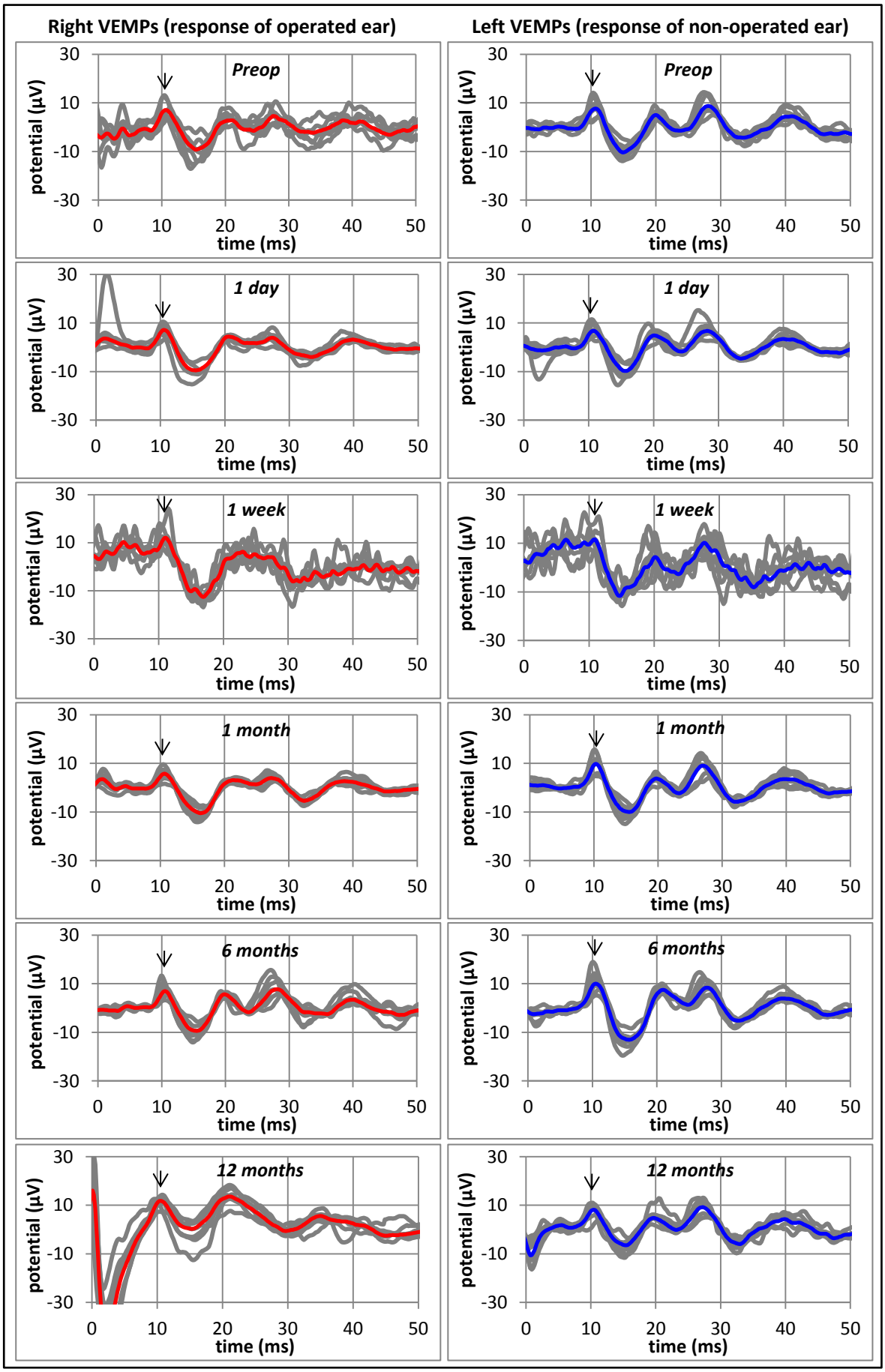

Figure 84. oVEMPs recorded preoperatively and postoperatively from patient 1. Red traces show the averaged response across tap intensities from the right eye (left vestibule), and blue traces show the averaged response across tap intensities recorded from the left eye (right vestibule). Grey traces are the averaged responses at each tap intensity bracket from 2 – 7. n10 peaks are indicated by arrows.

Pre- and postoperative audiograms for Patient 1 are presented in Figure 85. Preoperatively, the patient had a moderate to moderately-severe mixed hearing loss in the operated (left) ear, with thresholds measureable up to 11.2 kHz. One week after surgery, all air-conduction thresholds at 0.25 to 10 kHz increased between 5 and 45 dB HL. The threshold at 11.2 kHz increased by at least 5 dB to the point that it was no longer measureable before the limits of the audiometer were reached. Bone-conduction thresholds increased by 20 dB at 0.5 kHz, 5 dB at 1 and 3 kHz, and 15 dB at 4 kHz. Recovery of up to 20 dB HL was noted in air-conduction thresholds at postoperative assessments from 1 month onward, primarily at the lowest test frequencies. At the final assessment, air-conduction thresholds were within 5 – 10 dB of preoperative thresholds below 4 kHz, but remained between 15 and 20 dB above preoperative levels at frequencies where thresholds could be measured at 4 kHz and above. The thresholds at 11.2 kHz and above remained unmeasurable throughout the postoperative course. Bone-conduction thresholds recovered almost completely by 3 months after surgery, although the 3 kHz threshold remained 10 dB above the preoperative level until 6 months, where it improved to only 5 dB higher than before surgery.

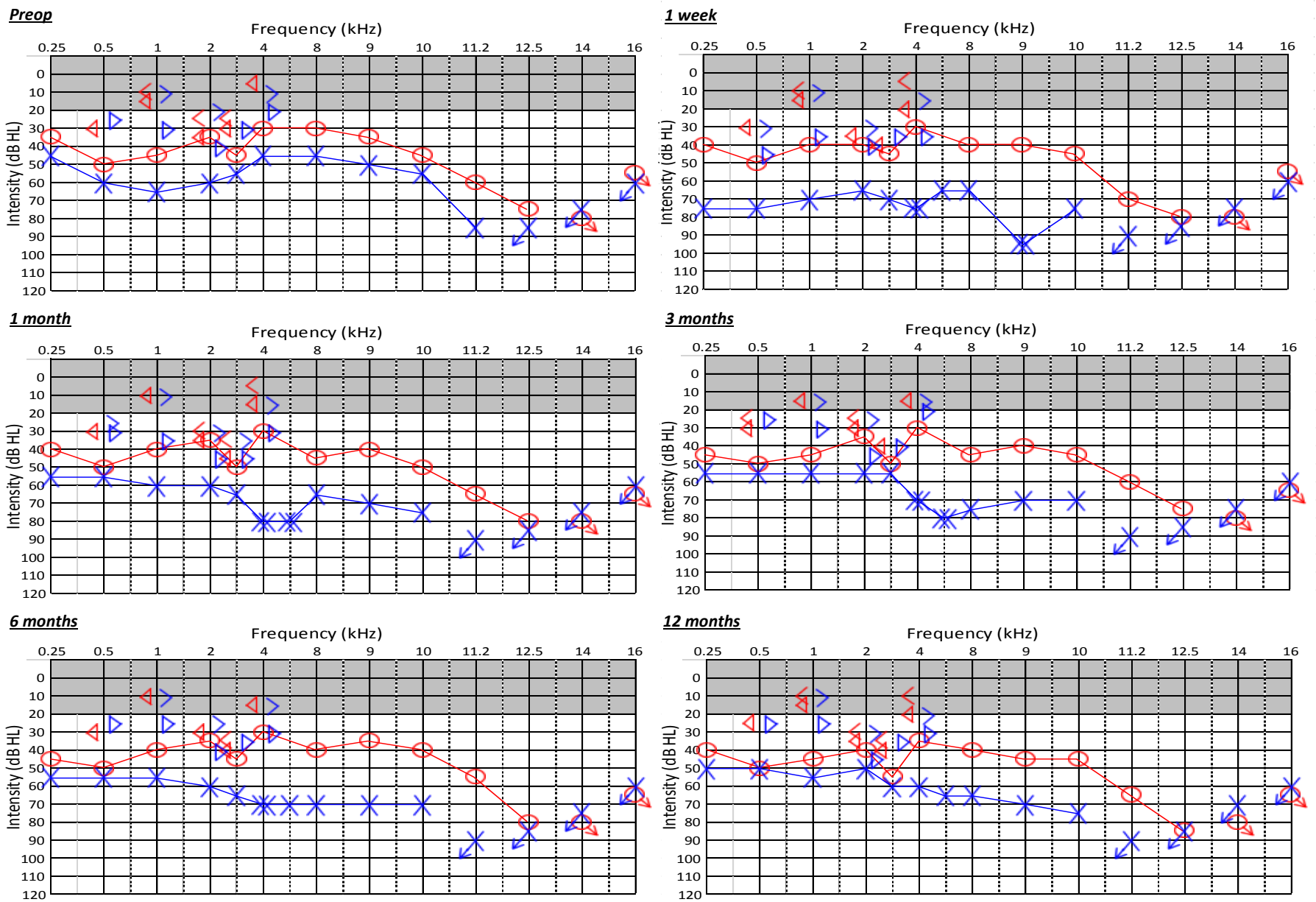

Figure 85. Audiograms recorded before and after left stapedectomy for Patient 1.

8.3.5.2 Case study 2: Patient 96

Patient 96 was a 42 year old female who underwent a primary left stapedotomy to correct a moderate conductive hearing loss, presumed to be due to otosclerosis. A stapedotomy had been performed on the right ear approximately six years earlier with a good hearing result and no reported complications. No balance concerns were reported preoperatively.

Intraoperatively, the left stapes footplate was noted to be thin and fixed in the oval window, with a mobile incus and malleus. A 0.7 mm stapedotomy was created using an argon laser and a microdrill, and a 0.6 mm SMart prosthesis was placed into the vestibule. No intraoperative or early postoperative complications were documented.

The first VEMP assessment was performed at the patient's bedside approximately 20 hours after surgery. At that time, the patient reported being somewhat light-headed and unsteady when she stood, but no other symptoms of balance disturbance. Three days after surgery, the patient began experiencing rotary vertigo, accompanied by nausea and vomiting, which persisted for approximately 24 hours. VEMP testing was performed around 24 hours after the acute vertigo had subsided (five days after surgery), at which point the patient continued to report an occasional sensation of movement with head turns. At the next assessment, 1 month after surgery, an occasional sensation of shifting of the visual field was noted with quick head movements, but otherwise, balance symptoms had resolved. No further symptoms of vestibular dysfunction were reported at subsequent assessments.

VEMP waveforms recorded for Patient 96 are presented in Figure 85, and the amplitude, asymmetry ratio, and latencies associated with the waveforms are provided in Table 26. VEMP results were not available for assessments at 3 and 6 months. The variability in VEMP recordings, and particularly absolute amplitude measurements, is clear from these results. If the asymmetry ratio is assessed, it is clear that a large decrease in the relative response of the operated ear compared to the non-operated ear was present 1 day and 1 week after surgery. At the 1 day assessment the latency of n10 in the operated ear also increased by 2.9 ms, whereas the latency in the non-operated ear increased by 0.6 ms. No latency changes were found at 1 week compared to the preoperative assessment. Interestingly, the response from the operated ear appears most disrupted 1 day after surgery, whereas subjective balance symptoms were most severe 3 – 4 days postoperatively.

The asymmetry ratio reverses in favour of a stronger response of the operated ear 1 month after surgery. Examination of the relevant traces in Figure 86 shows some interference early

in the trace recorded from the non-operated side, which may have influenced the comparison of amplitude between sides. Regardless, there was no longer evidence of a reduced response from the operated side at that measurement. At 12 months, the response from the operated side was again smaller than the operated side, with an asymmetry ratio of 21%.

Table 26. Summary of pre- and postoperative VEMP n10 characteristics in Participant 96.

	Preop	1 day	1 week	1 month	12 months
Amplitude – Operated ear (μV)	9.8	2.8	1.4	5.3	1.3
Amplitude – Non-operated ear (μV)	11.3	6.9	3.8	2.9	2.0
Asymmetry ratio (%)	7	42	46	-29	21
Latency – Operated ear (ms)	10.4	13.3	10.7	10.7	11.5
Latency – Non-operated ear (ms)	10.1	10.7	10.1	10.1	10.7

Pre- and postoperative audiograms for Patient 96 are presented in Figure 87. Prior to surgery, Patient 96 had a mild to moderate conductive hearing loss in the operated (left ear), with measureable audiometric thresholds up to 16 kHz. At the first postoperative assessment, hearing improved between 10 and 35 dB at 3 kHz and below. Above 4 kHz air-conduction thresholds increased by 10 to 40 dB and thresholds could no longer be recorded at 14 and 16 kHz. Continued improvement at lower frequencies was recorded until 12 months after surgery. Recovery of EHF hearing thresholds also continued until 12 months after surgery, at which point the only residual hearing loss was a 5 dB increase at 11.2 – 14 kHz, and an unmeasurable threshold at 16 kHz. Bone-conduction thresholds were initially elevated after surgery, particularly at 4 kHz, which increased by 25 dB. Recovery of these thresholds to preoperative levels was complete by 1 month after surgery.

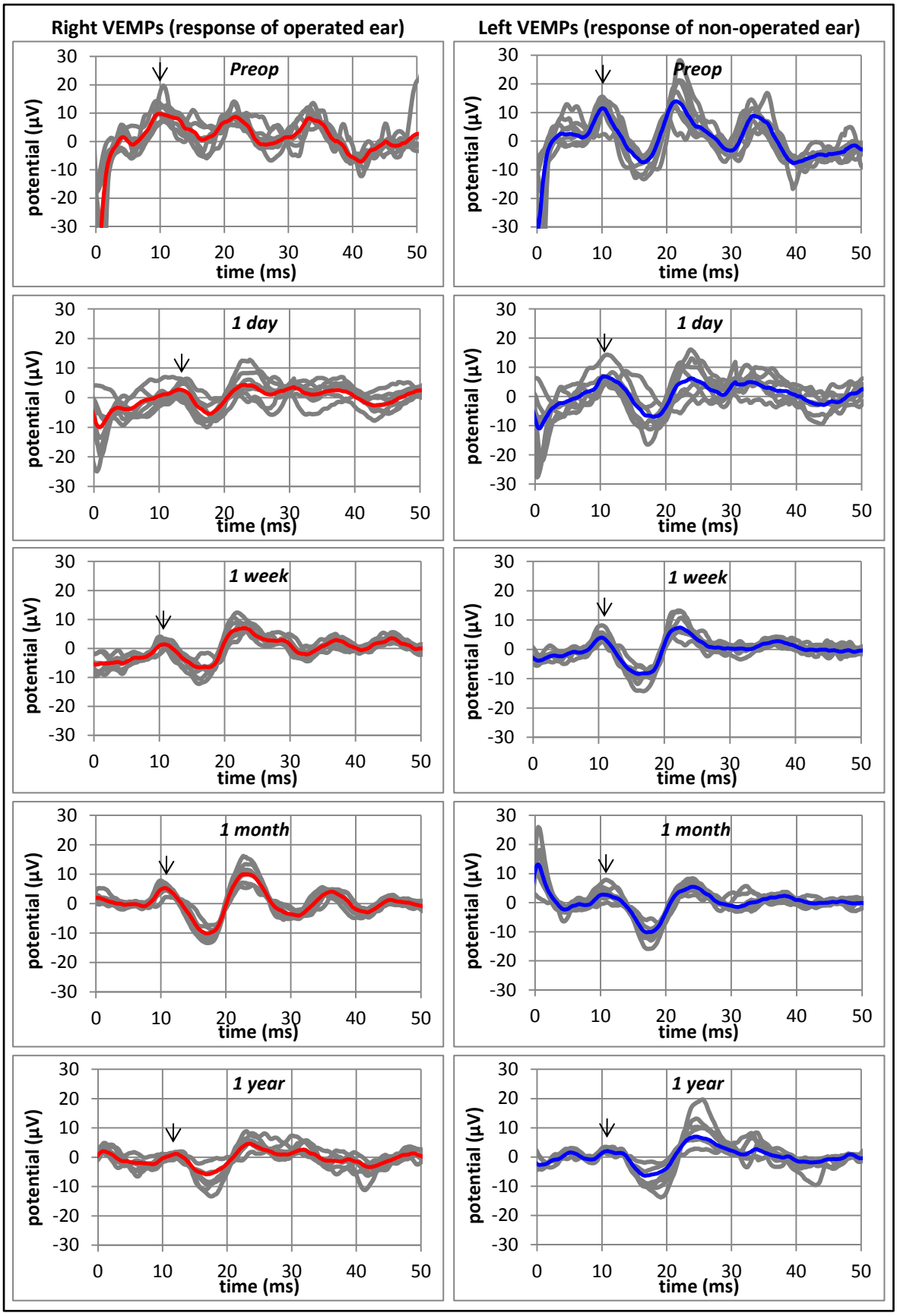

Figure 86. oVEMPs recorded preoperatively and postoperatively from Patient 96. Red traces show the averaged response across tap intensities from the right eye (left vestibule), and blue traces show the averaged response across tap intensities recorded from the left eye (right vestibule). Grey traces are the averaged responses at each tap intensity bracket from 2 – 7. n10 peaks are indicated by arrows.

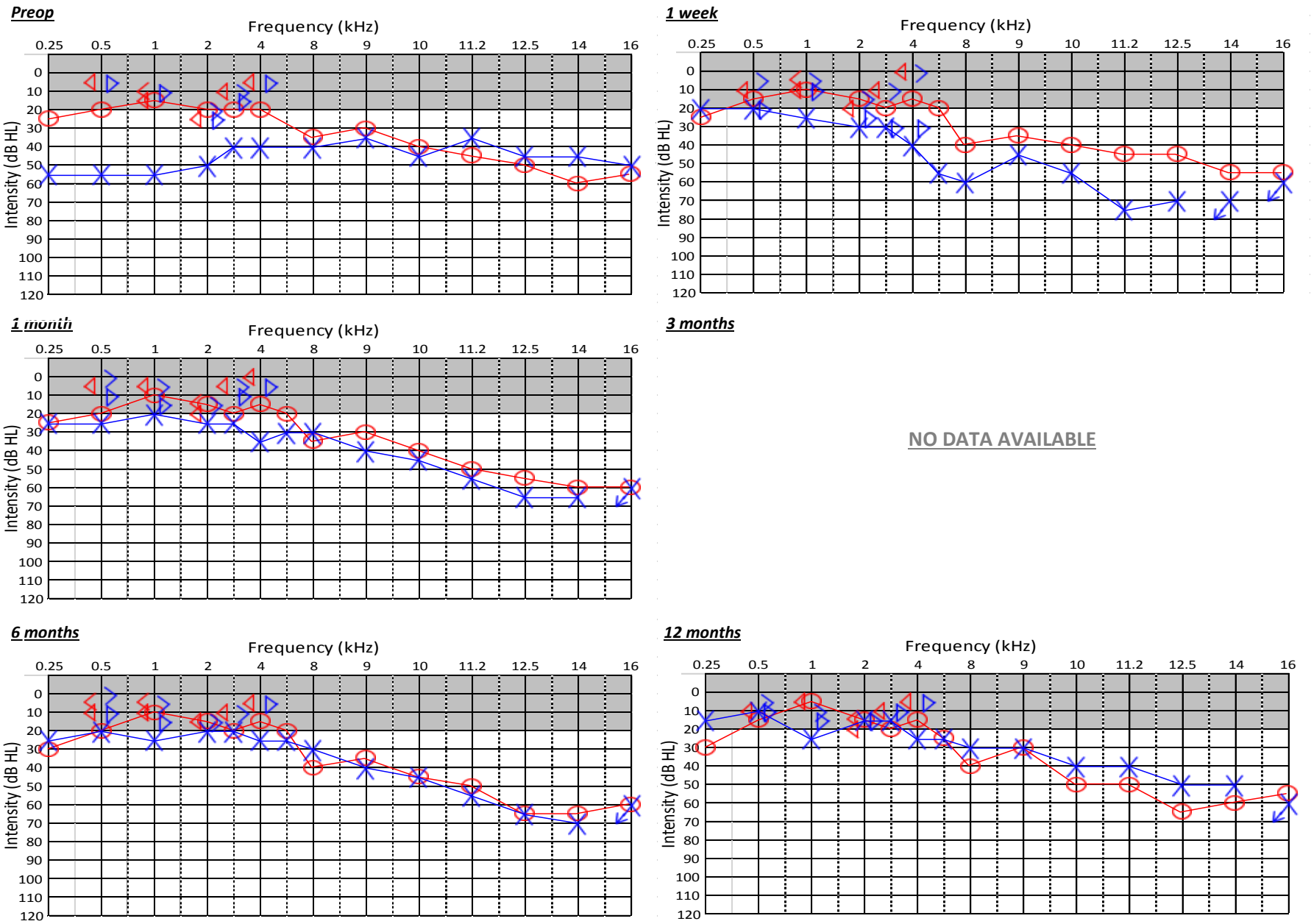

Figure 87. Audiograms recorded before and after left stapedotomy for Patient 96.

8.3.6 oVEMPs in patients with and without postoperative EHF hearing loss

Across all surgeries, 11 patients with available pre- and postoperative VEMP data were identified that presented with a loss of three or more measureable EHF thresholds at the 1 week postoperative assessment. Twenty-two patients (23 procedures) with VEMP data either experienced no loss of measureable EHF thresholds, or a gain in measureable thresholds at the first postoperative assessments. Characteristics of each group are presented in Table 27.

Table 27. Distribution of patients included in the oVEMP/EHF hearing loss analysis across surgery types.

Surgery	Ears	Procedures	Procedure type		
	n	*n*	Primary	Revision	Second stage
EHF hearing loss group					
Stapedectomy	9	9	6	3	-
Ossiculoplasty	0	0	0	0	0
Tympanoplasty	2	2	1	1	-
Total	*11*	*11*	*7*	*4*	*0*
No EHF loss group					
Stapedectomy	8	9	6	3	-
Ossiculoplasty	10	10	2	3	5
Tympanoplasty	4	4	2	2	-
Total	*22*	*23*	*10*	*8*	*5*

As with all analyses, postoperative data was not available for all patients at all assessments. Patient numbers for each assessment bracket are shown in Table 28. Analysis of oVEMPs in each group was performed using data from all surgeries combined and for stapedectomy patients alone. Given the small number of patients with "significant" EHF hearing losses after tympanoplasty and ossiculoplasty, data for these surgeries was not analysed separately.

Table 28. Number of patients with data available each postoperative assessment according to surgery.

	Approximate time since surgery					
Surgery	1 day	1 week	1 month	3 months	6 months	12 months
EHF hearing loss group - n						
Stapedectomy	6	7	7	6	7	6
Ossiculoplasty	0	0	0	0	0	0
Tympanoplasty	1	1	1	2	0	1
Total	*7*	*8*	*8*	*8*	*7*	*7*
No EHF loss group – n						
Stapedectomy	6	8	6	5	5	6
Ossiculoplasty	7	5	6	5	5	3
Tympanoplasty	2	4	3	3	3	3
Total	*15*	*17*	*15*	*13*	*13*	*12*

8.3.6.1 oVEMP changes across all surgeries

As shown in Figure 88, mean changes in the oVEMP asymmetry ratio were smaller (i.e. closer to zero) for the group without EHF hearing loss than the group with hearing loss at most assessments. Mean changes in asymmetry ratios tended to be more negative for the hearing loss group, indicating an increase in the relative response of the operated ear to the non-operated ear. A mixed factor ANOVA showed a significant overall difference between groups ($F(1, 15) = 3.51$, $p = .04$), and pairwise comparisons indicated that the difference between groups was statistically significant only at the assessment 12 months after surgery ($p < .001$). No significant difference in the mean change in asymmetry ratios across postoperative assessments was detected ($F(5, 75) = 1.12$, $p = .36$), nor was there a significant interaction between assessment bracket and hearing group ($F(5, 75) = 2.17$, $p = .07$).

Interestingly, the largest changes in oVEMP asymmetry ratios occurred for both groups at this final assessment, but in opposite directions. That the smallest difference between groups was documented at the first assessment and the largest at the final assessment weakens the argument that inner ear damage is the cause of both the EHF hearing loss and the changes in oVEMPs.

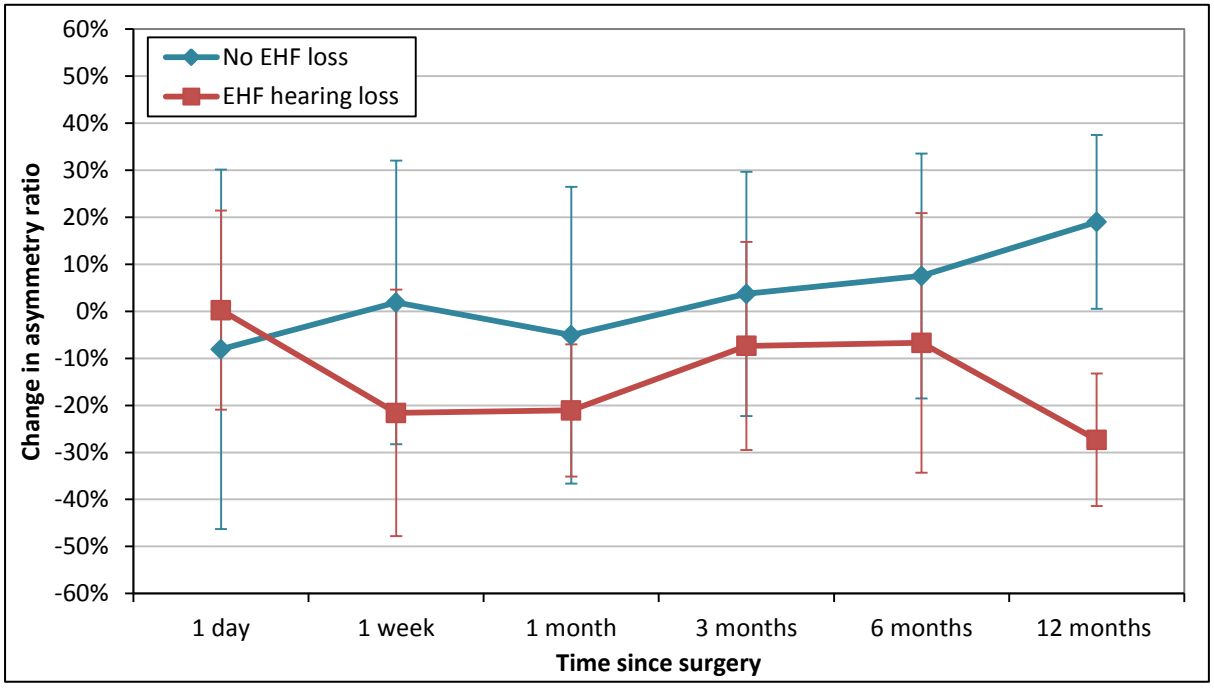

Figure 88. Change in mean oVEMP asymmetry ratio relative to the preoperative assessment for all patients with and without significant EHF hearing loss 1 week after surgery. Error bars represent standard deviation.

8.3.6.2 oVEMP changes following stapedectomy

Assessment of mean asymmetry ratio change in only stapedectomy patients with a significant EHF hearing loss or no loss of EHF thresholds showed no significant overall difference berween the two groups ($F(1, 9) = 0.80$, $p = .39$). An overall significant effect of assessment was identified ($F(5, 45) = 2.71$, $p = .03$) and this effect was significantly influenced by the hearing group ($F(5, 45) = 4.60$, $p = .002$). Unlike the pattern in the overall surgery data, the difference in mean asymmetry ratio change was larger 1 day after surgery than for assessments at 1 week to 6 months. One day after surgery, the mean change in the group without EHF hearing loss was more negative, at -34%, than the group with EHF hearing loss, for which the mean change relative to preoperative measurements was 0%. Pairwise comparisons indicated that this difference did not reach statistical significance.

The largest difference between groups was recorded 12 months after surgery, where the mean asymmetry ratio for the no EHF hearing loss group was 21%; significantly higher than the mean value of -27% recorded for the group without hearing loss ($p = .003$). As noted above, the larger difference between groups at 12 months than in other brackets raises questions regarding whether this result is related to surgery and inner ear trauma, or to measurement variability or non-surgical vestibular factors.

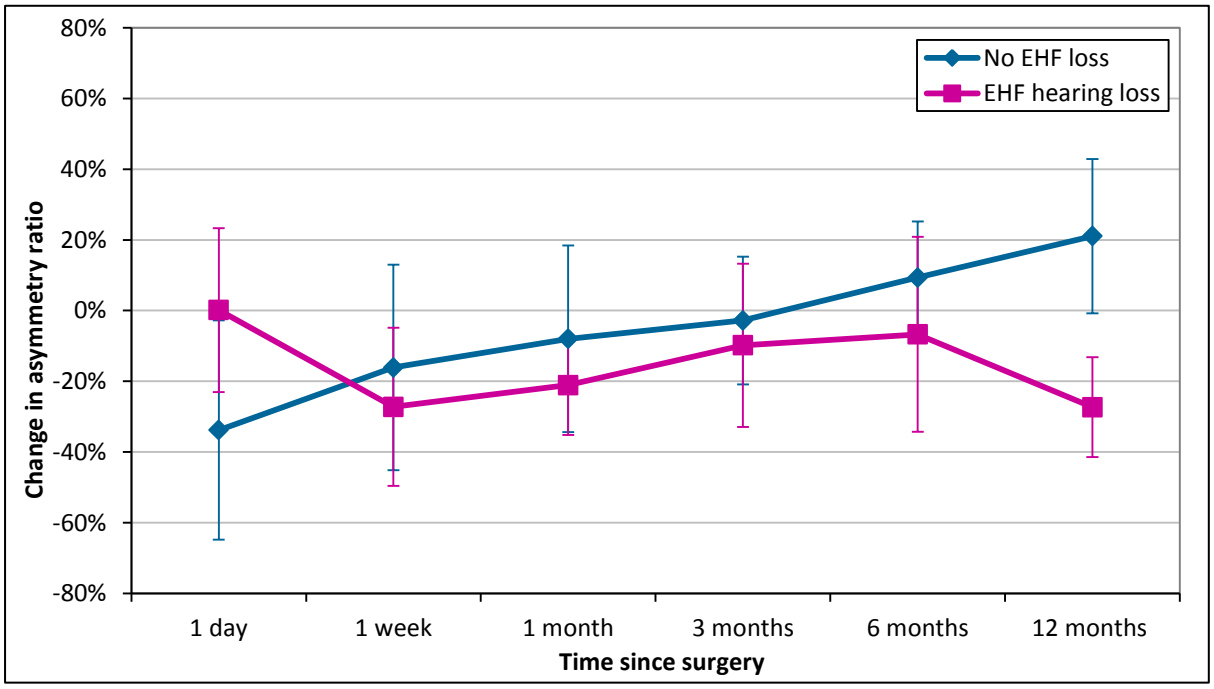

Figure 89. Change in mean oVEMP asymmetry ratio relative to the preoperative assessment for stapedectomy patients with and without significant EHF hearing loss 1 week after surgery. Error bars represent standard deviation.

8.4 Discussion

The present study used tap-evoked oVEMPs pre- and post-middle ear surgery to assess changes in the responses of the utricle. We expected that, given the close proximity of the utricle to the stapes footplate, utricular function would be particularly impaired following stapedectomy and ossiculoplasty, which involve manipulation of the ossicles, and thus the potential transmission of large hydrostatic forces to the inner ear. As symptoms of vestibular dysfunction are most prevalent in the early postoperative period, it was further predicted that oVEMP changes would be most common when vestibular testing was performed 1 day and 1 week after surgery.

Overall, the mean results provided no clear evidence to support the hypothesis that mild symptoms of balance disturbance in the early postoperative period following middle ear surgery are a result of trauma to the utricle. Significant differences between ears in the mean n10 amplitude and latency were not found at any assessment for any surgery, nor were there significant differences in mean amplitude, asymmetry ratio, or latency between preoperative and postoperative assessments. Analyses of oVEMP changes in patients with significant postoperative vertigo did, however, provide some preliminary evidence that trauma to the utricle may be responsible for severe balance dysfunction after surgery in some cases. These results are discussed in detail with respect to the potential causes of inner ear damage following each type of middle ear surgery.

8.4.1 Effect of surgery on mean oVEMP amplitude and asymmetry ratio

Many of the patients in this study reported mild dizziness, light-headedness, or unsteadiness at the time of the first postoperative oVEMP assessment within 24 hours of surgery. If symptoms were a result of surgical injury to the utricle, a change in oVEMP amplitude from the operated ear would be expected, at least at the assessment performed when symptoms were present. The absence of either a significant difference in the response amplitude between operated and non-operated ears or a difference in pre- and postoperative n10 amplitude in the operated ear suggests that cases of mild balance disturbance following stapedectomy, tympanoplasty, and ossiculoplasty are not typically the result of significant utricular injury. The assumption here, of course, is that tap-evoked oVEMPs are a sensitive enough tool to detect what may be reasonably subtle changes in the function of the utricle.

This assumption is considered with regards to the variability of amplitude in the non-test ear in the following sections.

8.4.1.1 n10 amplitude changes following stapes surgery

The absence of a significant change or difference between ears in the mean n10 amplitude following stapes surgery is in agreement with the unchanged vibration-evoked oVEMP responses documented by Winters et al. (2013) a minimum of eight weeks after stapes surgery. We had, however, theorised that by performing assessments early in the postoperative period, when balance symptoms were common, our protocol may detect changes in responses that were no longer evident when testing was performed by Winters et al. Assessment of the mean change in n10 amplitude relative to preoperative measurements appears to support this hypothesis, showing a statistically significant mean difference between operated and non-operated ears across all assessments and at the 1 week postoperative assessment. However, the difference between ears, particularly 1 week after surgery, is created by both an increase in the operated ear response and a decrease in the amplitude in the response from the non-operated ear. Ideally, the response of the non-operated ear should not change after surgery so that any changes in the operated ear can be attributed to genuine changes in otolithic function, and not test-retest variability. It is possible that the increase in the n10 amplitude in the operated ear reflects a genuine increase in activity from the utricle following surgery, however, given the changes in the contralateral ear, such a conclusion would be premature.

The divergent directions of amplitude changes between the operated and non-operated ears resulted in a negative shift in the mean asymmetry ratio at all assessments except those at 3 months, consistent with a non-significant postoperative increase in the amplitude of the response of the operated ear compared to the non-operated ear. Again, the variability in the n10 amplitude in the non-operated ear weakens this finding, however, if we assume that the result is genuine, it would be in agreement with Tribukait and Bergenius (1998) hypothesis that the resting activity of the utricular afferents increases following stapes surgery. Tribukait and Bergenius reported SVH results from 4 – 8 weeks after stapes surgery showing a tilt away from the operated side, indicative of increased utricular activity. Potential causes of increased utricular reponses may be surgical irritation of the utricle, or mechanical stimulation of the otolithic organs by the piston (Singbartl et al., 2006). Utricular stimulation

is predicted to occur more frequently in the early postoperative period if inflation of the otolithic organs to restore fluid pressure balance occurs secondary to minor perilymph leakage occurred post-stapedectomy (Wang et al. (2005). An increased n10 response amplitude in the operated ear relative to the non-operated ear 1 week after surgery and not later in the postoperative period, as was documented here, would be consistent with the theory that mechanical stimulation of the utricle continues until healing is complete postoperatively.

It seems likely that the effect of surgery on VEMPs will depend on the mechanism of trauma. Whereas mechanical stimulation of the otolithic organs may explain some instances of postoperative balance disturbance, we would expect that factors such as labyrinthitis or force trauma are responsible for other cases. These factors would be expected to depress vestibular activity, rather than increase responses. In one study of bone-conducted cVEMPs, responses could be elicited preoperatively in 16 of 41 ears, and disappeared post-stapedectomy in one ear, with the rest remaining unaffected (Trivelli et al., 2010). This is suggestive of decreased otolithic responsiveness in at least one case in a series with no cases of increased responses. If both increases and decreases in responses are possible after stapes surgery, the use of group mean data will be limited in determining whether significant changes have occurred. For this reason percentages of patients with increases and decreases in n10 were calculated, however, once more, no differences in the rates of increased or decreased oVEMPs were documented between operated and non-operated ears at any assessment. Again, overall, these data provide no clear evidence of a change in the function of the utricle following stapedectomy.

8.4.1.2 n10 amplitude changes following ossiculoplasty and tympanoplasty

Following ossiculoplasty and tympanoplasty, we hypothesised that the potential causes of vestibular trauma, such as compressive forces transmitted to the labyrinth during ossicular manipulation or serous labyrinthitis, would decrease, but not increase, the oVEMP amplitude in the operated ear. Presumably, if postoperative balance dysfunction is a result of the transmission of excessive force to the inner ear due to manipulation of the ossicles, the rate of both balance symptoms and VEMP changes will be higher following ossiculoplasty than tympanoplasty. We are not aware of any previous studies that have investigated oVEMPs following middle ear surgical procedures other than stapedectomy; however, air-conduction evoked cVEMPs have been monitored for changes following surgery for COM by Wang et

al. (2009). Following various types of tympanoplasty with or without mastoidectomy, Wang et al. found that the VEMP response rate increased from 41.7% before surgery to 66.7% three months after surgery in their 24 patients, although p13 latencies remained significantly longer than those for healthy controls. As air-conduction stimulation were used in that study, it is not clear if the continued p13 prolongation and absence of cVEMPs in many ears was the result of persistent abnormalities in the conductive mechanism, or to a true vestibular abnormality. This limitation was the impetus for the use of bone-conduction stimuli in the present study.

As stated above, in the current study no significant differences were present between ears in mean n10 amplitude or mean amplitude change at any assessment for either tympanoplasty or ossiculoplasty. In agreement with the stapedectomy results, this suggests that significant trauma to the utricle did not occur during either tympanoplasty or ossiculoplasty. Although there were some significant results found in the evaluation of n10 amplitude and asymmetry ratio across assessments following ossiculoplasty and tympanoplasty, these again seem to highlight the variability across repeated tap-evoked oVEMP measurements, rather than demonstrating any significant effect of surgery. For example, post-ossiculoplasty, a significant difference between the mean change in asymmetry ratio recorded at 6 and 12 months was documented, although the absolute mean asymmetry ratio did not differ between these two assessments. Given that the absolute mean asymmetry ratio was 5% at 12 months (compared to 8% at 6 months) and was not significantly different to that in any other bracket, the significantly different degree of change relative to the 6 month assessment seems more likely to have occurred because of the smaller group of participants assessed at 12 months (n = 13) compared to 6 months (n = 16). Although a positive asymmetry ratio shift would usually indicate a stronger response from the non-operated ear compared to the operated ear, in this case the mean amplitudes in both ears were very similar.

In the case of tympanoplasty, the mean change in the asymmetry ratio postoperatively was smallest at the first three postoperative assessments and increased (although not significantly) over time, as did the range of values recorded. If surgical factors are the cause of VEMP changes, greater differences are expected immediately after surgery, with possible recovery over time in line with subjective symptoms of balance disturbance. The increase in VEMP changes over time may be reflective of changes in vestibular function unrelated to surgery, and potentially related to recurrence of middle ear disease. However, in no cases were large changes accompanied by reports of new symptoms of vestibular dysfunction. These results highlight the degree of uncertainty in the results analysed over a one year period when many

variables may change. This uncertainty is magnified in cases where the clinical presentation does not correspond with the oVEMP results recorded.

Although much has been discussed regarding the reliability of oVEMP measurements, what is clear from the present results documenting n10 amplitude changes following stapedectomy, tympanoplasty, and ossiculoplasty, is that any changes in utricular responses that did occur were not substantial enough to be clearly identified above normal variability in the measurements. The purpose of testing the non-operated ear was to provide a measure of variability that could be used to ascertain whether changes in the operated ear were significant, and comparisons between ears proved a useful tool to evaluate whether statistically significant changes were truly in agreement with our hypotheses. In particular, the need to examine the absolute amplitude changes from each ear in addition to assessing the change in the asymmetry ratio was identified. As most cases of balance disturbance, with the exception of the two discussed below, were mild, it is perhaps not surprising that, on average, significant oVEMP amplitude changes were not found.

8.4.2 Effect of surgery on mean oVEMP latency

Following each of the three middle ear surgeries included in this study, the mean latency and the mean change in latency of n10 varied minimally in both the operated and non-operated ears and at no assessments was a significant difference detected between ears. These findings are again in agreement with those reported by Winters et al. (2013) showing no significant change in the n10 latency of vibration-evoked oVEMPs in 11 ears that underwent primary stapes surgery. Although Wang et al. (2009) showed some reduction in the p13 latency of cVEMPs following COM surgery, these responses were evoked by air-conduction stimuli, and the improvement is likely to be related to an increase in acoustic energy reaching the saccule, rather than a change in vestibular function.

A significant difference in mean n10 latency change was found across assessment post-tympanoplasty in the present study, with larger latency increases apparent at the 1 day assessment than at assessments later in the postoperative course. This effect was comparable in both the operated and non-operated ears, therefore the likely explanation is test-retest variability in the latency of the oVEMP n10 response, which is likely to be amplified when mean values are calculated for the small group of tympanoplasty patients seen at each postoperative assessment. Nguyen et al. (2010) found that the latency of the oVEMP n10 had

the poorest test-retest reliability of any of the measurement parameters they examined. Certainly our results showed variability in the n10 latencies of individual ears across assessments; however latency changes tended to be similar in both ears of each participant. When data was examined for individual patients, it was apparent that where a change of greater than 1 ms was present in one ear, a similar change was usually recorded for the other ear. These results suggest that while n10 latency may be variable over repeated recordings, the relative latency between the responses from each labyrinth is relatively stable. It is therefore possible that calculating a ratio of the latency of each ear may provide a more useful measurement to evaluate changes in responses across time compared to the comparison of absolute latencies from each ear.

8.4.3 Effect of surgery on oVEMP slope

The use of finger taps as stimuli allows the stimulus intensity to be varied and an input-output function relating tap strength to response amplitude to be created (Wahat & Patuzzi, 2012). Wahat and Patuzzi showed that variation in the intensity of finger taps to the bridge of the nose produced a clear increase in oVEMP n10 amplitude with increasing tap strength up to approximately 1 g. Above this stimulus level, saturation of VEMP amplitude was documented. We hypothesised that changes in utricular function after surgery may alter the characteristics of the VEMP input-output function, particularly the slope. The present results were not consistent with this hypothesis and analyses revealed no significant changes in mean slope across assessments for any surgery. Differences in the mean slope between operated and non-operated ears were small and, again, no significant differences were present for any of the three surgeries studied.

Overall, the mean slopes at all assessments for all surgeries was, as expected, positive, however of concern were the few cases in which the slope of the input-output function was negative. These findings were inconsistent with the expected increase in n10 amplitude with increasing tap intensity. Closer inspection of the data in these cases generally showed that interference or artefact was present in at least one intensity bracket. This contamination of the traces shifted the input-output function so that the gradient calculated did not represent the change in amplitude with intensity that may have been present in other brackets. We did not find any large changes in slope that clearly corresponded to a genuine change in amplitude growth with stimulus strength in only one ear. During testing, visual examination of

increased response strength with increasing stimulus intensity did provide a useful cross-check during testing that responses were genuine and not artefactual, however, based on the present data, the clinical importance of the input-output function currently seems limited.

8.4.4 Subjective symptoms of balance dysfunction

Informal observations of balance disturbance are not reported due to the marked variation in how patients described symptoms and, without a formal measurement tool, it was not possible to distinguish symptoms related to surgical manipulation of the ear from the effects of anaesthesia, medications, or other surgical factors. Ideally, a formal assessment of subjective balance symptoms should have been used to more accurate assess balance symptoms, however, a large survey of vestibular symptoms was beyond the scope of this study, and instead our aim was to detect significant symptoms that may be indicative of otolithic injury so that these could be correlated with changes in oVEMPs.

In agreement with previous studies, when symptoms of balance disturbance were present, they were most common and severe in the first week following surgery (Kujala et al., 2007; Molony & Marais, 1996; Özmen et al., 2009). In only two cases, both patients who had undergone stapes surgery, were balance symptoms persistent and intense enough that they were unable to move without evoking symptoms. This rate seems low compared to some previous reports, and Özmen et al. (2009) reported that vestibular disturbance of this degree or worse was present immediately after stapes surgery in 15 of their 33 patients. This difference may be a reflection of differences in assessment techniques, rather than the true rate of balance dysfunction.

8.4.5 Case studies: Patients with significant postoperative vertigo

The analysis of oVEMPs recorded pre- and postoperatively in Case 1 provides an example of a case of significant postoperative balance dysfunction without any corresponding changes in tap-evoked oVEMPs. This data is unique in that previous studies that have shown a lack of oVEMP changes following middle ear surgery have not included measurements in patients with significant postoperative vertigo (Winters et al., 2013). Immediately upon waking following total stapedectomy, necessitated by mobilisation of the footplate during stapedotomy, Patient 1 reported rotary vertigo accompanied by vomiting. Contrary to our expectations, at the first two assessments of oVEMPs over the six week period when

unsteadiness walking persisted, no changes in n10 parameters were recorded in operated ear that exceeded the variations in the non-operated ear. Assuming that the severity of the symptoms are indicative of significant injury that could be detected using oVEMPs if the utricle was involved, the results in this case suggest that the trauma did not involve the utricle.

The VEMP results obtained from Patient 1 at 1 month varied from those at earlier assessments, with an increase in the asymmetry ratio to 27%, suggesting that the responses from the operated ear decreased relative to the non-operated ear. The correct interpretation of this result is unclear given that no corresponding symptom changes were recorded and that the result does not align with those recorded in other brackets. It is possible that the reduced response in the operated ear resulted from an error in electrode placement or differences in impedance between the electrodes. A positive asymmetry ratio was also found at the 6 month assessment, suggesting that the 1 month result may have been genuine and indicative of a temporary change in vestibular function. This conclusion seems generous, however, and highlights the two key limitations in the present study; the lack of criteria by which to judge whether a significant change has occurred, and the lack of preliminary measurements to check for symmetrical electrode placement prior to beginning recordings.

The most likely site of trauma in Case 1, assuming that the utricle has been discounted by early oVEMP results, is the saccule. Cases have been made for both the saccule and the utricle being the most vulnerable to surgical insult during middle ear surgery. Whereas Backous et al. (1999), showed that the utricle was, on average, slightly closer to the stapes footplate in temporal bone specimens than the utricle, Wang et al. (2005) reported the opposite result. Enhanced vulnerability of the saccule in otosclerotic ears is suggested by distension and increased fragility of the organ documented in some studies (Igarashi et al., 1983; Yoon et al., 1990). The exclusion of utricular injury in Case 1 may suggest that it was the saccule that was the more vulnerable organ than the utricle in this patient.

The development of BPPV in the operated ear during the months following surgery, however, provides evidence that the SCCs have been affected. Indeed, Atacan et al. (2001) reported that characteristic symptoms of BPPV were more common in patients who had undergone stapedectomy 8 to 348 months previously than in control subjects. While it seems probable that the BPPV was a consequence of surgical trauma to the inner ear, Grayeli et al. (2009) propose that postoperative BPPV is a coincidence and does not occur more frequently following stapedectomy than in patients with otosclerosis who do not undergo surgery. The

development of BPPV does not exclude the possibility that trauma to the otolithic organs has occurred, as Hughes and Proctor (1997) propose that it is surgical injury to the saccule and/or utricle that facilitates detachment of the otoliths, which move into the SCCs to cause BPPV symptoms. In this case it seems plausible that significant trauma to the saccule could have resulted in both the initial symptoms of vertigo and imbalance, and the later symptoms of BPPV.

Unlike Case 1, in Case 96 no complications occurred during the primary stapedotomy procedure and severe vertigo did not present until three days after surgery. This case is interesting in that while postoperative changes in oVEMPs were documented, the timing of changes did not align precisely with the presentation of symptoms of balance dysfunction. oVEMPs performed on day 1, prior to the onset of vertigo showed a large decrease in the amplitude of the operated ear n10 relative to the non-operated ear and a 2.9 ms increase in the latency of the response in the operated ear. These results indicate that utricular responses from the operated ear were markedly depressed initially following surgery, despite the absence of major symptoms of balance dysfunction. At the one week assessment, approximately 24 hours after Patient 96 had recovered from the episode of vertigo, the asymmetry ratio again indicated a decreased response amplitude in the operated ear compared to the non-operated ear, with similar n10 latencies from both sides. The results from 1 month onwards provide no clear evidence of persistent vestibular dysfunction.

It is noteworthy that responses from the operated ear were most disturbed 1 day after surgery, while the onset of severe symptoms was delayed until the third postoperative day. Possible causes include the development of serous labyrinthitis in response to the initial trauma to the vestibule, or a slow leakage of perilymph through the stapedotomy. In contrast to Case 1, the changes in responses were consistent with decreased, rather than increased otolithic responses, therefore stimulation of the utricle by the piston is an unlikely explanation for the results in this case.

8.4.6 Association between EHF hearing loss and oVEMP changes

The relationship between postoperative EHF hearing loss and oVEMP changes was examined in two ways; by closely assessing audiometric changes in each of the two patients with postoperative vertigo, and by comparing changes in oVEMP asymmetry ratios in patients with and without significant EHF hearing loss.

In Case 1, in which trauma to the inner ear was recognised during surgery and postoperative vertigo was severe, both air- and bone-conduction thresholds across the entire test frequency range were initially poorer following surgery. The majority of recovery in bone-conduction thresholds and low-frequency air-conduction thresholds to preoperative levels occurred by 3 months after surgery, however a continued elevation of air-conduction thresholds at 4 kHz and above was recorded 12 months after surgery. A reduction in the highest frequency at which a threshold was measureable from 11.2 kHz to 10 kHz persisted across all assessments. The initial bone-conduction threshold deterioration in this case is indicative of a cochlear injury that, at least based on conventional frequency bone-conduction thresholds, recovers over time. As vestibular symptoms were most severe over the same period that bone-conduction thresholds were depressed, labyrinthine trauma affecting both the hearing and balance organs seems likely, although oVEMP results suggest the utricle was not involved. The question of EHF hearing loss remains unanswered here. Certainly, there is evidence that significant inner ear trauma occurred, and there is evidence of a long-term, although partially recoverable, EHF hearing loss. It is possible that EHF hearing loss resulted from that inner ear trauma, but the enduring air-bone gap in the low-frequencies means that a conductive component to the EHF hearing loss cannot be ruled out.

Successful closure of the air-bone gap was achieved from early in the postoperative course in Case 96, although air-conduction thresholds above 4 kHz and bone-conduction thresholds, particularly at 4 kHz, initially increased. Recovery of bone-conduction thresholds to preoperative levels was complete by 1 month after surgery and recovery of air-conduction thresholds to only slightly poorer than preoperative levels continued until 12 months after surgery. In view of the short-term increase in bone-conduction thresholds and changes in oVEMPs in this case, which provide clear evidence that inner ear trauma occurred, it seems reasonable that the initial EHF hearing loss was also a consequence of injury to the inner ear. This hypothesis is supported by the closure of the low-frequency air-bone gap, which reduces the probability that a change to the conductive transmission pathway caused the temporary EHF hearing loss.

If EHF hearing loss is due to iatrogenic trauma to the inner ear, we may expect that oVEMPs will be more frequently altered in patients with EHF hearing loss as the same inner ear insult affects the nearby otolithic organs. In both the analysis across all surgeries and that for stapedectomy alone, mean changes in the oVEMP asymmetry ratio tended to be larger and more negative for the hearing loss group, and these differences between groups were

significant at the 12 month assessment. The more negative shift in the asymmetry ratio in ears with EHF hearing loss is consistent with a larger increase in the relative response of the operated ear to the non-operated ear in this group than in ears with stable EHF hearing. It is possible that the trend for more negative shifts in the asymmetry ratio in the group with EHF hearing loss is indicative of surgical irritation of the labyrinth that affected both hearing and vestibular responses. However, it is concerning that differences were largest 12 months after surgery. In the across surgery analysis the smallest difference between groups was documented at the first assessment and the largest at the final assessment, which is the opposite pattern to that observed for EHF hearing loss. Although the difference was larger at the first assessment in the stapedectomy only analysis, this was not statistically significant and the difference decreased markedly by 1 week. This pattern over time significantly compromises the argument that the same inner ear trauma is the cause of both the EHF hearing loss and the changes in oVEMPs. If the mechanism was the same, we would expect to see a reduced difference in oVEMPs between the two groups over time, as the differences greatly decreased.

Overall, these analyses suggest that either if trauma to the inner ear is the cause of postoperative EHF hearing loss, this trauma has a greater effect on the cochlea than the vestibular system, such that any change in the function of the otolithic organs cannot be detected using tap-evoked oVEMPs. A possible explanation for this is that the cochlear duct is anatomically closer to the footplate than the otolithic organs (Pauw et al., 1991), and therefore presumably more likely to be affected by mechanical trauma or the spread of toxins or inflammatory agents. The vestibular system, being phylogenically older than the cochlea, may also be more resistant to trauma (Hinchcliffe, Bochenek, Pulec, Stroud, & Wilmot, 1971). Of course, these hypotheses apply only to early postoperative data and may not necessarily apply to persistent EHF hearing loss.

The absence of a significant relationship between oVEMP changes and whether or not early EHF hearing loss occurred does not necessarily rule out the theory that inner ear trauma caused EHF hearing loss. A strong possibility is that the variability in VEMP measurements in the small group of patients included in the analysis prevented any significant differences from being detected. In addition, the definition of "significant" EHF hearing loss was chosen somewhat arbitrarily as a loss of three or more measureable thresholds at the first postoperative assessment. Patients with every good hearing preoperatively who experienced a large increase in EHF thresholds after surgery, but not to the point that they became

unmeasurable, would have been excluded. In fact, patients such as this could have been included in the group without a significant EHF hearing loss. A brief review of the data suggests this was not the case and that patients with large EHF losses did lose at least one measureable frequency and thus were not included in the "no EHF loss" group. These limitations do, however, significantly reduce the chances that a significant relationship could be detected.

8.4.7 Limitations of the study

As noted above, the major limitation of this study was the variability of the oVEMP measurements over time. The study was designed so that the non-operated ear provided a control for each patient on the assumption that changes in the operated ear could be compared to changes to the non-operated ear to exclude effects of physiological variation or environmental changes on measurements. We still believe this is a valid method, however we were concerned that the non-operated ear varied so much. In general, the direction of changes was similar in both ears, however, as demonstrated by the large asymmetry ratio changes in some patients late in the postoperative course, in a few cases only one ear, and not always the operated ear, was affected. As has been acknowledged, further research regarding test-retest reliability and the establishment of criteria to determine when a significant change has occurred in essential.

While it is important that thorough reliability data is established, a more direct way of addressing the validity of differences between ears in individual patients would have been to perform preliminary saccade testing to ensure symmetrical responses from each eye. This procedure is described by Winters et al. (2013) as a means of ensuring symmetrical electrode placement and impedance between eyes before testing was performed. This certainly would have improved the confidence we had in changes in asymmetry ratios.

Ideally, all participants would have had clear and robust oVEMPs preoperatively, so that changes could be measured over time. Unfortunately this was not the case. In the majority of cases, contamination of waveforms by artefact of electrical interference seemed to be the main concern, however some aspects of the study population may have reduced the likelihood that oVEMPs could be measured, even in an ideal setting. In particular, bone-conducted oVEMPs are known to decline in amplitude with age and increasing sensorineural hearing loss (Chang et al., 2014; Nguyen et al., 2010). It has also previously been

demonstrated that VEMPs to bone-conducted stimuli are often abnormal in cases of COM or otosclerosis (Chang et al., 2014; Trivelli et al., 2010; Yang & Young, 2007). In several cases participants were excluded because of preoperatively absent VEMPs on the basis that it was not possible to measure n10 properties for later comparison. However, Singbartl et al. (2006) found that bone-conducted cVEMPs reappeared in the operated ear three to six weeks after stapedotomy in three of 23 cases, suggesting that it may have been valuable to include these patients regardless of absent responses and monitor for any postoperative recovery of oVEMPs. Participant numbers were small, particularly in the tympanoplasty group, therefore the inclusion of more participants with absent preoperative responses may have strengthened our analyses of postoperative changes.

8.4.8 Directions for future research

While our results provide some evidence in one case that vertigo was related to utricular injury, more data is needed from patients presenting with significant postoperative vertigo to determine whether the cause is trauma to the saccule and/or the utricle. Future studies would benefit from employing a more comprehensive test battery approach to the assessment of postoperative vestibular function. In particular the use of cVEMPs together with oVEMPs would be useful to elucidate whether the utricle or saccule is more frequently the site of surgical trauma. The limitation in this approach is that whereas studies of patients with superior vestibular neuritis have clearly demonstrated that oVEMPs to bone-conducted stimuli primarily reflect the function of the utricles (Rosengren & Kingma, 2013), the origins of vibration-evoked cVEMPs are not yet certain. Curthoys (2012) presented evidence that the saccule was the primary generator of cVEMPs in response to bone-conducted stimuli, however, other researchers have proposed the utricle and the superior vestibular nerve at least partially contributes to these responses (Brantberg et al., 2003; Govender et al., 2011). Until this issue is clarified, interpretation of changes in responses with respect to the location of injury will be restricted.

Although vestibular compensation limits the usefulness of SVH and SVV testing beyond the acute stage of vestibular trauma (Tribukait & Bergenius, 1998), these tests could be used together with oVEMPs to provide a useful cross-check of changes in utricular function early in the postoperative course. The case for or against postoperative utricular trauma would

certainly be strengthened if both tests showed evidence for increased or decreased otolithic responses.

It was also noted that apparent symptoms of vestibular trauma immediately following may have been related to anaesthesia, rather than inner ear injury. This issue could be clarified by performing oVEMP measurements and assessing symptoms in a control group of patients who have undergone surgery requiring a similar duration of anaesthesia, but without manipulation of the ear.

8.4.9 Summary and conclusions

Overall, we can conclude that there is no evidence from the group analyses in this study population that utricular function was significantly affected by middle ear surgery. What cannot be concluded is whether this result is entirely due to the absence of utricular damage, to limitations in the testing equipment or protocol, or to an insensitivity of tap-evoked oVEMPs in general to changes in otolithic responses. As at least some patients reported symptoms of balance dysfunction, we would have expected that if the utricle was the source, oVEMPs would be affected. It may be that, in these cases, trauma was not severe enough for changes in responses to be recorded, considering the overall variability in recordings.

In the two cases in which severe vertigo occurred post-stapedectomy, oVEMP changes that corresponded to the timeline of symptoms and the measurement of sensorineural hearing loss were documented in one patient. Although limited to one case, this example does suggest the utricle may be vulnerable during surgery in at least some patients. The absence of oVEMP changes in the other case of significant vertigo indicates that multiple causal mechanisms are likely to be responsible for post-stapedectomy vertigo.

These findings provide an interesting starting point that suggests further assessment of oVEMPs in cases of significant balance disturbance, particularly following stapedectomy, may provide some insight into the causes of postoperative vestibular symptoms. Several methodological issues regarding the reliability of oVEMPs must first be addressed to ensure that results can be accurately interpreted.

PART V: THE CLINICAL IMPORTANCE OF EHF HEARING ACUITY

Chapter 9: The importance of extended high-frequency hearing acuity to localisation abilities

9.1 The contribution of spectral information in the EHF range to auditory performance

There is increasing evidence that sensitivity to information contained in the EHF range plays an important role in auditory perception. That middle ear surgery is frequently detrimental to hearing acuity in this EHF range therefore suggests that further investigation is required to ascertain the impact that such hearing loss may have on auditory functioning.

9.1.1 Speech intelligibility

While the spectral information in speech is greatest below 8 kHz, there is also a significant amount of energy contained above 8 kHz and up to 20 kHz (Best, Carlile, Jin, & van Schaik, 2005; Moore, Stone, Fullgrabe, Glasberg, & Puria, 2008; Shoji, Regenbogen, Yu, & Blaugrund, 1991; Valencia, Mendoza, Mateo, & Carballo, 1994). In a recent study, Moore et al. (2008) used high quality recording techniques to analyse the spectro-temporal characteristics of normal conversational speech across a wide frequency range. Their analyses showed that for speech with an overall level of 65 dB SPL, the mean spectrum level fell with increasing frequency over 500 Hz – however, a mean 1/3-octave level of 37 dB SPL was still measureable at a centre frequency of 10 kHz. The distribution of spectrographic content is clearly demonstrated in Best et al. (2005)'s recording of the word "sludge" shown in Figure 90, in which substantial energy is present above 8 kHz.

We are not aware of any studies directly examining the effects of an elevation of EHF hearing thresholds on speech intelligibility; however some inferences may be drawn from research using filtered speech to investigate the effects of a reduction in high-frequency spectral information on speech perception in normal hearing and hearing impaired subjects. These few published studies have indicated that spectral information above 8 kHz does contribute to speech perception, particularly for fricatives such as /s/ and /z/ (Boothroyd & Medwetsky, 1992; Fullgrabe, Baer, Stone, & Moore, 2010; Lippmann, 1996; Monson, Lotto, & Ternstrom, 2011; Moore, Fullgrabe, & Stone, 2010; Pittman, 2008; Stelmachowicz, Pittman, Hoover, & Lewis, 2001). To ensure accurate perception of /s/ produced by female

and child speakers, both normal hearing and hearing impaired listeners require an upper bandwidth limit of at least 9 – 10 kHz (Boothroyd & Medwetsky, 1992; Stelmachowicz et al., 2001). Although these upper bandwidth limit requirements are intended as recommendations for the manufacturing and fitting of hearing aids, they imply that when spectral information above 8 kHz is inaccessible, such as in the case of an EHF hearing loss, perception of high-frequency fricatives may be compromised.

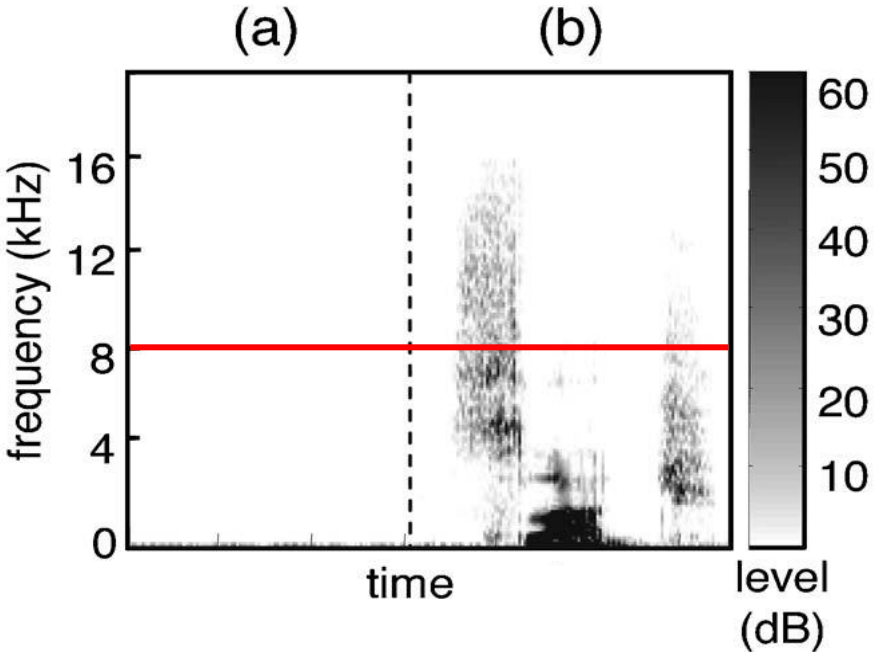

Figure 90. Spectrograms of (a) a silent period demonstrating the noise floor of the measurement equipment, and (b) a recording of the word "sludge" showing the considerable spectral information present above 8 kHz. Adapted from Best et al. (2005), with permission.

Given that the perception of /s/ serves several linguistic functions, including indicating plurality, possession, and tense (Denes, 1963; Rudmin, 1983; Tobias, 1959), it would be expected that loss of high-frequency bandwidth that limits access to this phoneme would be detrimental to speech intelligibility. However, for adults with acquired hearing losses, the use of additional acoustic cues, such as coarticulation effects, and linguistic knowledge may at least partially compensate for the reduction in audibility of high-frequency cues (Kortekaas & Stelmachowicz, 2000; Whalen, 1981). Knowledge and experience with language also assist listeners to use other semantic and syntactical cues in speech to limit the loss of intelligibility resulting from misperceived individual phonemes (Kalikow, Stevens, & Elliott, 1977). For this reason, if a hearing loss reduces access to high-frequency spectral information in speech either prelingually, or early in the process of speech and language development, the effects on speech perception would be expected to be greater (Stelmachowicz et al., 2001).

9.1.2 Subjective sound quality

Spectral information above 8 kHz also appears to affect the perceived sound quality of both speech and music (Fullgrabe et al., 2010; Moore & Tan, 2003; Ricketts, Dittberner, & Johnson, 2008; Snow, 1931). Moore and Tan (2003) found that subjective ratings of naturalness of music and speech by normal hearing listeners decreased as the upper cut-off frequency was lowered. For music stimuli, ratings of naturalness were highest when a broadband signal was presented, and ratings progressively decreased as the low-pass filter cut-off frequency was decreased from 16854 to 3547 Hz. A comparatively lower low-pass filter cut-off frequency was required for maximum perceived naturalness of speech, with a progressive reduction in subjective quality found when the upper cut-off frequency was decreased from 10869 to 3547 Hz.

Contrasting preferences for a narrower bandwidth have been shown for hearing impaired listeners. Ricketts et al. (2008) used paired-comparison judgements by listeners with mild to moderate hearing losses to demonstrate a significant relationship between the slope of the audiogram at 4 – 12 kHz and bandwidth preference. High-frequency audiograms with steeper slopes associated with a preference for music and movie soundtracks filtered using a cut-off frequency of 5.5 kHz over 9 kHz. Fullgrabe et al. (2010) also showed that in contrast to normal hearing listeners, for hearing impaired subjects presented with amplified speech, decreasing bandwidth from 10 kHz to 7.5 or 5 kHz was associated with increased pleasantness and decreased clarity. No correlation was found between either the slope of the audiogram or audiometric thresholds and quality ratings of stimuli. It is unclear whether differences between normal hearing and hearing impaired subjects would have been maintained if hearing impaired subjects who were unused to hearing such high-frequency stimuli were allowed to adapt to the new sound before testing.

9.1.3 Sound localisation

The cues available to discriminate the location of a sound are dependent on the position of the sound source in space and the spectral content of the stimulus. EHF hearing acuity could potentially disrupt localisation accuracy when the cues required to locate a sound in a certain plane are dependent on high-frequency content that is made inaccessible by hearing loss. Prior to discussion of these possible effects, the auditory cues to sound location and the importance of high-frequency spectral information to those cues will be reviewed here.

9.1.3.1 Mechanisms of sound localisation

Determining the location of a sound relies on three primary cues: the interaural differences in the timing and in the intensity of the sound, and the spectral information created by the filtering effects of the pinna. When a sound source is located away from the midline, the signal must travel a greater distance to reach the ear further from the source compared to the ear nearer the source. This creates a time delay between the ears which enables localisation in the horizontal dimension (Blauert, 1997; Middlebrooks, 1992). These interaural timing difference (ITD) cues are available in the components of a signal below 1.5 kHz, for which interaural time differences can be encoded meaningfully into interaural phase differences (Macpherson & Middlebrooks, 2002; Wightman & Kistler, 1992, 1997). Humans are also able to extract ITDs from the envelopes of sounds above 1.5 kHz (Henning, 1974; Henning & Ashton, 1981; McFadden & Pasanen, 1976). Although envelope cues can influence lateralisation, they are thought to be an inferior high-frequency cue relative to interaural level differences (ILDs) (Edmonds & Culling, 2005; Ewert, Kaiser, Kernschmidt, & Wiegrebe, 2012; Macpherson & Middlebrooks, 2002).

Interaural differences in the intensity or level of a signal arise when a sound "shadow" is cast by the head as it interacts with the signal, reducing the intensity of the stimulus that reaches the ear on the side opposite to the source location. This ILD, known as the "head shadow" effect, is measureable from approximately 1.5 – 2 kHz and increases progressively with increasing frequency (Bronkhorst & Plomp, 1988, 1989; Festen & Plomp, 1986; Middlebrooks, Makous, & Green, 1989; Shaw, 1974; Wightman & Kistler, 1993). ILDs provide an additional cue to the lateral angle of a sound source which, unlike low-frequency ITDs, may be disrupted if access to the high-frequency information that provides these cues is reduced by hearing loss.

ITDs and ILDs provide robust horizontal plane localisation cues, but are minimally informative for the coding of elevation and front-back location (Langendijk & Bronkhorst, 2002; Middlebrooks, 1992; Oldfield & Parker, 1984; Wightman & Kistler, 1997). Interaural cues are inherently ambiguous as, due to symmetrical placement of the ears on the head, different sound locations may result in the same interaural value when they fall within the "cone of confusion"; an approximately cone-shaped area centred on the interaural axis (Mills, 1972; Moore, 2007). These ambiguities may be resolved using spectral information provided by the pinna. The convoluted shape of the pinna results in location-dependent filtering as the signal is reflected into the meatus off one or more of its folds. Sound may also enter the EAC

directly, or via reflections from the head, shoulders, and upper torso (Batteau, 1967; Gardner & Gardner, 1973; Moore, 2007). The spectrum of the sound that reaches the TM is a combination of the direct and reflected signals, and varies systematically with the location of the sound source (Blauert, 1997; Carlile, 1996; Shaw, 1974; Wightman & Kistler, 1989).

Pinna filtering is dependent on the frequency content of the stimulus and will only be effective when the stimulus contains frequencies with wavelengths short enough to interact with the folds of the pinna. In humans, the incoming sound must contain high-frequencies; typically above 6 kHz, for spectral cues for localisation to be generated by the pinna (Hebrank & Wright, 1974; Heffner & Heffner, 2008; Middlebrooks & Green, 1991). This high-frequency spectral information is thought to be critical for preventing front-back confusions and determining the elevation of a sound (Middlebrooks, 1997; Wightman & Kistler, 1989).

9.1.3.2 Effects of EHF hearing loss on sound localisation

Based on experimental data that examines the effect on localisation performance of filtering stimuli to reduce spectral content in selected frequency ranges, there is a general consensus that limiting noise stimuli to frequencies below approximately 8 to 10 kHz results in a deterioration of vertical localisation and front-back discrimination (Bronkhorst, 1995; Carlile, Delaney, & Corderoy, 1999; Hebrank & Wright, 1974; Hofman & Van, 2003; King & Oldfield, 1997; Langendijk & Bronkhorst, 2002; Middlebrooks, 1992; Zhang & Hartmann, 2010). At least in normal listeners, accurate elevation discrimination has been found to rely on spectral information in a slightly lower frequency band than front-back discrimination (King & Oldfield, 1997; Langendijk & Bronkhorst, 2002). King and Oldfield (1997) used progressive low-pass filtering to demonstrate that a minimum high-frequency limit of 9 kHz is required for accurate localisation of elevation, but that this increased to 10 – 13 kHz for accurate discrimination of front and back location. Similarly, Langendijk and Bronkhorst (2002) reported that elevation discrimination relies on spectral information in the frequency band 5.7 – 11.3 kHz, whereas for front-back discrimination information in the frequency range 8 – 16 kHz was critical.

Studies manipulating the bandwidth of speech stimuli have also found that localisation errors associated with the cone of confusion (elevation and front-back discrimination errors) increase when high-frequency spectral content is removed (Best et al., 2005; Jin, Best,

Carlile, Baer, & Moore, 2002). Best et al. (2005) examined localisation of speech stimuli presented through headphones in a virtual auditory space created using individualised head-related transfer functions for five young adult listeners. Consistent with studies using filtered noise stimuli, Best et al. demonstrated that low-pass filtering of speech at 8 kHz significantly increased the rate of polar angle errors (a metric primarily reflecting front-back confusions and errors in elevation discrimination) compared to performance with a speech corpus with a 300 Hz to 16 kHz bandwidth. In addition, specific words in the corpus containing more energy above 8 kHz were localised more accurately in the polar dimension than words with less high-frequency information. The horizontal angle of stimuli was estimated accurately regardless of spectral content. These findings clearly illustrate the role of spectral information above 8 kHz in accurate disambiguation of elevation and front-back position.

The accuracy of speech localisation performance has also been found to depend on the *intensity* of the spectral content above 8 kHz in the stimulus. Best et al. (2005) found a gradual decline in polar angle localisation performance when the level of information above 8 kHz in speech stimuli was attenuated by 20 and then 40 dB. Although localisation performance was degraded when high-frequency information was reduced, even low levels of content above 8 kHz provided some benefit for polar angle localisation. This has implications for our understanding of the impact of the degree of hearing loss in the EHF range, as such a hearing loss can essentially be thought of as low-pass filtering of sound. Without adequate hearing sensitivity to detect spectral information above 6 kHz, optimal localisation performance is unlikely to be achieved when the direction of a sound corresponds with ambiguous ITD and ILD cues.

The contribution of high-frequency spectral information to the localisation of target sounds appears to be particularly important in the presence of competing noise. Brungart and Simpson (2009) demonstrated the requirement for an increased high-frequency cut-off frequency to determine elevation in spatially separated noise compared to discrimination in quiet in eight normal hearing listeners. Whereas filtering to include information at 12 to 16 kHz assisted localisation of a pulsed-noise target in quiet, it became more critical for accurate localisation of elevation in the presence of a spatially-separated low-level continuous masking. At a signal-to-noise ratio (SNR) of 0 dB, the addition of spectral information between 12 and 16 kHz corresponded with approximately a 30% decrease in overall localisation errors. The advantage conveyed by this EHF information diminished at negative SNR values. Overall, these results indicate that whereas accurate front-back

localisation requires a minimum upper bandwidth limit of 10 kHz in quiet conditions, this is increased up to 16 kHz when a low-level noise masker is present. The increased advantage of EHF content in the presence of noise was posited to be related to the larger head-shadow effect present at higher frequencies.

The relationship between EHF hearing loss and auditory localisation performance has also been investigated using experimental designs in which the accuracy of localisation of variously filtered target is compared in older and younger listeners. The premise on which these studies are based is that as EHF hearing loss occurs at a much higher rate in older adults, if hearing acuity at these frequencies is important to elevation and front-back localisation, impaired localisation in these dimensions should be more evident in older subjects. In agreement with studies showing the importance of high-frequency stimuli in localisation of elevation, a decline in performance in the vertical plane has been documented with advancing age (Abel & Hay, 1996; Dobreva, O'Neill, & Paige, 2011, 2012; Noble, Byrne, & Lepage, 1994; Otte, Agterberg, Van Wanrooij, Snik, & Van Opstal, 2013; Rakerd, Vander Velde, & Hartmann, 1998). However, studies of auditory performance in older adults have also found evidence central age-related deficits in temporal processing, which could impair localisation abilities irrespective of hearing thresholds (Grose & Mamo, 2010; Lister & Roberts, 2005; Martin & Jerger, 2005; Roberts & Lister, 2004; Schneider & Hamstra, 1999; Strouse, Ashmead, Ohde, & Grantham, 1998). Given the dependence of elevation, but not lateral angle, on discrimination on high-frequency spectral cues, it would be expected that peripheral high-frequency hearing loss would impair vertical localisation performance only, whereas a central processing deficit would disrupt localisation in both planes. Results have, however, been mixed as to whether horizontal plane localisation is also impaired in older adults (Dobreva et al., 2011; Noble et al., 1994; Otte et al., 2013; Rakerd et al., 1998).

9.1.3.3 Effects of cochlear EHF hearing loss on sound localisation

A reduction in access to high-frequency spectral cues provided by the pinna is certainly likely to occur in cases of EHF hearing loss, but localisation deficits may be compounded by the effects of cochlear damage. Cochlear pathology is typically associated with a reduction in frequency selectivity and temporal processing abilities (Moore, 1985). It has been suggested that the loss of these fine discrimination abilities would prohibit the resolution of patterns of spectral peaks and dips that convey the directional information provided by pinna filtering

(Moore et al., 2008). Indeed, one laboratory study examining localisation of "spectrally-smeared" speech stimuli, which had been filtered to simulate the effects of reduced frequency selectivity, demonstrated that localisation abilities are impaired under such conditions (Jin et al., 2002). From the current literature it is not possible to determine the extent that a reduction of audibility in the EHF range versus a loss of temporal and frequency selectivity in the cochlea contributes to localisation difficulties. This may be an important issue to consider when determining the localisation difficulties that an individual is likely to experience if a postoperative hearing loss is sensorineural rather than conductive.

There is currently a lack of data distinguishing between conductive and sensorineural EHF hearing losses in general and in particular with regards to possible localisation difficulties experienced by each group. Research comparing localisation abilities with bilateral conductive and sensorineural hearing losses in the conventional frequency range has shown that localisation abilities may be less impaired for listeners with sensorineural hearing losses (Noble et al., 1994; Noble, Byrne, & Ter-Horst, 1997). Noble et al. (1994) aimed to separate the effects on localisation ability of the type of hearing loss from those of audiometric configuration by comparing performance in 13 subjects with bilateral conductive/mixed hearing loss to subjects with the same degree of sensorineural hearing loss. Both groups showed deficits in elevation discrimination; however the conductive/mixed group showed an additional impairment in horizontal plane localisation. These group differences were replicated by Noble et al. (1997), suggesting that, at least in the conventional frequency range, the additional effects of reduced temporal and frequency selectivity in sensorineural loss compared to conductive loss are less detrimental for localisation accuracy than may be expected.

9.1.3.4 Effects of unilateral EHF hearing loss on sound localisation

Another key issue regarding the effects of EHF hearing loss following middle ear surgery is the comparative difficulties experienced with unilateral, as opposed to bilateral, hearing loss. There is a general consensus that auditory localisation difficulties are greater for listeners with unilateral or asymmetrical hearing losses than those with bilateral, symmetrical hearing losses. In particular, individuals with unilateral or asymmetrical losses require larger interaural differences to be present before binaural localisation cues can be identified (Moore, 2007). Unfortunately, published data regarding the effect of asymmetrical hearing thresholds

on localisation abilities do not include an evaluation of EHF thresholds. Given that the EHF range is thought to contribute most to localisation through the spectral cues of the pinna, it is appropriate to review the literature regarding the use of monaural spectral cues in localisation to attempt to infer the localisation effects of the unilateral loss of EHF hearing sensitivity.

The contribution of monaural spectral information to localisation performance has frequently been assessed by comparing binaural localisation accuracy to performance under experimental conditions where the spectral cues at one ear are disrupted, for example, by plugging one ear (e.g. Jin, Corderoy, Carlile, & van Schaik, 2004; Macpherson & Sabin, 2007; Morimoto, 2001; Musicant & Butler, 1984; Slattery & Middlebrooks, 1994; Wightman & Kistler, 1999; Zhang & Hartmann, 2010). In general, these studies have demonstrated that spectral cues from both ears contribute to vertical plane localisation when the sound source is located at the midline; however when a sound is located in the sagittal plane away from the midline, the lateral angle of the sound determines the relative contribution of each ear to the perception of localisation. The influence of the ear closest to the sound source gradually increases as the sound shifts laterally from the median plane towards that ear, whereas the contribution of the "far" ear decreases (Humanski & Butler, 1988; Wightman & Kistler, 1999). The contribution of the contralateral ear is negligible for sounds displaced 40 to 60 degrees from the midline (Macpherson & Sabin, 2007; Morimoto, 2001).

Based on evidence in the extant literature, we would expect that in the case of a unilateral high-frequency hearing loss localisation in the vertical and front-back dimensions would be disrupted when the sound source deviated more than 40 to 60 degrees from the midline towards the poorer hearing ear. Although this appears to be true for normal hearing listeners when the signal to one ear is disrupted, it has also been shown that at least some listeners with a partial or total unilateral hearing loss are able to localise sounds with reasonable accuracy in both the horizontal and vertical dimensions (Slattery & Middlebrooks, 1994). In addition, evidence suggests that when a long-term spectral disruption is applied, normal hearing listeners may learn to determine elevation accurately with those altered spectral cues (Hebrank & Wright, 1974; Van Wanrooij & Van Opstal, 2005). This suggests that the auditory system can partially adapt to changes in spectral cues to enable localisation on the poorer hearing side. Optimal localisation performance is not completely regained as far ipsilateral elevation gain remains below normal in most listeners (Van Wanrooij & Van Opstal, 2005).

9.1.4 Perception of speech in noise

In addition to providing a cue for localisation, the head shadow effect provides significant benefit for signal perception in the presence of background noise. For example, if a speech signal is coming from in front of a listener and the noise source is positioned to the right, the SNR will be higher at the left ear relative to the right. The listener is then able to selectively attend to the left ear, which has the more optimal SNR, in order to improve speech intelligibility. As the head shadow effect is greatest for high-frequencies (Bronkhorst & Plomp, 1988, 1989; Shaw, 1974), this is the frequency region at which the improvement in the SNR will be most prominent.

In binaural listening situations where speech and noise sources are separated, normal hearing listeners have been shown to benefit from the improved SNR due to head shadow effects, whereas individuals with sensorineural loss generally benefit less from the spatial separation of speech and noise (Arbogast, Mason, & Kidd, 2005; Bronkhorst & Plomp, 1989, 1992; Dubno, Ahlstrom, & Horwitz, 2002; Duquesnoy, 1983; Gelfand, Ross, & Miller, 1988; Helfer & Freyman, 2008; Marrone, Mason, & Kidd, 2008; Noble et al., 1997; Ter-Horst, Byrne, & Noble, 1993). The reduced advantage of the spatial separation of signal and noise in hearing impaired listeners is believed to result from the dependence of the head shadow effect on frequency information that is not accessible to listeners with high-frequency hearing losses (Dubno et al., 2002). The additional signal information available when the SNR is improved at high-frequencies will not be perceived in these individuals and therefore no functional improvement in signal-to-noise ratio will be available. The degree of high-frequency hearing loss appears to determine the size of the advantage demonstrated when speech and noise are separated compared to when both are located in front of a subject (Bronkhorst & Plomp, 1989). Deficits in the ability to access head shadow advantages is thought to be a primary contributor to the speech recognition difficulties in background noise reported by many people with high-frequency hearing loss (Dubno et al., 2002; Festen & Plomp, 1986; Hawkins & Yacullo, 1984; Leeuw & Dreschler, 1991).

9.1.5 Aims and hypotheses

The present study was conceived to address the absence of studies in the literature directly examining the effects of EHF hearing loss on auditory function in participants with such hearing loss. Given the strength of the published data illustrating that filtering out EHF

information from sound stimuli impairs localisation performance in the vertical plane in normal hearing listeners, this topic was selected for further investigation. The central goal of this study was therefore to determine whether any significant differences in localisation accuracy exist between listeners with normal hearing up to at least 14 kHz, and listeners with hearing loss at 4 kHz and above. Localisation was compared for speech stimuli and noise stimuli with spectral content above 8 kHz either present or removed using filtering.

Interaural cues are considered robust cues to sound location in the horizontal plane and, given that ITDs are present at frequencies below 1.5 kHz (Macpherson & Middlebrooks, 2002; Wightman & Kistler, 1992, 1997) and ILDs are measureable from approximately 1.5 – 2 kHz (Bronkhorst & Plomp, 1988, 1989; Festen & Plomp, 1986; Middlebrooks et al., 1989; Shaw, 1974; Wightman & Kistler, 1993), they should be relatively unaffected by the presence or absence of EHF spectral information. The exception is the discrimination of front-back sound source, for which confusions occur that may be resolved using high-frequency pinna cues (Langendijk & Bronkhorst, 2002; Middlebrooks, 1992; Middlebrooks & Green, 1991; Musicant & Butler, 1984; Oldfield & Parker, 1984; Wightman & Kistler, 1997). Based on this data, it was expected that in the lateral horizontal plane, the rate of front-back confusions, but not mean localisation error, would increase when the upper limit of the stimulus bandwidth was decreased from 16 to 8 kHz, or when EHF information was inaccessible due to hearing loss. Manipulations of EHF content were not expected to influence localisation in the frontal horizontal plane.

A stimulus presented on the median plane will not generate any interaural difference cues, therefore accurate judgement of elevation will be entirely dependent on the use of high-frequency spectral cues (Hebrank & Wright, 1974; Heffner & Heffner, 2008; Middlebrooks & Green, 1991). In contrast, stimuli in the lateral vertical plane can be localised with reasonable precision based on interaural cues alone, but performance is significantly improved when pinna based spectral cues are also available to the listener (Butler & Humanski, 1992; Butler, Humanski, & Musicant, 1990). The frontal vertical plane was therefore the critical condition in which we expected to see the strongest decline in localisation accuracy when EHF information was unavailable. A significant influence of EHF content was also predicted for the lateral vertical plane, although the strength of the effects were expected to be weaker than in the frontal vertical plane.

A Master of Audiology student, Sarah Gray, collected the data presented in this chapter. This data was initially analysed and presented in Sarah's master's thesis (Gray, 2014).

9.2 Method

9.2.1 Participants

To be eligible to take part in this study, participants were required to meet the hearing criteria listed below for either of two groups; an EHF hearing loss group and a normal hearing group.

Normal hearing group:

- Pure-tone hearing thresholds did not exceed 20 dB HL in either ear at any test frequency from 0.25 to 14 kHz; and
- The difference in thresholds between the ears was not greater than 15 dB HL at any test frequency.

EHF hearing loss group:

- Pure-tone hearing thresholds did not exceed 20 dB HL in either ear at any test frequency up to and including 2 kHz;
- The pure-tone threshold at 4 kHz did not exceed 30 dB HL in either ear;
- The threshold for at least one test frequency from 8 to 14 kHz in each ear reached a minimum of 55 dB HL; and
- The difference in thresholds between the ears was not greater than 15 dB HL at any test frequency.

To recruit participants that met one of the sets of inclusion criteria, an initial pool of volunteers participated in a hearing screening phase of the study. The inclusion criteria for this screening phase were that the participants were at least 18 years of age and had no significant history of middle ear disease or auditory processing disorders. Participants were recruited from staff and students from the University of Canterbury and residents of Christchurch. The invitation to participate in this phase of the study was issued by word of mouth, Department of Communication Disorders internal email, and brochures available at the University of Canterbury Speech and Language Clinic (provided in Appendix C). Participants meeting the screening inclusion criteria were invited to participate in the study and given a written information sheet (Appendix A). Written consent was obtained from all participants prior to the commencement of the hearing assessment, in accordance with the ethical approval obtained for this study from the University of Canterbury Ethics Committee

(reference: HEC 2013/68). Sixty-nine participants were recruited, including 44 females and 25 males with an age range of 18 to 67 years (*M* = 34.48, *SD* = 7.60).

Following hearing screening, 47 eligible participants were identified as meeting the criteria for one of the two groups and invited to participate in the second phase of the study. This group included 24 participants who met the inclusion criteria for the EHF hearing loss group and 23 for the normal hearing group. One participant in the hearing loss group declined to participate further, leaving 23 participants in each group.

The normal hearing group included 16 females and 7 males between the ages of 18 and 39 years (*M* = 24.65 years, *SD* = 4.80). Of the 23 participants in the hearing loss group, 16 were female and 7 were male, and ages ranged from 30 to 67 years (*M* = 53.70, *SD* = 9.10). Mean thresholds for each group are shown in Figure 90. It is evident from Figure 90 that mean thresholds were higher in in the conventional frequency range, as well as in the EHFs for the EHF hearing loss group in comparison to the normal hearing group, although thresholds remain below 20 dB HL at 2 kHz and below. The standard deviations associated with the mean thresholds are also greater for the EHF hearing loss group, particularly above 4 kHz.

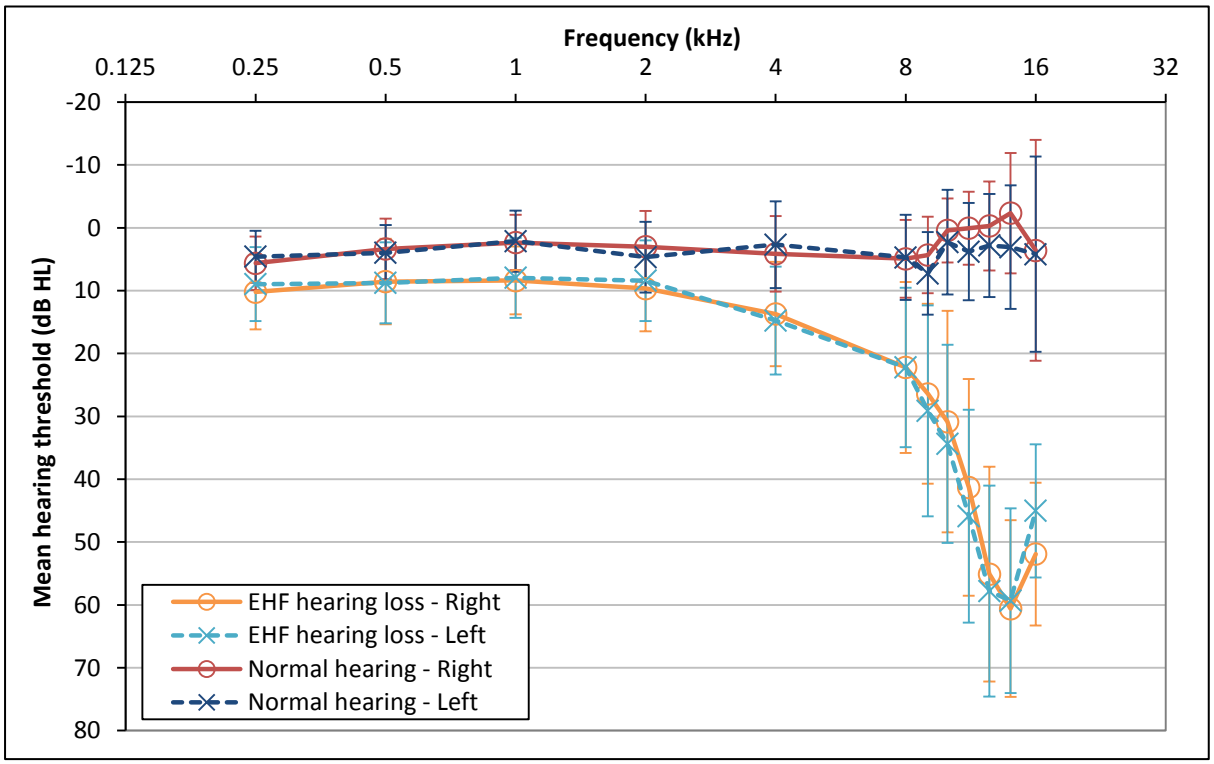

Figure 91. Mean hearing thresholds at each test frequency and for each ear for the "normal hearing" and "EHF hearing loss" groups of participants. Error bars represent standard deviation.

9.2.2 Equipment

9.2.2.1 Audiometry instrumentation

Pure-tone thresholds were measured using a calibrated GSI-61 audiometer (Grason-Stadler, Eden Prairie, MN). Air-conduction stimuli were presented in the conventional frequency range (0.25 – 8 kHz) via TDH-39 supra-aural headphones (Telephonics Corporation, Farmingdale, NY) and in the EHF range (8 – 16 kHz) using Sennheiser HDA200 circumaural headphones (Sennheiser electronic GmbH & Co., Wennebostel, Germany). When bone-conduction threshold measurement was indicated, stimuli were presented using a Radioear B -71 bone-conduction vibrator (Radioear Corporation, New Eagle PA). All audiometric testing was carried out in sound treated rooms at the University of Canterbury which met the criteria of ISO 8253-1 (2010).

9.2.2.2 Localisation task instrumentation

9.2.2.2.1 Room set-up

The localisation tasks were performed with the participant seated in a sound attenuating booth at the University of Canterbury, which had a floor area of 2900 x 2730 mm and a height of 2000 mm. Reverberation in the booth was reduced by lining the walls and ceiling with 25 – 20 mm thick sound absorbing foam and covering the floor with a layer of blankets and soft mats. As shown in Figure 92, the participant was seated in the centre of the room and the speaker array was positioned with the long, straight side close to the back wall and the speakers facing towards the participant. The sound card and amplifiers were placed on the floor in the space between the speaker array and the back wall of the booth.

The researcher, seated in a connecting control room with the computer running the stimulus presentation software, was able to observe the participant through an internal window measuring 610 x 760 mm. A wireless intercom system (Oricom, Sydney, Australia) provided a means for the participant to communicate with the researcher.

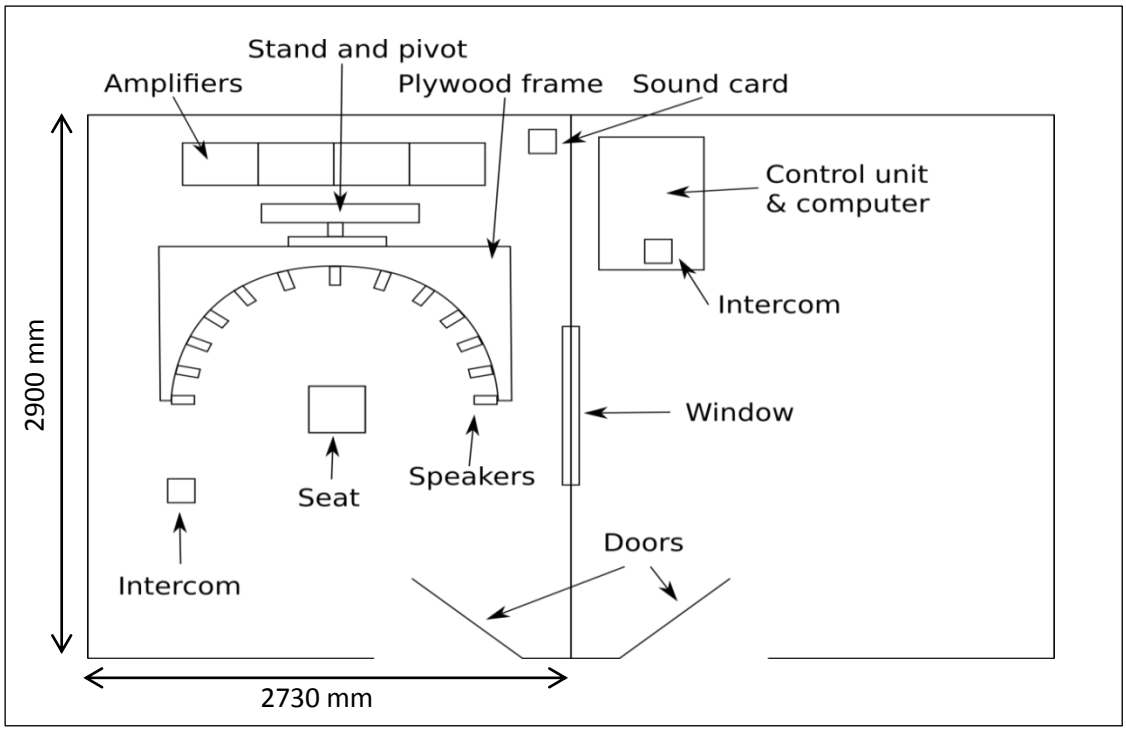

Figure 92. Diagram showing the layout of the localisation task test room from above.

9.2.2.2.2 Speaker array

The speaker array consisted of 13 loudspeakers arranged on an arc constructed of 20 mm thick plywood. A detailed diagram of the speaker array showing the dimensions of the stand is shown in Figure 93. The sheet of plywood from which the arc was cut measured 1970 x 1185 mm. The radius of the arc was 1085 mm. The plywood arc was attached to a modified engine hoist using a mounting bracket that allowed the plywood sheet to be rotated into horizontal and vertical positions.

Thirteen Inspire T6160 5.1 speakers (Creative Labs, Singapore) were attached to angle brackets screwed into the edge of the arc using hook and loop strips. The speakers were 100 mm in depth, so the final radius of the arc from the cone of each speaker to the centre was 985 mm. The front surfaces of the speakers were 125 x 75 mm. The first speaker was positioned at the centre of the arc, and the remaining 12 speakers were placed at 15 degree

intervals from the centre speaker to the front edges of the arc. Speakers were marked with location numbers 1 to 13 using labels affixed to the bottom of each speaker. Location 1 was defined as the leftmost speaker relative to the participant when the array was in the frontal horizontal position, and numbering continued consecutively so that the rightmost speaker was labelled location 13. Numbering used in other array orientations is shown in Figure 94 a - d.

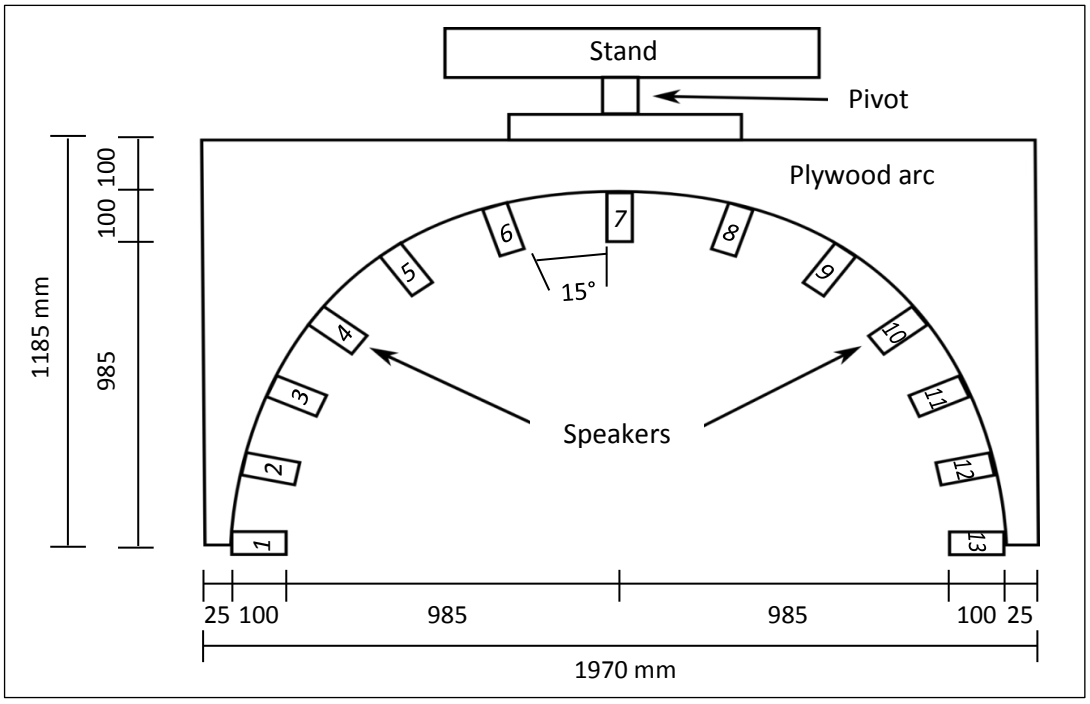

Figure 93. Diagram of the speaker array showing the stand, plywood arc, and speaker placement. Measurements are given in millimetres. Speaker numbers are shown in italics.

The speakers were driven by four amplifiers supplied with the Inspire T6160 5.1 speaker systems (Creative Labs, Singapore) and a MOTU Ultralite mk3 multi-channel soundcard (MOTU, Cambridge, MA). Each of the amplifiers was connected to two speakers. Of the remaining five speakers, four (speakers 2, 5, 8, and 12) were used as “virtual” speakers, meaning that the sound perceived at each of these speaker location swas actually produced by the combination of the signals from the two adjacent speakers. No sound was produced either physically or virtually by speaker 10. This was due to the limited number of amplifier outputs available from the multi-channel soundcard.

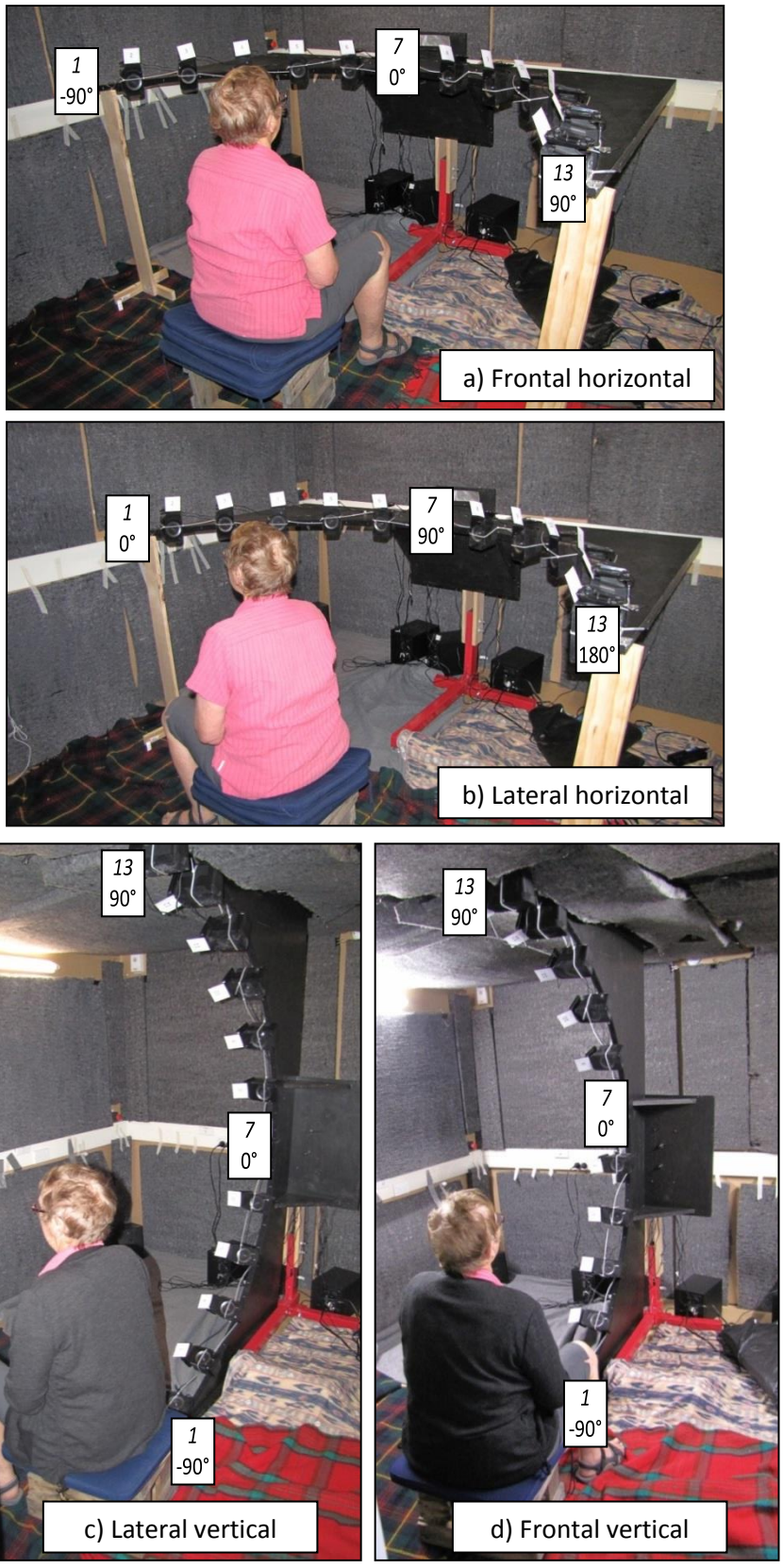

Figure 94. The experimental set-up showing the positions of the speaker array and the participant in each of the four array orientations: a) frontal horizontal, b) lateral horizontal, c) lateral horizontal, and d) frontal horizontal.

9.2.2.2.3 Localisation software

Stimulus characteristics and speaker presentation location were controlled using custom software; UC Directional Hearing Array (O'Beirne, 2013), created using LabVIEW 2012 (National Instruments, Austin, TX) and run through an HP Compaq nx6120 laptop (Hewlett Packard, Palo Alto, CA). As shown in the screenshot of the control panel in Figure 95, the software controlled the stimulus type, bandwidth, and intensity, and the speaker through which the stimulus was presented. The software was also used to record responses and calculate errors in localisation. A confusion matrix was produced for each participant, showing presented location vs. selected location for each condition, as shown in the lower half of Figure 94.

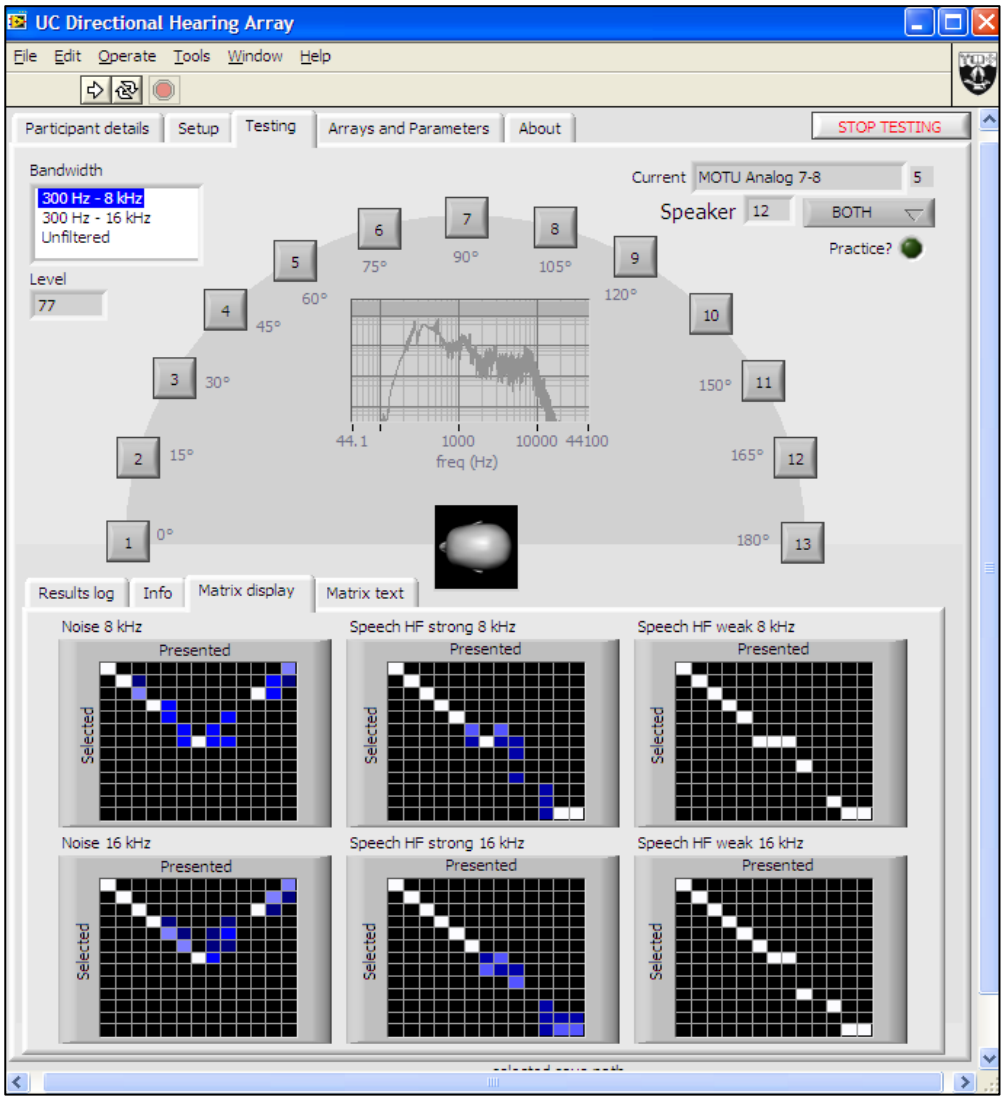

Figure 95. Screenshot of the stimulus and presentation control panel of the UC Directional Hearing Array software. The upper half shows the stimulus presentation selection options and the buttons labelled with speaker number which were used to input responses. The lower half shows the matrix displays of presented vs. selected locations for each test condition.

9.2.2.2.4 Stimuli

Two categories of stimuli; noise and speech, were each filtered to create a broadband stimulus and a reduced-high-frequency stimulus. In the broadband conditions, the stimuli were bandpass filtered using 10^{th} order Butterworth filters with a high-pass cut-off of 300 Hz and a low-pass cut-off of 16 kHz. The reduced-high-frequency stimuli were created by lowering the low-pass filter cut-off frequency to 8 kHz.

The noise stimuli were 150 ms noise bursts with rise-fall cosines of 10 ms. Speech stimuli were recordings of the Harvard word lists (Egan, 1948) generously provided by Assoc. Prof. Simon Carlile (Department of Physiology, University of Sydney). This speech corpus was comprised on ten lists of 100 phonetically balanced words spoken by an Australian female actor. Stimuli were recorded, as described in detail by Best et al. (2005), using a Brüel & Kjær 2610 amplifier (Brüel & Kjær, Nærum, Denmark) and digitised at a sample rate of 80 kHz using an anti-aliasing filter with a 30 kHz cut off.

Speech stimuli were divided with respect to the strength of spectral content in the EHF range to create two further stimulus conditions; strong high-frequency content (HF strong speech) and weak high-frequency content speech (HF weak speech). The purpose of creating these stimulus sets was to examine whether the amount of EHF content in speech influenced localisation performance. These stimulus sets were created by ranking the words from all ten lists according to the level (in arbitrary decibel units) of their content between 8 and 16 kHz (Figure 96). The 144 words with the highest level of EHF content were selected to create the strong high-frequency content stimulus set (HF strong speech) and the 48 words with the lowest EHF content formed the weak high-frequency content (HF weak speech) group.

To summarise, there were six stimulus conditions:

1. Noise stimuli:
    a. Bandpass filtered between 300 Hz and 16 kHz
    b. Bandpass filtered between 300 Hz and 8 kHz
2. Speech stimuli:
    a. Words with strong high-frequency content
        i. Bandpass filtered between 300 Hz and 16 kHz
        ii. Bandpass filtered between 300 Hz and 8 kHz

b. Words with weak high-frequency content

i. Bandpass filtered between 300 Hz and 16 kHz

ii. Bandpass filtered between 300 Hz and 8 kHz

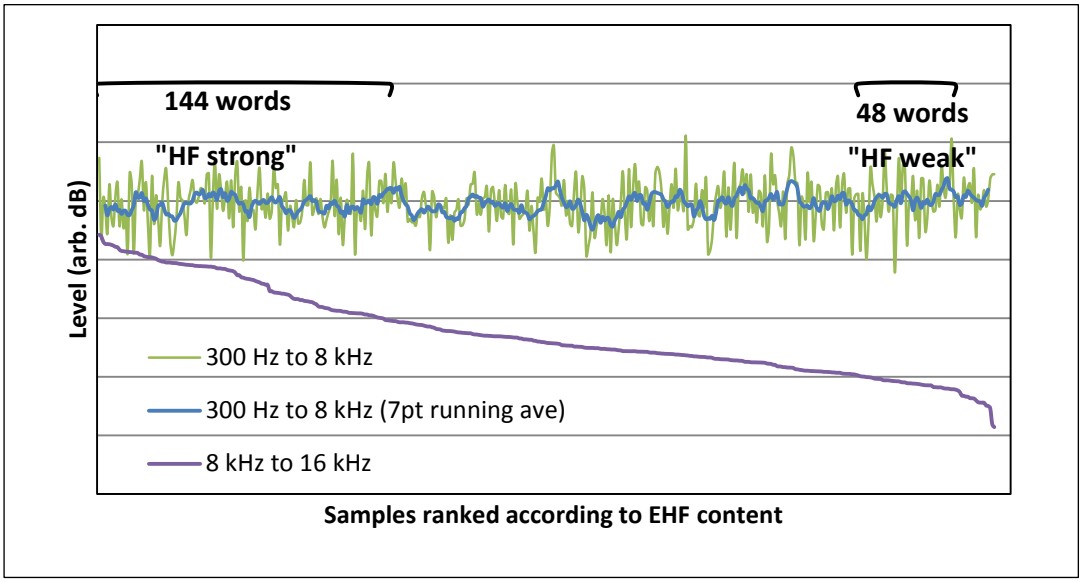

Figure 96. Words from the broadband speech corpus as described in Best et al. (2005) ranked according to the level of spectral energy between 8 and 16 kHz. The level of information between 300 Hz and 8 kHz, shown in blue, did not vary as a function of content at 8 – 16 kHz. The 144 words with the greatest content at 8 – 16 kHz were selected as the strong high-frequency content stimulus set ("HF strong") and the 48 words with the lowest level of spectral information at 8 – 16 kHz formed the weak high-frequency content stimulus set ("HF weak").

9.2.2.2.5 System calibration

Calibration of the each speaker was performed to ensure presentation levels were accurate and consistent across speakers so that other spectral coloration effects could not be used to identify individual speakers in the absence of reliable localisation information. Speaker sound pressure output level was measured as a function of frequency at the centre of the array (i.e. at the location of the participant's head) in response to the presentation of a broadband noise stimulus. Recordings were made using a calibrated Brüel & Kjær 4942 ½" diffuse field microphone (Brüel & Kjær, Nærum, Denmark) and PULSE LabShop recording and analysis software (version 16, Brüel & Kjær, Nærum, Denmark) run through an HP Compaq nx6120 laptop (Hewlett Packard, Palo Alto, CA). An A-weighted Fast Fourier Transform (FFT) of each speaker output was calculated in PULSE LabShop using a bandwidth of 200 kHz, a df of 125 Hz and an averaging time window of 4 seconds. Based on the FFT recorded, inverse

FFT filters were applied in the UC Directional Hearing Array software to flatten the frequency response of the output of each speaker. The FFT measurement process was repeated and an additional inverse filter applied to the 300 Hz to 8 kHz bandpass filtered stimuli to maintain an overall sound output level that was the same as that for the broadband noise and speech stimuli.

The output level of each of the 12 speaker channels in response to a continuous noise with a bandwidth of 300 Hz to 16 kHz was checked using a sound level meter (IVIE IE33J, Ivie Technologies Inc., Springville, UT). Again, measurements were made from the centre of the speaker array at the intended position of the participant's head. A correction factor based on the sound level recorded for each channel was then applied to each speaker channel in the UC Directional Array software to set the output level at the desired presentation level.

9.2.3 Procedure

9.2.3.2 Pure-tone audiometry

Following otoscopic assessment to rule out occlusion of the EAC or conductive abnormalities, pure-tone thresholds were measured in 5 dB steps using the modified Hughson-Westlake technique. Air-conduction thresholds were measured at 0.25, 0.5, 1, 2, 4, 6, 8, 9, 10, 11.2, 12.5, 14 and 16 kHz in each ear. Where air-conduction thresholds were greater than 20 dB HL at any frequency(s) from 0.5 - 4 kHz, bone-conduction thresholds were measured to distinguish between conductive and sensorineural hearing losses. "No response" was recorded when the participant did not respond to a tone presented at the limits of the audiometer for the frequency and ear being tested. As described in section 9.3.1, pure-tone thresholds were assessed for eligibility for either the EHF hearing loss or normal hearing test groups, and participants who met the inclusion criteria were invited to participate in the localisation assessments described below.

9.2.3.3 Localisation testing

Localisation of each of the six stimulus sets created by the three stimuli and two filter conditions were tested with the speaker array in four orientations; frontal horizontal plane, lateral horizontal plane, frontal vertical plane, and lateral vertical plane (see Figure 94 a – d). For all conditions the participant remained sitting on an adjustable stool in the centre of the

room. As shown in Figure 94, in the frontal horizontal condition, the participant was seated facing the centre speaker, and in the lateral horizontal condition they were turned so that they were side-on to the speakers. In the vertical plane conditions, the arc of speakers was turned to the vertical orientation and the participant sat either facing the arc (frontal vertical), or with the arc to one side of them, in line with their ear (lateral vertical). The height of the stool was adjusted to ensure the centre speaker was maintained at ear level.

Participants were verbally given the instructions that their task was to identify which speaker the sound they would hear was presented from and to call out the number marked on that speaker. They were asked to focus on a dot marked straight-ahead on the wall between presentations, but advised that they could turn to the speaker location after the sound played if they wished. Guessing was encouraged in cases where the participant was uncertain of the location, but the need to be as fast and accurate as possible was also stated. The speaker number reported was then recorded in the software by the tester. Recording the response triggered the presentation of the next stimulus.

The stimulus presentation level was varied across four different intensities; 73.00, 74.33, 75.67, and 77.0 dB A, that provided an average level of 75 dB A. The purpose of roving the stimulus presentation level was to counteract effects of slight head or body movements by the participant between presentations.

Prior to each change in the type of stimulus or the speaker array orientation, four practice stimuli were presented and the participant was asked to identify the speaker location for each stimulus. No feedback on accuracy was provided. The four practice stimuli for each of the speech and noise stimulus sets consisted of one stimulus presentation at each intensity level. Two of the stimuli in each set had a bandwidth of 300 Hz – 8 kHz and two had a bandwidth of 300 Hz to 16 kHz. The presentation location of each practice stimulus was selected randomly, with each stimulus in the set coming from a different speaker channel. Practice speech stimuli were all chosen from the “HF strong” stimulus set.

In each speaker array orientation, 96 noise burst stimuli were presented; 48 with a bandwidth of 300 Hz – 8 kHz and 48 with a bandwidth of 300 Hz to 16 kHz. For each filter bandwidth, 12 of the 48 stimuli were randomly presented at each of the four presentation levels and four presentations were made at each of the 12 speaker channels. Ninety-six speech stimuli were also presented in each speaker array orientation. Again, half of these presentations were of speech filtered using an upper cut-off frequency of 8 kHz and the other half were filtered with

an upper cut-off frequency of 16 kHz. In each filter condition, 36 of the 48 stimuli were categorised as "HF strong" speech stimuli and 12 were "HF weak" stimuli. For the "HF strong" stimuli, nine presentations were made at each intensity level and three presentations (each at a different intensity) at each speaker channel. The 12 "HF weak" stimuli were presented three times at each level and once at each speaker channel.

The order in which stimulus conditions were presented was counterbalanced across participants to avoid effects of practise or fatigue. To minimise the need to physically move the speaker array, participants were tested with either both horizontal plane conditions and then both vertical plane conditions, or vice versa. The participant was given a short rest period in the middle of the test session while the tester changed the speaker orientation.

9.2.4 Data analysis

9.2.4.1 Mean localisation error

Localisation errors were calculated as the difference in degrees between the speaker at which the stimulus was presented and the speaker at which the participant selected as the presentation location. Mean localisation errors were calculated for each stimulus type and low-pass filter frequency combination in each speaker array orientation. The effect of each experimental variable was assessed using a five-way mixed factor ANOVA performed using the within subjects factors stimulus type (HF strong speech, HF weak speech, noise), filter bandwidth (300 Hz – 8 kHz, 300 Hz – 16 kHz), speaker orientation (frontal horizontal, lateral horizontal, frontal vertical, lateral vertical), speaker location (1-13, with data from dummy speaker 10 removed), and the between subjects factor; hearing status (normal hearing, EHF hearing loss). Post-hoc pairwise comparisons were performed with Bonferroni corrections for multiple comparisons and significant results were defined as those where $p < .05$. Prior to analyses of mean error, "large" errors (defined below) were always removed from the data set.

9.2.4.2 Large errors

Large errors were defined as those greater than 90°, reflecting primarily front-back or up-down confusions. These large errors were removed from the main data set and analysed separately as they reflect a different type of error to the smaller inaccuracies in localisation.

The percentage of large errors was calculated for each stimulus condition based on the number of large errors that occurred as a proportion of the number of stimulus presentations. Although front-back and up-down errors cannot occur in the frontal horizontal plane, large errors were calculated for this condition as well as the other three to avoid any bias in the mean error data that could result comparatively larger mean errors in the frontal horizontal plane. A second five-way mixed factor ANOVA was performed to assess the effect of stimulus and speaker orientation variable on large errors. Dependent variables were the same as those described for mean localisation error, with the exception of speaker location, which was removed based on the fact that large errors are not expected to occur at all locations. Again, post-hoc pairwise comparisons were performed with Bonferroni corrections for multiple comparisons and "significant" results were defined as those where $p < .05$.

9.2.4.3 Relationship between hearing thresholds and mean error

Regression analyses were performed to assess the relationship between mean hearing thresholds at 0.25 – 8 kHz and 9 – 16 kHz and mean localisation error in each stimulus condition for each group. Prior to analysis, large errors were removed as described above, as were outlier values, defined as values greater than 2.2 times the 75^{th} percentile value or less than 2.2 times the 25^{th} percentile value for each stimulus condition data set. R^2 values were considered significant when the associated *p* value was less than .05.

All statistical analyses were performed using IBM SPSS version 22 (2013, IBM Corp., Armonk, NY).

9.3 Results

A summary of the means and standard deviations of the localisation error recorded for each stimulus combination in each of the four speaker array orientations is provided in Table 29.

Table 29. Mean localisation error (degrees) according to hearing group for each stimulus in each of the four speaker array orientations.

	Stimulus type and filter cut-off frequency					
	Noise		HF strong speech		HF weak speech	
Array orientation	8 kHz mean *(SD)*	16 kHz mean *(SD)*	8 kHz mean *(SD)*	16 kHz mean *(SD)*	8 kHz mean *(SD)*	16 kHz mean *(SD)*
EHF hearing loss group						
Frontal horizontal	5.67° *(6.37)*	4.55° *(5.50)*	2.95° *(4.63)*	2.21° *(4.09)*	3.04° *(6.44)*	2.88° *(6.06)*
Lateral horizontal	9.11° *(12.57)*	8.52° *(10.86)*	4.98° *(7.70)*	4.46° *(7.11)*	5.00° *(9.37)*	5.00° *(9.12)*
Frontal vertical	20.95° *(16.16)*	18.49° *(14.65)*	18.03° *(12.00)*	15.96° *(13.01)*	18.15° *(18.22)*	16.41° *(15.91)*
Lateral vertical	10.80° *(9.27)*	9.92° *(7.62)*	9.89° *(9.92)*	9.34° *(10.26)*	11.74° *(13.69)*	9.67° *(12.44)*
Normal hearing group						
Frontal horizontal	5.65° *(6.48)*	5.56° *(6.47)*	2.48° *(4.56)*	2.08° *(4.25)*	3.04° *(6.31)*	2.01° *(5.12)*
Lateral horizontal	8.89° *(11.45)*	8.87° *(10.73)*	5.47° *(8.22)*	4.89° *(7.73)*	5.81° *(4.95)*	7.95° *(9.18)*
Frontal vertical	19.24° *(15.45)*	18.32° *(15.43)*	17.74° *(14.50)*	14.15° *(13.15)*	18.32° *(17.53)*	18.87° *(16.12)*
Lateral vertical	10.24° *(9.84)*	9.93° *(8.94)*	6.29° *(6.77)*	6.63° *(7.04)*	7.28° *(11.76)*	6.52° *(10.07)*

9.3.1 Effect of hearing status

The mean localisation error across all experimental conditions was slightly, but not significantly higher for the EHF hearing loss group (9.51°, *SD* = 12.19°) compared to the normal hearing group (8.75°, *SD* = 11.87°). While no significant differences in mean error between groups were present when examined in the frontal horizontal, lateral horizontal, and frontal vertical orientations, mean error in the lateral vertical plane was significantly greater for the hearing loss group (10.23°, *SD* = 10.74) than for the normal hearing group (7.82°, *SD* = 9.36) ($F(1, 44) = 13.35$, $p = .001$) (Figure 97).

The overall mean percentage of large errors (> 90°) was not significantly different between participants in the EHF hearing loss group (*M* = 2.63%, *SD* = 6.30) and the normal hearing

group (M = 2.15%, SD = 5.54) (p = .52), nor were significant differences found between groups when localisation in each of the planes was examined individually (Figure 98).

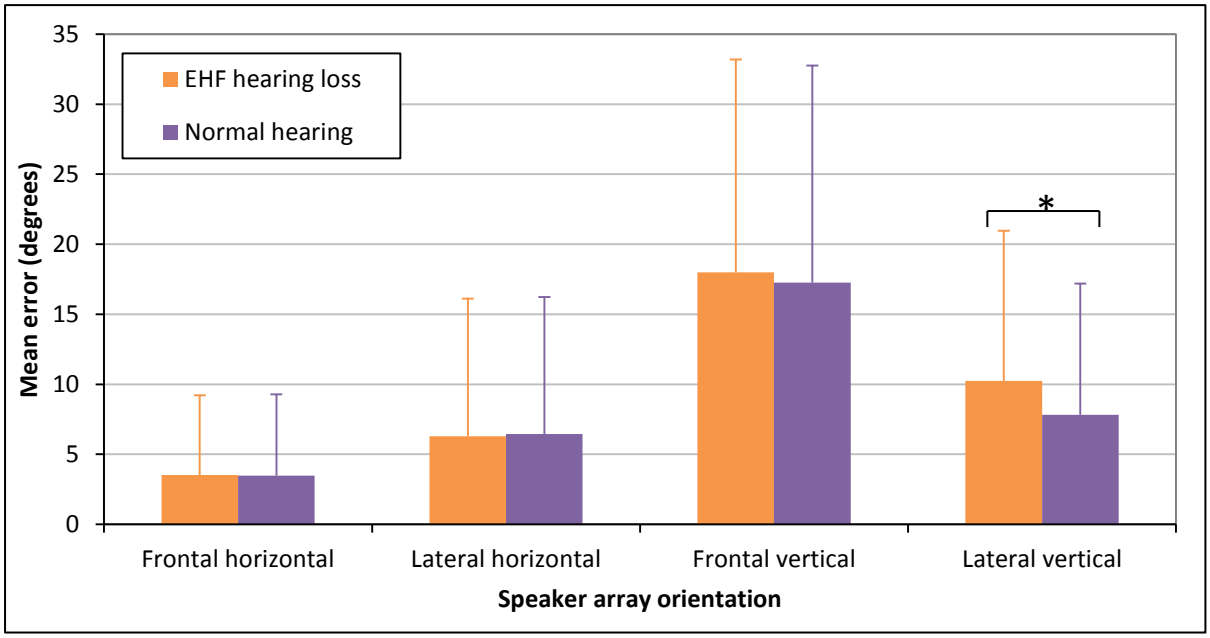

Figure 97. Mean localisation error for EHF hearing loss and normal hearing participants in each of the four planes tested. Error bars show standard deviation. Significant differences between groups (p < .05) are marked with an asterisk.

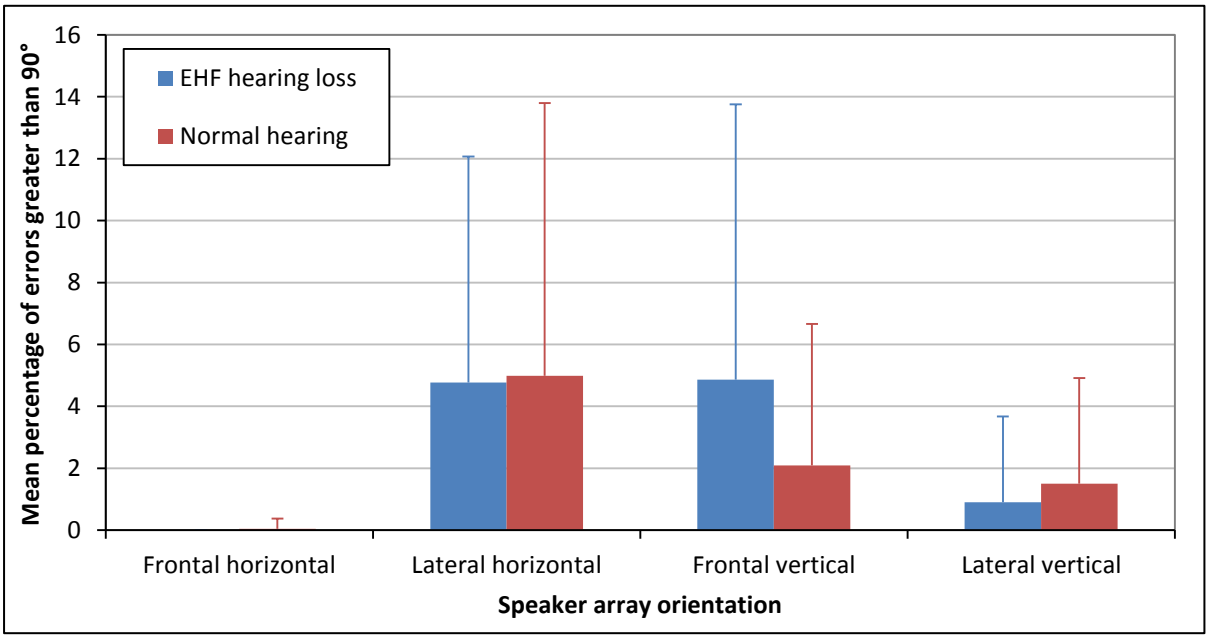

Figure 98. Mean percentage of large cross-quadrant localisation errors for EHF hearing loss and normal hearing participants in each of the four planes tested. Error bars represent standard deviation. No differences between groups were present in any of the four array orientations.

9.3.2 Effect of speaker array orientation

9.3.2.1 Mean localisation error

Localisation performance differed significantly across the four array orientations tested ($F(3, 132) = 149.52$, $p < .001$) and pairwise comparisons indicated that mean error in each condition differed significantly from each other condition (all $p < .001$). As shown in Figure 98, mean localisation error across all stimulus conditions was lowest when speakers were in the frontal horizontal plane (3.49°, *SD* = 5.76°) and highest when speakers were in the frontal vertical position (17.64°, *SD* = 15.35°). In the lateral horizontal and lateral vertical planes mean localisation error was 6.36° (*SD* = 9.80) and 9.02° (*SD* = 10.14), respectively.

9.3.2.2 Rate of large errors

A statistically significant effect of speaker array orientation on the percentage of errors greater than 90° was detected ($F(3, 132) = 9.89$, $p < .001$). As expected, the mean percentage of large errors across all participants was significantly lower in the frontal horizontal orientation (*M* = .02%, *SD* = .23) than in all other orientations (all $p < .05$) with only two normal hearing participants making a single large error each (Figure 97). The mean percentage of large errors was highest in the lateral horizontal plane (*M* = 4.87%, *SD* = 8.09), although this percentage was not significantly different to the mean percentage of large errors recorded in the frontal vertical plane (*M* = 3.48%, *SD* = 7.19; $p = 1.00$). In the frontal vertical plane error was significantly higher than that for the lateral vertical plane ($p = .03$).

9.3.3 Effect of filter cut-off frequency

9.3.3.1 Mean localisation error

Overall, average localisation accuracy was significantly better when the upper cut-off frequency of the bandpass filter was at 16 kHz (*M* = 8.62°, *SD* = 11.50) compared to when stimuli were low-pass filtered at 8 kHz (*M* = 9.63°, *SD* = 12.52) ($F(1, 44) = 42.44$, $p < .001$). The advantage of increased EHF spectral information was evident when localisation was tested in all speaker orientations (all $p < .05$), however post-hoc comparisons of mean error in the lateral horizontal plane showed that when the data was analysed for each hearing group separately, no significant difference in accuracy depending on the filter cut-off frequency was present for either group. No significant interactions were documented between filter cut-off

frequency and hearing group either for data across all speaker orientations ($F(1, 44) = .43$, $p = .52$), or when data was analysed for each speaker array individually. However, as shown in Figure 99, pairwise comparisons showed that in the lateral vertical plane the advantage of the 16 kHz filter over the 8 kHz filter frequency was significant for the EHF hearing loss group ($p = .02$), but not for the normal hearing group ($p = .61$).

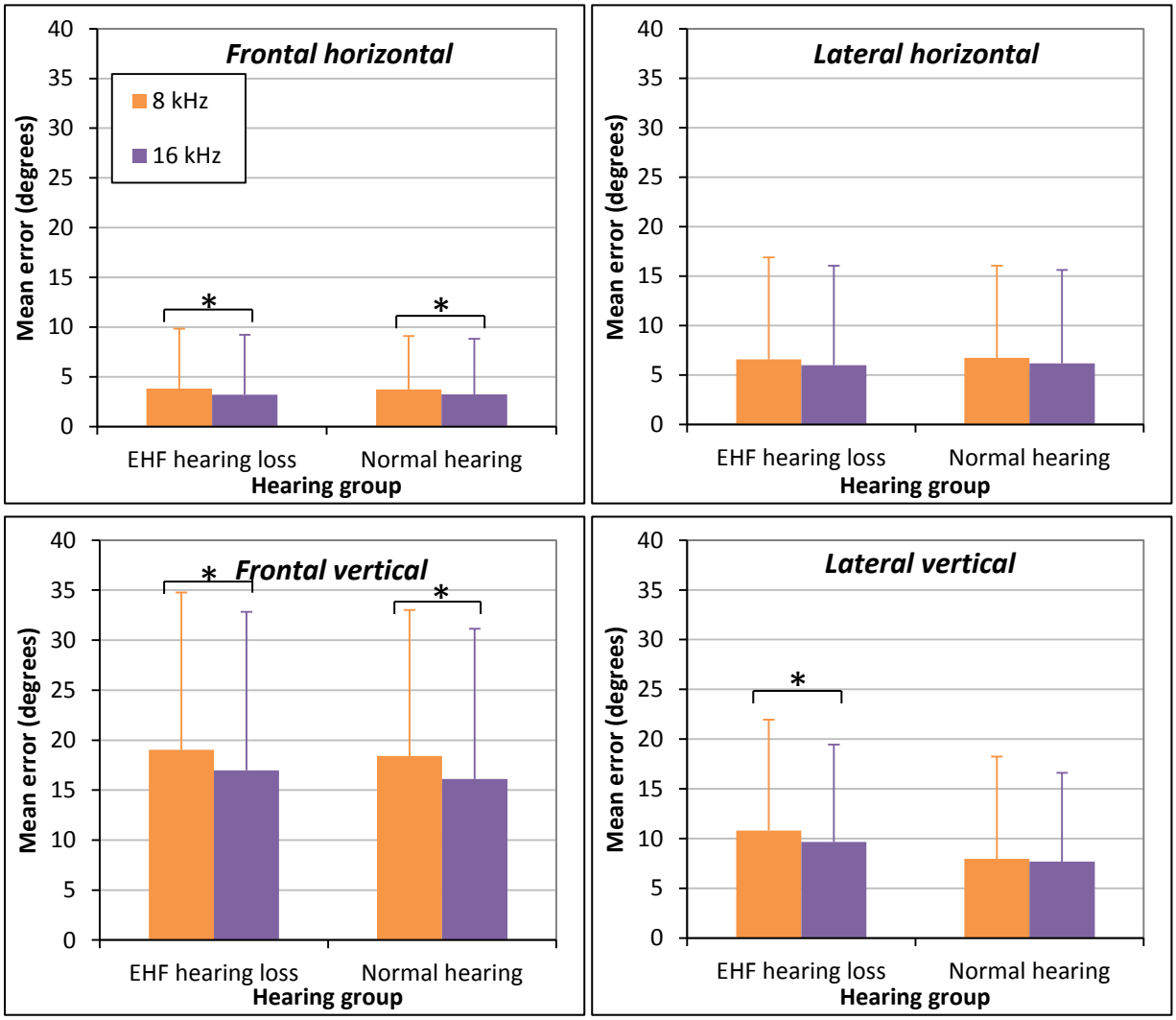

Figure 99. The effect of low-pass filter cut-off frequency on mean localisation error for EHF hearing loss and normal hearing participants in each of the four planes tested. Significant differences ($p < .05$) in mean error depending on filter cut-off frequency are marked with asterisks. Error bars show standard deviation.

9.3.3.2 Rate of large errors

In contrast to the mean error results, the assessment of the mean percentage of large errors across all array orientations showed no difference between stimuli filtered at 16 kHz (M =

2.27%, *SD* = 5.79) and at 8 kHz (*M* = 2.52%, *SD* = 6.08 (*p* = .10). As shown in Figure 100, although the rate of large errors was higher when stimuli were low-pass filtered at 8 kHz compared to 16 kHz in the lateral horizontal, frontal vertical, and lateral vertical planes, the differences were not significant for any speaker orientation. No significant interactions were found between filter cut-off frequency and hearing group in any plane.

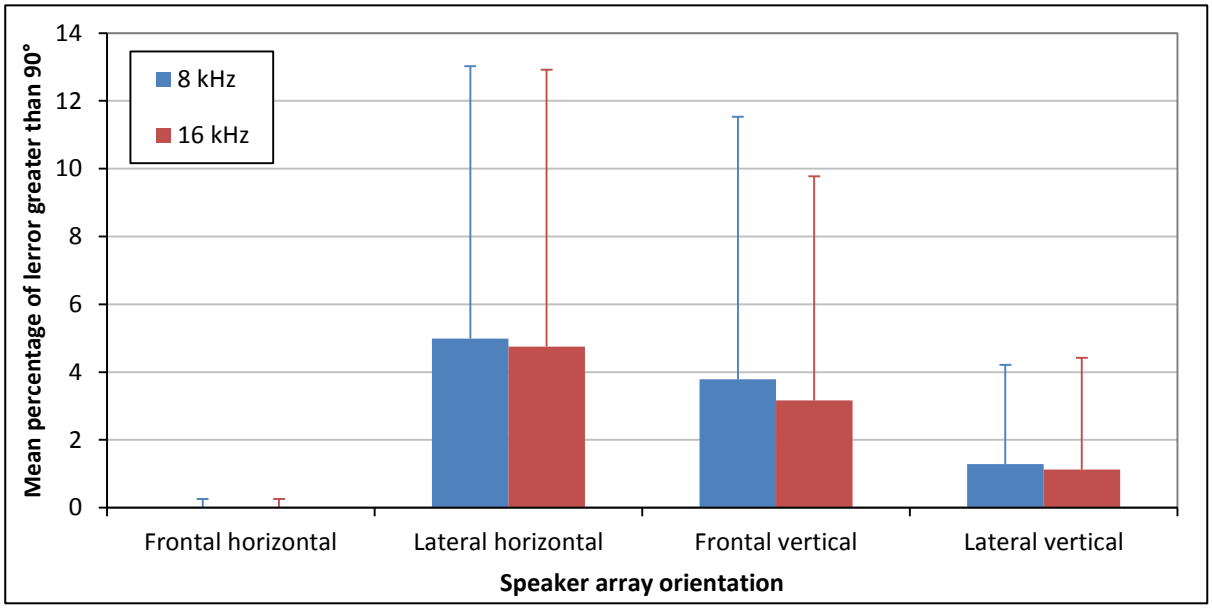

Figure 100. Mean percentage of large localisation errors for stimuli low-pass filtered at 8 kHz and at 16 kHz across all participants in each of the four planes. Error bars represent standard deviation.

9.3.4 Effect of type of stimulus

9.3.4.1 Mean localisation error

Analysis of mean error across all orientations showed a strong, significant effect of stimulus type ($F(2, 88) = 67.73$, $p < .001$). Pairwise comparisons indicated that mean localisation error across all conditions is best when speech with strong EHF content was used (*M* = 7.96°, *SD* = 10.54), followed by speech with weak EHF content (*M* = 8.48°, *SD* = 13.05), and that localisation was poorest when noise stimuli are presented (*M* = 10.94°, *SD* = 12.17). The overall effect of stimulus was not influenced by hearing status ($F(2, 88) = 1.20$, $p = .31$).

In both horizontal orientations and in the frontal vertical orientation, mean error for noise stimuli was significantly higher than for either type of speech stimulus (all $p < .05$). In the lateral vertical plane, mean error was again significantly higher with noise stimuli than with HF strong speech stimuli ($p = .001$), but no difference in performance was found between the noise and HF weak speech conditions ($p = .06$). In the frontal horizontal and lateral vertical

planes, error was significantly lower with HF strong speech stimuli compared to HF weak speech stimuli (both $p = .03$), however in the lateral horizontal and frontal vertical planes no difference in mean error depending on the strength of EHF content in speech stimuli was evident (lateral horizontal: $p = .91$, frontal vertical: $p = .60$).

The effect of stimulus type was significantly influenced by hearing status in only the lateral vertical plane ($F(2, 88) = 7.28$, $p = .001$). In response to both types of speech stimuli presented in the lateral vertical plane, participants with normal hearing localised significantly more accurately than participants in the EHF hearing loss group ($p < .001$) (Figure 101).

No significant interactions were found between stimulus type and filter frequency across speaker array orientations ($F(2, 88) = .34$, $p = .71$), or for any individual orientation. In the frontal horizontal plane there was a significant three-way interaction between hearing group, stimulus type and filter frequency ($F(2, 88) = 6.62$, $p = .002$), however pairwise comparisons showed no significant differences between groups for any stimulus-filter combinations.

9.3.4.2 Rate of large cross-quadrant errors

The significant overall effect of stimulus type on large errors ($F(2, 88) = 7.95$, $p = .001$) paralleled the results found for mean error, with the highest percentage of large errors found for noise stimuli (3.21%, $SD = 7.02$). Compared to noise stimuli, the percentage of large errors across both groups was significantly lower for HF strong speech ($M = 1.89\%$, $SD = 4.83$, $p = .01$) and HF weak speech stimuli ($M = 2.08\%$, $SD = 5.69$, $p = .04$), however no significant difference was evident between the two types of speech stimuli ($p = .70$). The effect of stimulus type on large errors differed significantly across array orientations ($F(6, 264) = 4.84$, $p < .001$) (Figure 102). No differences in mean large error rates with different stimuli were evident in the frontal horizontal or lateral vertical planes. In the lateral horizontal plane, the error rate for noise was higher than that for either HF strong ($p = .003$) or HF weak speech ($p = .04$), with no difference between the two sets of speech stimuli ($p = 1.00$). Finally, in the frontal vertical plane, the mean percentage of large errors was again higher for noise stimuli than for HF strong speech ($p = .04$), however the error rate for HF weak speech was not significantly different from either if the other conditions. Again, hearing status group did not influence the effect of stimulus type of large errors in any array orientation. No significant interactions were identified overall ($F(2, 88) = .96$, $p = .43$), or in any array orientation between stimulus type and filter cut-off frequency.

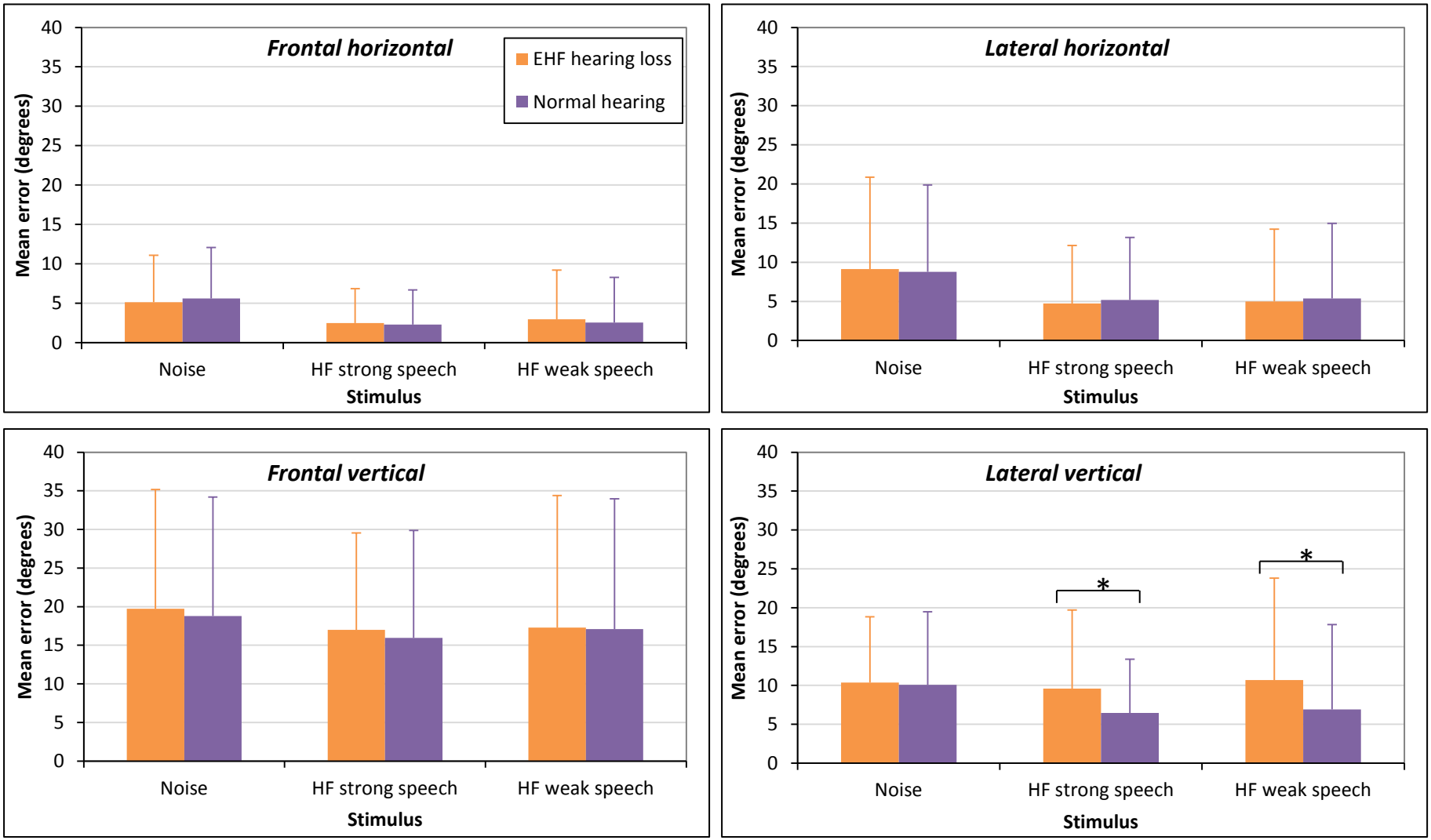

Figure 101. Mean localisation error as a function of the type of stimulus and hearing group. Data are presented for each speaker array orientation tested. Error bars represent standard deviation. Significant differences ($p < .05$) in mean error between groups are marked with an asterisk.

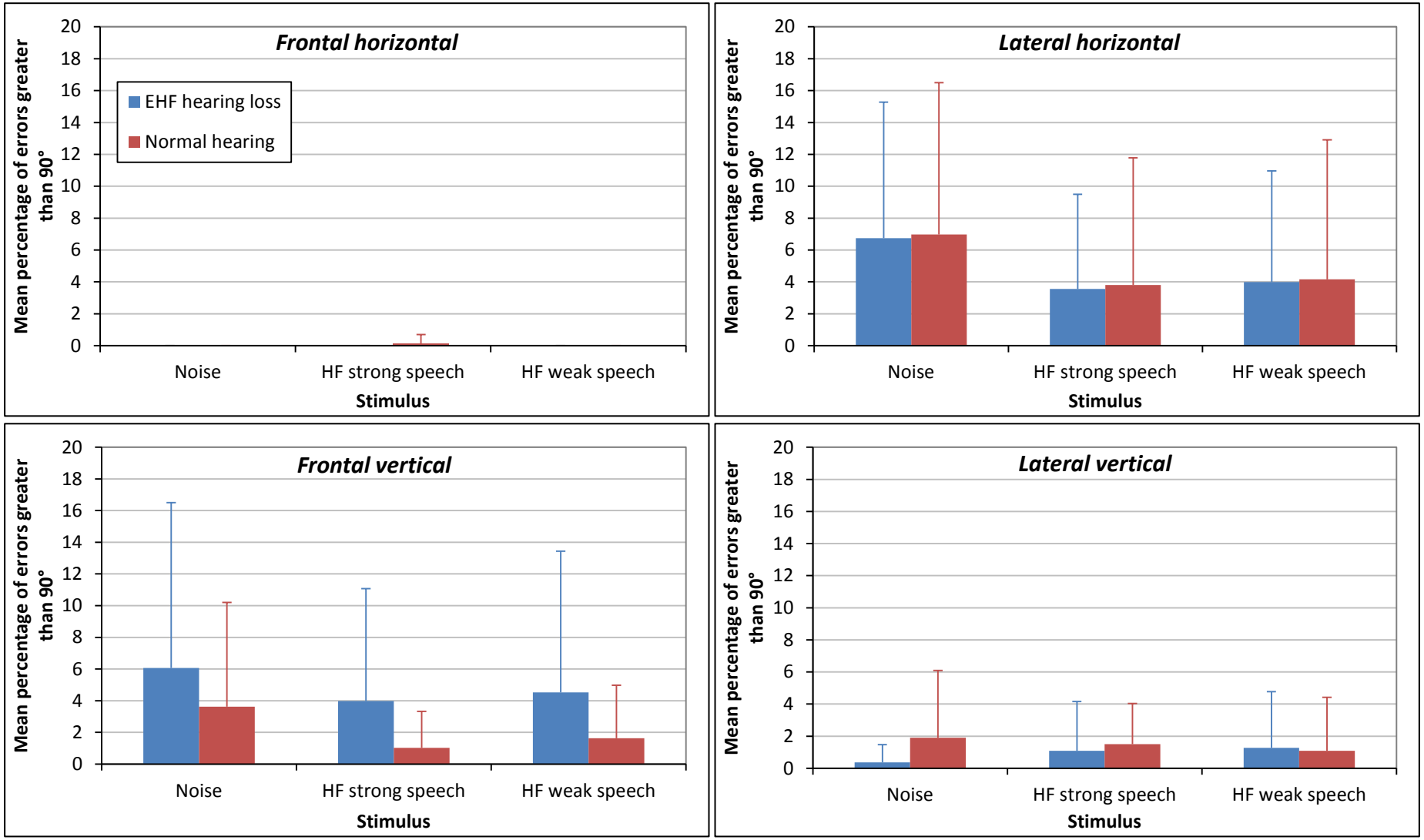

Figure 102. Mean percentage of large (> 90 degrees) errors as a function of the type of stimulus and the hearing group. Data are presented for each speaker array orientation tested. Error bars represent standard deviation. No differences between groups reached statistical significance.

9.3.5 Effect of speaker location

In the frontal horizontal condition, (Figure 103) mean localisation error for speakers at the centre of the array tended to be lower than that for more peripheral speakers. Mean error was lowest for the speaker located at -15° (.08°, *SD* = .55) and highest for stimuli presented through the speaker located at 90° (8.47°, *SD* = 7.74). A significant interaction between speaker location and hearing group was present ($F(11, 484) = 2.92$, $p = .001$). Post-hoc pairwise comparisons showed a significant difference between the two groups for the speaker located at 90° only ($p = .02$), where mean error was 10.10° (*SD* = 7.53) for the EHF hearing loss group and 6.84° (*SD* = 7.63) for the normal hearing group.

In the lateral horizontal plane, mean error was significantly influenced by speaker location ($F(11, 484) = 47.98$, $p < .001$) and tended to be lower around 0° than at locations further from the front-centre position (Figure 103). Mean error was greatest when stimuli were presented at 120° (17.58°, *SD* = 15.37), where error was significantly higher than every other speaker except that at 150°. Although error was highest at the two rear-most speakers when large errors were included, following their removal, mean error for the speakers at 165 and 180° was significantly lower than that for speakers at 120 and 150°. The effect of speaker location on mean error varied depending on hearing ($F(11, 484) = 2.12$, $p = .02$). At 15 and 45° error was significantly higher for normal hearing participants, and at the 150° speaker mean error was significantly higher for the group with EHF hearing loss.

The effect of speaker position on localisation accuracy was less clear when the array was in the vertical plane. While overall mean error was highest at 90°; the speaker directly above the participants head (*M* = 22.95°, *SD* = 16.91), error at this location was significantly higher than mean error for four, relatively spread out, other speaker locations (-90°, 0°, 30°, and 60°). Similarly, mean error was lowest for the speaker at 0°, but this was significantly different to only five of the remaining 11 locations (-45°, -30°, -15°, 75°, and 90°). A significant interaction between speaker location and hearing group was present ($F(11, 484) = 3.66$, $p < .001$), with contrasting effects of hearing group depending on speaker location. As shown in Figure 102, at two central locations (0° and -15°), mean error was significantly higher for the EHF hearing loss group compared to the normal hearing group ($p = .02$). In contrast, at 75° error was significantly higher for the normal hearing group ($p = .001$). The asymmetrical effect of each hearing group on speaker location in this orientation and in the lateral horizontal plane was not found in the frontal horizontal or lateral vertical orientations, however, visual inspection of the data shows similar non-significant trends.

Finally, in the lateral vertical plane, post-hoc investigation of the significant effect of speaker location ($F(11, 484) = 13.03$, $p < .001$), showed a trend for mean error to increase as speaker location shifted from -90°, directly below the participant, up to a maximum at -30°. Mean error declined as stimuli were presented at speakers progressively higher than -30°, down to a minimum at 90°. No significant interaction was found between speaker location and hearing group ($F(11, 484) = 1.77$, $p = .06$).

9.3.5.1 Interactions between speaker location and filter cut-off frequency

The effect of speaker location was significantly influenced by the low-pass filter cut-off frequency in the frontal horizontal ($F(11, 484) = 5.55$, $p < .001$), frontal vertical ($F(11, 484) = 9.70$, $p < .001$), and lateral vertical planes ($F(11, 484) = 10.70$, $p < .001$). In the frontal horizontal plane, error was significantly greater for stimuli filtered to an upper limit of 8 kHz compared to 16 kHz for speakers located towards the ends of the array (Figure 104). At -45° this trend was reversed and error was significantly higher for stimuli filtered at 16 kHz ($p = .03$). No significant effect of hearing group on the interaction between filter frequency and speaker location was found in the frontal horizontal plane ($F(11, 484) = 1.21$, $p = .28$).

In both vertical planes, mean error was significantly lower for the 16 kHz filtered stimuli than the 8 kHz stimuli for the speakers close to the centre of the array. Interestingly, this pattern was reversed at -75° and 75° in both vertical orientations, as well as at -90° in the lateral vertical orientation, and error was significantly higher when the higher filter cut-off frequency of 16 kHz was used (Figure 104). The relationship between low-pass filter cut-off and speaker location was not influenced by hearing status in either vertical plane.

9.3.5.2 Interactions between speaker location and type of stimulus

A significant interaction between speaker location and stimulus type was documented for the frontal horizontal ($F(22, 968) = 8.24$, $p < .001$) and lateral horizontal planes ($F(22, 968) = 9.08$, $p < .001$). In the frontal horizontal plane, mean localisation error was significantly greater for noise compared to both speech stimuli, with no difference between HF strong and HF weak speech at the majority of speakers, the exceptions being 0°, 15°, and 75°. In the lateral horizontal plane no significant effect of stimulus type on mean error was found at 0°, 165°, or 180°, where overall mean error was low following removal of large errors. As in the frontal horizontal plane, mean localisation error was greater for noise compared to both

speech stimuli with no difference between the two speech stimuli at the majority of speaker locations where an effect of stimulus was present. No significant three-way interaction was found between stimulus type, speaker location, and hearing in either horizontal plane.

In the frontal vertical plane, no significant interaction between speaker location and stimulus type was present ($F(22, 968) = 1.35$, $p = .13$), however, a significant interaction was found between stimulus, location, and hearing ($F(22, 968) = 1.91$, $p = .01$). Post-hoc analyses showed that statistically significant differences in mean error between groups were present for noise stimuli for speakers located at -15°, 0°, 15°, and 60°. The direction of the effect depended on speaker location, with higher mean error recorded for the EHF hearing loss group for speakers at -15°, 0°, 15°, but the opposite effect at the 60° location. Similarly, for HF strong speech stimuli, significant differences between groups showing more accurate performance for the normal hearing group were present for speakers positioned at 0° and 15°, but at 30°, 60°, and 75°, mean error was higher for the normal hearing group. For HF weak speech stimuli there was a significant difference between groups for the speaker located at 75° only, where mean error was again higher for the normal hearing group.

A significant interaction between stimulus type, filter frequency, and speaker location was also evident in the frontal vertical plane ($F(22, 968) = 2.31$, $p = .001$). Pairwise comparisons showed that for noise stimuli a significant advantage of 16 kHz filtered stimuli over 8 kHz filtered stimuli was present at the central speakers at -15°, 0°, and 15°, but at the speaker located at -75°, mean error increased in the 16 kHz condition. Similar patterns with improved performance with wider bandwidth for centre speakers were found for HF strong speech stimuli at all locations from -30° to 30°, and for HF weak speech stimuli at -30° and at 0°. Again, the relationship reversed and higher mean error was recorded for the 16 kHz stimuli over the 8 kHz filtered stimuli at the more peripheral locations of -75° and -45° for HF strong speech stimuli and 75° for HF weak speech stimuli.

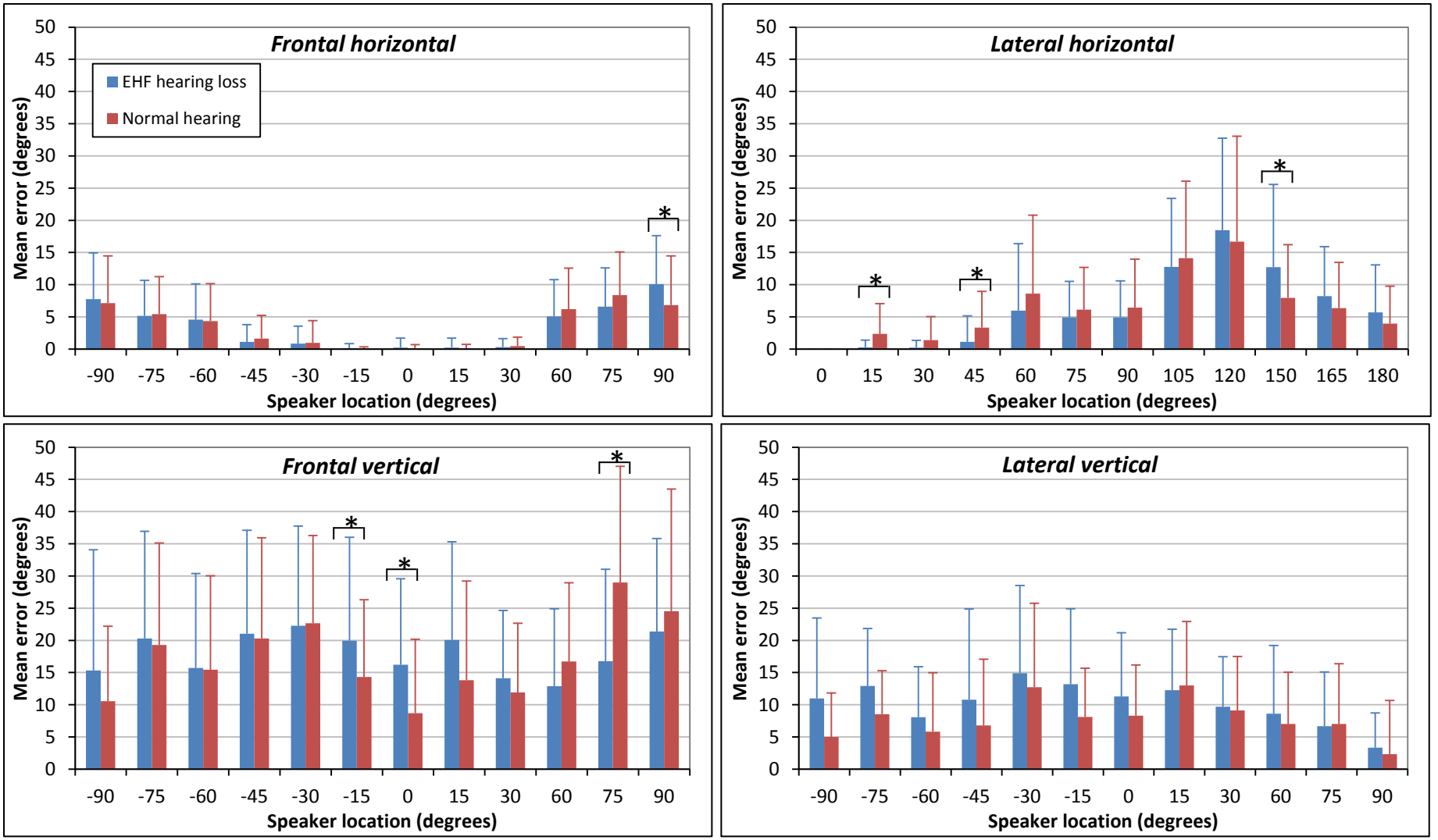

Figure 103. Mean localisation error as a function of speaker location and hearing group. Data are presented for each speaker array orientation tested. No data is presented for the dummy speaker location; 135° in the lateral horizontal location, and 45° in all other orientations. Error bars represent standard deviation. Significant differences ($p < .05$) in mean error between groups are marked with an asterisk.

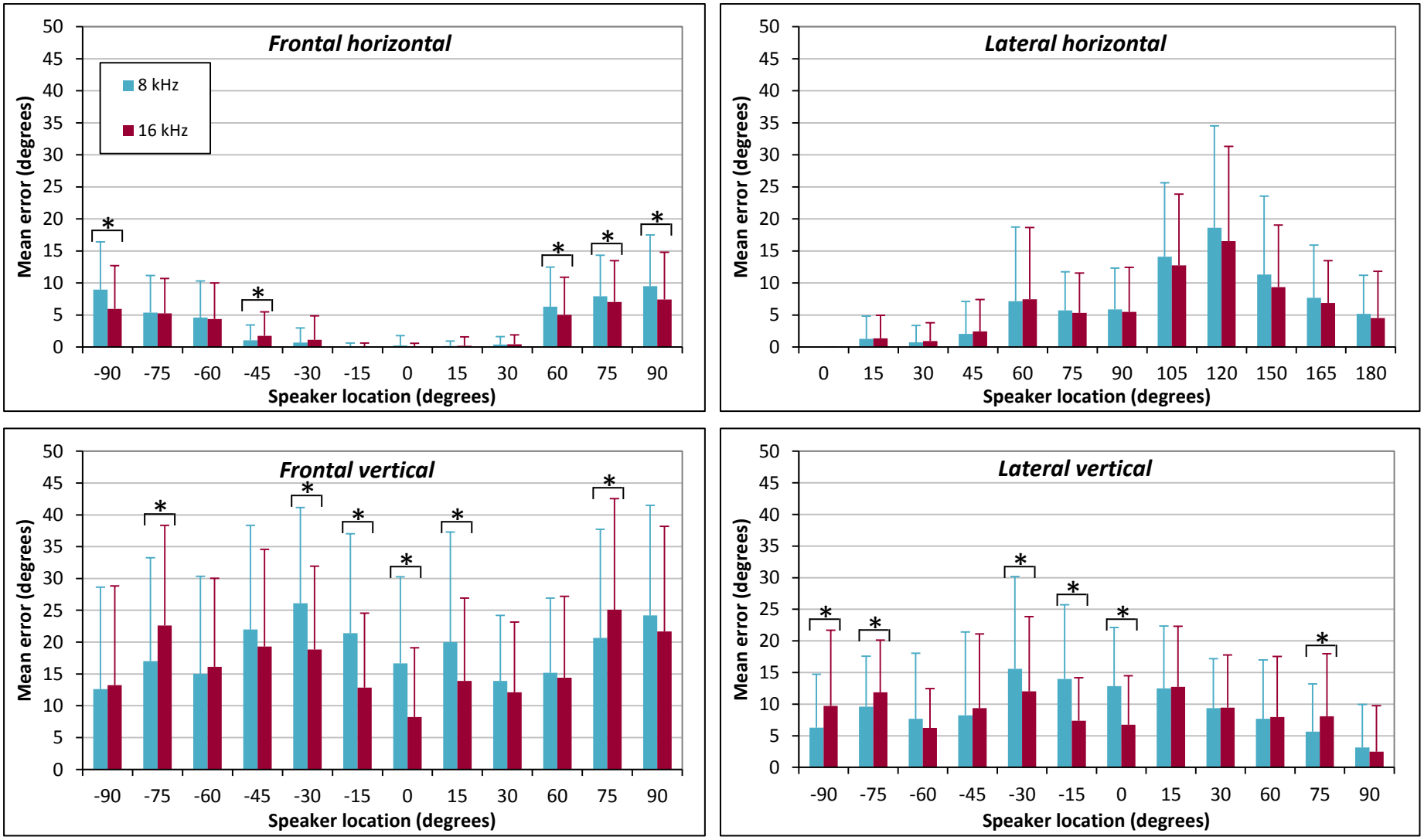

Figure 104. Mean localisation error as a function of speaker location and low-pass filter cut-off frequency. Data are presented for each speaker array orientation tested. No data is presented for the dummy speaker location; 135° in the lateral horizontal location, and 45° in all other orientations. Error bars represent standard deviation. Significant differences ($p < .05$) in mean error between groups are marked with an asterisk.

9.3.6 Relationship between hearing thresholds and mean localisation error

Results of regression analyses performed for each stimulus condition in each speaker array orientation are presented in Table 30.

Table 30. R^2 values showing the relationship between mean error (in degrees) in each condition and the mean hearing thresholds of each group at 0.25 – 8 kHz and 9 – 16 kHz.

	Normal hearing		EHF hearing loss	
Condition	0.25 – 8 kHz	9 – 16 kHz	0.25 – 8 kHz	9 – 16 kHz
Frontal horizontal				
Noise 8 kHz	.086	.057	.002	.014
Noise 16 kHz	.052	.204*	.002	.047
HF strong speech 8 kHz	.001	.115	.014	.003
HF strong speech 16 kHz	.007	.206*	.052	.085
HF weak speech 8 kHz	.001	.156	.032	.019
HF weak speech 16 kHz	.002	.190*	.221*	.021
Lateral horizontal				
Noise 8 kHz	.020	.086	.002	.012
Noise 16 kHz	.029	.045	.002	.000
HF strong speech 8 kHz	.023	.097	.018	.047
HF strong speech 16 kHz	.023	.080	.093	.198*
HF weak speech 8 kHz	.002	.136	.000	.002
HF weak speech 16 kHz	.022	.046	.000	.049
Frontal vertical				
Noise 8 kHz	.124	.048	.008	.080
Noise 16 kHz	.000	.020	.003	.008
HF strong speech 8 kHz	.001	.034	.013	.000
HF strong speech 16 kHz	.000	.076	.014	.001
HF weak speech 8 kHz	.005	.123	.008	.007
HF weak speech 16 kHz	.020	.064	.014	.089
Lateral vertical				
Noise 8 kHz	.090	.014	.009	.025
Noise 16 kHz	.017	.022	.006	.039
HF strong speech 8 kHz	.005	.018	.006	.099
HF strong speech 16 kHz	.006	.070	.121	.364*
HF weak speech 8 kHz	.017	.003	.061	.046
HF weak speech 16 kHz	.017	.009	.303*	.552**

* = significant relationship, $p < .05$
** = significant relationship, $p < .001$

Significant relationships between average pure-tone hearing thresholds and mean localisation error were not evident in the frontal vertical plane, however in each other speaker orientation at least one significant R^2 value was documented. In the lateral horizontal orientation, a weak significant relationship was found only between mean localisation error for HF strong speech with a low-pass filter of 16 kHz and the mean hearing threshold at 9 – 16 kHz for participants

with EHF hearing loss. The data in this case indicated a significant trend for mean error to increase as the mean EHF hearing threshold increased (R^2 = .198, F(1, 21) = 5.19, p = .03).

The only significant predictive relationships between hearing thresholds in the normal hearing group and mean localisation error were observed in the frontal horizontal plane. As shown in Table 30, significant relationships were present between average thresholds at 9 – 16 kHz for all three stimulus conditions filtered at 16 kHz, and in all cases mean localisation error increased with increasing EHF hearing threshold. For the EHF hearing loss group the one significant regression value with the speaker array in the frontal horizontal orientation was the positive relationship between the average thresholds in the conventional frequency range (0.25 – 8 kHz) and mean localisation error for HF weak speech low-pass filtered at 16 kHz (R^2 = .221, F(1, 21) = 5.96, p = .02).

The strongest predictive relationships between hearing thresholds and mean localisation error occurred for the EHF hearing loss group when testing in the lateral vertical plane. As shown in Table 30, with the speaker array in this orientation, R^2 values reaching the 95% level of significance were calculated for the EHF hearing loss group for the relationship between the mean thresholds at 9 – 16 kHz and error for HF strong speech stimuli low-pass filtered at 16 kHz (R^2 = .364, F(1, 21) = 12.12, p = .002), and for the mean thresholds at 0.25 – 8 kHz and mean error for HF weak speech stimuli low-pass filtered at 16 kHz (R^2 = .303, F(1, 21) = 8.70, p = .01). The strongest association was found between EHF average thresholds in the EHF hearing loss group and mean error in localising HF weak speech stimuli low-pass filtered at 16 kHz (R^2 = .552, F(1, 21) = 24.60, p < .001). In all cases of significant R^2 values in the lateral vertical plane, the trend was for error to increase with increasing hearing thresholds.

9.4 Discussion

The key question addressed in this study was whether spectral content in the 8 to 16 kHz range influenced localisation accuracy. This question was addressed by manipulating the bandwidth of the signal to either include or exclude EHF content, and by comparing localisation performance in participants with EHF hearing loss to those with normal hearing sensitivity. We expected that when localisation was measured in planes where cues contained in the EHF range significantly contributed to localisation accuracy, mean error would increase when access to spectral content above 8 kHz was restricted, either through filtering, or due to the presence of EHF hearing loss.

When data was examined across both groups and all four speaker array orientations tested, mean localisation error was slightly, but not significantly, higher for the EHF hearing loss group compared to the normal hearing group. Analysis of the effect of the low-pass filter cut-off frequency showed that average localisation accuracy was significantly better when the upper cut-off frequency of the bandpass filter was at 16 kHz compared to 8 kHz. Localisation in each of the four planes tested relies on a different cue or combination of cues, therefore it is critical that effects of restricting access to EHF spectral information are interpreted for array orientation individually.

9.4.1 Effect of low-pass filter cut-off frequency

Contrary to our hypothesis, in all speaker array orientations a significant reduction in mean error was observed when the low-pass filter cut-off frequency was increased from 8 kHz to 16 kHz. In the frontal vertical plane, this effect was expected for normal hearing listeners, and in agreement with the results of Best et al. (2005), however we had predicted that as the EHF hearing loss group would have limited access to the additional high-frequency information, they would not benefit from the extended bandwidth. In conflict with this prediction, no difference in the degree of improvement with increased bandwidth was documented between groups. Similarly, in the lateral vertical plane, we found that overall localisation error was lower when stimuli were low-pass filtered at 16 kHz to include EHF content, however when results from each hearing group were evaluated separately, the advantage of 16 kHz over 8 kHz low-pass filtered stimuli was significant only for the EHF hearing loss, rather than being stronger for the normal hearing group as expected. The presence of a significant effect of filter for the EHF hearing loss group suggests that at the

chosen stimulus presentation level, the group with EHF hearing loss could detect and use some degree of EHF spectral information. This does not explain why the advantage of increased bandwidth was not present for the normal hearing group.

The significant advantage of the higher low-pass filter frequency documented in the frontal horizontal plane contradicts the results of previous studies using low-pass filtering to remove EHF content (Best et al., 2005; Middlebrooks, 1992). Although the absolute differences in error with filter frequency were small, the significant results are suggestive of some contribution of spectral content in the 8 to 16 kHz range to localisation in the periphery of the frontal horizontal plane. Past research suggests that spectral information above 8 kHz is not necessary for accurate localisation in the frontal horizontal plane, however that is not to say that it has no role at all. ILD cues and envelope ITDs are present at higher-frequencies, typically from approximately 1.5 kHz (Henning, 1974; Henning & Ashton, 1981; McFadden & Pasanen, 1976). It is traditionally believed that when low-frequency content and robust ITDs are available, this is sufficient for accurate localisation, however, it is possible that our results reflect an advantage obtained from higher frequency interaural cues.

In the lateral horizontal plane, despite a significant advantage for the 16 kHz low-pass filtered stimuli over 8 kHz filtered stimuli, we found no evidence of the expected significant effect of stimulus bandwidth on large errors, such as front-back confusions. In addition, when the two groups were examined separately, the effect of low-pass filter cut-off frequency was no longer significant. The absence of a decrease in large errors when the low-pass filter cut-off frequency was increased from 8 to 16 kHz contradicts reports that front-back confusions are resolved using spectral information above 8 kHz and up to 13 – 16 kHz (Best et al., 2005; Jin et al., 2002; King & Oldfield, 1997; Langendijk & Bronkhorst, 2002). These previous studies have all supported the role of EHF spectral content in the disambiguation of front and back locations based on a decrease in such errors when information above 8 kHz is present in the sound stimulus.

We suspect that the reason for at least some of the unexpected effects of filter cut-off frequency may be related to our experimental set-up. In both vertical orientations and in the frontal horizontal orientation, the effect of filter cut-off frequency varied to some degree with the position of the sound source in the speaker array. For example, in both the frontal vertical and lateral vertical arrays whereas mean error was significantly lower for the 16 kHz filtered stimuli than the 8 kHz stimuli for the speakers close to the centre of the array, this pattern was reversed at three of the more peripheral speaker locations in each orientation. It is

possible, given that the advantage of 16 kHz filtered stimuli was not present at all eleven speaker locations in any array orientation, that some type of reverberation was present that altered the spectral content of the stimuli, and thus the effect of filter manipulations. The position of the speaker array in the lateral horizontal orientation was such that rear locations were towards the side of the booth with the viewing window, and the front speakers were towards the acoustically treated wall. It may be that the hard surface of the window created sound reflections that were particularly disruptive to localisation in this plane. This could have potentially obscured any effects of stimulus manipulation by distorting the localisation cues available to listeners.

9.4.2 Effect of hearing

The effect of spectral information in the EHF range on localisation ability was further examined by comparing accuracy in normal hearing adults to those with hearing loss confined to frequencies above 4 kHz. We predicted that EHF hearing loss would act in a similar manner to low-pass filtering by restricting access to spectral content in the signal above 8 kHz. Based on this, we hypothesised that the effects of hearing loss would parallel those expected with low-pass filtering, and that localisation errors would increase when the EHF hearing loss group was tested in plane that required the use of spectral cues for accurate localisation. Overall, we found very mixed results regarding the effect of EHF hearing thresholds on localisation ability. Whereas there was no significant effect of hearing in the frontal horizontal, lateral horizontal, or frontal vertical planes, the results were in agreement with our hypotheses only for the frontal horizontal plane. As predicted, localisation error was significantly higher for the participants with EHF hearing loss in the lateral vertical plane, however the conclusions that can be drawn from this result are limited by the absence of expected effects in the frontal vertical plane, where a stronger influence of EHF hearing loss was anticipated.

The absence of a significant effect of hearing group on mean localisation errors in the frontal horizontal plane was in agreement with the results of Otte et al. (2013), who found no difference in localisation performance in the horizontal plane between older listeners with poorer EHF hearing and younger listeners. However, despite the absence of an effect of hearing group on mean localisation, regression analyses showed that for the normal hearing group only, significant relationships were present between mean localisation error and

average thresholds at 9 – 16 kHz for all three stimuli filtered at 16 kHz (noise, HF strong speech and HF weak speech). In each instance, mean error increased with increasing hearing threshold. This finding, in agreement with the effects of low-pass filter cut-off frequency, suggests a contribution of EHF spectral content to localisation in the frontal horizontal plane, at least in our experimental set-up. This effect was absent for the EHF hearing loss group, perhaps reflecting the reduced access to EHF information, and therefore the decreased influence of hearing level on this spectral content. For the EHF hearing loss group, there was, however, a significant positive relationship between average thresholds at 0.25 – 8 kHz and mean localisation error for HF weak speech low-pass filtered at 16 kHz. The reason for this significant regression value is unclear given that there should have been little difference in the spectral content in the conventional frequency range across any of the speech stimuli, regardless of filter condition. It is possible that the significant effect is a result of the lower number of trials for weak stimuli, and therefore an increased chance for outlier responses to influence the data.

As discussed in relation to filter cut-off frequency, if EHF spectral information is used to reduce front-back confusions, this should be evident from the increase in large errors in the lateral horizontal plane when EHF information is removed. In conflict with this theory, but consistent with the results found for filter frequency, no significant effect of hearing status on localisation accuracy was found in the lateral horizontal plane. Again, although there was no main effect of hearing status, a weakly significant increase in mean error with increasing hearing thresholds at 9 – 16 kHz was found for HF strong speech with a low-pass filter of 16 kHz for participants with EHF hearing loss. This is the only evidence in this plane that supports the hypothesis that a reduction in access to EHF content could increase localisation error; therefore this relationship must be interpreted very cautiously in terms of the level of support it provides for the hypothesis.

Surprisingly, given the supposed strong contribution of EHF spectral cues to localisation accuracy in the median vertical plane and the significant effect of filter cut-off frequency, no significant overall differences in overall mean error or the rate of large error were documented between the two hearing groups, nor did regression analyses reveal any significant relationships between average pure-tone hearing thresholds and mean localisation error. A previous study by Noble et al. (1994) demonstrated that median vertical plane localisation of noise bursts with an upper cut-off frequency of 8 kHz was readily compromised when hearing loss was present at 4 – 8 kHz. We expected that as cues to

elevation extend above 8 kHz, we would find at least comparable, if not more pronounced deficits than those reported by Noble et al. when spectral information above 8 kHz was presented in the present study. Based strictly on a comparison of our results with those of Noble et al., we might suggest that together the results imply that it is high-frequency hearing within the conventional frequency range, but not in the EHF range, that is important for localisation in the frontal vertical plane. However, based on both our comparison of 8 and 16 kHz low-pass filtered stimuli, and the results of studies of the effect of altering spectral content on vertical localisation in normal hearing listeners, there is a general consensus that information above 8 kHz is critical to accurate discrimination of elevation (Best et al., 2005; Jin et al., 2002; King & Oldfield, 1997; Langendijk & Bronkhorst, 2002).

There are several possible explanations for the apparent conflict between our results showing that localisation was impaired in the frontal horizontal, lateral horizontal, and frontal vertical planes when EHF spectral content was reduced through filtering, but not when access was limited by hearing loss. The most likely scenario is that given the presentation level of our stimuli and the level of their hearing thresholds, the EHF hearing loss group retained adequate access to EHF content to maintain near normal localisation. Clearly, the amount of EHF spectral content available to most listeners will be significantly less when it is removed by filtering, rather than rendered inaudible by some degree of hearing loss, and this difference could explain our results. Regardless, we would have expected that if this were the case, there would have been some correlation between hearing thresholds and localisation performance in the frontal vertical plane that showed that accuracy became poorer with increasing hearing loss, in agreement with the effect of filtering.

Another possibility is that, considering the concerns regarding reflections from the window in the test booth mentioned earlier, the cues to sound locations were disrupted by reflected signals. Acoustic treatments of the floor and ceiling also differed so that, while every effort was made to reduce reverberation in the room, there may have been differences in sound reflections depending on speaker location that provided a cue to the sound source. In support of this theory is the differential effect of hearing group and either or both of stimulus type and low-pass filter cut-off frequency at a small number of speaker locations. For example, at two central speaker locations in the frontal vertical plane, mean error was significantly higher for the EHF hearing loss group compared to the normal hearing group, but for the speaker located at 75°, error was higher for the normal hearing group. Although these findings at only a few speakers could be the result of reasonably low numbers of trials and low participant

numbers, as discussed in relation to filtering, they may suggest effects of the sound environment on the spectrum of the stimulus and associated localisation cues.

The lateral vertical plane was the only plane for which a significant overall effect of hearing group was evident. Regression analyses showed that mean error for the EHF hearing loss group significantly increased with increasing average hearing thresholds in the 9 – 16 kHz range for both HF weak and HF strong speech low-pass filtered at 16 kHz. For the HF weak speech filtered at 16 kHz, there was also a weaker, but significant, predictive relationship between average thresholds at 0.25 – 8 kHz and mean error for the EHF hearing loss group. These relationships were not significant for the normal hearing group, or for any other stimuli. Noble et al. (1994) also found that for listeners with sensorineural or conductive hearing loss, localisation accuracy in the lateral vertical plane was correlated with hearing thresholds, although in their study error increased with increasing thresholds at 4, 6, and 8 kHz, and EHF thresholds were not assessed. Our significant correlation between average thresholds in the conventional frequency range and error for the HF weak speech, 16 kHz filter condition, may also be related to high-frequency thresholds in the conventional range. Alternatively, the slightly poorer conventional frequency thresholds in the EHF hearing loss group may have had an influence on localisation by disrupting the interaural cues that contribute to localisation in the lateral horizontal plane.

The significant effect of hearing group on lateral vertical plane localisation accuracy is in agreement with our hypotheses and with previous research (Best et al., 2005; Butler & Humanski, 1992; Noble et al., 1994), and together with the results of the regression analyses, suggests that poorer localisation occurs when listeners have a reduced ability to access EHF spectral cues due to hearing loss. The regression analyses are particularly interesting in that whereas there was no significant correlation between EHF hearing thresholds and stimuli low-pass filtered at 8 kHz, these relationships were significant when the 16 kHz filter cut-off frequency was applied. We propose that the significant relationship between hearing and localisation performance only when the EHF content was presented, and only for the EHF hearing loss group where access to this information was supposedly restricted, is due to varying levels of hearing loss and therefore benefit of this spectral information.

9.4.3 Effect of type of stimulus

In contradiction to the hypothesis and the results of previous studies, localisation performance was consistently poorer for noise stimuli than for speech stimuli. In both horizontal orientations and in the frontal vertical orientation, mean localisation error for noise stimuli was significantly higher than for either type of speech stimulus. In the lateral vertical plane mean error was again significantly higher with noise stimuli than only HF strong speech stimuli. When we examined the percentage of errors greater than 90° we again found that the error rate was higher for noise compared to both speech stimuli in the lateral horizontal plane and compared to HF strong speech only in the frontal vertical plane. No differences in mean large error rates with different stimuli were evident in the lateral vertical or frontal horizontal planes.

The first conflict between our findings and the literature is that previous studies have shown that there is no difference in the accuracy with which the lateral angle was estimated between speech and non-speech stimuli (Best et al., 2005; Gilkey & Anderson, 1995). The second way in which the present data differs is that where previous studies have found a difference in localisation accuracy between speech and non-speech stimuli in the vertical plane, improved accuracy has been associated with the non-speech stimuli (Best et al., 2005; Gilkey & Anderson, 1995). For example, Gilkey and Anderson (1995) demonstrated that localisation accuracy was comparable for 25 μs clicks and speech stimuli in the horizontal plane of a large sphere, but error was higher for speech stimuli in elevation and front-back discrimination. Similarly, Best et al. (2005) found that there was no difference in the accuracy of lateral angle estimation between broadband noise and speech stimuli, but in the vertical plane the rate of errors associated with the cone of confusion increased when speech stimuli were used rather than noise.

These earlier findings have been interpreted as evidence that interaural difference cues available for stimuli in the horizontal plane are sufficiently robust that lateral angle can be estimated accurately regardless of the spectral characteristics of a stimulus (Best et al., 2005; Carlile, Leong, & Hyams, 1997; Gilkey & Anderson, 1995; Ricard & Meirs, 1994). The discrimination of elevation and front versus back are, however, reliant on spectral cues that are stronger in the high frequencies, and an increase in cone of confusion type errors therefore tend to occur when these spectral cues are ambiguous. It is proposed that whereas speech has a non-flat spectrum that varies over time, broadband noise is more spectrally stable, and thus it is easier for the listener to distinguish between spectral location cues and

spectral features of the stimulus when noise is presented (Best et al., 2005; Butler, 1986; Makous & Middlebrooks, 1990; Middlebrooks, 1992). For array orientations that require spectral cues for accurate localisation, but not those where interaural cues are robust, noise is therefore expected to be easier to localise than speech stimuli.

The most obvious cause of the conflict between our results and previous findings is the longer duration of our speech stimuli; which was on average 710 ms, than the 150 ms noise bursts. We would expect that a longer stimulus would give participants more time to extract the cues required to more accurately determine the location of the sound. However, the speech corpus used here and the length of the noise bursts are identical to those used by Best et al. (2005), who found a clear advantage of noise over speech. It is possible that the difference between our results and those of Best et al. results from the ability of our participants to move their heads as a stimulus was presented, which may have allowed them to shift their head towards the stimulus as it was being presented (despite being instructed not to), providing additional cues to its precise location. As speech was a longer stimulus, if participants were turning as the speech stimulus was presented, they would have had longer to do so than for noise. In the Best et al. study, stimuli were presented in a virtual auditory space, therefore any movement of the head would not have influenced localisation accuracy. Although the contribution of head movement to localisation accuracy is not well understood, the available evidence suggests that at least a modest improvement in the discrimination of elevation and a reduction in front-back confusions occurs when listeners are allowed to move their heads during sound stimulus presentation (Kato, Uematsu, Kashino, & Hirahara, 2003; Perrett & Noble, 1997a, 1997b; Thurlow, Mangels, & Runge, 1967; Wallach, 1939, 1940).

It was expected that when speech stimuli were divided into groups based on the strength of their spectral content at 8 – 16 kHz, localisation performance would be superior for words with greater EHF content in the planes in which localisation was dependent on high-frequency information, particularly in the frontal vertical plane. In partial agreement with this hypothesis, we found that mean error was slightly, but significantly, lower for HF strong speech than for HF weak speech in the lateral vertical plane, as expected, as well as the frontal horizontal plane, in which had predicted no significant difference would be present. This effect was absent in the lateral horizontal and frontal vertical planes, where we had predicted, based on the contribution of spectral cues to localisation in these orientations, that localisation accuracy would be improved with stronger EHF content in the speech stimuli. No differences in mean large error rates with HF strong and HF weak speech stimuli were

evident in any plane. Again, these results contradict those of Best et al. (2005), who found a trend for mean polar angle error to decrease with increasing spectral energy above 8 kHz in their set of 250 words. It is likely that the small numbers of each type of speech stimuli we presented, particularly HF weak stimuli, weakened our analysis and reduced our ability to identify significant effects of the strength of EHF content in speech. Interestingly, no interactions were found between stimulus type and low-pass filter cut-off frequency. We expected that the application of a low-pass filter at 8 kHz to all speech stimuli would reduce any differences between HF strong and HF weak speech, although again the small number of HF weak stimuli presented would have hindered such an effect being detected.

Although significant increases in mean error (but not large errors) with weaker EHF content in speech were documented in the frontal horizontal and lateral vertical planes, these differences were small, and it is unclear whether they represent a genuine advantage for HF strong speech. While such an advantage may be explained in the lateral vertical plane in terms of providing additional spectral information that helps to resolve cone of confusion errors, this effect is not in accordance with known localisation mechanisms in the frontal horizontal plane.

9.4.4 Limitations of the study

As discussed above, a key limitation in this study was that testing was performed in an environment that we could not be sure did not create reverberation and distortion of the signals. Although every effort was made to reduce reverberation and sound reflections by lining the walls and ceiling with sound absorbing foam, and covering the floor with blankets, the window remained exposed. This issue should have been recognised and addressed prior to the study. The reason for using a test booth with a window was so that the experimenter could view the participant and ensure that they did not move during stimulus presentations. Despite this surveillance, we were also unable to rule out an effect of slight head movement during presentations, particularly, as noted above, when the longer speech stimuli were presented. Previous studies have implemented solutions to this issue such as using a bite bar (e.g. Gilkey & Anderson, 1995), or having participants focus a laser attached to their head on a marked spot (e.g. Brungart & Simpson, 2009). Such issues are also resolved using virtual auditory space paradigms, where the effects of head movement can be completely eliminated (e.g. Best et al., 2005).

It is widely recognised that localisation experiments will be more limited in their ability to detect significant effects of stimulus of subject variables when a fixed number of visible sound source locations are used and when these are only in a single plane (Carlile et al., 1997). As Carlile et al. (1997) point out, under such conditions participants are constrained in their responses by the known potential locations. They are therefore forced to select a location that does not necessarily correspond to the exact location at which they perceived the sound was presented. By limiting response options to a small range of locations, smaller errors could be obscured, weakening the ability to detect any differences resulting from experimental variables. Ideally, the speaker array should provide the possibility of stimulus presentations in any plane, and sound sources should not be visible to participants. Rather than asking the participants to call out the location of the sound, a method of pointing to the perceived location would also have provided a less constrained response mode, that enabled participants to more precisely indicate the perceived sound source without being restricted to a limited number of options (Carlile et al., 1997; Gilkey & Anderson, 1995; Makous & Middlebrooks, 1990; Mason, Ford, Rumsey, & De Bruyn, 2001; Oldfield & Parker, 1986).

Another possibility to increase the sensitivity of the experimental design to small localisation errors would have been to use a greater number of speakers, with spacing of less than 15°, no dummy speaker, and no virtual speaker channels. Makous and Middlebrooks (1990) demonstrated that, when tested with broadband stimuli, normal hearing adult listeners could resolve sound locations separated by 2° for horizontal locations and 3.5° for vertical locations in the frontal hemisphere. Using speakers separated by such small amounts would therefore be expected to increase our ability to detect much smaller differences in error between groups and stimuli. Whereas our speaker spacing of 15° is certainly consistent with some other published studies, such as Yost, Loiselle, Dorman, Burns, and Brown (2013) and Brungart and Simpson (2009), who both positioned their sound sources in 15° increments, others have effectively increased the sensitivity of their experimental designs by reducing spacing down to as little as 2.5° (Otte et al., 2013).

Although many studies of localisation test only a small number of participants, for example Best et al. (2005), Carlile et al. (1999), Gilkey and Anderson (1995), Langendijk and Bronkhorst (2002), Makous and Middlebrooks (1990) Middlebrooks (1992), and Wightman and Kistler (1992) all tested less than ten subjects, ideally more participants would have been included in each group to increase the statistical power of the study design. This seems particularly important given that we found large inter-subject variation, suggesting if only a

small number of participants were used, they may not be representative of the "normal" population. A greater and more equal range of participant ages and a more equal number of males and female participants across the two experimental groups would also have been ideal. In both groups there were more than twice as many females as males, which may have influenced results as males tend to have larger pinnae, which can influence localisation accuracy (Otte et al., 2013).

Of greater concern is the difference in ages between the two groups. The mean age of the hearing loss group was 53.7 years (*SD* = 9.1), which was much higher and had a greater range than the normal hearing group (*M* = 24.7 years, *SD* = 4.8). Studies of auditory performance in older adults have found evidence central age-related deficits in temporal processing unrelated to changes in pure-tone thresholds, which could impair localisation abilities regardless of EHF thresholds (Grose & Mamo, 2010; Lister & Roberts, 2005; Martin & Jerger, 2005; Roberts & Lister, 2004; Schneider & Hamstra, 1999; Strouse et al., 1998). Although more difficult to recruit, ideally two groups of participants with equivalent age, but differing thresholds in the EHF range only, would have been found to participate in the present study to rule out any other effects of age on localisation processes.

As noted above, the degree of hearing loss for the EHF hearing loss group meant that at least some degree of EHF spectral information would have been audible to most participants. Again, this is a result of difficulties in recruiting a group of listeners with an "ideal" EHF hearing loss. To isolate the effects of EHF hearing loss, ideally listeners in the EHF hearing loss group would have had normal hearing up to at least 4 kHz, with a moderate or greater hearing loss at 8 kHz and above. This would have meant that the spectral information across the entire EHF range would have been equally and completely inaccessible to only these participants. Unfortunately for research purposes, such hearing losses rarely occur. Although our participants had better hearing than desired at some EHF frequencies, and therefore could access some EHF cues, we do believe that the group realistically represents the population with EHF hearing loss, and therefore could be validly employed to investigate the effects of such hearing loss.

9.4.5 Directions for further research

Once the methodological issues above have been resolved and the effects of bilateral, symmetrical EHF hearing loss on localisation has been clarified, the next step is to determine

whether comparable effects are present when EHF hearing loss is unilateral and/or asymmetrical. This is of particular interest when examining the effects of EHF hearing loss resulting from middle ear surgery, as such procedures are rarely performed on both ears simultaneously, and therefore the resulting hearing loss will be unilateral. Also important when considering the effects of surgically-induced EHF hearing loss is whether the auditory system can adapt to changes in spectral cues created by unilateral hearing loss to enable accurate localisation. There is some evidence that such adaptation to unilateral losses may occur (e.g. Hebrank & Wright, 1974; Van Wanrooij & Van Opstal, 2005), however any effects specific to EHF hearing loss have not been assessed. In some cases, EHF hearing loss following surgery is likely be at least partially conductive in nature, rather than sensorineural. Whether this influences localisation abilities in a different manner also warrants investigation.

EHF hearing sensitivity is also thought to influence speech perception in noise, and this is certainly an area that warrants further research. Hearing in noise is believed to be related to localisation ability by way of the head shadow effect and the ability to benefit from spatial separation of sound. As this ability has been shown to be impaired in listeners with sensorineural hearing loss (e.g. Arbogast et al., 2005; Bronkhorst & Plomp, 1989, 1992; Dubno et al., 2002; Helfer & Freyman, 2008; Marrone et al., 2008; Noble et al., 1997; Ter-Horst et al., 1993), it would certainly be interesting to assess whether comparable deficits occur with EHF hearing loss.

As discussed, we hypothesised that some participants with lesser EHF hearing losses may have had adequate access to spectral cues that enabled them to accurately localise sound. Further research is needed to clarify what degree (if any) of EHF hearing loss begins to impair localisation abilities, and whether hearing sensitivity at all frequencies in the EHF range is equally important to localisation.

9.4.6 Summary and conclusions

This study was designed to examine the influence of access to EHF spectral information on localisation accuracy. When the availability of spectral localisation cues in the EHF range was restricted by lowering the low-pass filter cut-off frequency from 16 to 8 kHz, we found an overall increase in localisation error, consistent with the results of Best et al. (2005). However, our results showed that the increase in error with reduced EHF information was

present in all planes tested, which contradicts the theory that only localisation in planes where EHF spectral cues are utilised would be affected. While this finding does offer some evidence that spectral content above 8 kHz aids localisation, methodological issues need to be resolved before any clear conclusions can be drawn.

When the effect of reduced access to spectral content in the EHF range was assessed by comparing localisation ability in normal hearing participants and participants with EHF hearing loss, the results were less clear. Although the trend was for increased error when hearing loss was present, the difference between groups was only significant when speakers were positioned in the lateral vertical orientation. This suggests some decrease in localisation accuracy occurs when EHF hearing loss is present, at least under specific conditions, but the results in the remaining three orientations were less consistent with this theory. In particular, in the frontal vertical plane, where we expected the largest effect of reduced EHF access on performance, we failed to find any significant influence of hearing loss. Overall, although we have found some evidence of a contribution of EHF spectral information to localisation ability, there is limited evidence that reduction in EHF sensitivity causes localisation deficits comparable to those observed in previous studies (e.g. Best et al., 2005) where information above 8 kHz is removed by filtering.

PART VI: SUMMARY AND CONCLUSIONS

Chapter 10: Summary and conclusions

The overarching aim of the studies presented in this thesis was to obtain detailed information regarding the effects of middle ear surgery on short- and long-term auditory function. The impetus for this research was the common occurrence of postoperative hearing deterioration at 4 to 8 kHz noted by surgeons and audiologists testing patients who had undergone otherwise successful middle ear surgery. It was hypothesised that this high-frequency hearing loss may be the result of iatrogenic cochlear trauma and would be more evident when thresholds were measured in the EHF range. Previous studies (Bauchet St Martin et al., 2008; Doménech & Carulla, 1988; Mair & Laukli, 1986; Tange & Dreschler, 1990) provided evidence that postoperative EHF hearing transpired relatively often after surgeries with good low-frequency hearing results, however the extant literature provided a distinct lack of information describing whether the hearing loss was transient or permanent, and conductive or sensorineural. This research was conceived to address these gaps in the literature. This chapter provides a summary of the key findings of the present research and discusses the clinical implications of these results.

10.1 Summary of results: changes in postoperative hearing and balance

10.1.1 Immediate EHF postoperative hearing loss and recovery of hearing

The study presented in Chapter 3 is the first comprehensive, prospective study to establish the rate of EHF hearing loss in the early postoperative period following reconstructive middle ear surgery and to describe the patterns of recovery in EHF thresholds occurring over the first postoperative year. The results of this study provided clear evidence that elevation of EHF air-conduction thresholds occurs frequently in the 1 – 2 weeks following stapedectomy, ossiculoplasty, and tympanoplasty. Significant recovery of EHF hearing acuity was documented over the first one to three months after surgery; the same timeframe as air- and bone-conduction threshold improvement in the conventional frequency range. Although improvement in EHF thresholds that had increased after surgery was recorded in the vast majority of patients, in many cases thresholds did not return to preoperative levels. Twelve months after surgery, 50% of patients who underwent stapedectomy and 42% who had a tympanoplasty retained a reduction in their highest audible frequency, relative to that measured before surgery. In most cases of stapedectomy, this EHF loss occurred despite

successful closure of the air-bone gap at lower frequencies and an absence of bone-conduction hearing loss at 0.5 – 4 kHz. The rate of audible frequency loss in the group of ossiculoplasty patients one year postoperatively was comparable to that in the non-operated ear, suggesting a limited long-term detrimental effect of ossiculoplasty on EHF thresholds in the majority of patients.

The two major trends emerging from the data presented in Chapter 3 were that EHF hearing loss was most common and most severe in the early postoperative period, and that it occurred more frequently following stapedectomy than tympanoplasty and especially ossiculoplasty. This is of note given that stapedectomy was associated with the greatest improvements in hearing at lower frequencies, whereas more limited gains were achieved in tympanoplasty and ossiculoplasty. As was discussed, the differential effect of surgery type may partly reflect the limitations of monitoring changes in EHF audiometric thresholds when extensive hearing loss is present. However, that this effect was apparent for mean and median thresholds, and for the rate of audible frequency loss, suggests it is not purely the result of methodological issues. Instead, the results imply that either the injury to the cochlea or the disruption to middle ear transmission of high-frequency stimuli that causes EHF hearing loss following stapedectomy occurs more often or is more extensive during stapes surgery than in other middle ear procedures.

10.1.2 The nature of postoperative EHF hearing loss

The second aim to be addressed by this programme of research was to ascertain whether the frequent elevation of EHF thresholds following middle ear surgery was indeed reflective of cochlear injury, or whether the hearing loss was related to changes to the transmission of high-frequency sounds through the reconstructed middle ear. As discussed in Chapter 5, there are many potential causes of EHF hearing loss and based on air-conduction thresholds alone it is not possible to distinguish between middle and inner ear origins. Chapter 6 described the modification and validation of the TEAC HP-F100 bone-conduction transducer for use in the assessment of cochlear function at 8 – 16 kHz.

The pilot study presented in Chapter 7 provides unique data showing that early postoperative EHF hearing loss following stapedectomy may be composed of both conductive and sensorineural elements. In this small series of four patients, two cases were documented in which both EHF air- and bone-conduction thresholds (as measured with the HP-F100

transducer) markedly increased following stapes surgery. In both of these cases, EHF air-conduction thresholds at least partially recovered over the three months following surgery. The immediate postoperative development of an EHF conductive hearing loss, with significant recovery over the subsequent weeks, suggests that factors directly related to surgery in the tympanic cavity, such as the presence of blood, oedema, and packing material, are the most likely cause of this hearing loss. Alternatively, the replacement membrane covering the oval window may impair transmission of high-frequency vibration to the cochlea until healing is complete (Antoli-Candela et al., 2009).

In contrast to the pattern of recovery of postoperatively elevated EHF air-conduction thresholds documented in the two cases of post-stapedectomy EHF hearing loss, the elevated EHF bone-conduction thresholds showed little improvement over the three month follow-up period. The persistent elevation of EHF bone-conduction thresholds, despite unchanged bone-conduction thresholds in the conventional frequency range, is consistent with surgical injury to the basal cochlea. In the case of stapedectomy, the most likely potential causes of such cochlear trauma include transmission of excessive force to the inner ear, exposure to high levels of noise from surgical instruments, or laser induced injury. Any of these factors may exert their effects by triggering inflammation and/or oxidative stress, disturbance to the ionic balance of the labyrinthine fluids, metabolic stress, or causing structural damage to the cells of the inner ear. At least in these two cases, the trauma was sufficient that persistent damage to the inner ear could be documented.

10.1.3 Effects of middle ear surgery on vestibular function

The nature of iatrogenic inner ear damage was further investigated by assessing postoperative changes in the responses of the vestibular system. Given the anatomical proximity of the otolithic organs to the stapes footplate, it was hypothesised that changes to utricular responses reflective of trauma to the inner ear would occur following middle ear surgery. Overall, the oVEMP data collected from patients undergoing middle ear surgery provided no evidence of a postoperative change in utricular responses. The strength of this study design was that the first vestibular assessments were performed within 48 hours of surgery, a time at which at least mild vestibular symptoms were most likely to be present, and indeed were in several patients. Given that VEMP responses, on average, remained unchanged despite mild balance disturbance often being reported, the results suggest that the source of symptoms was not

trauma to the utricle. Alternatively, if the utricle was injured, tap-evoked oVEMPs were not a sensitive enough tool to detect the change in function above the overall variability in recordings.

The second advance over previous studies was that pre- and postoperative VEMPs were compared in patients who reported significant postoperative vertigo. oVEMP changes that corresponded to the timeline of symptoms and the measurement of sensorineural hearing loss were documented in one of the two cases in which severe vertigo occurred post-stapedectomy. Although limited to one case, this example does provide new evidence that the utricle may be vulnerable during surgery, and the cause of significant postoperative balance dysfunction in at least some patients. The absence of oVEMP changes in the other case of significant vertigo suggests that multiple causal mechanisms are responsible for vertigo following stapedectomy, some of which do not involve injury to the utricle. Exploration of the relationship between postoperative EHF hearing loss and symptoms of balance disturbance or changes in oVEMPs did not provide any evidence of a common inner ear cause.

10.2 Summary of results: methodological issues and advancements

An important aim of this research was to develop a method of reliably measuring ear-specific EHF bone-conduction thresholds. Chapter 6 described modifications made to the TEAC HP-F100 transducer to enable it to be used in audiometric testing and presented a series of investigations performed to assess the test-retest reliability of the transducer, obtain calibration values, and develop the optimal protocol for clinical use. These tests supported the findings of Popelka et al. (2010) that the transducer had characteristics appropriate for clinical use, and it also extended their findings by clarifying the optimal position for the transducer during testing and the way in which the ears should be occluded and masking should be applied. The pilot study presented in Chapter 7 is the first to show that HP-F100 transducer can reliably be used to monitor changes in EHF hearing acuity over repeated assessments in listeners with conductive hearing loss. Previous studies of changes in cochlear function following middle ear surgery had employed electrostimulation techniques (Doménech & Carulla, 1988; Doménech et al., 1989; Hegewald et al., 1989) or used the KH-70 electromagnetic transducer (Mair & Hallmo, 1994), which both have significant limitations for clinical use, as discussed in Chapter 6. The results obtained using the HP-F100

device suggest that it is both reliable and appropriate for clinical use, thus representing a significant advancement from previous techniques. Future research will certainly benefit from this technology in studies performed to clarify the nature of EHF hearing loss after middle ear surgery.

10.3 Clinical implications

While the primary importance of frequencies within the conventionally tested audiometric range for the understanding of speech is not disputed, there is an increasing body of research illustrating the contribution of EHF spectral information to optimal auditory performance. The literature suggests that the audibility of EHF content may influence speech intelligibility, sound quality, and localisation accuracy (e.g. Best et al., 2005; Carlile et al., 1999; Fullgrabe et al., 2010; Moore et al., 2010; Stelmachowicz et al., 2001). By extension, one could predict that when a loss of hearing acuity in the EHF range restricts access to spectral information in this range, any of these functions may be compromised. There is, however, currently a lack of evidence to support this hypothesis.

10.3.1 Localisation accuracy

The study presented in Chapter 9 was performed with the aim of addressing questions regarding the importance of EHF hearing loss to one aspect of auditory performance. Localisation accuracy was selected for investigation based on the strength of the literature suggesting removing spectral content above 8 kHz using low-pass filtering significantly influenced some aspects of localisation performance (Best et al., 2005; Brungart & Simpson, 2009; Jin et al., 2002). Overall, the results of this study showed that localisation accuracy of speech and noise stimuli decreased when EHF spectral content was reduced by lowering the low-pass filter cut-off frequency from 16 to 8 kHz. Unexpectedly, the increase in mean error with decreased EHF content was observed in all four planes tested; lateral vertical, lateral horizontal, frontal vertical, and frontal horizontal. This contradicts the theory that EHF spectral information provided by the pinna are a cue to sound source location only in the frontal vertical and lateral vertical planes, but do not contribute to horizontal localisation accuracy. It is possible that this data reflects a greater role than previously thought of content in a signal above 8 kHz to localisation in both vertical and horizontal planes. However, at this stage it seems more likely that methodological issues (such as the possibility of reflections

within the test booth) contributed to the unexpected finding and these concerns need to be addressed before any clear conclusions can be drawn.

An effect of removing EHF content by filtering on localisation accuracy had previously been demonstrated in the literature (Best et al., 2005; Brungart & Simpson, 2009; Jin et al., 2002), but this study was the first to compare localisation abilities in listeners with and without EHF hearing loss. It was hypothesised that hearing loss limited to the EHF range would act in a similar manner to a low-pass filter with a cut-off frequency at 8 kHz, and thus similar effects on localisation accuracy would be observed. Although the trend was for increased error when hearing loss was present, the difference between groups was statistically significant only when speakers were positioned in the lateral vertical orientation. Most notably, we failed to find any significant influence of EHF hearing loss on mean localisation accuracy in the frontal vertical plane, in which localisation is thought to be highly dependent on EHF cues (King & Oldfield, 1997; Langendijk & Bronkhorst, 2002). Again, it was hypothesised that the conflicts between these results and what is known regarding the frequency dependence of localisation cues in each plane, were at least partly related to methodological issues. The smaller effect of EHF hearing loss than filtering on localisation accuracy is likely to be related to the intensity of spectral content that remains accessible to the listener. Presumably, hearing loss of the extent that many participants presented with allowed some access to EHF pinna cues that could be used by listeners to improve localisation accuracy. Certainly, the results suggest that the effects of EHF hearing loss in the configuration and degree that presents in most adult listeners on localisation ability are not as extensive as those that occur when information above 8 kHz is removed by filtering.

10.3.2 EHF hearing loss as a model for research

While the clinical importance of EHF hearing loss to individual listeners remains unresolved, we propose that a more critical implication of the present results is in the use of postoperative EHF audiometry as a framework for future research. Specifically, that EHF hearing loss occurs so frequently postoperatively, particularly after stapedectomy, and that it sometimes includes a sensorineural component, indicates that this is a much more sensitive indicator of inner ear harm than conventional audiometry. In any investigation of the effects of inner ear manipulations, whether surgical or therapeutic, it is optimal to use the most sensitive tool available to detect any consequences of interventions. This not only provides more complete

and accurate information regarding the effects of experimental or clinical treatments, but also improves the efficiency with which such data can be collected.

As the data presented in Chapter 3 shows, significant sensorineural hearing loss rarely occurs in the conventional frequency range after middle ear surgery, particularly when hearing is tested more than two weeks postoperatively. It may be that more subtle differences in cochlear trauma that are not reflected in comparisons of conventional frequency bone-conduction thresholds, at least on average across a series of patients, will be more easily detected in the EHF range. If the basal cochlea is indeed more sensitive to trauma, it is probable that differences in the risks presented by different types of lasers, surgical tools, materials, and techniques will be most evident when EHF thresholds are tested. Assessing changes in EHF thresholds will inform the debate regarding the advantages and disadvantages of surgical variables without requiring the recruitment and testing of so many patients with what may be an inferior, more damaging tool.

The sensitivity of EHF hearing to surgical trauma may also be of particular use when investigating the efficacy of interventions designed to protect the cochlea from surgical trauma. As was discussed in Chapter 5, the stressors to the inner ear during middle ear surgery, such as excessive force or noise exposure, could potentially cause inner ear damage through inflammation, oxidative stress, vascular changes, infection, metabolic stress, and disturbances in ionic fluid balance. Each of these mechanisms of damage provides a target for pharmaceutical interventions to prevent permanent cochlear injury. For example, corticosteroids such as dexamethasone have anti-inflammatory actions in the cochlea as well anti-apoptotic activity by altering the expression level of apoptosis-related genes (Dinh et al., 2008; Haake et al., 2009). The protective effects of dexamethasone on the cochlea following high intensity noise exposure and cochlear implant insertion trauma have been previously documented (e.g. Eastwood et al., 2010; Eshraghi et al., 2007; van de Water et al., 2010; Vivero et al., 2008). Other ototherapeutic treatments shown to protect the cochlea from trauma or improve recovery post-trauma, such as electrode insertion, or noise, include the corticosteroid triamcinolone (Kiefer et al., 2007; Ye et al., 2007) and the amino acid D-methionine (Campbell et al., 2011; Campbell et al., 2007). If any of these agents have similar protective effects on the cochlea during middle ear surgery, which is a reasonable expectation given the success of such treatments during cochlear implant electrode insertion, EHF audiometry provides a strong measure with which the success of treatment can be assessed. If a pharmaceutical treatment can be shown to significantly reduce the rate of EHF hearing loss,

we may expect that the rate of rarer cases of significant hearing loss at frequencies below 8 kHz may also be reduced if a sufficient number of patients are tested.

The presence of a conductive component to postoperative EHF hearing loss provides similar opportunities to sensitively assess the impact of changes to ossicular prostheses or grafts on middle ear transmission. The development of postoperative conductive hearing loss that was dominant above 4 kHz in the presence of a reduction in the low-frequency air-bone gap indicates that middle ear transmission can have significant effects on EHF hearing, even when transmission of lower frequency stimuli is near normal. This raises interesting questions regarding the function of the healthy and reconstructed middle ear conductive mechanism at higher frequencies and the effects of manipulations to the physical characteristics of the system on hearing acuity. Differences in thresholds in the EHF range only that depend on the technique or material used could be used to inform the debate regarding optimal middle ear reconstruction.

10.3.3 Long-term effects of cochlear damage

As noted in Chapter 7, more rapid deterioration of air- and bone-conduction thresholds within the conventional frequency range has been reported in the ten years following stapedectomy than in control patients (Vartiainen et al., 1993). If this deterioration is related to cochlear fragility subsequent to surgery, as suggested by Sperling et al. (2013), it may be that more subtle damage and thus the risk of later hearing deterioration can be identified using postoperative EHF audiometry. Regardless of whether prevention of further deterioration is possible at this stage, identification of patients at risk of developing hearing loss would definitely warrant increased hearing monitoring and patient counselling. Long-term, these patients may be identified as candidates for preventive treatments if they become available.

10.4 Future research

There are many aspects of the present work which would benefit from further investigation. In the course of audiometric data collection for the phase of the study presented in Chapter 3, concerns arose regarding the frequency-specificity of EHF pure-tone stimuli produced by the audiometers used, and thus the validity of thresholds measured with this equipment. Such concerns regarding spurious tones in the EHF output of some audiometers have previously

been reported (Kurakata et al., 2010; Schmuziger et al., 2007), but appear to have gone largely unacknowledged by most clinicians. Objective measurements of the electrical output of the two audiometers used for data collection throughout this thesis confirmed the presence of unwanted lower-frequency energy in the output of GSI 61 audiometers at 14 and 16 kHz. Measurements performed for two audiometers of this model indicated that while the output was consistent across repeated testing in a single audiometer, the spectrum produced by each audiometer when 14 and 16 kHz pure-tones were presented was distinctly different. These results strongly suggest that for changes in EHF thresholds to be accurately interpreted, the same audiometer must be used for repeated testing. As this was the protocol followed throughout data collection, this provided reassuring confirmation that intermittent changes in the spectra should not have influenced results. The other issue to be considered, however, was whether the unwanted lower frequency output reduced the level at which a supposedly EHF threshold was recorded.

In the majority of cases of postoperative EHF hearing loss, particularly after stapedectomy, thresholds improved at lower frequencies where unintended tones or noise was strongest. If listeners were responding to lower frequency tones that became audible only when hearing improved postoperatively, we would expect a corresponding improvement in EHF thresholds to be recorded. The fact that in most cases EHF thresholds deteriorated, even when thresholds in the conventional frequency range dramatically improved, led us to conclude that EHF threshold changes reported in Chapter 3 were not the result of unintended tones in the audiometer output, at least in the majority of cases. The documentation of low-frequency audiometer output that could exceed listeners' thresholds during EHF testing is, regardless, an area of concern and should be considered whenever interpreting EHF audiograms and changes in EHF thresholds. This is an area that would benefit greatly from further research, particularly in developing methods of preventing unwanted noise from influencing the audiogram while maintaining an adequate dynamic range for testing.

The assessment of tap-evoked oVEMPs documented in Chapter 8 showed that measurements were highly variable over time. In the series reported, the non-operated contralateral ear was used as a control measure by which to judge whether significant changes in the responses of operated ear had occurred. The variability of measurements in the non-operated ear suggests that further development of the technique is required in order to optimise the reliability of recordings. In addition, criteria by which significant changes can be judged in the absence of a healthy contralateral ear for comparison would be beneficial. While no mean group changes

in oVEMPs were documented in this series, the findings in one case of significant postoperative vertigo suggest that further assessment of utricular function in cases of significant balance disturbance after middle ear surgery may provide some insight into the causes of postoperative vestibular symptoms. If methodological limitations can be resolved, the use of tap-evoked oVEMPs may therefore be a useful tool as part of an assessment battery to detect surgical injury to the vestibular system.

There are many aspects of auditory function that could be affected by EHF hearing loss. While this research selected the area of localisation to begin to assess the effects of EHF hearing loss on auditory function, additional aspects of auditory function that warrant further research include the detection and understanding of speech in noise. Given that many listeners with high-frequency hearing loss report significant difficulty understanding speech in the presence of background noise, the effects of isolated EHF hearing loss on this ability are certainly of interest. Brungart and Simpson (2009) reported a need for an increased low-pass filter cut-off frequency when localisation accuracy was assessed in the presence of a masking noise, relative to localisation of a target signal in quiet. Whether a similar requirement for EHF information is required for speech perception in noise, and whether this requirement is reflected in impaired performance in listeners with EHF hearing loss, is an interesting topic that requires further investigation.

Chapter 7 presented a pilot study that shows that the TEAC HP-F100 can successfully be used to distinguish between conductive and sensorineural EHF hearing loss postoperatively. The results of the pilot study indicate that EHF hearing loss may contain both conductive and sensorineural elements, however in this small group the relative rates of each type of hearing loss cannot be determined. It is important that data demonstrating the frequency with which conductive and sensorineural losses occur is completed prior to the development of any intervention or treatment studies.

In determining the causes of iatrogenic cochlear damage, recordings made using the HP-F100 during surgery could also provide valuable information regarding surgical manoeuvres that are most traumatic to the cochlea. Intraoperative tracking of EHF bone-conduction thresholds could potentially be a highly sensitive method of monitoring the instantaneous effects of surgery on inner ear function. The assessment of the relationship between intraoperative threshold changes and postoperative hearing outcomes will provide additional information regarding how surgery causes transient versus permanent changes to cochlear function. This information will aid surgeons in determining the optimal technique and equipment to protect

cochlear function wherever possible. The development of the equipment and protocols required for this research is already underway.

REFERENCES

à Wengen, D. F. (1993). Change of bone conduction thresholds by total footplate stapedectomy in relation to age. *American Journal of Otolaryngology, 14*(2), 105-110.
à Wengen, D. F., Pfaltz, C. R., & Uyar, Y. (1992). The influence of age on the results of stapedectomy. *European Archives of Oto-Rhino-Laryngology, 249*(1), 1-4.
Aantaa, E., & Virolainen, E. (1979). Vestibular neuronitis; a follow-up study. *Acta Oto-Rhino-Laryngologica Belgica, 33*(3), 401-404.
Aarnisalo, A. A., Cheng, J. T., Ravicz, M. E., Hulli, N., Harrington, E. J., Hernandez-Montes, M. S., . . . Rosowski, J. J. (2009). Middle ear mechanics of cartilage tympanoplasty evaluated by laser holography and vibrometry. *Otology & Neurotology, 30*(8), 1209-1214.
Abel, S. M., & Hay, V. H. (1996). Sound localization. The interaction of aging, hearing loss and hearing protection. *Scandinavian Audiology, 25*(1), 3-12.
Abi-Hachem, R. N., Zine, A., & Van De Water, T. R. (2010). The injured cochlea as a target for inflammatory processes, initiation of cell death pathways and application of related otoprotectives strategies. *Recent patents on CNS drug discovery, 5*(2), 147-163.
Adelman, C., Fraenkel, R., Kriksunov, L., & Sohmer, H. (2012). Interactions in the cochlea between air conduction and osseous and non-osseous bone conduction stimulation. *European Archives of Oto-Rhino-Laryngology, 269*(2), 425-429.
Adelman, C., & Sohmer, H. (2013). Thresholds to soft tissue conduction stimulation compared to bone conduction stimulation. *Audiology and Neurotology, 18*(1), 31-35.
Ahmed, H. O., Dennis, J. H., Badran, O., Ismail, M., Ballal, S. G., Ashoor, A., & Jerwood, D. (2001). High-frequency (10-18 kHz) hearing thresholds: reliability, and effects of age and occupational noise exposure. *Occupational Medicine (Oxford, England), 51*(4), 245-258.
Alaani, A., & Raut, V. V. (2010). Kurz titanium prosthesis ossiculoplasty--follow-up statistical analysis of factors affecting one year hearing results. *Auris Nasus Larynx, 37*(2), 150-154.
Albers, A. E., Schonfeld, U., Kandilakis, K., & Jovanovic, S. (2013). CO(2) laser revision stapedotomy. *The Laryngoscope, 123*(6), 1519-1526.
Alian, W. A., Majdalawieh, O. F., Van Wijhe, R. G., Ejnell, H., & Bance, M. (2012). Prosthetic reconstruction from the tympanic membrane to the stapes head or to the stapes footplate? A laser Doppler study. *Journal of Otolaryngology - Head & Neck Surgery, 41*(2), 84-93.
American Academy of Otolaryngology. (1995). Committee on Hearing and Equiolibrium guidelines for the evaluation of results of treatment of conductive hearing loss. *Otolaryngology - Head and Neck Surgery, 113*, 186-187.
American National Standards Institue. (1987). American National Standard Mechanical Coupler for Measurement of Bone Vibrators *(ANSI S3.13-1987)*. New York: Acoustical Society of America.
American National Standards Institue. (2010). American National Standard Specifications for Audiometers *(ANSI S3.6-2010)*. New York: Acoustical Society of America.
American Speech–Language–Hearing Association. (1990). Guidelines for screening for hearing impairments and middle ear disorders.
Antoli-Candela, F., Jr., Gomez-Molinero, F., & Busturia-Berrade, I. (2009). Otosclerosis: The effect of stapes surgery on the bone conduction audiogram. *Otology & Neurotology, 30*(3), 286-294.
Antonelli, P. J., Gianoli, G. J., Lundy, L. B., LaRouere, M. J., & Kartush, J. M. (1998). Early Post-Laser Stapedotomy Hearing Thresholds. *The American Journal of Otology, 19*(4), 443-446.
Arbogast, T. L., Mason, C. R., & Kidd, G., Jr. (2005). The effect of spatial separation on informational masking of speech in normal-hearing and hearing-impaired listeners. *The Journal of the Acoustical Society of America, 117*(4 Pt 1), 2169-2180.
Aritomo, H., & Goode, R. (1992). Comparative study of incus replacement prostheses using a temporal bone model. In N. Yanagihara & J. I. Suzuki (Eds.), *Transplants and Implants in Otology II.* (pp. 223-225). New York, NY: Kugler Publications.
Arlinger, S. D., Kylen, P., & Hellqvist, H. (1978). Skull distortion of bone conducted signals. *Acta Oto-Laryngologica, 85*(5-6), 318-323.
Arnold, W., Ferekidis, E., & Hamann, K. F. (2007). The influence of the footplate-perilymph interface on postoperative bone conduction. *Advances in Oto-Rhino-Laryngology, 65*, 155-157.

Arnoldner, C., Schwab, B., & Lenarz, T. (2006). Clinical results after stapedotomy: a comparison between the erbium: yttrium-aluminum-garnet laser and the conventional technique. *Otology & Neurotology, 27*(4), 458-465.

Aschan, G., Bergstedt, M., & Stahle, J. (1956). Nystagmography; recording of nystagmus in clinical neuro-otological examinations. *Acta Oto-Laryngologica. Supplementum, 129*, 1-103.

Aslam, M. A. (2010). Effect of ear surgery on bone conduction thresholds of patients with chronic middle ear disease. *Pakistan Journal of Medical Sciences, 26*(4), 764-768.

Atacan, E., Sennaroglu, L., Genc, A., & Kaya, S. (2001). Benign paroxysmal positional vertigo after stapedectomy. *The Laryngoscope, 111*(7), 1257-1259.

Athanasiadis-Sismanis, A. (2010). Tympanoplasty: tympanic membrane repair. In A. J. Gulya, L. B. Minor & D. Poe (Eds.), *Glasscock Shambaugh - Surgery of the Ear* (pp. 465-488). Shelton, CT: People's Medical Publishing House.

Athanasiadis-Sismanis, A., & Poe, D. (2010). Ossicular chain reconstruction. In A. J. Gulya, L. B. Minor & D. Poe (Eds.), *Glasscock Shambaugh - Surgery of the Ear* (pp. 489-500). Shelton, CT: People's Medical Publishing House.

Atherley, G. R., & Dingwall-Fordyce, I. (1963). The Reliability of Repeated Auditory Threshold Determination. *British Journal of Industrial Medicine, 20*, 231-235.

Axelsson, A., & Ryan, A. (2001). Circulation of the inner ear: comparative study of the vascular anatomy in the mammalian cochlea. In A. Jahn & J. Santos-Sacchi (Eds.), *Physiology of the ear* (pp. 301 - 320). San Diego, CA: Singular.

Ayache, D., Lejeune, D., & Williams, M. T. (2007). Imaging of Postoperative Sensorineural Complications of Stapes Surgery: a pictorial essay. *Advances in Oto-Rhino-Laryngology, 65*, 308-313.

Az-ma, T., Saeki, N., & Yuge, O. (1999). Cytosolic Ca2+ movements of endothelial cells exposed to reactive oxygen intermediates: role of hydroxyl radical-mediated redox alteration of cell-membrane Ca2+ channels. *British Journal of Pharmacology, 126*(6), 1462-1470.

Babighian, G. G., & Albu, S. (2009). Failures in stapedotomy for otosclerosis. *Otolaryngology - Head and Neck Surgery, 141*(3), 395-400.

Backous, D. D., Coker, N. J., & Jenkins, H. A. (1993). Prospective study of resident-performed stapedectomy. *Otology & Neurotology, 14*(5), 451-454.

Backous, D. D., Minor, L. B., Aboujaoude, E. S., & Nager, G. T. (1999). Relationship of the utriculus and sacculus to the stapes footplate: anatomic implications for sound-and/or pressure-induced otolith activation. *The Annals of Otology, Rhinology, and Laryngology, 108*(6), 548-553.

Bailey, H. A., Jr., Pappas, J. J., & Graham, S. S. (1983). Small fenestra stapedectomy technique: reducing risk and improving hearing. *Otolaryngology - Head and Neck Surgery, 91*(5), 516-520.

Baloh, R. W., & Honrubia, V. (1989). *Clinical neurophysiology of the vestibular system*. New York, NY: Oxford University Press.

Baloh, R. W., Honrubia, V., Yee, R. D., & Hess, K. (1984). Changes in the human vestibulo-ocular reflex after loss of peripheral sensitivity. *Annals of Neurology, 16*(2), 222-228.

Baloh, R. W., Sills, A. W., & Honrubia, V. (1979). Impulsive and sinusoidal rotatory testing: a comparison with results of caloric testing. *The Laryngoscope, 89*(4), 646-654.

Bance, M., Morris, D. P., & Van Wijhe, R. (2007). Effects of ossicular prosthesis mass and section of the stapes tendon on middle ear transmission. *The Journal of Otolaryngology, 36*(2), 113-119.

Bance, M., Morris, D. P., Vanwijhe, R. G., Kiefte, M., & Funnell, W. R. (2004). Comparison of the mechanical performance of ossiculoplasty using a prosthetic malleus-to-stapes head with a tympanic membrane-to-stapes head assembly in a human cadaveric middle ear model. *Otology & Neurotology, 25*(6), 903-909.

Bárány, E. (1938). *A contribution to the physiology of bone conduction*. Thesis. Thaning and Appels forlag.

Barbara, M., Monini, S., de Seta, E., & Filipo, R. (1994). Early hearing evaluation after microdrill stapedotomy. *Clinical Otolaryngology and Allied Sciences, 19*(1), 9-12.

Barbara, M., Ronchetti, F., Cerruto, R., Bandiera, G., Monini, S., & Filipo, R. (2005). Early Audiometric Evaluations May Predict Cochlear Damage After Stapes Surgery. *The Mediterranean Journal of Otology, 2*, 1 - 5.

Barry, S. J., & Vaughan, R. B. (1981). Loudness balance calibration of bone conduction vibrators. *Journal of Speech and Hearing Research, 24*(3), 454-459.
Bartels, L. J. (1990). KTP laser stapedotomy: is it safe? *Otolaryngology - Head and Neck Surgery, 103*(5 (Pt 1)), 685-692.
Batteau, D. W. (1967). The role of the pinna in human localization. *Proceedings of the Royal Society of London, 168*(1011), 158-180.
Bauchet St Martin, M., Rubinstein, E. N., & Hirsch, B. E. (2008). High-frequency sensorineural hearing loss after stapedectomy. *Otology & Neurotology, 29*(4), 447-452.
Beahan, N., Kei, J., Driscoll, C., Charles, B., & Khan, A. (2012). High-frequency pure-tone audiometry in children: a test-retest reliability study relative to ototoxic criteria. *Ear and Hearing, 33*(1), 104-111.
Beentjes, B. I. (1972). The cochlear aqueduct and the pressure of cerebrospinal and endolabyrinthine fluids. *Acta Oto-Laryngologica, 73*(2), 112-120.
Beiter, R. C., & Talley, J. N. (1976). High-frequency audiometry above 8,000 Hz. *Audiology, 15*(3), 207-214.
Bell, I., Goodsell, S., & Thornton, A. R. (1980). A brief communication on bone conduction artefacts. *British Journal of Audiology, 14*(3), 73-75.
Bellucci, R. J. (1979). Trends and profiles in stapes surgery. *Annals of Otology, Rhinology and Laryngology, 88*(5 Pt 1), 708-713.
Benitez, J. T., & Schuknecht, H. F. (1962). Otosclerosis: a human temporal bone report. *The Laryngoscope, 72*, 1-9.
Bennett, M., Warren, F., & Haynes, D. (2006). Indications and technique in mastoidectomy. *Otolaryngologic Clinics of North America, 39*(6), 1095-1113.
Beranek, L. (1949). *Acoustic Measurements*. Hoboken, NJ: John Wiley & Sons, Incorporated.
Berenholz, L. P., Rizer, F. M., Burkey, J. M., Schuring, A. G., & Lippy, W. H. (2000). Ossiculoplasty in Canal Wall Down Mastoidectomy. *Otolaryngology - Head and Neck Surgery, 123*(1), 30-33.
Bergin, M. J. (2011). *Inner Ear Effects of Middle Ear Surgery*. Thesis. University of Otago.
Bergstrom, B. (1973a). Morphology of the vestibular nerve. 3. Analysis of the calibers of the myelinated vestibular nerve fibers in man at various ages. *Acta Oto-Laryngologica, 76*(5), 331-338.
Bergstrom, B. (1973b). Morphology of the vestibular nerve. II. The number of myelinated vestibular nerve fibers in man at various ages. *Acta Oto-Laryngologica, 76*(2), 173-179.
Best, V., Carlile, S., Jin, C., & van Schaik, A. (2005). The role of high frequencies in speech localization. *The Journal of the Acoustical Society of America, 118*(1), 353-363.
Bhansali, S. A., & Honrubia, V. (1999). Current status of electronystagmography testing. *Otolaryngology - Head and Neck Surgery, 120*(3), 419-426.
Bicknell, P. G. (1971). Sensorineural deafness following myringoplasty operations. *The Journal of Laryngology & Otology, 85*(9), 957-961.
Birch, L., & Elbrond, O. (1985). Stapedectomy and vertigo. *Clinical Otolaryngology and Allied Sciences, 10*(4), 217-223.
Black, B. (1992). Ossiculoplasty prognosis: the spite method of assessment. *The American Journal of Otology, 13*(6), 544-551.
Black, F. O., Pesznecker, S., Norton, T., Fowler, L., Lilly, D. J., Shupert, C., . . . Jacobson, E. S. (1991). Surgical management of perilymph fistulas. A new technique. *Archives of Otolaryngology - Head and Neck Surgery, 117*(6), 641-648.
Blauert, J. (1997). *Spatial hearing: the psychophysics of human sound localization*. Cambridge, MA: MIT press.
Bohmer, A., & Rickenmann, J. (1995). The subjective visual vertical as a clinical parameter of vestibular function in peripheral vestibular diseases. *Journal of Vestibular Research, 5*(1), 35-45.
Boonchoo, R., & Puapermpoonsiri, P. (2007). Early and Late Hearing Outcomes after CO2 Laser Stapedotomy. *Journal of the Medical Association of Thailand, 90*(8), 1647-1653.
Boothroyd, A., & Medwetsky, L. (1992). Spectral distribution of /s/ and the frequency response of hearing aids. *Ear and Hearing, 13*(3), 150-157.

Brackmann, D. E., & Sheehy, J. L. (1979). Tympanoplasty: TORPS and PORPS. *The Laryngoscope, 89*(1), 108-114.
Brandt, T., & Strupp, M. (2005). General vestibular testing. *Clinical Neurophysiology, 116*(2), 406-426.
Brannstrom, K. J., & Lantz, J. (2010). Interaural attenuation for Sennheiser HDA 200 circumaural earphones. *International Journal of Audiology, 49*(6), 467-471.
Brantberg, K., Granath, K., & Schart, N. (2007). Age-related changes in vestibular evoked myogenic potentials. *Audiology and Neurotology, 12*(4), 247-253.
Brantberg, K., Tribukait, A., & Fransson, P. A. (2003). Vestibular evoked myogenic potentials in response to skull taps for patients with vestibular neuritis. *Journal of Vestibular Research, 13*(2-3), 121-130.
Brase, C., Keil, I., Schwitulla, J., Mantsopoulos, K., Schmid, M., Iro, H., & Hornung, J. (2013). Bone conduction after stapes surgery: comparison of CO2 laser and manual perforation. *Otology & Neurotology, 34*(5), 821-826.
Brinkmann, R., & Richter, U. (1980). A determination of the normal threshold of hearing by bone conduction. *Proceedings of the 10th International Congres on Acoustics., paper B-11.2*.
Bronkhorst, A. W. (1995). Localization of real and virtual sound sources. *The Journal of the Acoustical Society of America, 98*(5), 2542-2553.
Bronkhorst, A. W., & Plomp, R. (1988). The effect of head-induced interaural time and level differences on speech intelligibility in noise. *The Journal of the Acoustical Society of America, 83*(4), 1508-1516.
Bronkhorst, A. W., & Plomp, R. (1989). Binaural speech intelligibility in noise for hearing-impaired listeners. *The Journal of the Acoustical Society of America, 86*(4), 1374-1383.
Bronkhorst, A. W., & Plomp, R. (1992). Effect of multiple speechlike maskers on binaural speech recognition in normal and impaired hearing. *The Journal of the Acoustical Society of America, 92*(6), 3132-3139.
Brownell, W. E., Bader, C. R., Bertrand, D., & de Ribaupierre, Y. (1985). Evoked mechanical responses of isolated cochlear outer hair cells. *Science, 227*(4683), 194-196.
Brungart, D. S., & Simpson, B. D. (2009). Effects of bandwidth on auditory localization with a noise masker. *The Journal of the Acoustical Society of America, 126*(6), 3199-3208.
Buchler, M., Kompis, M., & Hotz, M. A. (2012). Extended frequency range hearing thresholds and otoacoustic emissions in acute acoustic trauma. *Otology & Neurotology, 33*(8), 1315-1322.
Buchman, C. A., Fucci, M. J., Roberson, J. B., Jr., & De La Cruz, A. (2000). Comparison of argon and CO2 laser stapedotomy in primary otosclerosis surgery. *American Journal of Otolaryngology, 21*(4), 227-230.
Buren, M., Solem, B. S., & Laukli, E. (1992). Threshold of hearing (0.125-20 kHz) in children and youngsters. *British Journal of Audiology, 26*(1), 23-31.
Burtner, D., & Goodman, M. L. (1974). Etiological factors in poststapedectomy granulomas. *Archives of Otolaryngology, 100*(3), 171-173.
Butler, R. A. (1986). The bandwidth effect on monaural and binaural localization. *Hearing Research, 21*(1), 67-73.
Butler, R. A., & Humanski, R. A. (1992). Localization of sound in the vertical plane with and without high-frequency spectral cues. *Perception & Psychophysics, 51*(2), 182-186.
Butler, R. A., Humanski, R. A., & Musicant, A. D. (1990). Binaural and monaural localization of sound in two-dimensional space. *Perception, 19*(2), 241-256.
Campbell, K., Claussen, A., Meech, R., Verhulst, S., Fox, D., & Hughes, L. (2011). D-methionine (D-met) significantly rescues noise-induced hearing loss: timing studies. *Hearing Research, 282*(1-2), 138-144.
Campbell, K. C., Meech, R. P., Klemens, J. J., Gerberi, M. T., Dyrstad, S. S., Larsen, D. L., . . . Hughes, L. F. (2007). Prevention of noise- and drug-induced hearing loss with D-methionine. *Hearing Research, 226*(1-2), 92-103.
Campbell, K. C., Rybak, L. P., Meech, R. P., & Hughes, L. (1996). D-methionine provides excellent protection from cisplatin ototoxicity in the rat. *Hearing Research, 102*(1-2), 90-98.
Carhart, R. (1971). Observations on relations between thresholds for pure tones and for speech. *The Journal of Speech and Hearing Disorders, 36*(4), 476-483.

Carhart, R., & Hayes, C. (1949). Clinical reliability of bone conduction audiometry. *The Laryngoscope, 59*(10), 1084-1101.
Carhart, R., & Jerger, J. F. (1959). Preferred method for clinical determination of pure-tone thresholds. *Journal of Speech & Hearing Disorders, 24*, 330-345.
Carlile, S. (1996). *Virtual auditory space: Generation and applications*. Austin, TX: RG Landes
Carlile, S., Delaney, S., & Corderoy, A. (1999). The localisation of spectrally restricted sounds by human listeners. *Hearing Research, 128*(1-2), 175-189.
Carlile, S., Leong, P., & Hyams, S. (1997). The nature and distribution of errors in sound localization by human listeners. *Hearing Research, 114*(1-2), 179-196.
Causse, J. B., Causse, J. R., Cezard, R., Briand, C., Bretlau, P., Wiet, R., & House, J. W. (1988). Vertigo in postoperative follow-up of otosclerosis. *The American Journal of Otology, 9*(3), 246-255.
Causse, J. B., Causse, J. R., & Parahy, C. (1985). Stapedotomy technique and results. *The American Journal of Otology, 6*(1), 68-71.
Causse, J. B., Causse, J. R., Wiet, R. J., & Yoo, T. J. (1983). Complications of stapedectomies. *The American Journal of Otology, 4*(4), 275-280.
Causse, J. R., Causse, J. B., Bretlau, P., Uriel, J., Berges, J., Chevance, L. G., . . . Bastide, J. M. (1989). Etiology of otospongiotic sensorineural losses. *The American Journal of Otology, 10*(2), 99-107.
Chandler, J. R., & Rodriguez-Torro, O. E. (1983). Changing patterns of otosclerosis surgery in teaching institutions. *Otolaryngology - Head and Neck Surgery, 91*(3), 239-245.
Chang, C. W., Cheng, P. W., & Young, Y. H. (2014). Inner ear deficits after chronic otitis media. *European Archives of Oto-Rhino-Laryngology 271*(8), 2165-2170.
Cheng, A. G., Cunningham, L. L., & Rubel, E. W. (2005). Mechanisms of hair cell death and protection. *Current opinion in Otolaryngology & Head and Neck Surgery, 13*(6), 343-348.
Cheng, J. T., Aarnisalo, A. A., Harrington, E., Hernandez-Montes Mdel, S., Furlong, C., Merchant, S. N., & Rosowski, J. J. (2010). Motion of the surface of the human tympanic membrane measured with stroboscopic holography. *Hearing Research, 263*(1-2), 66-77.
Chi, F. L., Wu, Y., Yan, Q. B., Shen, Y. H., Jiang, Y., & Fan, B. H. (2009). Sensitivity and fidelity of a novel piezoelectric middle ear transducer. *ORL; Journal for Oto-Rhino-Laryngology, 71*(4), 216-220.
Chien, W., Rosowski, J. J., Ravicz, M. E., Rauch, S. D., Smullen, J., & Merchant, S. N. (2009). Measurements of stapes velocity in live human ears. *Hearing Research, 249*(1-2), 54-61.
Chihara, Y., Iwasaki, S., Ushio, M., & Murofushi, T. (2007). Vestibular-evoked extraocular potentials by air-conducted sound: another clinical test for vestibular function. *Clinical Neurophysiology, 118*(12), 2745-2751.
Cho, Y. S., Lee, H. S., Hong, S. H., Chung, W. H., Min, J. Y., & Hwang, S. J. (2007). Effects of packing on the postoperative hearing after middle ear surgery. *Acta Oto-Laryngologica. Supplementum*(558), 67-72.
Choi, H. G., Lee, D. H., Chang, K. H., Yeo, S. W., Yoon, S. H., & Jun, B. C. (2011). Frequency-specific hearing results after surgery for chronic ear diseases. *Clinical and Experimental Otorhinolaryngology, 4*(3), 126-130.
Chung, F., Un, V., & Su, J. (1996). Postoperative symptoms 24 hours after ambulatory anaesthesia. *Canadian Journal of Anaesthesia, 43*(11), 1121-1127.
Cicchetti, D. V. (1994). Multiple comparison methods: establishing guidelines for their valid application in neuropsychological research. *Journal of Clinical and Experimental Neuropsychology, 16*(1), 155-161.
Ciorba, A., Gasparini, P., Chicca, M., Pinamonti, S., & Martini, A. (2010). Reactive oxygen species in human inner ear perilymph. *Acta Oto-Laryngologica, 130*(2), 240-246.
Clark, J. A., & Pickles, J. O. (1996). The effects of moderate and low levels of acoustic overstimulation on stereocilia and their tip links in the guinea pig. *Hearing Research, 99*(1-2), 119-128.
Clerici, W. J., & Yang, L. (1996). Direct effects of intraperilymphatic reactive oxygen species generation on cochlear function. *Hearing Research, 101*(1-2), 14-22.

Cody, A. R., & Johnstone, B. M. (1981). Acoustic trauma: single neuron basis for the "half-octave shift". *The Journal of the Acoustical Society of America, 70*(3), 707-711.
Coker, N. J., Ator, G. A., Jenkins, H. A., & Neblett, C. R. (1986). Carbon dioxide laser stapedotomy: a histopathologic study. *American Journal of Otolaryngology, 7*(4), 253-257.
Colebatch, J. G. (2001). Vestibular evoked potentials. *Current Opinion in Neurology, 14*(1), 21-26.
Colebatch, J. G., & Halmagyi, G. M. (1992). Vestibular evoked potentials in human neck muscles before and after unilateral vestibular deafferentation. *Neurology, 42*(8), 1635-1636.
Colebatch, J. G., Halmagyi, G. M., & Skuse, N. F. (1994). Myogenic potentials generated by a click-evoked vestibulocollic reflex. *Journal of Neurology, Neurosurgery, and Psychiatry, 57*(2), 190-197.
Coles, R. R., Lutman, M. E., & Robinson, D. W. (1991). The limited accuracy of bone-conduction audiometry: its significance in medicolegal assessments. *The Journal of Laryngology & Otology, 105*(7), 518-521.
Colletti, V., Sittoni, V., & Fiorino, F. G. (1988). Stapedotomy with and without stapedius tendon preservation versus stapedectomy: long-term results. *The American Journal of Otology, 9*(2), 136-141.
Corliss, L. M., Doster, M. E., Simonton, J., & Downs, M. (1970). High frequency and regular audiometry among selected groups of high school students. *The Journal of School Health, 40*(8), 400-405.
Correia, M., & Dickman, J. (1991). Peripheral vestibular system. In M. M. Paparella, D. A. Shumrick, J. L. Gluckman & W. L. Meyerhoff (Eds.), *Otolaryngology* (pp. 269-279). Philadelphia, PA: W.B. Saunders.
Corso, F. (1963). Bone-conduction thresholds for sonic and ultrasonic frequencies. *The Journal of the Acoustical Society of America, 35*, 1738-1743.
Cremers, C. W., Beusen, J. M., & Huygen, P. L. (1991). Hearing gain after stapedotomy, partial platinectomy, or total stapedectomy for otosclerosis. *The Annals of Otology, Rhinology, and Laryngology, 100*(12), 959-961.
Crowe, S. J., Guild, S. R., & Polvogt, L. M. (1934). Observations on the Pathology of High-tone Deafness. *Bulletin of the Johns Hopkins Hospital, 54*, 315-379.
Cuda, D., Murri, A., Mochi, P., Solenghi, T., & Tinelli, N. (2009). Microdrill, CO2-laser, and piezoelectric stapedotomy: a comparative study. *Otology & Neurotology, 30*(8), 1111-1115.
Cureoglu, S., Schachern, P. A., Rinaldo, A., Tsuprun, V., Ferlito, A., & Paparella, M. M. (2005). Round window membrane and labyrinthine pathological changes: an overview. *Acta Oto-Laryngologica, 125*(1), 9-15.
Curthoys, I. S. (2010). A critical review of the neurophysiological evidence underlying clinical vestibular testing using sound, vibration and galvanic stimuli. *Clinical Neurophysiology, 121*(2), 132-144.
Curthoys, I. S. (2012). The interpretation of clinical tests of peripheral vestibular function. *The Laryngoscope, 122*(6), 1342-1352.
Curthoys, I. S., Burgess, A. M., Iwasaki, S., Chihara, Y., Ushio, M., & McGarvie, L. A. (2011). Probability and the weight of evidence. Reply to Xie: ‘‘Comment on the ocular vestibular-evoked myogenic potential to air-conducted sound; probable superior vestibular nerve origin *Clinical Neurophysiology, 122*(6), 1269-1270.
Curthoys, I. S., Dai, M. J., & Halmagyi, G. M. (1991). Human ocular torsional position before and after unilateral vestibular neurectomy. *Experimental Brain Research, 85*(1), 218-225.
Curthoys, I. S., Iwasaki, S., Chihara, Y., Ushio, M., McGarvie, L. A., & Burgess, A. M. (2011). The ocular vestibular-evoked myogenic potential to air-conducted sound; probable superior vestibular nerve origin. *Clinical Neurophysiology, 122*(3), 611-616.
Curthoys, I. S., Kim, J., McPhedran, S. K., & Camp, A. J. (2006). Bone conducted vibration selectively activates irregular primary otolithic vestibular neurons in the guinea pig. *Experimental Brain Research, 175*(2), 256-267.
da Cruz, M. J., Fagan, P., Atlas, M., & McNeill, C. (1997). Drill-induced hearing loss in the nonoperated ear. *Otolaryngology - Head and Neck Surgery, 117*(5), 555-558.
Dallos, P. (1973). *The auditory periphery: Biophysics and physiology*. New York, NY: Academic Press.

Dallos, P. (1992). The Active Cochlea. *Journal of Neuroscience, 12*(12), 4575-4585.
Dawes, J. D., Cameron, D. S., Curry, A. R., & Rannie, I. (1973). Post-stapedectomy granuloma of the oval window. *The Journal of Laryngology & Otology, 87*(4), 365-378.
Dawes, J. D. K., & Curry, A. R. (1974). Types of stapedectomy Failure and prognosis of revision operations. *The Journal of Laryngology & Otology, 88*, 213-216.
Dawes, P. J. D. (1999). Early complications of surgery for chronic otitis media. *The Journal of Laryngology & Otology, 113*, 803-810.
de Bruijn, A. J., Tange, R. A., & Dreschler, W. A. (1999). Comparison of stapes prostheses: a retrospective analysis of individual audiometric results obtained after stapedotomy by implantation of a gold and a teflon piston. *The American Journal of Otology, 20*(5), 573-580.
de Bruijn, A. J., Tange, R. A., & Dreschler, W. A. (2001). Efficacy of evaluation of audiometric results after stapes surgery in otosclerosis. I. The effects of using different audiologic parameters and criteria on success rates. *Otolaryngology - Head and Neck Surgery, 124*(1), 76-83.
de Zinis, L. O., Cottelli, M., & Koka, M. (2010). Inner ear function following underlay myringoplasty. *Audiology and Neurotology, 15*(3), 149-154.
Dean, M. S., & Martin, F. N. (2000). Insert earphone depth and the occlusion effect. *American Journal of Audiology, 9*(2), 131-134.
Decraemer, W. F., & Khanna, S. M. (1994). Modelling the malleus vibration as a rigid body motion with one rotational and one translational degree of freedom. *Hearing Research, 72*(1-2), 1-18.
Decraemer, W. F., & Khanna, S. M. (1995). Malleus vibration modelled as rigid body motion. *Acta Oto-Rhino-Laryngologica Belgica, 49*(2), 139-145.
Decraemer, W. F., & Khanna, S. M. (2004). Measurement, visualization and quantitative analysis of complete three-dimensional kinematical data sets of human and cat middle ear. In K. Gyo, H. Wada, N. Hato & T. Koike (Eds.), *Middle Ear Mechanics in Research and Otology* (pp. 3 - 10). Singapore: World Scientific.
Decraemer, W. F., Khanna, S. M., & Funnell, W. R. (1989). Interferometric measurement of the amplitude and phase of tympanic membrane vibrations in cat. *Hearing Research, 38*(1-2), 1-17.
Del Bo, M., Zaghis, A., & Ambrosetti, U. (1987). Some observations concerning 200 stapedectomies: fifteen years postoperatively. *The Laryngoscope, 97*(10), 1211-1213.
Demir, U. L., Karaca, S., Ozmen, O. A., Kasapoglu, F., Coskun, H. H., & Basut, O. (2012). Is it the middle ear disease or the reconstruction material that determines the functional outcome in ossicular chain reconstruction? *Otology & Neurotology, 33*(4), 580-585.
Dempsey, J. J., & Levitt, H. (1990). Bone vibrator placement and the cancellation technique. *Ear and Hearing, 11*(4), 271-281.
Denes, P. B. (1963). On the statistics of spoken English. *The Journal of the Acoustical Society of America, 35*(6), 892-904.
Desai, A. A., Aiyer, R. G., Pandya, V. K., & Nair, U. (2004). Post Operative Sensorineural Hearing Loss after Middle Ear Surgery. *Indian Journal of Otolaryngology and Head and Neck Surgery, 56*(3), 240-242.
DiBartolomeo, J. R., & Ellis, M. (1980). The argon laser in otology. *The Laryngoscope, 90*(11 Pt 1), 1786-1796.
Dinh, C. T., Haake, S., Chen, S., Hoang, K., Nong, E., Eshraghi, A. A., . . . Van De Water, T. R. (2008). Dexamethasone protects organ of corti explants against tumor necrosis factor-alpha-induced loss of auditory hair cells and alters the expression levels of apoptosis-related genes. *Neuroscience, 157*(2), 405-413.
Dirks, D. (1964). Factors Related to Bone Conduction Reliability. *Archives of Otolaryngology - Head and Neck Surgery, 79*, 551-558.
Dirks, D., & Kamm, C. (1975). Bone-vibrator measurements: physical characteristics and behavioral thresholds. *Journal of Speech, Language and Hearing Research, 18*(2), 242-260.
Dirks, D., Malmquist, C., & Bower, D. (1968). Toward the specification of normal bone-conduction threshold. *The Journal of the Acoustical Society of America, 43*(6), 1237-1242.
Dirks, D., & Malmquist, G. (1969). Comparison of frontal and mastoid bone-conduction thresholds in various conductive lesions. *Journal of Speech and Hearing Research, 12*(4), 725-746.

Dirks, D., & Swindeman, J. (1967). The variability of occluded and unoccluded bone-conduction thresholds. *Journal of Speech and Hearing Research, 10*(2), 232.
Dobreva, M. S., O'Neill, W. E., & Paige, G. D. (2011). Influence of aging on human sound localization. *Journal of Neurophysiology, 105*(5), 2471-2486.
Dobreva, M. S., O'Neill, W. E., & Paige, G. D. (2012). Influence of age, spatial memory, and ocular fixation on localization of auditory, visual, and bimodal targets by human subjects. *Experimental Brain Research, 223*(4), 441-455.
Dolan, T. G., & Morris, S. G. (1990). Administering audiometric speech tests via bone conduction: a comparison of transducers. *Ear and Hearing, 11*(6), 446-449.
Doménech, J., & Carulla, M. (1988). High-frequency audiometric changes after stapedectomy. *Scandinavian Audiology. Supplementum, 30*, 233-235.
Doménech, J., Carulla, M., & Traserra, J. (1989). Sensorineural high-frequency hearing loss after drill-generated acoustic trauma in tympanoplasty. *Archives of Oto-Rhino-Laryngology, 246*(5), 280-282.
Dornhoffer, J. L. (2003). Cartilage tympanoplasty: indications, techniques, and outcomes in a 1,000-patient series. *The Laryngoscope, 113*(11), 1844-1856.
Drake, R. L., Vogl, A. W., & Mitchell, A. W. M. (2009). *Gray's Anatomy for Students*. Philadelphia, PA: Churchill Livingstone.
Dreschler, W. A., & van der Hulst, R. J. (1987). High frequency audiometry using headphones. *Audiology Practices, 4*, 1-3.
Dreschler, W. A., van der Hulst, R. J., Tange, R. A., & Urbanus, N. A. (1985). The role of high-frequency audiometry in early detection of ototoxicity. *Audiology, 24*(6), 387-395.
Du, X., Choi, C. H., Chen, K., Cheng, W., Floyd, R. A., & Kopke, R. D. (2011). Reduced formation of oxidative stress biomarkers and migration of mononuclear phagocytes in the cochleae of chinchilla after antioxidant treatment in acute acoustic trauma. *International Journal of Otolaryngology, 2011*, 612690.
Dubno, J. R., Ahlstrom, J. B., & Horwitz, A. R. (2002). Spectral contributions to the benefit from spatial separation of speech and noise. *Journal of Speech, Language and Hearing Research, 45*(6), 1297-1310.
Duquesnoy, A. J. (1983). Effect of a single interfering noise or speech source upon the binaural sentence intelligibility of aged persons. *The Journal of the Acoustical Society of America, 74*(3), 739-743.
Eastwood, H., Chang, A., Kel, G., Sly, D., Richardson, R., & O'Leary, S. J. (2010). Round window delivery of dexamethasone ameliorates local and remote hearing loss produced by cochlear implantation into the second turn of the guinea pig cochlea. *Hearing Research, 265*(1-2), 25-29.
Edmonds, B. A., & Culling, J. F. (2005). The spatial unmasking of speech: evidence for within-channel processing of interaural time delay. *The Journal of the Acoustical Society of America, 117*(5), 3069-3078.
Eeg-Olofsson, M., Stenfelt, S., Tjellstrom, A., & Granstrom, G. (2008). Transmission of bone-conducted sound in the human skull measured by cochlear vibrations. *International Journal of Audiology, 47*(12), 761-769.
Egan, J. P. (1948). Articulation testing methods. *The Laryngoscope, 58*(9), 955-991.
Elpern, B. S., & Naunton, R. F. (1963). The stability of the occlusion effect. *Archives of Otolaryngology - Head and Neck Surgery, 77*(4), 376.
Eshraghi, A. A., Wang, J., Adil, E., He, J., Zine, A., Bublik, M., . . . Van De Water, T. R. (2007). Blocking c-Jun-N-terminal kinase signaling can prevent hearing loss induced by both electrode insertion trauma and neomycin ototoxicity. *Hearing Research, 226*(1-2), 168-177.
Evans, P., & Halliwell, B. (1999). Free radicals and hearing. Cause, consequence, and criteria. *Annals of the New York Academy of Sciences, 884*, 19-40.
Ewert, S. D., Kaiser, K., Kernschmidt, L., & Wiegrebe, L. (2012). Perceptual sensitivity to high-frequency interaural time differences created by rustling sounds. *Journal of the Association for Research in Otolaryngology, 13*(1), 131-143.

Fausti, S. A., Erickson, D. A., Frey, R. H., Rappaport, B. Z., & Schechter, M. A. (1981). The effects of noise upon human hearing sensitivity from 8000 to 20 000 Hz. *The Journal of the Acoustical Society of America, 69*(5), 1343-1347.

Fausti, S. A., Frey, R. H., Erickson, D. A., Rappaport, B. Z., Cleary, E. J., & Brummett, R. E. (1979). A system for evaluating auditory function from 8000–20 000 Hz. *The Journal of the Acoustical Society of America, 66*(6), 1713-1718.

Fausti, S. A., Frey, R. H., Henry, J. A., Knutsen, J. L., & Olson, D. J. (1990). Reliability and validity of high-frequency (8-20 kHz) thresholds obtained on a computer-based audiometer as compared to a documented laboratory system. *Journal of the American Academy of Audiology, 1*(3), 162-170.

Fausti, S. A., Frey, R. H., Henry, J. A., Olson, D. J., & Schaffer, H. I. (1992). Early detection of ototoxicity using high-frequency, tone-burst-evoked auditory brainstem responses. *Journal of the American Academy of Audiology, 3*(6), 397-404.

Fausti, S. A., Henry, J. A., Helt, W. J., Phillips, D. S., Frey, R. H., Noffsinger, D., . . . Fowler, C. G. (1999). An individualized, sensitive frequency range for early detection of ototoxicity. *Ear and Hearing, 20*(6), 497-505.

Fausti, S. A., Henry, J. A., Schaffer, H. I., Olson, D. J., Frey, R. H., & Bagby, G. C., Jr. (1993). High-frequency monitoring for early detection of cisplatin ototoxicity. *Archives of Otolaryngology - Head and Neck Surgery, 119*(6), 661-666.

Fausti, S. A., Mitchell, C. R., Frey, R. H., Henry, J. A., & O'Connor, J. L. (1994). Multiple-stimulus method for rapid collection of auditory brainstem responses using high-frequency (> or = 8 kHz) tone bursts. *Journal of the American Academy of Audiology, 5*(2), 119-126.

Fausti, S. A., Rappaport, B. Z., Schechter, M. A., & Frey, R. H. (1982). An investigation of the validity of high-frequency audition. *The Journal of the Acoustical Society of America, 71*(3), 646-649.

Fayad, J. N., Semaan, M. T., Meier, J. C., & House, J. W. (2009). Hearing results using the SMart piston prosthesis. *Otology & Neurotology, 30*(8), 1122-1127.

Fayad, J. N., Ursick, J., Brackmann, D. E., & Friedman, R. A. (2014). Total ossiculoplasty: short- and long-term results using a titanium prosthesis with footplate shoe. *Otology & Neurotology, 35*(1), 108-113.

Fernández, C., & Goldberg, J. M. (1976a). Physiology of peripheral neurons innervating otolith organs of the squirrel monkey. I. Response to static tilts and to long-duration centrifugal force. *Journal of Neurophysiology, 39*(5), 970-984.

Fernández, C., & Goldberg, J. M. (1976b). Physiology of peripheral neurons innervating otolith organs of the squirrel monkey. II. Directional selectivity and force-response relations. *Journal of Neurophysiology, 39*(5), 985-995.

Fernández, C., & Goldberg, J. M. (1976c). Physiology of peripheral neurons innervating otolith organs of the squirrel monkey. III. Response dynamics. *Journal of Neurophysiology, 39*(5), 996-1008.

Ferrazzini, M. (2003). *Virtual Middle Ear: a dynamic mathematical model based on finite element method*. Unpublished Thesis. Swiss Federal Institute of Technology.

Festen, J. M., & Plomp, R. (1986). Speech-reception threshold in noise with one and two hearing aids. *The Journal of the Acoustical Society of America, 79*(2), 465-471.

Fisch, U. (1982). Stapedotomy versus stapedectomy. *The American Journal of Otology, 4*(2), 112-117.

Fletcher, H., & Munson, W. A. (1933). Loudness, its definition, measurement and calculation. *The Journal of the Acoustical Society of America, 5*(2), 82-111.

Fletcher, J. L., Cairns, A. B., Collins, F. G., & Endicott, J. (1967). High frequency hearing following meningitis. *Journal of Auditory Research, 7*(3), 223-227.

Floc'h, J. L., Tan, W., Telang, R. S., Vlajkovic, S. M., Nuttall, A., Rooney, W. D., . . . Thorne, P. R. (2014). Markers of cochlear inflammation using MRI. *Journal of Magnetic Resonance Imaging, 39*(1), 150-161.

Forge, A., & Li, L. (2000). Apoptotic death of hair cells in mammalian vestibular sensory epithelia. *Hearing Research, 139*(1-2), 97-115.

Forge, A., & Schacht, J. (2000). Aminoglycoside antibiotics. *Audiology and Neurotology, 5*(1), 3-22.

Forge, A., & Van De Water, T. R. (2008). Protection and Repair of Inner Ear Sensory Cells. In R. J. Salvi, A. N. Popper & R. R. Fay (Eds.), *Hair Cell Regeneration, Repair, and Protection* (pp. 199-256). New York, NY: Springer.

Forton, G. E., Wuyts, F. L., Delsupehe, K. G., Verfaillie, J., & Loncke, R. (2009). CO2 laser-assisted stapedotomy combined with aWengen titanium clip stapes prosthesis: superior short-term results. *Otology & Neurotology, 30*(8), 1071-1078.

Frank, T. (1982). Influence of contralateral masking on bone-conduction thresholds. *Ear and Hearing, 3*(6), 314-319.

Frank, T. (1990). High-frequency hearing thresholds in young adults using a commercially available audiometer. *Ear and Hearing, 11*(6), 450-454.

Frank, T. (2001). High-frequency (8 to 16 kHz) reference thresholds and intrasubject threshold variability relative to ototoxicity criteria using a Sennheiser HDA 200 earphone. *Ear and Hearing, 22*(2), 161-168.

Frank, T., & Crandell, C. C. (1986). Acoustic radiation produced by B-71, B-72, and KH 70 bone vibrators. *Ear and Hearing, 7*(5), 344-347.

Frank, T., & Dreisbach, L. E. (1991). Repeatability of high-frequency thresholds. *Ear and Hearing, 12*(4), 294-295.

Frank, T., & Holmes, A. (1981). Acoustic radiation from bone vibrators. *Ear and Hearing, 2*(2), 59-63.

Frank, T., & Ragland, A. E. (1987). Repeatability of high-frequency bone conduction thresholds. *Ear and Hearing, 8*(6), 343-346.

Fredelius, L., & Rask-Andersen, H. (1990). The role of macrophages in the disposal of degeneration products within the organ of corti after acoustic overstimulation. *Acta Oto-Laryngologica, 109*(1-2), 76-82.

Fucci, M. J., Lippy, W. H., Schuring, A. G., & Rizer, F. M. (1998). Prosthesis size in stapedectomy. *Otolaryngology - Head and Neck Surgery 118*(1), 1-5.

Fujioka, M., Kanzaki, S., Okano, H. J., Masuda, M., Ogawa, K., & Okano, H. (2006). Proinflammatory cytokines expression in noise-induced damaged cochlea. *Journal of Neuroscience Research, 83*(4), 575-583.

Fullgrabe, C., Baer, T., Stone, M. A., & Moore, B. C. (2010). Preliminary evaluation of a method for fitting hearing aids with extended bandwidth. *International Journal of Audiology, 49*(10), 741-753.

Funnell, W. R., & Laszlo, C. A. (1982). A critical review of experimental observations on ear-drum structure and function. *ORL; Journal for Oto-Rhino-Laryngology, 44*(4), 181-205.

Gacek, R. R. (1968). The innervation of the vestibular labyrinth. *The Annals of Otology, Rhinology, and Laryngology, 77*(4), 676-685.

Galli, J., Parrilla, C., Fiorita, A., Marchese, M. R., & Paludetti, G. (2005). Erbium: yttrium-aluminum-garnet laser application in stapedotomy. *Otolaryngology - Head and Neck Surgery, 133*(6), 923-928.

Gallichan, M., Ravenna, S., Giguere, C., Leroux, T., Wu, L., & Wong, G. (1998). High-frequency bone conduction audiometry using a piezoelectric transducer. *Canadian Acoustics, 26*(3), 70-71.

Galy-Bernadoy, C., Akkari, M., Mathiolon, C., Mondain, M., Uziel, A., & Venail, F. (2014). Comparison of early hearing outcomes of type 2 ossiculoplasty using hydroxyapatite bone cement versus other materials. *European Annals of Otorhinolaryngology, Head and Neck Diseases, 131*(5), 289-292.

Gamra, O. B., Mbarek, C., Khammassi, K., Methlouthi, N., Ouni, H., Hariga, I., . . . El Khedim, A. (2008). Cartilage graft in type I tympanoplasty: audiological and otological outcome. *European Archives of Oto-Rhino-Laryngology, 265*(7), 739-742.

Gan, R. Z., Dyer, R. K., Wood, M. W., & Dormer, K. J. (2001). Mass loading on the ossicles and middle ear function. *The Annals of Otology, Rhinology, and Laryngology, 110*(5 Pt 1), 478-485.

Gardner, E. K., Jackson, C. G., & Kaylie, D. M. (2004). Results with titanium ossicular reconstruction prostheses. *The Laryngoscope, 114*(1), 65-70.

Gardner, M. B., & Gardner, R. S. (1973). Problem of localization in the median plane: effect of pinnae cavity occlusion. *The Journal of the Acoustical Society of America, 53*(2), 400-408.
Gelfand, S. A. (1997). *Essentials of Audiology.* New York, NY: Theme Medical Publishers.
Gelfand, S. A., Ross, L., & Miller, S. (1988). Sentence reception in noise from one versus two sources: effects of aging and hearing loss. *The Journal of the Acoustical Society of America, 83*(1), 248-256.
Gerard, J., Serry, P., & Gersdorff, M. C. (2008). Outcome and Lack of Prognostic Factors in Stapes Surgery. *Otology & Neurotology, 29*, 290-294.
Gilkey, R. H., & Anderson, T. R. (1995). The accuracy of absolute localization judgments for speech stimuli. *Journal of Vestibular Research, 5*(6), 487-497.
Gjuric, M., Schneider, W., Buhr, W., Wolf, S. R., & Wigand, M. E. (1997). Experimental sensorineural hearing loss following drill-induced ossicular chain injury. *Acta Oto-Laryngologica, 117*(4), 497-500.
Glasberg, B. R., & Moore, B. C. (1990). Derivation of auditory filter shapes from notched-noise data. *Hearing Research, 47*(1-2), 103-138.
Glasscock, M. E. (1973). Tympanic membrane grafting with fascia: overlay vs. undersurface technique. *The Laryngoscope, 83*(5), 754-770.
Gloddek, B., Lamm, K., & Haslov, K. (1992). Influence of middle ear immune response on the immunological state and function of the inner ear. *The Laryngoscope, 102*(2), 177-181.
Goldberg, J. M., & Fernández, C. (1984). The Vestibular System. In I. D. Smith (Ed.), *Handbook of Physiology*. Baltimore, MD: Williams and Wilkins.
Gomez Garcia, A., & Jauregui-Renaud, K. (2003). Subjective assessment of visual verticality in follow-up of patients with acute vestibular disease. *Ear, Nose, & Throat Journal, 82*(6), 442-444, 446.
Goode, R. L., Ball, G., Nishihara, S., & Nakamura, K. (1996). Laser Doppler vibrometer (LDV)--a new clinical tool for the otologist. *The American Journal of Otology, 17*(6), 813-822.
Goode, R. L., Friedrichs, R., & Falk, S. (1977). Effect on hearing thresholds of surgical modification of the external ear. *The Annals of Otology, Rhinology, and Laryngology, 86*(4 Pt 1), 441-450.
Goode, R. L., Killion, M., Nakamura, K., & Nishihara, S. (1994). New knowledge about the function of the human middle ear: development of an improved analog model. *Otology & Neurotology, 15*(2), 145-154.
Goodhill, V., & Holcomb, A. L. (1955). Cochlear potentials in the evaluation of bone conduction. *Annals of Otology, Rhinology and Laryngology, 64*(4), 1213-1233.
Gopen, Q. (2010). Pathology and Clinical Course of the Inflammatory Diseases of the Middle Ear. In A. J. Gulya, L. B. Minor & D. Poe (Eds.), *Glasscock Shambaugh - Surgery of the Ear* (pp. 425-436). Shelton, CT: People's Medical Publishing House.
Gordon, J. S., Phillips, D. S., Helt, W. J., Konrad-Martin, D., & Fausti, S. A. (2005). Evaluation of insert earphones for high-frequency bedside ototoxicity monitoring. *Journal of Rehabilitation Research and Development, 42*(3), 353-361.
Govender, S., Rosengren, S. M., & Colebatch, J. G. (2009). The effect of gaze direction on the ocular vestibular evoked myogenic potential produced by air-conducted sound. *Clinical Neurophysiology, 120*(7), 1386-1391.
Govender, S., Rosengren, S. M., & Colebatch, J. G. (2011). Vestibular neuritis has selective effects on air- and bone-conducted cervical and ocular vestibular evoked myogenic potentials. *Clinical Neurophysiology, 122*(6), 1246-1255.
Gray, S. (2014). *The role of hearing sensitivity above 8 kHz in auditory localization*. Thesis. University of Canterbury.
Grayeli, A. B., Sterkers, O., & Toupet, M. (2009). Audiovestibular function in patients with otosclerosis and balance disorders. *Otology & Neurotology, 30*(8), 1085-1091.
Green, D. M., Kidd, G., Jr., & Stevens, K. N. (1987). High-frequency audiometric assessment of a young adult population. *The Journal of the Acoustical Society of America, 81*(2), 485-494.
Grose, J. H., & Mamo, S. K. (2010). Processing of temporal fine structure as a function of age. *Ear and Hearing, 31*(6), 755-760.
Guinan, J. J., Jr., & Peake, W. T. (1967). Middle-ear characteristics of anesthetized cats. *The Journal of the Acoustical Society of America, 41*(5), 1237-1261.

Gulya, A. J. (2010). Developmental anatomy of the temporal bone and skull base. In A. J. Gulya, L. B. Minor & D. Poe (Eds.), *Glasscock Shambaugh - Surgery of the Ear* (pp. 3-27). Shelton, CT: People's Medical Publishing House.

Gundersen, T. (1971). *Prostheses in the ossicular chain: experimental and clinical studies*. Baltimore, MD: University Park Press Baltimore.

Gyo, K., Aritomo, H., & Goode, R. L. (1987). Measurement of the ossicular vibration ratio in human temporal bones by use of a video measuring system. *Acta Oto-Laryngologica, 103*(1-2), 87-95.

Gyo, K., Goode, R. L., & Miller, C. (1986). Effect of middle ear modification on umbo vibration. Human temporal bone experiments with a new vibration measuring system. *Archives of Otolaryngology - Head and Neck Surgery, 112*(12), 1262-1268.

Haake, S. M., Dinh, C. T., Chen, S., Eshraghi, A. A., & Van De Water, T. R. (2009). Dexamethasone protects auditory hair cells against TNFalpha-initiated apoptosis via activation of PI3K/Akt and NFkappaB signaling. *Hearing Research, 255*(1-2), 22-32.

Hain, T. C., & Helminski, J. O. (2007). Anatomy and physiology of the normal vestibular system. In S. J. Herdman (Ed.), *Vestibular Rehabilitation* (pp. 2 - 18). Philadelphia, PA: FA Davis Co.

Håkansson, B. E. (2003). The balanced electromagnetic separation transducer a new bone conduction transducer. *The Journal of the Acoustical Society of America, 113*(2), 818-825.

Hall, E. D., Andrus, P. K., & Yonkers, P. A. (1993). Brain hydroxyl radical generation in acute experimental head injury. *Journal of Neurochemistry, 60*(2), 588-594.

Halliwell, B., & Gutteridge, J. M. (1985). The importance of free radicals and catalytic metal ions in human diseases. *Molecular aspects of medicine, 8*(2), 89-193.

Halliwell, B., & Gutteridge, J. M. (1999). The chemistry of free radicals and related 'reactive species' *Free radicals in biology and medicine* (Vol. 3, pp. 36-104). Oxford, England: Oxford University Press.

Hallmo, P., & Mair, I. W. (1996). Drilling in ear surgery: A comparison of pre- and postoperative bone-conduction thresholds in both the conventional and extended high-frequency ranges. *Scandinavian Audiology, 25*(1), 35-38.

Hallmo, P., Sundby, A., & Mair, I. W. (1991). High-frequency audiometry. Response characteristics of the KH70 vibrator. *Scandinavian Audiology, 20*(2), 139-143.

Hallmo, P., Sundby, A., & Mair, I. W. (1992). High-frequency audiometry. Masking of air- and bone-conduction signals. *Scandinavian Audiology. Supplementum, 21*(2), 115-121.

Hallmo, P., Sundby, A., & Mair, I. W. (1994). Extended high-frequency audiometry. Air- and bone-conduction thresholds, age and gender variations. *Scandinavian Audiology, 23*(3), 165-170.

Halmagyi, G. M., & Curthoys, I. S. (1999). Clinical testing of otolith function. *Annals of the New York Academy of Sciences, 871*, 195-204.

Halmagyi, G. M., Yavor, R. A., & Colebatch, J. G. (1995). Tapping the head activates the vestibular system: a new use for the clinical reflex hammer. *Neurology, 45*(10), 1927-1929.

Hamilton, J. W. (2010). Systematic preservation of the ossicular chain in cholesteatoma surgery using a fiber-guided laser. *Otology & Neurotology, 31*(7), 1104-1108.

Hammerschlag, P. E., Fishman, A., & Scheer, A. A. (1998). A review of 308 cases of revision stapedectomy. *The Laryngoscope, 108*(12), 1794-1800.

Handley, G. H., & Hicks, J. N. (1990). Stapedectomy in residency--the UAB experience. *The American Journal of Otology, 11*(2), 128-130.

Handzel, O., & McKenna, M. (2010). Surgery for Otosclerosis. In A. J. Gulya, L. B. Minor & D. Poe (Eds.), *Glasscock Shambaugh - Surgery of the Ear* (pp. 529 - 546). Shelton, CT: People's Medical Publishing House.

Harder, H., Jerlvall, L., Kylén, P., & Ekvall, L. (1982). Calculation of hearing results after tympanoplasty. *Clinical Otolaryngology, 7*(4), 221-229.

Harrell, R. W. (2000). Puretone Evaluation. In J. Katz (Ed.), *Handbook of Clinical Audiology* (pp. 71 - 87). Philadelphia, PA: Lippincott Williams & Wilkins.

Harris, J. D., Haines, H. L., & Myers, C. K. (1953). A helmet-held bone conduction vibrator. *The Laryngoscope, 63*(10), 998-1007.

Harrison, W. H., Shambaugh, G. E., Jr., Derlacki, E. L., & Clemis, J. D. (1967). Perilymph fistula in stapes surgery. *The Laryngoscope, 77*(5), 836-849.

Hart, C. W., & Naunton, R. F. (1961). Frontal bone conduction tests in clinical audiometry. *The Laryngoscope, 71*, 24-29.
Hashimoto, K., Seki, M., Miyasaka, H., & Watanabe, K. (2006). Effect of steroids on increased permeability of blood vessels of the stria vascularis after auditory ossicle vibration by a drill in otologic surgery. *The Annals of Otology, Rhinology, and Laryngology, 115*(10), 769-774.
Hato, N., Stenfelt, S., & Goode, R. L. (2003). Three-dimensional stapes footplate motion in human temporal bones. *Audiology and Neurotology, 8*(3), 140-152.
Häusler, R., Messerli, A., Romano, V., Burkhalter, R., Weber, H. P., & Altermatt, H. J. (1996). Experimental and clinical results of fiberoptic argon laser stapedotomy. *European Archives of Oto-Rhino-Laryngology, 253*(4-5), 193-200.
Häusler, R., Schär, P. J., Pratisto, H., Weber, H. P., & Frenz, M. (1999). Advantages and Dangers of Erbium Laser Application in Stapedotomy. *Acta Oto-Laryngologica, 119*, 207-213.
Hawkins, D. B., & Yacullo, W. S. (1984). Signal-to-noise ratio advantage of binaural hearing aids and directional microphones under different levels of reverberation. *The Journal of Speech and Hearing Disorders, 49*(3), 278-286.
Haynes, D., & Wittkopf, J. (2010). Canal-Wall-Up Mastoidectomy. In A. J. Gulya, L. B. Minor & D. Poe (Eds.), *Glasscock Shambaugh - Surgery of the Ear* (pp. 501-514). Shelton, CT: People's Medical Publishing House.
Hebrank, J., & Wright, D. (1974). Spectral cues used in the localization of sound sources on the median plane. *The Journal of the Acoustical Society of America, 56*(6), 1829-1834.
Hedgecock, L. D. (1961). Clinical calibration of bone-conduction measurements. *Archives of Otolaryngology - Head and Neck Surgery, 73*, 186-195.
Heffner, H. E., & Heffner, R. S. (2008). High-frequency hearing *Handbook of the Senses: Audition* (pp. 55-60). New York, NY: Elsevier.
Hegarty, J. L., Patel, S., Fischbein, N., Jackler, R. K., & Lalwani, A. K. (2002). The value of enhanced magnetic resonance imaging in the evaluation of endocochlear disease. *The Laryngoscope, 112*(1), 8-17.
Hegewald, M., Heitman, R., Wiederhold, M. L., Cooper, J. C., & Gates, G. A. (1989). High-frequency electrostimulation hearing after mastoidectomy. *Otolaryngology - Head and Neck Surgery, 100*(1), 49-56.
Heiland, K. E., Goode, R. L., Asai, M., & Huber, A. M. (1999). A human temporal bone study of stapes footplate movement. *The American Journal of Otology, 20*(1), 81-86.
Helfer, K. S., & Freyman, R. L. (2008). Aging and speech-on-speech masking. *Ear and Hearing, 29*(1), 87-98.
Helms, J. (1976). Acoustic trauma from the bone cutting burr. *The Journal of Laryngology & Otology, 90*(12), 1143-1149.
Henderson, D., Bielefeld, E. C., Harris, K. C., & Hu, B. H. (2006). The role of oxidative stress in noise-induced hearing loss. *Ear and Hearing, 27*(1), 1-19.
Henning, G. B. (1974). Lateralization and the binaural masking-level difference. *The Journal of the Acoustical Society of America, 55*(6), 1259-1262.
Henning, G. B., & Ashton, J. (1981). The effect of carrier and modulation frequency on lateralization based on interaural phase and interaural group delay. *Hearing Research, 4*(2), 185-194.
Henry, P., & Letowski, T. (2007). Bone conduction: Anatomy, physiology, and communication: DTIC Document.
Hess, K., Baloh, R. W., Honrubia, V., & Yee, R. D. (1985). Rotational testing in patients with bilateral peripheral vestibular disease. *The Laryngoscope, 95*(1), 85-88.
Hibst, R. (1992). Mechanical effects of erbium:YAG laser bone ablation. *Lasers in Surgery and Medicine, 12*(2), 125-130.
Hickling, S. (1966). Studies on the reliability of auditory threshold values. *Journal of Auditory Research, 6*, 39-46.
Hildyard, V. H., Sando, I., & Davison, S. L. (1972). Diagnosis and management of far-advanced otosclerosis. *Archives of Otolaryngology - Head and Neck Surgery, 96*(6), 530-534.
Hillman, D. E., & McLaren, J. W. (1979). Displacement configuration of semicircular canal cupulae. *Neuroscience, 4*(12), 1989-2000.

Hilmi, O. J., McKee, R. H., Abel, E. W., Spielmann, P. M., & Hussain, S. S. (2012). Do high-speed drills generate high-frequency noise in mastoid surgery? *Otology & Neurotology, 33*(1), 2-5.
Hinchcliffe, R., Bochenek, Z., Pulec, J., Stroud, M., & Wilmot, T. J. (1971). Iatrogenic vestibular disorders. *The Journal of Laryngology & Otology, 85*(12), 1268- 1273.
Hirose, K., Discolo, C. M., Keasler, J. R., & Ransohoff, R. (2005). Mononuclear phagocytes migrate into the murine cochlea after acoustic trauma. *The Journal of Comparative Neurology, 489*(2), 180-194.
Hirose, K., Hockenbery, D. M., & Rubel, E. W. (1997). Reactive oxygen species in chick hair cells after gentamicin exposure in vitro. *Hearing Research, 104*(1-2), 1-14.
Hirvonen, T. P., & Aalto, H. (2013). Immediate postoperative nystagmus and vestibular symptoms after stapes surgery. *Acta Oto-Laryngologica, 133*(8), 842-845.
Hodgson, R. S., & Wilson, D. F. (1991). Argon Laser Stapedotomy. *The Laryngoscope, 101*(3), 230-233.
Hofman, M., & Van, O. J. (2003). Binaural weighting of pinna cues in human sound localization. *Experimental Brain Research, 148*(4), 458-470.
Holmquist, J., Oleander, R., & Hallen, O. (1979). Peroperative drill-generated noise levels in ear surgery. *Acta Oto-Laryngologica, 87*(5-6), 458-460.
Homma, K., Du, Y., Shimizu, Y., & Puria, S. (2009). Ossicular resonance modes of the human middle ear for bone and air conduction. *Acoustical Society of America, 125*(2), 968-979.
Hood, J. D. (1957). The Principles and Practice of Bone Conduction Audiometry : A Review of the Present Position. *Proceedings of the Royal Society of Medicine, 50*(9), 689 - 697.
Hough, J. V. D. (1966). Recent advances in otosclerosis. *Archives of Otolaryngology - Head and Neck Surgery, 83*(4), 379.
House, H. P. (1967). The fistula problem in otosclerosis surgery. *The Laryngoscope, 77*(8), 1410-1426.
Huang, T., Cheng, A. G., Stupak, H., Liu, W., Kim, A., Staecker, H., . . . Van De Water, T. R. (2000). Oxidative stress-induced apoptosis of cochlear sensory cells: otoprotective strategies. *International Journal of Developmental Neuroscience, 18*(2-3), 259-270.
Huang, Y. C., Yang, T. L., & Young, Y. H. (2012). Feasibility of ocular vestibular-evoked myogenic potentials (oVEMPs) recorded with eyes closed. *Clinical Neurophysiology, 123*(2), 376-381.
Huber, A., Linder, T., & Fisch, U. (2001). Is the Er:YAG laser damaging to inner ear function? *Otology & Neurotology, 22*(3), 311-315.
Hughes, C. A., & Proctor, L. (1997). Benign paroxysmal positional vertigo. *The Laryngoscope, 107*(5), 607-613.
Humanski, R. A., & Butler, R. A. (1988). The contribution of the near and far ear toward localization of sound in the sagittal plane. *The Journal of the Acoustical Society of America, 83*(6), 2300-2310.
Hunter, L. L., Margolis, R. H., Rykken, J. R., Le, C. T., Daly, K. A., & Giebink, G. S. (1996). High frequency hearing loss associated with otitis media. *Ear and Hearing, 17*(1), 1-11.
Huttenbrink, K. B. (2003). Biomechanics of stapesplasty: a review. *Otology & Neurotology, 24*(4), 548-557; discussion 557-559.
Igarashi, M., O Uchi, T., Isago, H., & Wright, W. K. (1983). Utricular and saccular volumetry in human temporal bones. *Acta Oto-Laryngologica, 95*(1-2), 75-80.
Ikeda, R., Nakaya, K., Oshima, H., Oshima, T., Kawase, T., & Kobayashi, T. (2011). Effect of aspiration of perilymph during stapes surgery on the endocochlear potential of guinea pig. *Otolaryngology - Head and Neck Surgery, 145*(5), 801-805.
Iniguez-Cuadra, R., Alobid, I., Bores-Domenech, A., Menendez-Colino, L. M., Caballero-Borrego, M., & Bernal-Sprekelsen, M. (2010). Type III tympanoplasty with titanium total ossicular replacement prosthesis: anatomic and functional results. *Otology & Neurotology, 31*(3), 409-414.
International Electrotechnical Commission. (1971). An IEC mechanical coupler for the calibration of bone vibrators having a specified contact area and being applied with a specified static force *(IEC 373:1971)*.
International Electrotechnical Commission. (1998). Specification for an acoustic coupler (IEC reference type) for calibration of earphones used in audiometry *(IEC 60318-3:1998)*.

International Electrotechnical Commission. (2012). Electroacoustics - Audiometric equipment - Part 1: Equipment for pure-tone audiometry *(IEC 60645-1:2012)*.
International Organization for Standardization. (1998). Acoustics -- Reference zero for the calibration of audiometric equipment -- Part 1: Reference equivalent threshold sound pressure levels for pure tones and supra-aural earphones *(ISO 389-1:1998)*.
International Organization for Standardization. (2005). Acoustics - Reference zero for the calibration of audiometric equipment. Part 7 - Reference threshold of of hearing under free-field and diffuse-field listening conditions. *(ISO 398-7:2005)*.
International Organization for Standardization. (2006). Acoustics -- Reference zero for the calibration of audiometric equipment -- Part 5: Reference equivalent threshold sound pressure levels for pure tones in the frequency range 8 kHz to 16 kHz *(ISO 389-5:2006)*.
International Organization for Standardization. (2010). Acoustics - Audiometric test methods - Part 1: Basic pure tone air and bone conduction threshold audiometry *(ISO 8253-1:2010)*.
Ito, T., Röösli, C., Kim, C. J., Sim, J. H., Huber, A. M., & Probst, R. (2011). Bone conduction thresholds and skull vibration measured on the teeth during stimulation at different sites on the human head. *Audiology and Neurotology, 16*(1), 12-22.
Iwasaki, S., Chihara, Y., Smulders, Y. E., Burgess, A. M., Halmagyi, G. M., Curthoys, I. S., & Murofushi, T. (2009). The role of the superior vestibular nerve in generating ocular vestibular-evoked myogenic potentials to bone conducted vibration at Fz. *Clinical Neurophysiology, 120*(3), 588-593.
Iwasaki, S., McGarvie, L. A., Halmagyi, G. M., Burgess, A. M., Kim, J., Colebatch, J. G., & Curthoys, I. S. (2007). Head taps evoke a crossed vestibulo-ocular reflex. *Neurology, 68*(15), 1227-1229.
Iwasaki, S., Smulders, Y. E., Burgess, A. M., McGarvie, L. A., Macdougall, H. G., Halmagyi, G. M., & Curthoys, I. S. (2008). Ocular vestibular evoked myogenic potentials to bone conducted vibration of the midline forehead at Fz in healthy subjects. *Clinical Neurophysiology, 119*(9), 2135-2147.
Jacobson, E. J., Downs, M. P., & Fletcher, J. L. (1969). Clinical findings in high-frequency thresholds during known ototoxic drug usage. *Journal of Auditory Research, 9*(4), 379-385.
Jacobson, G. P., & Newman, C. W. (1991). Rotational testing. *Seminars in Hearing, 12*(3), 199-224.
Jang, C. H. (2002). Changes in external ear resonance after mastoidectomy: open cavity mastoid versus obliterated mastoid cavity. *Clinical Otolaryngology and Allied Sciences, 27*(6), 509-511.
Jansson, K. F., Hakansson, B., Johannsen, L., & Tengstrand, T. (2014). Electro-acoustic performance of the new bone vibrator Radioear B81: A comparison with the conventional Radioear B71. *International Journal of Audiology*, 1-7.
Javel, E., Grant, I. L., & Kroll, K. (2003). In vivo characterization of piezoelectric transducers for implantable hearing AIDS. *Otology & Neurotology, 24*(5), 784-795.
Jesberger, J. A., & Richardson, J. S. (1991). Oxygen free radicals and brain dysfunction. *The International Journal of Neuroscience, 57*(1-2), 1-17.
Jia, H., Wang, J., Francois, F., Uziel, A., Puel, J. L., & Venail, F. (2013). Molecular and cellular mechanisms of loss of residual hearing after cochlear implantation. *The Annals of Otology, Rhinology, and Laryngology, 122*(1), 33-39.
Jiang, D., Bibas, A., Santuli, C., Donnelly, N., Jeronimidis, G., & O'Connor, A. F. (2007). Equivalent noise level generated by drilling onto the ossicular chain as measured by laser Doppler vibrometry: a temporal bone study. *The Laryngoscope, 117*(6), 1040-1045.
Jin, C., Best, V., Carlile, S., Baer, T., & Moore, B. (2002). *Speech localization.* Paper presented at the Audio Engineering Society Convention 112.
Jin, C., Corderoy, A., Carlile, S., & van Schaik, A. (2004). Contrasting monaural and interaural spectral cues for human sound localization. *The Journal of the Acoustical Society of America, 115*(6), 3124-3141.
Johar, D., Roth, J. C., Bay, G. H., Walker, J. N., Kroczak, T. J., & Los, M. (2004). Inflammatory response, reactive oxygen species, programmed (necrotic-like and apoptotic) cell death and cancer. *Roczniki Akademii Medycznej w Bialymstoku, 49*, 31-39.

Jongkees, L. B., & Philipszoon, A. J. (1964). Electronystagmography. *Acta Oto-Laryngologica. Supplementum, 189*, Suppl 189.
Jovanovic, S. (2005). Lasers in Otology. In K. B. Huttenbrink (Ed.), *Lasers in Otorhinolaryngology* (pp. 21 - 52). Stuttgart, Germany: Thieme.
Jovanovic, S., Anft, D., Schonfeld, U., Berghaus, A., & Scherer, H. (1999). Influence of CO2 laser application to the guinea-pig cochlea on compound action potentials. *The American Journal of Otology, 20*(2), 166-173.
Jovanovic, S., Schonfeld, U., Fischer, R., Doring, M., Prapavat, V., Muller, G., & Scherer, H. (1995). Thermal stress of the inner ear during laser stapedotomy. I: Continuous-wave laser. *HNO, 43*(12), 702-709.
Jovanovic, S., Schonfeld, U., Fischer, R., Doring, M., Prapavat, V., Muller, G., & Scherer, H. (1998). Thermic effects in the "vestibule" during laser stapedotomy with pulsed laser systems. *Lasers in Surgery and Medicine, 23*(1), 7-17.
Jovanovic, S., Schonfeld, U., & Scherer, H. (2004). CO2 laser stapedotomy with the "one-shot" technique--clinical results. *Otolaryngology - Head and Neck Surgery, 131*(5), 750-757.
Juhn, S. K., Hunter, B. A., & Odland, R. M. (2001). Blood-labyrinth barrier and fluid dynamics of the inner ear. *The Iinternational Tinnitus Journal, 7*(2), 72-83.
Just, T., Guder, E., & Pau, H. W. (2011). Effect of the stapedotomy technique on early post-operative hearing results--Preliminary results. *Auris Nasus Larynx, 39*(4), 383-386.
Kalikow, D. N., Stevens, K. N., & Elliott, L. L. (1977). Development of a test of speech intelligibility in noise using sentence materials with controlled word predictability. *The Journal of the Acoustical Society of America, 61*(5), 1337-1351.
Kamal, S. A. (1996). Vein Graft in Stapes Surgery. *The American Journal of Otology, 17*(2), 230-235.
Kantner, C., & Gurkov, R. (2012). Characteristics and clinical applications of ocular vestibular evoked myogenic potentials. *Hearing Research, 294*(1-2), 55-63.
Kapteyn, T. S., Boezeman, E. H., & Snel, A. M. (1983). Bone-conduction measurement and calibration using the cancellation method. *The Journal of the Acoustical Society of America, 74*(4), 1297-1299.
Karatas, E., Miman, M. C., Ozturan, O., Erdem, T., & Kalcioglu, M. T. (2007). Contralateral normal ear after mastoid surgery: evaluation by otoacoustic emissions (mastoid drilling and hearing loss). *ORL; Journal for Oto-Rhino-Laryngology, 69*(1), 18-24.
Kartush, J., & McGee, T. (1991). Controversies in laser stapedotomy. *Insights in Otolaryngology, 6*, 14-18.
Kato, M., Uematsu, H., Kashino, M., & Hirahara, T. (2003). The effect of head motion on the accuracy of sound localization. *Acoustical Science and Technology, 24*(5), 315-317.
Kaufman, R. S., & Schuknecht, H. F. (1967). Reparative granuloma following stapedectomy: a clinical entity. *The Annals of Otology, Rhinology, and Laryngology, 76*(5), 1008-1017.
Kaufmann, M., Adelman, C., & Sohmer, H. (2012). Mapping Sites on Bone and Soft Tissue of the Head, Neck and Thorax at Which a Bone Vibrator Elicits Auditory Sensation. *Audiology and Neurotology Extra, 2*(1), 9-15.
Keck, T., Burner, H., & Rettinger, G. (2005). Prospective clinical study on cochlear function after erbium:yttrium-aluminum-garnet laser stapedotomy. *The Laryngoscope, 115*(9), 1627-1631.
Keck, T., Wiebe, M., Rettinger, G., & Riechelmann, H. (2002). Safety of the Erbium:Yttrium-Aluminum-Garnet Laser in Stapes Surgery in Otosclerosis. *Otology & Neurotology, 23*, 21-24.
Keithley, E. M., Wang, X., & Barkdull, G. C. (2008). Tumor necrosis factor alpha can induce recruitment of inflammatory cells to the cochlea. *Otology & Neurotology, 29*(6), 854-859.
Kelley, N., & Reger, S. (1937). The effect of binaural occlusion of the external auditory meati on the sensitivity of the normal ear for bone conducted sound. *Journal of Experimental Psychology, 21*(2), 211.
Kelly, D. J., Prendergast, P. J., & Blayney, A. W. (2003). The effect of prosthesis design on vibration of the reconstructed ossicular chain: a comparative finite element analysis of four prostheses. *Otology & Neurotology, 24*(1), 11-19.
Kemp, D. T. (1978). Stimulated acoustic emissions from within the human auditory system. *The Journal of the Acoustical Society of America, 64*(5), 1386-1391.

Kerr, A. G., & Smyth, G. D. (1970). Experimental evaluation of tympanoplasty methods. *Archives of Otolaryngology, 91*(4), 327-333.
Kerth, J. D., & Allen, G. W. (1963). Comparison of the perilymphatic and cerebrospinal fluid pressures. *Archives of Otolaryngology, 77*, 581-585.
Khanna, S. M., & Stinson, M. R. (1985). Specification of the acoustical input to the ear at high frequencies. *The Journal of the Acoustical Society of America, 77*(2), 577-589.
Khanna, S. M., & Tonndorf, J. (1972). Tympanic membrane vibrations in cats studied by time-averaged holography. *The Journal of the Acoustical Society of America, 51*(6), 1904-1920.
Khanna, S. M., Tonndorf, J., & Queller, J. E. (1976). Mechanical parameters of hearing by bone conduction. *The Journal of the Acoustical Society of America, 60*(1), 139-154.
Kiefer, J., Ye, Q., Tillein, J., Adunka, O., Arnold, W., & Gstottner, W. (2007). Protecting the cochlea during stapes surgery: is there a role for corticosteroids? *Advances in Oto-Rhino-Laryngology, 65*, 300-307.
Kim, H. J., Kim, M. J., Jeon, J. H., Kim, J. M., Moon, I. S., & Lee, W. S. (2014). Functional and practical outcomes of inlay butterfly cartilage tympanoplasty. *Otology & Neurotology, 35*(8), 1458-1462.
King, R. B., & Oldfield, S. R. (1997). The impact of signal bandwidth on auditory localization: Implications for the design of three-dimensional audio displays. *Human Factors: The Journal of the Human Factors and Ergonomics Society, 39*(2), 287-295.
Kingma, H. (2006). Function tests of the otolith or statolith system. *Current Opinion in Neurology, 19*(1), 21-25.
Kirikae, I. (1959). An experimental study on the fundamental mechanism of bone conduction. *Acta Oto-Laryngologica, 145*, 1-111.
Kiukaanniemi, H., Lopponen, H., & Sorri, M. (1992). Noise-induced low- and high-frequency hearing losses in Finnish conscripts. *Military Medicine, 157*(9), 480-482.
Koike, T., Wada, H., & Kobayashi, T. (2002). Modeling of the human middle ear using the finite-element method. *The Journal of the Acoustical Society of America, 111*, 1306-1317.
Koizuka, I., Sakagami, M., Doi, K., Takeda, N., & Matsunaga, T. (1995). Nystagmus measured by ENG after stapes surgery. *Acta Oto-Laryngologica. Supplementum, 520 Pt 2*, 258-259.
Konrádsson, K. S., Ivarsson, A., & Bank, G. (1987). Computerized laser doppler interferometric scanning of the vibrating tympanic membrane. *Scandinavian Audiology, 16*(3), 159-166.
Kopke, R. D., Coleman, J. K. M., Liu, J., Jackson, R. L., & Van De Water, T. R. (2005). Mechanism of Noise-Induced Hearing Loss and Otoprotective Stratergies. In T. R. Van De Water & H. Staecker (Eds.), *Otolaryngology* (pp. 395 - 408). New York, NY: Thieme Medical Publishers.
Kopke, R. D., Liu, W., Gabaizadeh, R., Jacono, A., Feghali, J., Spray, D., . . . Van de Water, T. R. (1997). Use of organotypic cultures of Corti's organ to study the protective effects of antioxidant molecules on cisplatin-induced damage of auditory hair cells. *The American Journal of Otology, 18*(5), 559-571.
Koppula, S., Kumar, H., Kim, I. S., & Choi, D. K. (2012). Reactive oxygen species and inhibitors of inflammatory enzymes, NADPH oxidase, and iNOS in experimental models of Parkinson's disease. *Mediators of Inflammation, 2012*, 823-902.
Korres, S. G., & Balatsouras, D. G. (2004). Diagnostic, pathophysiologic, and therapeutic aspects of benign paroxysmal positional vertigo. *Otolaryngology - Head and Neck Surgery, 131*(4), 438-444.
Kortekaas, R. W., & Stelmachowicz, P. G. (2000). Bandwidth effects on children's perception of the inflectional morpheme /s/: acoustical measurements, auditory detection, and clarity rating. *Journal of Speech, Language and Hearing Research, 43*(3), 645-660.
Kos, M. I., Castrillon, R., Montandon, P., & Guyot, J. P. (2004). Anatomic and functional long-term results of canal wall-down mastoidectomy. *Annals of Otology Rhinology and Laryngology, 113*(11), 872-876.
Kringlebotn, M., & Gundersen, T. (1985). Frequency characteristics of the middle ear. *The Journal of the Acoustical Society of America, 77*(1), 159-164.
Kubo, T., Anniko, M., Stenqvist, M., & Hsu, W. (1998). Interleukin-2 affects cochlear function gradually but reversibly. *ORL; Journal for Oto-Rhino-Laryngology, 60*(5), 272-277.

Küçük, B., Abe, K., Ushiki, T., Inuyama, Y., Fukuda, S., & Ishikawa, K. (1991). Microstructures of the bony modiolus in the human cochlea: a scanning electron microscopic study. *Journal of Electron Microscopy, 40*(3), 193-197.
Kujala, J., Aalto, H., & Hirvonen, T. P. (2005). Video-oculography findings in patients with otosclerosis. *Otology & Neurotology, 26*(6), 1134-1137.
Kujala, J., Aalto, H., & Hirvonen, T. P. (2010). Video-oculography findings and vestibular symptoms on the day of stapes surgery. *European Archives of Oto-Rhino-Laryngology, 267*(2), 187-190.
Kujala, J., Aalto, H., Ramsay, H., & Hirvonen, T. (2007). Simultaneous bilateral stapes surgery--a pilot study. *Acta Oto-Laryngologica, 127*(12), 1255-1258.
Kurakata, K., Mizunami, T., Matsushita, K., & Shiraishi, K. (2010). Unwanted sounds generated with test tone presentation can spoil extended high-frequency audiometry. *The Journal of the Acoustical Society of America, 128*(4), El157-1162.
Kveton, J. (2010). Open Cavity Mastoid Operations. In A. J. Gulya, L. B. Minor & D. Poe (Eds.), *Glasscock Shambaugh - Surgery of the Ear* (pp. 515-528). Shelton, CT: People's Medical Publishing House.
Kylén, P., & Arlinger, S. (1976). Drill-generated noise levels in ear surgery. *Acta Oto-Laryngologica, 82*(5-6), 402-409.
Kylén, P., Arlinger, S., Jerlvall, L., & Harder, H. (1980). Ossicular manipulation in chronic ear surgery. An electrocochleographic study. *Archives of Otolaryngology, 106*(10), 598-601.
Kylén, P., Arlinger, S. D., & Bergholtz, L. M. (1977). Peroperative temporary threshold shift in ear surgery. An electrocochleographic study. *Acta Oto-Laryngologica, 84*(5-6), 393-401.
Kylén, P., Stjernvall, J. E., & Arlinger, S. (1977). Variables affecting the drill-generated noise levels in ear surgery. *Acta Oto-Laryngologica, 84*(3-4), 252-259.
Laitakari, K., & Lopponen, H. (1994). Carhart notch and electric bone-conduction audiometry. *Scandinavian Audiology, 23*(2), 139-141.
Langendijk, E. H., & Bronkhorst, A. W. (2002). Contribution of spectral cues to human sound localization. *The Journal of the Acoustical Society of America, 112*(4), 1583-1596.
Langman, A. W., Jackler, R. K., & Sooy, F. A. (1991). Stapedectomy: long-term hearing results. *The Laryngoscope, 101*(8), 810-814.
Laske, R. D., Roosli, C., Chatzimichalis, M. V., Sim, J. H., & Huber, A. M. (2011). The influence of prosthesis diameter in stapes surgery: a meta-analysis and systematic review of the literature. *Otology & Neurotology, 32*(4), 520-528.
Laukli, E., & Mair, I. W. (1985). High-frequency audiometry. Normative studies and preliminary experiences. *Scandinavian Audiology, 14*(3), 151-158.
Lawrence, M. (1960). Acoustic effects of middle ear substitution. *Transactions - American Academy of Ophthalmology and Otolaryngology, 64*, 235-247.
Lawrence, M. (1973). In vivo studies of the microcirculation (with l6-mm color motion picture). *Advances in Oto-Rhino-Laryngology, 20*, 244-255.
Lee, H. S., Hong, S. D., Hong, S. H., Cho, Y. S., & Chung, W. H. (2008). Ossicular chain reconstruction improves bone conduction threshold in chronic otitis media. *The Journal of Laryngology & Otology, 122*(4), 351-356.
Lee, J. C., Lee, S. R., Nam, J. K., Lee, T. H., & Kwon, J. K. (2012). Comparison of different grafting techniques in type I tympanoplasty in cases of significant middle ear granulation. *Otology & Neurotology, 33*(4), 586-590.
Leeuw, A. R., & Dreschler, W. A. (1991). Advantages of directional hearing aid microphones related to room acoustics. *Audiology, 30*(6), 330-344.
Lefebvre, P. P., Malgrange, B., Lallemend, F., Staecker, H., Moonen, G., & Van De Water, T. R. (2002). Mechanisms of cell death in the injured auditory system: otoprotective strategies. *Audiology and Neurotology, 7*(3), 165-170.
Lemkens, N., Vermeire, K., Brokx, J. P., Fransen, E., Van Camp, G., & Van De Heyning, P. H. (2002). Interpretation of pure-tone thresholds in sensorineural hearing loss (SNHL): a review of measurement variability and age-specific references. *Acta Oto-Rhino-Laryngologica Belgica, 56*(4), 341-352.

Leonetti, J. P., Kircher, M. L., Jaber, J. J., Benscoter, B. J., Marmora, J. J., & Feustel, P. J. (2012). Inner ear effects of canal wall down mastoidectomy. *Otolaryngology - Head and Neck Surgery, 146*(4), 621-626.
Lesinski, S. G. (1990). Lasers for otosclerosis--which one if any and why. *Lasers in Surgery and Medicine, 10*(5), 448-457.
Lesinski, S. G. (2003). Revision stapedectomy. *Current opinion in Otolaryngology & Head and Neck Surgery, 11*(5), 347-354.
Lesinski, S. G. (2010). Lasers in Otology. In A. J. Gulya, L. B. Minor & D. Poe (Eds.), *Glasscock Shambaugh - Surgery of the Ear* (pp. 331-348). Shelton, CT: People's Medical Publishing House.
Lesinski, S. G., & Newrock, R. (1993). Carbon dioxide lasers for otosclerosis. *Otolaryngologic clinics of North America, 26*(3), 417-441.
Lesinski, S. G., & Stein, J. A. (1989). Stapedectomy revision with the CO2 laser. *The Laryngoscope, 99*(6 Pt 2 suppl 46), 13-19.
Levitt, H. (1987). A cancellation technique for the amplitude and phase calibration of hearing aids and nonconventional transducers. *Journal of Rehabilitation Research and Development, 24*(4), 261-270.
Levy, R., Shvero, J., & Hadar, T. (1990). Stapedotomy technique and results: ten years' experience and comparative study with stapedectomy. *The Laryngoscope, 100*(10 Pt 1), 1097-1099.
Liberman, M. C., & Dodds, L. W. (1987). Acute ultrastructural changes in acoustic trauma: serial-section reconstruction of stereocilia and cuticular plates. *Hearing Research, 26*(1), 45-64.
Liberman, M. C., & Kiang, N. Y. (1978). Acoustic trauma in cats. Cochlear pathology and auditory-nerve activity. *Acta Oto-Laryngologica. Supplementum, 358*, 1-63.
Liberman, M. C., & Mulroy, M. J. (1982). Acute and chronic effects of acoustic trauma: cochlear pathology and auditory nerve pathophysiology. In R. P. Hamernik, D. Henderson & R. J. Salvi (Eds.), *New perspectives on noise-induced hearing loss* (pp. 105-135). New York, NY: Raven Press.
Lim, D. J. (1984). Otoconia in health and disease. A review. *The Annals of Otology, Rhinology & Laryngology. Supplement, 112*, 17-24.
Lin, K. Y., & Young, Y. H. (2011). Correlation between subjective visual horizontal test and ocular vestibular-evoked myogenic potential test. *Acta Oto-Laryngologica, 131*(2), 149-155.
Linstrom, C., Silverman, C. A., Rosen, A., & Meiteles, L. Z. (2001). Bone conduction impairment in chronic ear disease. *Annals of Otology, Rhinology and Laryngology, 110*(1), 437-441.
Lippert, B. M., Gottschlich, S., Kulkens, C., Folz, B., Rudert, H., & Werner, J. A. (2001). Experimental and clinical results of Er:YAG laser stapedotomy. *Lasers in Surgery and Medicine, 28*(1), 11-17.
Lippmann, R. P. (1996). Accurate consonant perception without mid-frequency speech energy. *Speech and Audio Processing, 4*(1), 66.
Lippy, W. H., Burkey, J. M., Fucci, M. J., Schuring, A. G., & Rizer, F. M. (1996). Stapedectomy in the elderly. *The American Journal of Otology, 17*(6), 831-834.
Lippy, W. H., & Schuring, A. G. (1984). Stapedectomy revision following sensorineural hearing loss. *Otolaryngology - Head and Neck Surgery, 92*(5), 580-582.
Lister, J. J., & Roberts, R. A. (2005). Effects of age and hearing loss on gap detection and the precedence effect: narrow-band stimuli. *Journal of Speech, Language and Hearing Research, 48*(2), 482-493.
Löppönen, H. (1992). High-frequency audiometry. Masking in electric bone-conduction audiometry. *Scandinavian Audiology, 21*(1), 31-35.
Löppönen, H., & Laitakari, K. (2001). Carhart notch effect in otosclerotic ears measured by electric bone-conduction audiometry. *Scandinavian Audiology Supplementum, 52*, 160-162.
Löppönen, H., Laitakari, K., & Sorri, M. (1991). High-frequency audiometry. Accelerometric findings with electric bone-conduction audiometry. *Scandinavian Audiology, 20*(1), 61-67.
Löppönen, H., & Sorri, M. (1991). High-frequency air-conduction and electric bone-conduction audiometry. Comparison of two methods. *Scandinavian Audiology, 20*(3), 175-180.
Lopponen, H., Sorri, M., & Bloigu, R. (1991). High-frequency air-conduction and electric bone-conduction audiometry. Age and sex variations. *Scandinavian Audiology, 20*(3), 181-189.

Löppönen, H., Sorri, M., & Bloigu, R. (1991). High-Frequency Air-Conduction and Electric Bone-Conduction Audiometry: Age and Sex Variations. *Scandinavian Audiology, 20*(3), 181-189.
Lundy, L. (2009). The Effect of CO(2) and KTP laser on the cat saccule and utricle. *The Laryngoscope, 119*(8), 1594-1605.
Macpherson, E. A., & Middlebrooks, J. C. (2002). Listener weighting of cues for lateral angle: the duplex theory of sound localization revisited. *The Journal of the Acoustical Society of America, 111*(5 Pt 1), 2219-2236.
Macpherson, E. A., & Sabin, A. T. (2007). Binaural weighting of monaural spectral cues for sound localization. *The Journal of the Acoustical Society of America, 121*(6), 3677-3688.
Magliulo, G., Gagliardi, M., Cuiuli, G., Celebrini, A., Parrotto, D., & D'Amico, R. (2005). Stapedotomy and post-operative benign paroxysmal positional vertigo. *Journal of Vestibular Research, 15*(3), 169-172.
Mair, I. W., Fjermedal, O., & Laukli, E. (1989). Air conduction thresholds and secretory otitis media: a conventional and extra-high frequency audiometric comparison. *The Annals of Otology, Rhinology, and Laryngology, 98*(10), 767-771.
Mair, I. W., & Hallmo, P. (1994). Myringoplasy, A Conventional Extended High-Frequency, Air- and Bone-conduction Audiometric Study. *Scandinavian Audiology, 23*(3), 205-208.
Mair, I. W., & Laukli, E. (1986). Air conduction thresholds after myringoplasty and stapes surgery: a conventional and high frequency audiometric comparison. *Annals of Otology, Rhinology and Laryngology, 95*(4 Pt 1), 327-330.
Mair, I. W., Pedersen, S., & Laukli, E. (1989). Audiometric results of TORP and PORP middle ear reconstruction. *Annals of Otology, Rhinology and Laryngology, 98*(6), 429-433.
Maire, R., & van Melle, G. (2000). Dynamic asymmetry of the vestibulo-ocular reflex in unilateral peripheral vestibular and cochleovestibular loss. *The Laryngoscope, 110*(2 Pt 1), 256-263.
Makous, J. C., & Middlebrooks, J. C. (1990). Two-dimensional sound localization by human listeners. *The Journal of the Acoustical Society of America, 87*(5), 2188-2200.
Man, A., & Winerman, I. (1985). Does drill noise during mastoid surgery affect the contralateral ear? *The American Journal of Otology, 6*(4), 334-335.
Mann, W. J., Amedee, R. G., Fuerst, G., & Tabb, H. G. (1996). Hearing loss as a complication of stapes surgery. *Otolaryngology - Head and Neck Surgery, 115*(4), 324-328.
Manzari, L., Burgess, A. M., & Curthoys, I. S. (2010). Effect of bone-conducted vibration of the midline forehead (Fz) in unilateral vestibular loss (uVL). Evidence for a new indicator of unilateral otolithic function. *Acta Otorhinolaryngologica Italica, 30*(4), 175.
Manzari, L., Tedesco, A., Burgess, A. M., & Curthoys, I. S. (2010). Ocular vestibular-evoked myogenic potentials to bone-conducted vibration in superior vestibular neuritis show utricular function. *Otolaryngology - Head and Neck Surgery, 143*(2), 274-280.
Marchese, M. R., Paludetti, G., De Corso, E., & Cianfrone, F. (2007). Role of stapes surgery in improving hearing loss caused by otosclerosis. *The Journal of Laryngology & Otology, 121*(5), 438-443.
Marchese, M. R., Scorpecci, A., Cianfrone, F., & Paludetti, G. (2011). "One-shot" CO2 versus Er:YAG laser stapedotomy: is the outcome the same? *European Archives of Oto-Rhino-Laryngology 268*(3), 351-356.
Mardassi, A., Deveze, A., Sanjuan, M., Mancini, J., Parikh, B., Elbedeiwy, A., . . . Lavieille, J. P. (2011). Titanium ossicular chain replacement prostheses: prognostic factors and preliminary functional results. *European Annals of Otorhinolaryngology, Head and Neck Diseases, 128*(2), 53-58.
Margolis, R. (2008). The Vanishing Air-Bone Gap - Audiology's Dirty Little Secret. *Audiology Online*. Retrieved from http://www.audiologyonline.com/ website:
Mark, A. S., Seltzer, S., Nelson-Drake, J., Chapman, J. C., Fitzgerald, D. C., & Gulya, A. J. (1992). Labyrinthine enhancement on gadolinium-enhanced magnetic resonance imaging in sudden deafness and vertigo: correlation with audiologic and electronystagmographic studies. *The Annals of Otology, Rhinology, and Laryngology, 101*(6), 459-464.
Marrone, N., Mason, C. R., & Kidd, G., Jr. (2008). The effects of hearing loss and age on the benefit of spatial separation between multiple talkers in reverberant rooms. *The Journal of the Acoustical Society of America, 124*(5), 3064-3075.

Martin, A. D., & Harner, S. G. (2004). Ossicular reconstruction with titanium prosthesis. *The Laryngoscope, 114*(1), 61-64.
Martin, J. S., & Jerger, J. F. (2005). Some effects of aging on central auditory processing. *Journal of Rehabilitation Research and Development, 42*(4 Suppl 2), 25-44.
Mason, R., Ford, N., Rumsey, F., & De Bruyn, B. (2001). Verbal and nonverbal elicitation techniques in the subjective assessment of spatial sound reproduction. *Journal of the Audio Engineering Society, 49*(5), 366-384.
Massey, B. L., Kennedy, R. J., & Shelton, C. (2005). Stapedectomy outcomes: titanium versus teflon wire prosthesis. *The Laryngoscope, 115*(2), 249-252.
Matos, R. D., Valle, S. P., Dias, A. M., Santos, T. M., & Leite, I. C. (2010). Acoustic radiation effects on bone conduction threshold measurement. *Brazilian Journal of Otorhinolaryngology, 76*(5), 654-658.
Matthews, L. J., Lee, F. S., Mills, J. H., & Dubno, J. R. (1997). Extended high-frequency thresholds in older adults. *Journal of Speech, Language and Hearing Research, 40*(1), 208-214.
Maureen, T. H. (1993). Audiological characteristics of the patients with otosclerosis. *Otolaryngologic Clinics of North America, 26*, 373-387.
McBride, M., Letowski, T., & Tran, P. (2008). Bone conduction reception: Head sensitivity mapping. *Ergonomics, 51*(5), 702-718.
McDermott, J. C., Fausti, S. A., Henry, J. A., & Frey, R. H. (1990). Effects of contralateral masking on high-frequency bone-conduction thresholds. *Audiology, 29*(6), 297-303.
McFadden, D., & Pasanen, E. G. (1976). Lateralization of high frequencies based on interaural time differences. *The Journal of the Acoustical Society of America, 59*(3), 634-639.
McGee, T. M. (1981). Comparison of small fenestra and total stapedectomy. *The Annals of Otology, Rhinology, and Laryngology, 90*(6 Pt 1), 633-636.
McGee, T. M., Diaz-Ordaz, E. A., & Kartush, J. M. (1993). The role of KTP laser in revision stapedectomy. *Otolaryngology - Head and Neck Surgery, 109*(5), 839-843.
McLaren, J. W., & Hillman, D. E. (1979). Displacement of the semicircular canal cupula during sinusoidal rotation. *Neuroscience, 4*(12), 2001-2008.
McMenomey, S. O., & Gubbels, S. P. (2008). Labyrinthitis. In P. C. Weber (Ed.), *Vertigo and Disequilibrium : A Practical Guide to Diagnosis and Management* (pp. 91 - 98). New York, NY: Thieme.
Merchant, S. N., McKenna, M. J., Mehta, R. P., Ravicz, M. E., & Rosowski, J. J. (2003). Middle ear mechanics of Type III tympanoplasty (stapes columella): II. Clinical studies. *Otology & Neurotology, 24*(2), 186-194.
Merchant, S. N., & Rosowski, J. J. (2010). Surgical Reconstruction and Passive Prostheses. In S. Puria, R. R. Fay & A. N. Popper (Eds.), *The Middle Ear* (pp. 253-272). New York, NY: Springer.
Meulemans, J., Wuyts, F. L., & Forton, G. E. (2013). Middle ear reconstruction using the titanium Kurz Variac partial ossicular replacement prosthesis: functional results. *JAMA Otolaryngology - Head & Neck Surgery, 139*(10), 1017-1025.
Meurman, O. H., & Aantaa, E. (1966). Labyrinth irritation after otosclerosis operations. *Acta Oto-Laryngologica*, Suppl 224:118+.
Meyer, S. E. (1999). The effect of stapes surgery on high frequency hearing in patients with otosclerosis. *The American Journal of Otology, 20*(1), 36-40.
Meyerhoff, W. L., Marple, B. F., & Roland, P. S. (1996). Tympanic Membrane, Middle Ear, and Mastoid. In P. S. Roland, B. F. Marple & W. L. Meyerhoff (Eds.), *Hearing Loss* (pp. 155 - 194). New York, NY: Thieme.
Middlebrooks, J. C. (1992). Narrow-band sound localization related to external ear acoustics. *The Journal of the Acoustical Society of America, 92*(5), 2607-2624.
Middlebrooks, J. C. (1997). Spectral Shape Cues for Sound localization. In R. H. Gilkey & T. R. Anderson (Eds.), *Binaural and Spatial Hearing in Real and Virtual Environments* (pp. 77-98). Mahwah, NJ: Lawrence Erlbaum Associates.
Middlebrooks, J. C., & Green, D. M. (1991). Sound localization by human listeners. *Annual Review of Psychology, 42*, 135-159.

Middlebrooks, J. C., Makous, J. C., & Green, D. M. (1989). Directional sensitivity of sound-pressure levels in the human ear canal. *The Journal of the Acoustical Society of America, 86*(1), 89-108.
Migirov, L., & Wolf, M. (2009). Influence of drilling on the distortion product otoacoustic emissions in the non-operated ear. *ORL; Journal for Oto-Rhino-Laryngology, 71*(3), 153-156.
Miller, J. D., Engebretson, A. M., & Weston, P. B. (1964). Recording the Waveforms of Periodic Acoustic Signals at Levels near and below 0.0002 μbar. *The Journal of the Acoustical Society of America, 36*, 1591.
Miller, J. M., Brown, J. N., & Schacht, J. (2003). 8-iso-prostaglandin F(2alpha), a product of noise exposure, reduces inner ear blood flow. *Audiology and Neurotology, 8*(4), 207-221.
Mills, A. W. (1972). Auditory localization(Binaural acoustic field sampling, head movement and echo effect in auditory localization of sound sources position, distance and orientation). In J. Tobias (Ed.), *Foundations of Modern Auditory Theory* (Vol. 2, pp. 303-348).
Møller, A. R. (2000). *Hearing: Its Physiology and Pathophysiology*. New York, NY: Academic Press.
Molony, N. C., & Marais, J. (1996). Balance after stapedectomy: the measurement of spontaneous sway by posturography. *Clinical Otolaryngology and Allied Sciences, 21*(4), 353-356.
Monson, B. B., Lotto, A. J., & Ternstrom, S. (2011). Detection of high-frequency energy changes in sustained vowels produced by singers. *The Journal of the Acoustical Society of America, 129*(4), 2263-2268.
Moody, D. B., Stebbins, W. C., Hawkins, J. E., Jr., & Johnsson, L. G. (1978). Hearing loss and cochlear pathology in the monkey (Macaca) following exposure to high levels of noise. *Archives of Oto-Rhino-Laryngology, 220*(1-2), 47-72.
Moon, I. S., Song, M. H., Kim, H. N., Chung, M. H., Lee, W. S., & Lee, H. K. (2007). Hearing results after ossiculoplasty using Polycel prosthesis. *Acta Oto-Laryngologica, 127*(1), 20-24.
Moore, B. C. (1985). Frequency selectivity and temporal resolution in normal and hearing-impaired listeners. *British Journal of Audiology, 19*(3), 189-201.
Moore, B. C. (1995). *Perceptual consequences of cochlear damage*. Oxford, England: Oxford University Press.
Moore, B. C. (1996). Perceptual consequences of cochlear hearing loss and their implications for the design of hearing aids. *Ear and Hearing, 17*(2), 133-161.
Moore, B. C. (2007). *Cochlear hearing loss: Physiological, psychological and technical issues* (2nd ed.). West Sussex, England: John Wiley & Sons Ltd.
Moore, B. C., Fullgrabe, C., & Stone, M. A. (2010). Effect of spatial separation, extended bandwidth, and compression speed on intelligibility in a competing-speech task. *The Journal of the Acoustical Society of America, 128*(1), 360-371.
Moore, B. C., Stone, M. A., Fullgrabe, C., Glasberg, B. R., & Puria, S. (2008). Spectro-temporal characteristics of speech at high frequencies, and the potential for restoration of audibility to people with mild-to-moderate hearing loss. *Ear and Hearing, 29*(6), 907-922.
Moore, B. C., & Tan, C. T. (2003). Perceived naturalness of spectrally distorted speech and music. *The Journal of the Acoustical Society of America, 114*(1), 408-419.
Morimoto, M. (2001). The contribution of two ears to the perception of vertical angle in sagittal planes. *The Journal of the Acoustical Society of America, 109*(4), 1596-1603.
Morris, D. P., Bance, M., van Wijhe, R. G., Kiefte, M., & Smith, R. (2004). Optimum tension for partial ossicular replacement prosthesis reconstruction in the human middle ear. *The Laryngoscope, 114*(2), 305-308.
Morton, L. P., & Reynolds, L. (1991). High frequency thresholds: variations with age and industrial noise exposure. *The South African Journal of Communication Disorders, 38*, 13-17.
Moscillo, L., Imperiali, M., Carra, P., Catapano, F., & Motta, G. (2006). Bone conduction variation poststapedotomy. *American Journal of Otolaryngology, 27*(5), 330-333.
Motta, G., & Moscillo, L. (2002). Functional results in stapedotomy with and without CO(2) laser. *ORL; Journal for Oto-Rhino-Laryngology, 64*(5), 307-310.
Motta, G., Ruosi, M., & Motta, S. (1996). Stapedotomy vs stapedectomy. Comparison of hearing results. *Acta Otorhinolaryngologica Italica, 16*(2 Suppl 53), 36-41.

Murofushi, T., Curthoys, I. S., Topple, A. N., Colebatch, J. G., & Halmagyi, G. M. (1995). Responses of guinea pig primary vestibular neurons to clicks. *Experimental Brain Research, 103*(1), 174-178.
Murofushi, T., & Kaga, K. (2009a). Recording and Assessing VEMPs *Vestibular Evoked Myogenic Potential*. Tokyo, Japan: Springer.
Murofushi, T., & Kaga, K. (2009b). *Vestibular Evoked Myogenic Potential*. Tokyo, Japan: Springer.
Murugasu, E., Puria, S., & Roberson, J. B., Jr. (2005). Malleus-to-footplate versus malleus-to-stapes-head ossicular reconstruction prostheses: temporal bone pressure gain measurements and clinical audiological data. *Otology & Neurotology, 26*(4), 572-582.
Musicant, A. D., & Butler, R. A. (1984). The influence of pinnae-based spectral cues on sound localization. *The Journal of the Acoustical Society of America, 75*(4), 1195-1200.
Musiek, F. E., & Baran, J. A. (2007). *The auditory system: anatomy, physiology and clinical correlates*. Boston, MA: Allyn & Bacon.
Nagai, N., Ogawa, Y., Hagiwara, A., Otsuka, K., Inagaki, T., Shimizu, S., & Suzuki, M. (2014). Ocular vestibular evoked myogenic potentials induced by bone-conducted vibration in patients with unilateral inner ear disease. *Acta Oto-Laryngologica, 134*(2), 151-158.
Neff, B. A., Rizer, F. M., Schuring, A. G., & Lippy, W. H. (2003). Tympano-ossiculoplasty utilizing the Spiggle and Theis titanium total ossicular replacement prosthesis. *The Laryngoscope, 113*(9), 1525-1529.
Nguyen, K. D., Welgampola, M. S., & Carey, J. P. (2010). Test-retest reliability and age-related characteristics of the ocular and cervical vestibular evoked myogenic potential tests. *Otology & Neurotology, 31*(5), 793-802.
Nilo, E. R. (1968). The relation of vibrator surface area and static application force to the vibrator-to-head coupling. *Journal of Speech and Hearing Research, 11*(4), 805-810.
Nishihara, S., & Goode, R. L. (1994). Experimental study of the acoustic properties of incus replacement prostheses in a human temporal bone model. *The American Journal of Otology, 15*(4), 485-494.
Noble, W., Byrne, D., & Lepage, B. (1994). Effects on sound localization of configuration and type of hearing impairment. *The Journal of the Acoustical Society of America, 95*(2), 992-1005.
Noble, W., Byrne, D., & Ter-Horst, K. (1997). Auditory localization, detection of spatial separateness, and speech hearing in noise by hearing impaired listeners. *The Journal of the Acoustical Society of America, 102*(4), 2343-2352.
Northern, J. L., Downs, M. P., Rudmose, W., Glorig, A., & Fletcher, J. L. (1972). Recommended High-Frequency Audiometric Threshold Levels (8000–18 000 Hz). *The Journal of the Acoustical Society of America, 52*(2B), 585-595.
O'Beirne, G. A. (2013). *UC Directinoal Hearing Array*. Computer Software. University of Canterbury. Christchurch, New Zealand.
O'Connor, K. N., Tam, M., Blevins, N. H., & Puria, S. (2008). Tympanic membrane collagen fibers: a key to high-frequency sound conduction. *The Laryngoscope, 118*(3), 483-490.
Oberascher, G., Albegger, K., Gruber, W., & Baselides, P. (1992). Otosclerosis--diagnosis and therapy. *Wiener Medizinische Wochenschrift, 142*(20-21), 474-481.
Ohinata, Y., Miller, J. M., Altschuler, R. A., & Schacht, J. (2000). Intense noise induces formation of vasoactive lipid peroxidation products in the cochlea. *Brain Research, 878*(1-2), 163-173.
Ohlemiller, K. K., Wright, J. S., & Dugan, L. L. (1999). Early elevation of cochlear reactive oxygen species following noise exposure. *Audiology and Neurotology, 4*(5), 229-236.
Økstad, S., Laukli, E., & Mair, I. W. (1988). High-frequency audiometry: comparison of electric bone-conduction and air-conduction thresholds. *Audiology, 27*(1), 17-26.
Oldfield, S. R., & Parker, S. P. (1984). Acuity of sound localisation: a topography of auditory space. I. Normal hearing conditions. *Perception, 13*(5), 581-600.
Oldfield, S. R., & Parker, S. P. (1986). Acuity of sound localisation: a topography of auditory space. III. Monaural hearing conditions. *Perception, 15*(1), 67-81.
Osterhammel, D., & Osterhammel, P. (1979). High-frequency audiometry. Age and sex variations. *Scandinavian Audiology, 8*(2), 73-81.

Oswal, V. (2002). Lasers in Otology: General Considerations. In V. Oswal, M. Remacle, S. Jovanovic & J. P. Krespi (Eds.), *Principles and Practice of Lasers in Otorhinolaryngology and Head and Neck Surgery* (pp. 513 - 520). The Hague, Netherlands: Kugler Publications.

Otte, R. J., Agterberg, M. J., Van Wanrooij, M. M., Snik, A. F., & Van Opstal, A. J. (2013). Age-related hearing loss and ear morphology affect vertical but not horizontal sound-localization performance. *Journal of the Association for Research in Otolaryngology, 14*(2), 261-273.

Ou, H. C., Bohne, B. A., & Harding, G. W. (2000). Noise damage in the C57BL/CBA mouse cochlea. *Hearing Research, 145*(1-2), 111-122.

Özmen, A. O., Aksoy, S., Ozmen, S., Sarac, S., Sennaroglu, L., & Gursel, B. (2009). Balance after stapedotomy: analysis of balance with computerized dynamic posturography. *Clinical Otolaryngology, 34*(3), 212-217.

Packer, P., Mackendrick, A., & Solar, M. (1982). What's best in myringoplasty: underly or overlay, dura or fascia? *The Journal of Laryngology & Otology, 96*(1), 25-41.

Palmgren, O. (1979). Long-Term Results of Open Cavity and Tympanomastoid Surgery of the Chronic Ear. *Acta Oto-Laryngologica, 88*(1), 343-349.

Palva, A., & Sorri, M. (1979). Can an operation of deaf ear be dangerous for hearing? *Acta Oto-Laryngologica. Supplementum, 360*, 155-157.

Palva, T. (1987). Surgical treatment of chronic middle ear disease. II. Canal wall up and canal wall down procedures. *Acta Oto-Laryngologica, 104*(5-6), 487-494.

Palva, T., Kärjä, J., & Palva, A. (1973). High-Tone Sensorineural Losses Following Chronic Ear Surgery. *Archives of Otolaryngology - Head and Neck Surgery, 98*(3), 176-178.

Paparella, M. M. (1962). Acoustic trauma from the bone cutting bur. *The Laryngoscope, 72*, 116-126.

Paparella, M. M., Morizono, T., Le, C. T., Mancini, F., Sipila, P., Choo, Y. B., . . . Kim, C. S. (1984). Sensorineural hearing loss in otitis media. *The Annals of Otology, Rhinology, and Laryngology, 93*(6 Pt 1), 623-629.

Park, J. E., & Barbul, A. (2004). Understanding the role of immune regulation in wound healing. *American Journal of Surgery, 187*(5a), 11s-16s.

Parkin, J. L., Wood, G. S., Wood, R. D., & McCandless, G. A. (1980). Drill- and suction-generated noise in mastoid surgery. *Archives of Otolaryngology - Head and Neck Surgery, 106*(2), 92-96.

Parrilla, C., Galli, J., Fetoni, A. R., Rigante, M., & Paludetti, G. (2008). Erbium: yttrium-aluminum-garnet laser stapedotomy--a safe technique. *Otolaryngology - Head and Neck Surgery, 138*(4), 507-512.

Parving, A., & Elberling, C. (1982). High-pass masking in the classification of low-frequency hearing loss. *Scandinavian Audiology, 11*(3), 173-178.

Patterson, J. H., Jr., & Hamernik, R. P. (1997). Blast overpressure induced structural and functional changes in the auditory system. *Toxicology, 121*(1), 29-40.

Pauw, B. K., Pollak, A. M., & Fisch, U. (1991). Utricle, saccule, and cochlear duct in relation to stapedotomy. A histologic human temporal bone study. *The Annals of Otology, Rhinology, and Laryngology, 100*(12), 966-970.

Pennington, C. L. (1983). Incus interposition. A 15-year report. *Annals of Otology, Rhinology and Laryngology, 92*(6 Pt 1), 568-570.

Perrett, S., & Noble, W. (1997a). The contribution of head motion cues to localization of low-pass noise. *Perception & Psychophysics, 59*(7), 1018-1026.

Perrett, S., & Noble, W. (1997b). The effect of head rotations on vertical plane sound localization. *The Journal of the Acoustical Society of America, 102*(4), 2325-2332.

Persson, P., Harder, H., & Magnuson, B. (1997). Hearing Results in Otosclerosis Surgery after Partial Stapedectomy, Total Stapedectomy and Stapedotomy. *Acta Oto-Laryngologica, 117*(1), 94-99.

Pfalz, R., Hibst, R., & Bald, N. (1995). Suitability of different lasers for operations ranging from the tympanic membrane to the base of the stapes. *Advances in Oto-Rhino-Laryngology, 49*, 87-94.

Pickles, J. O. (2008). *An introduction to the physiology of hearing* (3rd ed.). Bingley, England: Emerald Group Publishing.

Pinar, H. S., Ardic, F. N., Topuz, B., & Kara, C. O. (2005). Subjective visual vertical and subjective visual horizontal measures in patients with chronic dizziness. *The Journal of Otolaryngology, 34*(2), 121-125.
Pirvola, U., Xing-Qun, L., Virkkala, J., Saarma, M., Murakata, C., Camoratto, A. M., . . . Ylikoski, J. (2000). Rescue of hearing, auditory hair cells, and neurons by CEP-1347/KT7515, an inhibitor of c-Jun N-terminal kinase activation. *The Journal of Neuroscience, 20*(1), 43-50.
Pittman, A. L. (2008). Short-term word-learning rate in children with normal hearing and children with hearing loss in limited and extended high-frequency bandwidths. *Journal of Speech, Language and Hearing Research, 51*(3), 785-797.
Plath, P., Lenart, R., Matschke, R. G., & Kruppa, E. (1992). Long-term results of stapedectomy and stapedotomy. *HNO, 40*(2), 52-55.
Poirrier, A. L., Pincemail, J., Van Den Ackerveken, P., Lefebvre, P. P., & Malgrange, B. (2010). Oxidative stress in the cochlea: an update. *Current Medicinal Chemistry, 17*(30), 3591-3604.
Pompeiano, O. (1975). Macular input to neurons of the spinoreticulocerebellar pathway. *Brain Research, 95*(2-3), 351-368.
Popelka, G. R., Telukuntla, G., & Puria, S. (2010). Middle-ear function at high frequencies quantified with advanced bone-conduction measures. *Hearing Research, 263*(1-2), 85-92.
Probst, R., Lonsbury-Martin, B. L., & Martin, G. K. (1991). A review of otoacoustic emissions. *The Journal of the Acoustical Society of America, 89*(5), 2027-2067.
Purcell, D., Kunov, H., & Cleghorn, W. (1999). Objective calibration of bone conductors using otoacoustic emissions. *Ear and Hearing, 20*(5), 375-392.
Purcell, D., Kunov, H., & Cleghorn, W. (2003). Estimating bone conduction transfer functions using otoacoustic emissions. *The Journal of the Acoustical Society of America, 114*(2), 907-918.
Puria, S., Kunda, L. D., Roberson, J. B., Jr., & Perkins, R. C. (2005). Malleus-to-footplate ossicular reconstruction prosthesis positioning: cochleovestibular pressure optimization. *Otology & Neurotology, 26*(3), 368-379.
Puria, S., Peake, W. T., & Rosowski, J. J. (1997). Sound-pressure measurements in the cochlear vestibule of human-cadaver ears. *The Journal of the Acoustical Society of America, 101*(5 pt 1), 2754-2770.
Puria, S., & Steele, C. (2010). Tympanic-membrane and malleus-incus-complex co-adaptations for high-frequency hearing in mammals. *Hearing Research, 263*(1-2), 183-190.
Quaranta, N., Besozzi, G., Fallacara, R. A., & Quaranta, A. (2005). Air and bone conduction change after stapedotomy and partial stapedectomy for otosclerosis. *Otolaryngology - Head and Neck Surgery, 133*(1), 116-120.
Quérat, C., Martin, C., Prades, J. M., & Richard, C. (2014). Canal wall up tympanoplasty for cholesteatoma with intact stapes. Comparison of hearing results between cartilage and PORP on stapes and impact of malleus removal and total reinforcement of the tympanic membrane by cartilage. *European Annals of Otorhinolaryngology, Head and Neck Diseases, 131*(4), 211-216.
Raeder, J., Gupta, A., & Pedersen, F. M. (1997). Recovery characteristics of sevoflurane- or propofol-based anaesthesia for day-care surgery. *Acta Anaesthesiologica Scandinavica, 41*(8), 988-994.
Ragheb, S. M., Gantz, B. J., & Mccabe, B. F. (1987). Hearing results after cholesteatoma surgery: The iowa experience. *The Laryngoscope, 97*(11), 1254-1263.
Rakerd, B., Vander Velde, T. J., & Hartmann, W. M. (1998). Sound localization in the median sagittal plane by listeners with presbyacusis. *Journal of the American Academy of Audiology, 9*(6), 466-479.
Raman, R. (1983). Poor high frequency results following total stapedectomy—Theoretical considerations. *Indian Journal of Otolaryngology, 35*(1), 9-11.
Rangheard, A. S., Marsot-Dupuch, K., Mark, A. S., Meyer, B., & Tubiana, J. M. (2001). Postoperative complications in otospongiosis: usefulness of MR imaging. *AJNR. American Journal of Neuroradiology, 22*(6), 1171-1178.
Rauch, S. D., & Bartley, M. L. (1992). Argon laser stapedectomy: comparison to traditional fenestration techniques. *The American Journal of Otology, 13*(6), 556-560.
Raut, V., & Halik, J. (2005). Argon laser assisted small fenestra stapedotomy for otosclerosis. *Auris Nasus Larynx, 32*(1), 11-15.

Ravi, R., Somani, S. M., & Rybak, L. P. (1995). Mechanism of cisplatin ototoxicity: antioxidant system. *Pharmacology & Toxicology, 76*(6), 386-394.
Redaelli de Zinis, L. O., Cottelli, M., & Koka, M. (2010). Inner Ear Function following Underlay Myringoplasty. *Audiology and Neurotology, 15*(3), 149-154.
Reuter, W., Schonfeld, U., Mansmann, U., Fischer, R., & Gross, M. (1998). Extended high frequency audiometry in pre-school children. *Audiology, 37*(5), 285-294.
Ricard, G. L., & Meirs, S. L. (1994). Intelligibility and localization of speech from virtual directions. *Human Factors, 36*(1), 120-128.
Richards, W. D., & Frank, T. (1982). Frequency response and output variations of Radioear B-71 and B-72 bone vibrators. *Ear and Hearing, 3*(1), 37-38.
Richter, U., & Brinkmann, K. (1981). Threshold of hearing by bone conduction. A contribution to international standardization. *Scandinavian Audiology. Supplementum, 10*(4), 235-237.
Richter, U., & Frank, T. (1985). Calibration of bone vibrators at high frequencies. *Audiologische Akustik, 24*, 52-62.
Ricketts, T. A., Dittberner, A. B., & Johnson, E. E. (2008). High-frequency amplification and sound quality in listeners with normal through moderate hearing loss. *Journal of Speech, Language and Hearing Research, 51*(1), 160-172.
Roach, R. E., & Carhart, R. (1956). A clinical method for calibrating the bone-conduction audiometer. *A.M.A. Archives of Otolaryngology, 63*(3), 270-278.
Roberts, R. A., & Lister, J. J. (2004). Effects of age and hearing loss on gap detection and the precedence effect: broadband stimuli. *Journal of Speech, Language and Hearing Research, 47*(5), 965-978.
Robinson, D. W., & Dadson, R. S. (1956). A re-determination of the equal-loudness relations for pure tones. *British Journal of Applied Physics, 7*(5), 166.
Robinson, D. W., & Shipton, M. S. (1982). A standard determination of paired air- and bone-conduction thresholds under different masking noise conditions. *Audiology, 21*(1), 61-82.
Robinson, M. (1974). Stapes prosthesis: stainless steel vs. teflon. *The Laryngoscope, 84*(11), 1982-1995.
Robinson, M., & Kasden, S. (1977). Bone Conduction Speech Discrimination An Indication of Cochlear Function in the Immediate Postoperative Period. *Archives of Otolaryngology - Head and Neck Surgery, 103*(4), 238-240.
Rocha, R. L., Atherino, C. C., & Frota, S. M. (2010). High-frequency audiometry in normal hearing military firemen exposed to noise. *Brazilian Journal of Otorhinolaryngology, 76*(6), 687-694.
Roosli, C., Sim, J. H., Chatzimichalis, M., & Huber, A. M. (2012). How does closure of tympanic membrane perforations affect hearing and middle ear mechanics? An evaluation in a patient cohort and temporal bone models. *Otology & Neurotology, 33*(3), 371-378.
Rose, D. E. (1978). *Audiological assessment*. Englewood Cliffs, NJ: Prentice-Hall.
Rosen, S., Plester, D., El-Mofty, A., & Rosen, H. V. (1964). High frequency audiometry in presbycusis. *Archives of Otolaryngology, 79*, 18-32.
Rosengren, S. M., Govender, S., & Colebatch, J. G. (2011). Ocular and cervical vestibular evoked myogenic potentials produced by air- and bone-conducted stimuli: comparative properties and effects of age. *Clinical Neurophysiology, 122*(11), 2282-2289.
Rosengren, S. M., & Kingma, H. (2013). New perspectives on vestibular evoked myogenic potentials. *Current Opinion in Neurology, 26*(1), 74-80.
Rosengren, S. M., McAngus Todd, N. P., & Colebatch, J. G. (2005). Vestibular-evoked extraocular potentials produced by stimulation with bone-conducted sound. *Clinical Neurophysiology, 116*(8), 1938-1948.
Rosengren, S. M., Welgampola, M. S., & Colebatch, J. G. (2010). Vestibular evoked myogenic potentials: past, present and future. *Clinical Neurophysiology, 121*(5), 636-651.
Rosowski, J. J., Cheng, J. T., Ravicz, M. E., Hulli, N., Hernandez-Montes, M., Harrington, E., & Furlong, C. (2009). Computer-assisted time-averaged holograms of the motion of the surface of the mammalian tympanic membrane with sound stimuli of 0.4-25 kHz. *Hearing Research, 253*(1-2), 83-96.
Rosowski, J. J., & Merchant, S. N. (1995). Mechanical and acoustic analysis of middle ear reconstruction. *The American Journal of Otology, 16*(4), 486-497.

Rudmin, F. (1983). False air-bone gap. *Ear and Hearing, 4*(2), 106-107.
Rybak, L. P., Ravi, R., & Somani, S. M. (1995). Mechanism of protection by diethyldithiocarbamate against cisplatin ototoxicity: antioxidant system. *Fundamental and Applied Toxicology, 26*(2), 293-300.
Sagalovich, B. M., & Bednin, F. V. (1982). Bone conduction receiver for the measurement of the auditory thresholds over a broad frequency range. *Meditsinskaia Tekhnika*(6), 14-18.
Sakai, Y., Karino, S., & Kaga, K. (2006). Bone-conducted auditory brainstem-evoked responses and skull vibratory velocity measurement in rats at frequencies of 0.5-30 kHz with a new giant magnetostrictive bone conduction transducer. *Acta Oto-Laryngologica, 126*(9), 926-933.
Sakamoto, M., Sugasawa, M., Kaga, K., & Kamio, T. (1998). Average thresholds in the 8 to 20 kHz range in young adults. *Scandinavian Audiology, 27*(3), 169-172.
Sando, I., Hemenway, W. G., Miller, D. R., & Black, F. O. (1974). Vestibular pathology in otosclerosis temporal bone nistopathological report. *The Laryngoscope, 84*(4), 593-605.
Sanford, C. A., Hunter, L. L., Feeney, M. P., & Nakajima, H. H. (2013). Wideband acoustic immittance: tympanometric measures. *Ear and Hearing, 34 Suppl 1*, 65s-71s.
Sataloff, J., Vassallo, L., & Menduke, H. (1967). Occupational hearing loss and high frequency thresholds. *Archives of Environmental Health, 14*(6), 832-836.
Sataloff, R. T., & Sataloff, J. (2006). The nature of hearing loss. In R. T. Sataloff & J. Sataloff (Eds.), *Occupational hearing loss* (pp. 23). Boca Raton, FL: CRC Press.
Schechter, M. A., Fausti, S. A., Rappaport, B. Z., & Frey, R. H. (1986). Age categorization of high-frequency auditory threshold data. *The Journal of the Acoustical Society of America, 79*(3), 767-771.
Schmerber, S., Troussier, J., Dumas, G., Lavieille, J. P., & Nguyen, D. Q. (2006). Hearing results with the titanium ossicular replacement prostheses. *European Archives of Oto-Rhino-Laryngology, 263*(4), 347-354.
Schmuziger, N., Brechbuehl, M., & Probst, R. (2007). Acoustic measures of low-frequency noise in extended high-frequency audiometry. *The Journal of the Acoustical Society of America, 121*(3), 120-1244.
Schmuziger, N., Probst, R., & Smurzynski, J. (2004). Test-retest reliability of pure-tone thresholds from 0.5 to 16 kHz using Sennheiser HDA 200 and Etymotic Research ER-2 earphones. *Ear and Hearing, 25*(2), 127-132.
Schneider, B. A., & Hamstra, S. J. (1999). Gap detection thresholds as a function of tonal duration for younger and older listeners. *The Journal of the Acoustical Society of America, 106*(1), 371-380.
Schuknecht, H. F. (1962). Sensorineural hearing loss following stapedectomy. *Acta Oto-Laryngologica, 54*, 336-348.
Schuknecht, H. F. (1993). *Pathology of the ear* (2nd ed.). Malvern, PA: Lea & Febiger.
Schuknecht, H. F., & Barber, W. (1985). Histologic variants in otosclerosis. *The Laryngoscope, 95*(11), 1307-1317.
Schuknecht, H. F., & Mendoza, A. M. (1981). Cochlear Pathology after stapedectomy. *American Journal of Otolaryngology, 2*(3), 173-187.
Schuknecht, H. F., & Neff, W. D. (1952). Hearing losses after apical lesions in the cochlea. *Acta Oto-Laryngologica, 42*(3), 263-274.
Schuknecht, H. F., & Tonndorf, J. (1960). Acoustic trauma of the cochlea from ear surgery. *The Laryngoscope, 70*, 479-505.
Seicshnaydre, M. A., Sismanis, A., & Hughes, G. B. (1994). Update of reparative granuloma: survey of the American Otological Society and the American Neurotology Society. *The American Journal of Otology, 15*(2), 155-160.
Seki, M., Miyasaka, H., Edamatsu, H., & Watanabe, K. (2001). Changes in permeability of strial vessels following vibration given to auditory ossicle by drill. *The Annals of Otology, Rhinology, and Laryngology, 110*(2), 122-126.
Seo, T., Miyamoto, A., Saka, N., Shimano, K., Nishida, T., Hashimoto, M., & Sakagami, M. (2008). Vestibular evoked myogenic potential induced by bone-conducted stimuli in patients with conductive hearing loss. *Acta Oto-Laryngologica, 128*(6), 639-643.

Sergi, B., Scorpecci, A., Parrilla, C., & Paludetti, G. (2010). Early hearing assessment after "one shot" CO2 laser stapedotomy: is it helpful to predict inner ear damage and the functional outcome? *Otology & Neurotology, 31*(9), 1376-1380.
Sha, S. H., & Schacht, J. (2000). Antioxidants attenuate gentamicin-induced free radical formation in vitro and ototoxicity in vivo: D-methionine is a potential protectant. *Hearing Research, 142*(1-2), 34-40.
Sha, S. H., Taylor, R., Forge, A., & Schacht, J. (2001). Differential vulnerability of basal and apical hair cells is based on intrinsic susceptibility to free radicals. *Hearing Research, 155*(1-2), 1-8.
Shaan, M., Landolfi, M. D., Taibah, A., Russo, A., Szyanski, M., & Sanna, M. (1995). Modified Bondy Technique. *The American Journal of Otology, 16*(5), 696-697.
Shabana, Y. K., Allam, H., & Pedersen, C. B. (1999). Laser stapedotomy. *The Journal of Laryngology & Otology, 113*(5), 413-416.
Shah, U. K., Poe, D. S., Rebeiz, E. E., Perrault, D. F., Jr., Pankratov, M. M., & Shapshay, S. M. (1996). Erbium laser in middle ear surgery: in vitro and in vivo animal study. *The Laryngoscope, 106*(4), 418-422.
Shambaugh, G. E. (1963). Summary - Unsolved problems - Panel Stapes Surgery. *Archives of Otolaryngology, 78*, 627.
Shaw, E. A. (1974). Transformation of sound pressure level from the free field to the eardrum in the horizontal plane. *The Journal of the Acoustical Society of America, 56*(6), 1848-1861.
Shea, J. J., Jr. (1963). Complications of the Stapedectomy Operation. *The Annals of Otology, Rhinology, and Laryngology, 72*, 1108-1123.
Shea, J. J., Jr. (1998). Forty years of stapes surgery. *The American Journal of Otology, 19*(1), 52-55.
Shea, J. J., Jr., Ge, X., & Orchik, D. J. (1995). Traumatic endolymphatic hydrops. *The American Journal of Otology, 16*(2), 235-240.
Sheehy, J. L. (1984). TORPs and PORPs: causes of failure--a report on 446 operations. *Otolaryngology - Head and Neck Surgery, 92*(5), 583-587.
Shelton, C., & Sheehy, J. L. (1990). Tympanoplasty: review of 400 staged cases. *The Laryngoscope, 100*(7), 679-681.
Shen, Y., Teh, B. M., Friedland, P. L., Eikelboom, R. H., & Atlas, M. D. (2011). To pack or not to pack? A contemporary review of middle ear packing agents. *The Laryngoscope, 121*(5), 1040-1048.
Sheykholeslami, K., Murofushi, T., Kermany, M. H., & Kaga, K. (2000). Bone-conducted evoked myogenic potentials from the sternocleidomastoid muscle. *Acta Oto-Laryngologica, 120*(6), 731-734.
Shin, B. S., Oh, S. Y., Kim, J. S., Kim, T. W., Seo, M. W., Lee, H., & Park, Y. A. (2012). Cervical and ocular vestibular-evoked myogenic potentials in acute vestibular neuritis. *Clinical Neurophysiology, 123*(2), 369-375.
Shinohara, T., Gyo, K., Saiki, T., & Yanagihara, N. (2000). Ossiculoplasty using hydroxyapatite prostheses: long-term results. *Clinical Otolaryngology and Allied Sciences, 25*(4), 287-292.
Shipton, M. S., John, A. J., & Robinson, D. W. (1980). Air-radiated sound from bone vibration transducers and its implications for bone conduction audiometry. *British Journal of Audiology, 14*(3), 86-99.
Shoji, K., Regenbogen, E., Yu, J. D., & Blaugrund, S. M. (1991). High-frequency components of normal voice. *Journal of Voice, 5*(1), 29-35.
Shott, S. R., & Pensak, M. L. (1992). Perilymphatic fistula. *Ear, Nose, & Throat Journal, 71*(11), 568, 571-562.
Silverstein, H., Bendet, E., Rosenberg, S., & Nichols, M. (1994). Revision stapes surgery with and without laser: a comparison. *The Laryngoscope, 104*(12), 1431-1438.
Silverstein, H., Rosenberg, S., & Jones, R. (1989). Small fenestra stapedotomies with and without KTP laser: a comparison. *The Laryngoscope, 99*(5), 485-488.
Sim, J. H., Chatzimichalis, M., Roosli, C., Laske, R. D., & Huber, A. M. (2012). Objective assessment of stapedotomy surgery from round window motion measurement. *Ear and Hearing, 33*(5), e24-31.

Singbartl, F., Basta, D., Seidl, R. O., Ernst, A., & Todt, I. (2006). Perioperative recordings of vestibular-evoked myogenic potentials in otosclerosis. *Otology & Neurotology, 27*(8), 1070-1073.
Singleton, G. T., & Schuknecht, H. F. (1959). Experimental fracture of the stapes in cats. *The Annals of Otology, Rhinology, and Laryngology, 68*, 1069 - 1081.
Slattery, W. H., 3rd, & Middlebrooks, J. C. (1994). Monaural sound localization: acute versus chronic unilateral impairment. *Hearing Research, 75*(1-2), 38-46.
Smyth, G. D. (1972). Tympanosclerosis. *The Journal of Laryngology & Otology, 86*(1), 9-14.
Smyth, G. D. (1976). Postoperative cholesteatoma in combined approach tympanoplasty. Fifteen year report on tympanoplasty. Part I. *The Journal of Laryngology & Otology, 90*(7), 597-621.
Smyth, G. D. (1977). Sensorineural hearing loss in chronic ear surgery. *The Annals of Otology, Rhinology, and Laryngology, 86*(1 Pt 1), 3-8.
Smyth, G. D., & Hassard, T. H. (1978). Eighteen years experience in stapedectomy. The case for the small fenestra operation. *The Annals of Otology, Rhinology & Laryngology. Supplement, 87*(3 Pt 2 Suppl 49), 3-36.
Snow, W. B. (1931). Audible Frequency Ranges of Music, Speech and Noise. *Bell System Technical Journal, 10*(4), 616-627.
Sohmer, H., Freeman, S., Geal-Dor, M., Adelman, C., & Savion, I. (2000). Bone conduction experiments in humans - a fluid pathway from bone to ear. *Hearing Research, 146*(1-2), 81-88.
Somers, T., Govaerts, P., Marquet, T., & Offeciers, E. (1994). Statistical analysis of otosclerosis surgery performed by Jean Marquet. *The Annals of Otology, Rhinology, and Laryngology, 103*(12), 945-951.
Somers, T., Vercruysse, J. P., Zarowski, A., Verstreken, M., & Offeciers, E. (2006). Stapedotomy with microdrill or carbon dioxide laser: influence on inner ear function. *Annals of Otology, Rhinology and Laryngology, 115*(12), 880-885.
Somers, T., Vercruysse, J. P., Zarowski, A., Verstreken, M., Schatteman, I., & Offeciers, F. E. (2007). Transient depression of inner ear function after stapedotomy: skeeter versus CO(2) laser technique. *Advances in Oto-Rhino-Laryngology, 65*, 267-272.
Somma, G., Pietroiusti, A., Magrini, A., Coppeta, L., Ancona, C., Gardi, S., . . . Bergamaschi, A. (2008). Extended high-frequency audiometry and noise induced hearing loss in cement workers. *American Journal of Industrial Medicine, 51*(6), 452-462.
Sone, M., Mizuno, T., Naganawa, S., & Nakashima, T. (2009). Imaging analysis in cases with inflammation-induced sensorineural hearing loss. *Acta Oto-Laryngologica, 129*(3), 239-243.
Song, B. B., & Schacht, J. (1996). Variable efficacy of radical scavengers and iron chelators to attenuate gentamicin ototoxicity in guinea pig in vivo. *Hearing Research, 94*(1-2), 87-93.
Sorom, A. J., Driscoll, C. L., Beatty, C. W., & Lundy, L. (2007). Retrospective analysis of outcomes after stapedotomy with implantation of a self-crimping Nitinol stapes prosthesis. *Otolaryngology -Head and Neck Surgery, 137*(1), 65-69.
Spandow, O., Soderberg, O., & Bohlin, L. (2000). Long-term results in otosclerotic patients operated by stapedectomy or stapedotomy. *Scandinavian Audiology, 29*(3), 186-190.
Spencer, M. G., & Reid, A. (1985). Drill-generated noise levels in mastoid surgery. *The Journal of Laryngology & Otology, 99*(10), 967-972.
Sperling, N. M., Sury, K., Gordon, J., & Cox, S. (2013). Early postoperative results in stapedectomy. *Otolaryngology - Head and Neck Surgery, 149*(6), 918-923.
Stach, B. (2010). Audiologic Evaluation of Otologic/Neurotolgoic Disease. In A. J. Gulya, L. B. Minor & D. Poe (Eds.), *Glasscock-Shambaugh - Surgery of the Ear* (pp. 189-222). Shelton, CT: People's Medical Publishing House.
Stapleton, E., Mills, R., & Tham, J. C. (2008). Sacculo-collic response in otosclerosis and following successful stapes surgery. *The Journal of Laryngology & Otology, 122*(4), 347-350.
Stelmachowicz, P. G., Beauchaine, K. A., Kalberer, A., & Jesteadt, W. (1989). Normative thresholds in the 8- to 20-kHz range as a function of age. *The Journal of the Acoustical Society of America, 86*(4), 1384-1391.

Stelmachowicz, P. G., Beauchaine, K. A., Kalberer, A., Kelly, W. J., & Jesteadt, W. (1989). High-frequency audiometry: test reliability and procedural considerations. *The Journal of the Acoustical Society of America, 85*(2), 879-887.
Stelmachowicz, P. G., Beauchaine, K. A., Kalberer, A., Langer, T., & Jesteadt, W. (1988). The reliability of auditory thresholds in the 8- to 20-kHz range using a prototype audiometer. *The Journal of the Acoustical Society of America, 83*(4), 1528-1535.
Stelmachowicz, P. G., Gorga, M. P., & Cullen, J. K. (1982). A calibration procedure for the assessment of thresholds above 8000 Hz. *Journal of Speech and Hearing Research, 25*(4), 618-623.
Stelmachowicz, P. G., Pittman, A. L., Hoover, B. M., & Lewis, D. E. (2001). Effect of stimulus bandwidth on the perception of /s/ in normal- and hearing-impaired children and adults. *The Journal of the Acoustical Society of America, 110*(4), 2183-2190.
Stenfelt, S. (2006). Middle ear ossicles motion at hearing thresholds with air conduction and bone conduction stimulation. *The Journal of the Acoustical Society of America, 119*(5 pt 1), 2848-2858.
Stenfelt, S. (2011). Acoustic and physiologic aspects of bone conduction hearing. *Advances in Oto-Rhino-Laryngology, 71*, 10-21.
Stenfelt, S., & Goode, R. L. (2005). Bone-conducted sound: physiological and clinical aspects. *Otology & Neurotology, 26*(6), 1245-1261.
Stenfelt, S., Hakansson, B., & Tjellstrom, A. (2000). Vibration characteristics of bone conducted sound in vitro. *The Journal of the Acoustical Society of America, 107*(1), 422-431.
Stenfelt, S., Hato, N., & Goode, R. L. (2002). Factors contributing to bone conduction: the middle ear. *The Journal of the Acoustical Society of America, 111*(2), 947-959.
Stenfelt, S., Puria, S., Hato, N., & Goode, R. L. (2003). Basilar membrane and osseous spiral lamina motion in human cadavers with air and bone conduction stimuli. *Hearing Research, 181*(1-2), 131-143.
Stenfelt, S., & Reinfeldt, S. (2007). A model of the occlusion effect with bone-conducted stimulation. *International Journal of Audiology, 46*(10), 595-608.
Stenfelt, S., Wild, T., Hato, N., & Goode, R. L. (2003). Factors contributing to bone conduction: the outer ear. *The Journal of the Acoustical Society of America, 113*(2), 902-913.
Stepp, C. E., & Voss, S. E. (2005). Acoustics of the human middle-ear air space. *The Journal of the Acoustical Society of America, 118*(2), 861-871.
Stevens, K. N., Berkovitz, R., Kidd Jr, G., & Green, D. M. (1987). Calibration of ear canals for audiometry at high frequencies. *The Journal of the Acoustical Society of America, 81*(2), 470-484.
Stinson, M. R. (1985). The spatial distribution of sound pressure within scaled replicas of the human ear canal. *The Journal of the Acoustical Society of America, 78*(5), 1596-1602.
Stinson, M. R., & Shaw, E. A. G. (1982). Wave effects and pressure distribution in the ear canal near the tympanic membrane. *The Journal of the Acoustical Society of America, 71*(S1), S88-S88.
Stinson, M. R., & Shaw, E. A. G. (1983). Sound pressure distribution in the human ear canal. *The Journal of the Acoustical Society of America, 73*(S1), S59-S60.
Strömbäck, K., Kobler, S., & Rask-Andersen, H. (2012). High frequency hearing following stapes surgery. *Acta Oto-Laryngologica, 132*(9), 944-950.
Stromberg, A. K., Yin, X., Olofsson, A., & Duan, M. (2010). Evaluation of the usefulness of a silicone tube connected to a microphone in monitoring noise levels induced by drilling during mastoidectomy and cochleostomy. *Acta Oto-Laryngologica, 130*(10), 1163-1168.
Strouse, A., Ashmead, D. H., Ohde, R. N., & Grantham, D. W. (1998). Temporal processing in the aging auditory system. *The Journal of the Acoustical Society of America, 104*(4), 2385-2399.
Studebaker, G. A. (1962a). On masking in bone-conduction testing. *Journal of Speech and Hearing Research, 5*, 215-227.
Studebaker, G. A. (1962b). Placement of vibrator in bone-conduction testing. *Journal of Speech and Hearing Research, 5*, 321-331.
Studebaker, G. A. (1967). Clinical masking of the nontest ear. *The Journal of Speech and Hearing Disorders, 32*(4), 360-371.

Su, H. C., Huang, T. W., Young, Y. H., & Cheng, P. W. (2004). Aging effect on vestibular evoked myogenic potential. *Otology & Neurotology, 25*(6), 977-980.
Sugiura, M., Naganawa, S., Teranishi, M., & Nakashima, T. (2006). Three-dimensional fluid-attenuated inversion recovery magnetic resonance imaging findings in patients with sudden sensorineural hearing loss. *The Laryngoscope, 116*(8), 1451-1454.
Sullivan, J. A., Gotlieb, C. C., & Hodges, W. E. (1947). Shift of bone conduction threshold on occlusion of the external ear canal. *The Laryngoscope, 57*(11), 690-703.
Syms, C. A., Syms, M. J., & Sheehy, J. L. (2010). Mastoidectomy - Intact Canal Wall Procedure. In D. E. Brackmann, C. Shelton & M. A. Arriaga (Eds.), *Otologic Surgery* (pp. 195-205). Philadelphia, PA: Elsevier.
Szyfter, W., Mielcarek-Kuchta, D., Mietkiewska-Leszniewska, D., Mlodkowska, A., & Laczkowska-Przybylska, J. (2013). Comparison between 2 laser systems, Er-Yag and CO2, in stapes surgery. *Otology & Neurotology, 34*(1), 29-35.
Tabak, S., Collewijn, H., & Boumans, L. J. (1997). Deviation of the subjective vertical in long-standing unilateral vestibular loss. *Acta Oto-Laryngologica, 117*(1), 1-6.
Tange, R., & Dreschler, W. (1990). Pre- and postoperative high-frequency audiometry in otosclerosis. *ORL; Journal for Oto-Rhino-Laryngology, 52*(1), 16-20.
Tange, R. A., Dreschler, W. A., & van der Hulst, R. J. (1985). The importance of high-tone audiometry in monitoring for ototoxicity. *Archives of Oto-Rhino-Laryngology, 242*(1), 77-81.
Tange, R. A., Schimanski, G., van Lange, J. W., Grolman, W., & Zuur, L. C. (2002). Reparative granuloma seen in cases of gold piston implantation after stapes surgery for otosclerosis. *Auris Nasus Larynx, 29*(1), 7-10.
Tasaki, I., & Spyropoulos, C. S. (1959). Stria vascularis as source of endocochlear potential. *Journal of Neurophysiology, 22*(2), 149-155.
Tashima, K., Tanaka, S., & Saito, H. (1986). Volumetric changes of the aerated middle ear and mastoid after insertion of tympanostomy tubes. *American Journal of Otolaryngology, 7*(4), 302-305.
Tenney, J., Arriaga, M. A., Chen, D. A., & Arriaga, R. (2008). Enhanced hearing in heat-activated-crimping prosthesis stapedectomy. *Otolaryngology - Head and Neck Surgery, 138*(4), 513-517.
Ter-Horst, K., Byrne, D., & Noble, W. (1993). Ability of hearing-impaired listeners to benefit from separation of speech and noise. *Australian Journal of Audiology, 15*, 71-84.
Thannickal, V. J., & Fanburg, B. L. (2000). Reactive oxygen species in cell signaling. *American journal of physiology. Lung cellular and molecular physiology, 279*(6), L1005-1028.
Thornton, A. R., Bell, I. E., & Phillipps, J. J. (1989). High-frequency monitoring using an electrostimulation audiometer. *British Journal of Audiology, 23*(1), 63-68.
Thurlow, W. R., Mangels, J. W., & Runge, P. S. (1967). Head movements during sound localization. *The Journal of the Acoustical Society of America, 42*(2), 489-493.
Tobias, J. V. (1959). Relative occurrence of phonemes in American English. *The Journal of the Acoustical Society of America, 31*(5), 631-631.
Todd, N. P., Rosengren, S. M., Aw, S. T., & Colebatch, J. G. (2007). Ocular vestibular evoked myogenic potentials (OVEMPs) produced by air- and bone-conducted sound. *Clinical Neurophysiology, 118*(2), 381-390.
Ton, C., & Parng, C. (2005). The use of zebrafish for assessing ototoxic and otoprotective agents. *Hearing Research, 208*(1-2), 79-88.
Toner, J. G., Smyth, G. D. L., & Kerr, A. G. (2007). Realities in ossiculoplasty. *The Journal of Laryngology & Otology, 105*(07), 529-533.
Tonndorf, J. (1964). Animal experiments in bone conduction: clinical conclusions. *Annals of Otology, Rhinology and Laryngology, 73*, 658-678.
Tonndorf, J. (1966). Bone conduction. Studies in experimental animals. *Acta Oto-Laryngologica, Supplementum, 213*, 1-132.
Tonndorf, J. (1971). Experiments on acoustic stimulated eye movement. *Archives of Otolaryngology - Head and Neck Surgery, 93*(2), 220.
Tonndorf, J. (1976). Endolymphatic hydrops: mechanical causes of hearing loss. *Archives of Oto-Rhino-Laryngology, 212*(4), 293-299.

Tonndorf, J., Campbell, R. A., Berstein, L., & Reneau, J. P. (1966). Quantitative evaluation of bone conduction components in cats. *Acta Oto-Laryngologica, 61*(s213), 10-38.
Tonndorf, J., & Khanna, S. M. (1970). The role of the tympanic membrane in middle ear transmission. *The Annals of Otology, Rhinology, and Laryngology, 79*(4), 743-753.
Tonndorf, J., & Khanna, S. M. (1971). The tympanic membrane as a part of the middle ear transformer. *Acta Oto-Laryngologica, 71*(2), 177-180.
Tonndorf, J., & Khanna, S. M. (1972). Tympanic-membrane vibrations in human cadaver ears studied by time-averaged holography. *The Journal of the Acoustical Society of America, 52*(4), 1221-1233.
Tonndorf, J., & Kurman, B. (1984). High frequency audiometry. *Annals of Otology, Rhinology and Laryngology, 93*, 576-582.
Tornabene, S. V., Sato, K., Pham, L., Billings, P., & Keithley, E. M. (2006). Immune cell recruitment following acoustic trauma. *Hearing Research, 222*(1-2), 115-124.
Tos, M., Lau, T., & Plate, S. (1984). Sensorineural hearing loss following chronic ear surgery. *Annals of Otology, Rhinology and Laryngology, 94*(4 Pt 1), 403-409.
Tos, M., Trojaborg, N., & Thomsen, J. (1989). The contralateral ear after translabyrinthine removal of acoustic neuromas: is there a drill-noise generated hearing loss? *The Journal of Laryngology & Otology, 103*(9), 845-849.
Tribukait, A., & Bergenius, J. (1998). The subjective visual horizontal after stapedotomy: evidence for an increased resting activity in otolithic afferents. *Acta Oto-Laryngologica, 118*(3), 299-306.
Tribukait, A., Bergenius, J., & Brantberg, K. (1998). Subjective visual horizontal during follow-up after unilateral vestibular deafferentation with gentamicin. *Acta Oto-Laryngologica, 118*(4), 479-487.
Trivelli, M., D'Ascanio, L., Pappacena, M., Greco, F., & Salvinelli, F. (2010). Air- and bone-conducted vestibular evoked myogenic potentials (VEMPs) in otosclerosis: recordings before and after stapes surgery. *Acta Otorhinolaryngologica Italica, 30*(1), 5-10.
Tsai, V., Ostroff, J., Korman, M., & Chen, J. M. (2005). Bone-conduction hearing and the occlusion effect in otosclerosis and normal controls. *Otology & Neurotology, 26*(6), 1138-1142.
Tsang, W. S., Woo, J. K., & Tong, M. C. (2006). Poststapedectomy reparative granuloma. *Ear, Nose, & Throat Journal, 85*(9), 562.
Tseng, C. L., Chou, C. H., & Young, Y. H. (2010). Aging effect on the ocular vestibular-evoked myogenic potentials. *Otology & Neurotology 31*(6), 959-963.
Tuz, M., Dogru, H., Uygur, K., & Gedikli, O. (2000). Improvement in bone conduction threshold after tympanoplasty. *Otolaryngology - Head and Neck Surgery, 123*(6), 775-778.
Uchino, Y., & Kushiro, K. (2011). Differences between otolith- and semicircular canal-activated neural circuitry in the vestibular system. *Neuroscience Research, 71*(4), 315-327.
Urquhart, A. C., McIntosh, W. A., & Bodenstein, N. P. (1992). Drill-generated sensorineural hearing loss following mastoid surgery. *The Laryngoscope, 102*(6), 689-692.
Valencia, N. N., Mendoza, L. E., Mateo, R. I., & Carballo, G. G. (1994). High-frequency components of normal and dysphonic voices. *Journal of Voice, 8*(2), 157-162.
Valente, M., Valente, M., & Goebel, J. (1992). High-frequency thresholds: circumaural earphone versus insert earphone. *Journal of the American Academy of Audiology, 3*(6), 410-418.
Valko, Y., Hegemann, S. C., Weber, K. P., Straumann, D., & Bockisch, C. J. (2011). Relative diagnostic value of ocular vestibular evoked potentials and the subjective visual vertical during tilt and eccentric rotation. *Clinical Neurophysiology, 122*(2), 398-404.
van de Water, T. R., Dinh, C. T., Vivero, R., Hoosien, G., Eshraghi, A. A., & Balkany, T. J. (2010). Mechanisms of hearing loss from trauma and inflammation: otoprotective therapies from the laboratory to the clinic. *Acta Oto-Laryngologica, 130*(3), 308-311.
Van Wanrooij, M. M., & Van Opstal, A. J. (2005). Relearning sound localization with a new ear. *The Journal of Neuroscience, 25*(22), 5413-5424.
Vartiainen, E. (1992). What is the best method of treatment for labyrinthine fistulae caused by cholesteatoma? *Clinical Otolaryngology and Allied Sciences, 17*(3), 258-260.
Vartiainen, E., & Seppa, J. (1997). Results of bone conduction following surgery for chronic ear disease. *European Archives of Oto-Rhino-Laryngology, 254*(8), 384-386.

Vartiainen, E., Virtaniemi, J., Kemppainen, M., & Karjalainen, S. (1993). Hearing levels of patients with otosclerosis 10 years after stapedectomy. *Otolaryngology - Head and Neck Surgery, 108*(3), 251-255.

Vassbotn, F. S., Moller, P., & Silvola, J. (2007). Short-term results using Kurz titanium ossicular implants. *European Archives of Oto-Rhino-Laryngology, 264*(1), 21-25.

Vaziri, N. D. (2008). Causal link between oxidative stress, inflammation, and hypertension. *Iranian Journal of Kidney Diseases, 2*(1), 1-10.

Velazquez-Villasenor, L., Merchant, S. N., Tsuji, K., Glynn, R. J., Wall, C., 3rd, & Rauch, S. D. (2000). Temporal bone studies of the human peripheral vestibular system. Normative Scarpa's ganglion cell data. *The Annals of Otology, Rrhinology & Laryngology. Supplement, 181*, 14-19.

Vibert, D., & Häusler, R. (2000). Long-term evolution of subjective visual vertical after vestibular neurectomy and labyrinthectomy. *Acta Oto-Laryngologica, 120*(5), 620-622.

Vibert, D., Häusler, R., & Safran, A. B. (1999). Subjective visual vertical in peripheral unilateral vestibular diseases. *Journal of Vestibular Research, 9*(2), 145-152.

Vincent, R., Bittermann, A. J., Oates, J., Sperling, N., & Grolman, W. (2012). KTP versus CO2 laser fiber stapedotomy for primary otosclerosis: results of a new comparative series with the otology-neurotology database. *Otology & Neurotology, 33*(6), 928-933.

Vincent, R., Sperling, N. M., Oates, J., & Jindal, M. (2006). Surgical findings and long-term hearing results in 3,050 stapedotomies for primary otosclerosis: a prospective study with the otology-neurotology database. *Otology & Neurotology, 27*(8 Suppl 2), S25-547.

Vital, V., Konstantinidis, I., Vital, I., & Triaridis, S. (2008). Minimizing the dead ear in otosclerosis surgery. *Auris Nasus Larynx, 35*(4), 475-479.

Vitte, E., & Semont, A. (1995). Assessment of vestibular function by videonystagmoscopy. *Journal of Vestibular Research, 5*(5), 377-383.

Vivero, R. J., Joseph, D. E., Angeli, S., He, J., Chen, S., Eshraghi, A. A., . . . Van de Water, T. R. (2008). Dexamethasone base conserves hearing from electrode trauma-induced hearing loss. *The Laryngoscope, 118*(11), 2028-2035.

Vlaming, M. S., & Feenstra, L. (1986). Studies on the mechanics of the reconstructed human middle ear. *Clinical Otolaryngology and Allied Sciences, 11*(6), 411-422.

von Békésy, G. (1932). Zur Theorie des Horens bei der Schallaufnahme durch Knochenleitung. *Annals of Physics, 13*, 111 - 136.

von Békésy, G. (1960). *Experiments in hearing*. New York, NY: McGraw Hill.

Wahat, N. H. A., & Patuzzi, R. (2012). *Ocular vestibular evoked myogenic potentials (oVEMPs) produced by finger taps to the head of normal subjects*. Department of Physiology. University of Western Australia. Nedlands, Australia.

Wallach, H. (1939). On sound localization. *The Journal of the Acoustical Society of America, 10*(4), 270-274.

Wallach, H. (1940). The role of head movements and vestibular and visual cues in sound localization. *Journal of Experimental Psychology, 27*(4), 339.

Wang, M. C., & Lee, G. S. (2007). Vestibular evoked myogenic potentials in middle ear effusion. *Acta Oto-Laryngologica, 127*(7), 700-704.

Wang, M. C., Liu, C. Y., Yu, E. C., Wu, H. J., & Lee, G. S. (2009). Vestibular evoked myogenic potentials in chronic otitis media before and after surgery. *Acta Oto-Laryngologica, 129*(11), 1206-1211.

Wang, Y., Hirose, K., & Liberman, M. C. (2002). Dynamics of noise-induced cellular injury and repair in the mouse cochlea. *Journal of the Association for Research in Otolaryngology, 3*(3), 248-268.

Wang, Z. M., Chi, F. L., & Dai, C. F. (2005). Modified stapes prosthesis to limit postoperative vertigo. *Otolaryngology - Head and Neck Surgery, 132*(1), 50-54.

Warner, D. S., Sheng, H., & Batinic-Haberle, I. (2004). Oxidants, antioxidants and the ischemic brain. *The Journal of Experimental Biology, 207*(Pt 18), 3221-3231.

Watanabe, T., Bertoli, S., & Probst, R. (2008). Transmission pathways of vibratory stimulation as measured by subjective thresholds and distortion-product otoacoustic emissions. *Ear and Hearing, 29*(5), 667-673.

Watcha, M. F., & White, P. F. (1992). Postoperative nausea and vomiting. Its etiology, treatment, and prevention. *Anesthesiology, 77*(1), 162-184.
Watson, N. (1938). Limits of audition for bone conduction. *The Journal of the Acoustical Society of America, 9*, 294-300.
Watson, N., & Gales, R. (1943). Bone-conduction threshold measurements: Effects of occlusion, enclosures, and masking devices. *The Journal of the Acoustical Society of America, 14*(4), 207-215.
Weber, K. P., Rosengren, S. M., Michels, R., Sturm, V., Straumann, D., & Landau, K. (2012). Single motor unit activity in human extraocular muscles during the vestibulo-ocular reflex. *The Journal of Physiology, 590*(Pt 13), 3091-3101.
Wegner, I., Kamalski, D. M., Tange, R. A., Vincent, R., Stegeman, I., van der Heijden, G. J., & Grolman, W. (2014). Laser versus conventional fenestration in stapedotomy for otosclerosis: a systematic review. *The Laryngoscope, 124*(7), 1687-1693.
Weir, J. (2005). Quantifying test-retest reliability using the intraclass correlation coefficient and the SEM. *The Journal of Strength & Conditioning Research, 19*(1), 231-240.
Welgampola, M. S., & Colebatch, J. G. (2001). Vestibulocollic reflexes: normal values and the effect of age. *Clinical Neurophysiology, 112*(11), 1971-1979.
Welgampola, M. S., & Colebatch, J. G. (2005). Characteristics and clinical applications of vestibular-evoked myogenic potentials. *Neurology, 64*(10), 1682-1688.
Welgampola, M. S., Migliaccio, A. A., Myrie, O. A., Minor, L. B., & Carey, J. P. (2009). The human sound-evoked vestibulo-ocular reflex and its electromyographic correlate. *Clinical Neurophysiology, 120*(1), 158-166.
Welgampola, M. S., Rosengren, S. M., Halmagyi, G. M., & Colebatch, J. G. (2003). Vestibular activation by bone conducted sound. *Journal of Neurology, Neurosurgery, and Psychiatry, 74*(6), 771-778.
Wersall, J. (1961). Vestibular receptor cells in fish and mammals. *Acta Oto-Laryngologica. Supplementum, 163*, 25-29.
Wersäll, J., & Bagger-Sjöbäck, D. (1974). Morphology of the vestibular sense organ. In H. H. Kornhuber (Ed.), *Handbook of Sensory Physiology, Vestibular System Part 1: Basic Mechanisms* (pp. 123-170). Berlin, Germany: Springer Verlag.
Weston, P. B., Gengel, R. W., & Hirsh, I. J. (1967). Effects of vibrator types and their placement on bone-conduction threshold measurements. *The Journal of the Acoustical Society of America, 41*(4), 788-792.
Whalen, D. H. (1981). Effects of vocalic formant transitions and vowel quality on the English [s]-[s] boundary. *The Journal of the Acoustical Society of America, 69*(1), 275-282.
Whitehead, M. L., Stagner, B. B., McCoy, M. J., Lonsbury-Martin, B. L., & Martin, G. K. (1995). Dependence of distortion-product otoacoustic emissions on primary levels in normal and impaired ears. II. Asymmetry in L1,L2 space. *The Journal of the Acoustical Society of America, 97*(4), 2359-2377.
Whittemore, K. R., Jr., Merchant, S. N., & Rosowski, J. J. (1998). Acoustic mechanisms: canal wall-up versus canal wall-down mastoidectomy. *Otolaryngology - Head and Neck Surgery, 118*(6), 751-761.
Wiesenthal, A. A., & Garber, L. Z. (1999). New method for packing the external auditory canal, middle ear space, and mastoid cavities after otologic surgery. *The Journal of Otolaryngology, 28*(5), 260-265.
Wiet, R. J., Harvey, S. A., & Bauer, G. P. (1993). Complications in stapes surgery. Options for prevention and management. *Otolaryngologic clinics of North America, 26*(3), 471-490.
Wiet, R. J., Kubek, D. C., Lemberg, P., & Byskosh, A. T. (1997). A meta-analysis review of revision stapes surgery with argon laser: effectiveness and safety. *The American Journal of Otology, 18*(2), 166-171.
Wiet, R. J., Morgenstein, S. A., Zwolan, T. A., & Pircon, S. M. (1987). Far-advanced otosclerosis. Cochlear implantation vs stapedectomy. *Archives of Otolaryngology - Head and Neck Surgery, 113*(3), 299-302.
Wightman, F. L., & Kistler, D. J. (1989). Headphone simulation of free-field listening. I: Stimulus synthesis. *The Journal of the Acoustical Society of America, 85*(2), 858-867.

Wightman, F. L., & Kistler, D. J. (1992). The dominant role of low-frequency interaural time differences in sound localization. *The Journal of the Acoustical Society of America, 91*(3), 1648-1661.
Wightman, F. L., & Kistler, D. J. (1993). Sound localization. In W. A. Yost, A. N. Popper & R. R. Fay (Eds.), *Human Psychophysics* (pp. 155-192). New York, NY: Springer.
Wightman, F. L., & Kistler, D. J. (1997). Monaural sound localization revisited. *The Journal of the Acoustical Society of America, 101*(2), 1050-1063.
Wightman, F. L., & Kistler, D. J. (1999). Resolution of front-back ambiguity in spatial hearing by listener and source movement. *The Journal of the Acoustical Society of America, 105*(5), 2841-2853.
Wilber, L. A., & Goodhill, V. (1967). Real ear versus artificial mastoid methods of calibration of bone-conduction vibrators. *Journal of Speech and Hearing Research, 10*(3), 405-416.
Wiley, T. L., Cruickshanks, K. J., Nondahl, D. M., Tweed, T. S., Klein, R., & Klein, B. (1998). Aging and high-frequency hearing sensitivity. *Journal of Speech, Language and Hearing Research, 41*(5), 1061-1072.
Willi, U. B., Ferrazzini, M. A., & Huber, A. M. (2002). The incudo-malleolar joint and sound transmission losses. *Hearing Research, 174*(1-2), 32-44.
Williams, K. R., Blayney, A. W., & Lesser, T. H. (1997). Mode shapes of a damaged and repaired tympanic membrane as analysed by the finite element method. *Clinical Otolaryngology and Allied Sciences, 22*(2), 126-131.
Williams, K. R., & Lesser, T. H. (1990). A finite element analysis of the natural frequencies of vibration of the human tympanic membrane. Part I. *British Journal of Audiology, 24*(5), 319-327.
Winters, S. M., Klis, S. F., Kool, A. C., Kraaijenga, S. A., Tange, R. A., & Grolman, W. (2013). Perioperative bone-conducted ocular vestibular-evoked myogenic potentials in otosclerosis patients. *Otology & Neurotology, 34*(6), 1109-1114.
Woldag, K., Meister, E. F., & Kosling, S. (1995). Diagnosis in persistent vertigo after stapes surgery. *Laryngo- Rhino- Otologie, 74*(7), 403-407.
Wolff, D., & Bellucci, R. J. (1956). The human ossicular ligaments. *Annals of Otology, Rhinology and Laryngology, 65*(4), 895-910.
Woods, O., Fata, F. E., & Saliba, I. (2009). Ossicular reconstruction: incus versus universal titanium prosthesis. *Auris Nasus Larynx, 36*(4), 387-392.
Wrightson, T., & Keith, A. (1918). *An Enquiry into the Analytical Mechanism of the Internal Ear*. London, England: Macmillan and Company, Limited.
Wullstein, H. (1956). Theory and practice of tympanoplasty. *The Laryngoscope, 66*(8), 1076-1093.
Wysocki, J., Kwacz, M., Mrowka, M., & Skarzynski, H. (2011). Comparison of round-window membrane mechanics before and after experimental stapedotomy. *The Laryngoscope, 121*(9), 1958-1964.
Yacullo, W. S. (1996). *Clinical Masking Procedures*. Boston, MA: Allyn and Bacon.
Yamashita, D., Jiang, H. Y., Schacht, J., & Miller, J. M. (2004). Delayed production of free radicals following noise exposure. *Brain Research, 1019*(1-2), 201-209.
Yang, T. L., & Young, Y. H. (2003). Comparison of tone burst and tapping evocation of myogenic potentials in patients with chronic otitis media. *Ear and Hearing, 24*(3), 191-194.
Yang, T. L., & Young, Y. H. (2007). Vestibular-evoked myogenic potentials in patients with otosclerosis using air- and bone-conducted tone-burst stimulation. *Otology & Nneurotology, 28*(1), 1-6.
Yawn, R. J., Carlson, M. L., Haynes, D. S., & Rivas, A. (2014). Lateral-to-malleus underlay tympanoplasty: surgical technique and outcomes. *Otology & Neurotology, 35*(10), 1809-1812.
Ye, Q., Tillein, J., Hartmann, R., Gstoettner, W., & Kiefer, J. (2007). Application of a corticosteroid (Triamcinolon) protects inner ear function after surgical intervention. *Ear and Hearing, 28*(3), 361-369.
Yilmaz, M. S., Guven, M., Kayabasoglu, G., & Varli, A. F. (2013). Comparison of the anatomic and hearing outcomes of cartilage type 1 tympanoplasty in pediatric and adult patients. *European Archives of Oto-Rhino-Laryngology*.

Yin, X., Stromberg, A. K., & Duan, M. (2011). Evaluation of the noise generated by otological electrical drills and suction during cadaver surgery. *Acta Oto-Laryngologica, 131*(11), 1132-1135.
Yoon, T. H., Paparella, M. M., & Schachern, P. A. (1990). Otosclerosis involving the vestibular aqueduct and Meniere's disease. *Otolaryngology - Head and Neck Surgery, 103*(1), 107-112.
Yost, W. A. (2000). *Fundamentals of hearing: An introduction*. San Diego, CA: Academic Press.
Yost, W. A., Loiselle, L., Dorman, M., Burns, J., & Brown, C. A. (2013). Sound source localization of filtered noises by listeners with normal hearing: a statistical analysis. *The Journal of the Acoustical Society of America, 133*(5), 2876-2882.
Young, Y. H. (2006). Vestibular evoked myogenic potentials: optimal stimulation and clinical application. *Journal of Biomedical Science, 13*(6), 745-751.
Yung, M. W., Oates, J., & Vowler, S. L. (2006). The learning curve in stapes surgery and its implication to training. *The Laryngoscope, 116*(1), 67-71.
Zapala, D. A., & Brey, R. H. (2004). Clinical experience with the vestibular evoked myogenic potential. *Journal of the American Academy of Audiology, 15*(3), 198-215.
Zemlin, W. R. (1998). *Speech and hearing science: Anatomy and physiology*. Boston, MA: Allyn & Bacon.
Zhang, P. X., & Hartmann, W. M. (2010). On the ability of human listeners to distinguish between front and back. *Hearing Research, 260*(1-2), 30-46.
Zheng, C., Guyot, J. P., & Montandon, P. (1996). Ossiculoplasty by interposition of a minor columella between the tympanic membrane and stapes head. *The American Journal of Otology, 17*(2), 200-202.
Zislis, T., & Fletcher, J. L. (1966). Relation of high frequency thresholds to age and sex. *Journal of Auditory Research, 6*, 189-198.
Zou, J., Bretlau, P., Pyykko, I., Starck, J., & Toppila, E. (2001). Sensorineural hearing loss after vibration: an animal model for evaluating prevention and treatment of inner ear hearing loss. *Acta Oto-Laryngologica, 121*(2), 143-148.
Zou, J., Pyykko, I., Sutinen, P., & Toppila, E. (2005). Vibration induced hearing loss in guinea pig cochlea: expression of TNF-α and VEGF. *Hearing Research, 202*(1-2), 13-20.
Zwislocki, J., Kruger, B., Miller, J. D., Niemoeller, A. F., Shaw, E. A., & Studebaker, G. (1988). Earphones in audiometry. Committee on Hearing, Bioacoustics, and Biomechanics. Commission on Behavioral and Social Sciences and Education. National Research Council Working Group. *The Journal of the Acoustical Society of America, 83*(4), 1688-1689.

APPENDICES

Appendix A: Participant information sheets and consent forms

Prinicipal investigator:
Mr Phil Bird
Department of Otolaryngology
Christchurch Hospital
2 Riccarton Avenue
Christchurch
03 3640640

Study assessing inner ear function after ear surgery

You are invited to take part in a study assessing the effect of middle ear surgery on the inner ear. Your participation is entirely voluntary (your choice). You do not have to take part in this study, and if you choose not to take part you will receive the standard treatment/care available.

Background information:

Ear surgery is performed for different reasons but a common reason is to improve hearing. It has been noticed that although hearing often improves in the normal hearing frequencies that are tested with a conventional audiogram there may be subtle decreases in hearing in the higher frequencies because of very subtle mechanical trauma during surgery to the inner ear. The inner ear (cochlea) is a very delicate specialized organ and there have been theories about the effect of some surgical trauma such as mechanical vibration and also the effect of inflammatory cells recruited during healing. When the cochlea is damaged the higher frequencies of hearing tend to be affected more easily. These frequencies are above the frequency levels that we usually test but the audiology department is able to test these frequencies with special equipment. We can also assess inner ear balance function by testing eye muscle responses to ear stimulation (Vestibular Evoked Myogenic Potential or VEMP test).

Our department is very interested in studying the effect of surgery on all frequencies of hearing (that measured and those high frequencies not commonly measured) and also assessing the change in VEMP measurements after surgery. We hope to get a good set of data following surgery in 60 patients. This will give us good information into whether inner ear function is affected after middle ear surgery and also help us plan for future studies into possible intervention to minimize the effect of surgery on the ear if indeed surgery does cause change to inner ear function.

We are hoping that you may want to take part in our study.

What does the study involve for you?

All that will be different for you is that you have an extra audiogram (ten minutes) performed after the standard audiogram before your surgery and then at your post-operative visits when you would be having an audiogram anyway. The hearing results will be freely available to you after the study. We will also perform VEMP testing that is very brief and involves some electrode recordings of your eye muscles.

The study will in no way affect the success of your surgery or affect healing. You can pull out of the study at anytime and this will have no effect on your care after surgery. Your General Practitioner will be informed that you are in the study. At the end of the study if you wish you will be sent the results of all of the study.

If you take part in the study your privacy and confidentiality will be protected and there will be no information shown to people outside the medical study staff that could be identified to you. No material that could personally identify you will be used in any reports on this study.

If you have any questions or would like any extra information please feel free to ask.

If you have any queries or concerns regarding your rights as a participant in this study, you may wish to contact an independent health and disability advocate:
Free phone: 0800 555 050
Free fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

This study has received ethical approval from the Upper South B Ethics Committee, ethics reference number URB/09/07/029

Please feel free to contact the researcher if you have any questions about this study.

Canterbury
District Health Board
Te Poari Hauora ō Waitaha

Study assessing inner ear function after ear surgery

Patient Consent Form

An interpreter is not readily available, if you would like an interpreter we will endeavour to find one:

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai
Samoan	Ou te mana'o ia i ai se fa'amatala upu.	Ioe	Leai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai

Please read and tick the appropriate box:

	Yes	No
I have read and understood the information sheet "Research assessing inner ear function after middle ear surgery"	☐	☐
◦ I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study. I am satisfied with the answers given to me.	☐	☐
◦ I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my future health care	☐	☐
◦ I understand that taking part in this study is confidential and no material that could identify me will be used in any reports of this study.	☐	☐
◦ I have had time to consider whether to take part in this study.	☐	☐

I, _____[insert your full name]

Hereby consent to taking part in this study. I understand that this will involve having an extra audiogram before my surgery and at follow-up appointments and also a balance study (VEMP).

Signed:_____ Date (day/month/year): ___/___/___

Project explained by:_____ Signed:_____

At the end of the study I would like a copy of the results to be sent to me ☐ Yes ☐ No

Thank you, for your assistance.

Mr Phil Bird
Consultant Otologist
Department of Otolaryngology
Christchurch Public Hospital
2 Riccarton Avenue
Christchurch

Melissa Babbage
Audiologist/PhD student

Mr Daran Murray
Consultant Otologist

Dr Greg O'Beirne
Lecturer in Audiology

Investigators:
Melissa Babbage, PhD student
Department of Communication Disorders
Tel: 021 172 2992
Email: melissa.babbage@pg.canterbury.ac.nz

Assoc Prof Greg O'Beirne, Audiology Programme Director
Department of Communication Disorders
Tel: + 64 3 364 2987 ext. 7085

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

Project Information

Study assessing a new bone-conduction device for the measurement of high-frequency hearing sensitivity

You are invited to take part in a study assessing new techniques for the measurement of inner ear hearing function at high-frequencies. Your participation is entirely voluntary (your choice). If you decide to participate, all testing will take place at the University of Canterbury Speech and Hearing Clinic.

Background information

Usually, a hearing test assesses how good your hearing is at the frequencies, or pitches, most important for understanding speech. However, in some cases testing hearing at higher frequencies allows us to detect damage to the inner ear earlier than we can when we test only at lower frequencies. For example, following exposure to loud noise, or some chemotherapy drugs, hearing may become worse at very high frequencies or pitches first.

The hearing sensitivity of the inner ear can be tested using a device that sends sound straight to the inner ear by gently vibrating the bone. Standard bone-vibrators are not capable of testing high-frequencies, so we are interested in testing a new vibration-headphone device that will allow us to test inner ear hearing sensitivity at these higher frequencies.

We hope to obtain data that will tell us how reliably the new device will measure hearing under different conditions, such as when it is positioned in different places on the head. We also intend to compare hearing measured with the new device to that measured with standard headphones. This information will allow us to set-up the device so we can accurately measure inner ear hearing function in people with or without middle ear problems, such as glue ear.

What does the study involve for you?

The first part of the study will involve checking your ears for any middle ear problems by performing a brief pressure test of the eardrum and testing your hearing sensitivity at the standard frequencies. If your results show no signs of abnormal middle ear function, you will be invited to participate in the second part of the study.

Part two of the study involves testing your hearing at higher frequencies using headphones and the new bone-conduction device. The bone-conduction headphone consists of a headband

with a small metal disk that is positioned on your head. You will be asked to listen for tones and indicate when you hear them by pressing a button. Thresholds (the quietest sounds you respond to) will be measured three or four times with the bone-conduction device to assess the repeatability of the measurements. Together, both parts of the study will take approximately 45 to 60 minutes. The hearing results will be freely available to you immediately after testing.

If any hearing loss is identified during the test, these results will be discussed with you and you will be invited to make an appointment at the University of Canterbury Speech and Hearing Clinic for a free diagnostic hearing assessment and consultation at your convenience.

The results of the tests you participate in will be used in the current study, and may also be used in future studies within the University of Canterbury. If you choose to take part, your privacy and confidentiality will be protected and there will be no information shown to people outside the researchers named above that could be identified to you. No material that could personally identify you will be used in any reports on this study. To ensure confidentiality all data collected for the study will be kept in locked and secure facilities and in password protected electronic form and will be destroyed after ten years.

You may receive a copy of the project results by contacting the researcher at the conclusion of the project.

You may end the tests at any time and are free to discontinue participation in this study, , without any consequences. You may contact the researcher to withdraw any information you have provided from being included in the results of the study within one month of doing the test.

If you have any questions or would like any extra information please feel free to ask.

This project has been reviewed and approved by the University of Canterbury Human Ethics Committee, and participants should address any complaints to The Chair, Human Ethics Committee, University of Canterbury, Private Bag 4800, Christchurch (human-ethics@canterbury.ac.nz).

If you have any queries or concerns regarding your rights as a participant in this study, you may wish to contact an independent health and disability advocate:
Free phone: 0800 555 050
Free fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

Study assessing a new bone-conduction device for the measurement of high-frequency hearing sensitivity

Participant Consent Form

An interpreter is not readily available, if you would like an interpreter we will endeavour to find one:

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai
Samoan	Ou te mana'o ia i ai se fa'amatala upu.	Ioe	Leai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai

Please read and tick the appropriate box:

	Yes	No
• I have read and understood the information sheet *"Study assessing a new bone-conduction device for the measurement of high-frequency hearing sensitivity"*	☐	☐
• I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study. I am satisfied with the answers given.	☐	☐
• I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without penalty. I understand that I can also withdraw the information I have provided within one month of participating by contacting the researcher.	☐	☐
• I understand that taking part in this study is confidential and no material that could identify me will be used in any reports of this study.	☐	☐
• I understand that all data collected for the study will be kept in locked and secure facilities and in password protected electronic form and will be destroyed after ten years.	☐	☐
• I have had time to consider whether to take part in this study.	☐	☐

I, _____[insert your full name]

Hereby consent to taking part in this study.

Signed:_____ Date (day/month/year): ___/___/___

Project explained by:_____ Signed:_____

Thank you, for your assistance.

If you have any concerns you can contact the researcher for further information. If I have any complaints, I can contact the Chair of the University of Canterbury Human Ethics Committee, Private Bag 4800, Christchurch (human-ethics@canterbury.ac.nz)

Melissa Babbage, PhD student
Department of Communication Disorders
Tel: 021 172 2992
Email: melissa.babbage@pg.canterbury.ac.nz

Assoc Prof Greg O'Beirne, Audiology Programme Director
Department of Communication Disorders
Tel: + 64 3 364 2987 ext. 7085
Email: gregory.obeirne@canterbury.ac.nz

Canterbury
District Health Board
Te Poari Hauora ō Waitaha

Prinicipal investigator:
Melissa Babbage
Department of Communication Disorders
University of Canterbury
Private Bag 4800
CHRISTCHURCH 8140
03 364 2431

Study assessing inner ear function after ear surgery

You are invited to take part in a study assessing the effect of middle ear surgery on the inner ear. Your participation is entirely voluntary (your choice). You do not have to take part in this study, and if you choose not to take part you will receive the standard treatment/care available.

Background information:

Ear surgery is performed for different reasons but a common reason is to improve hearing. It has been noticed that although hearing often improves in the normal hearing frequencies that are tested with a conventional audiogram there may be subtle decreases in hearing in the higher frequencies because of very subtle mechanical trauma during surgery to the inner ear. The inner ear (cochlea) is a very delicate specialized organ and there have been theories about the effect of some surgical trauma such as mechanical vibration and also the effect of inflammatory cells recruited during healing. When the cochlea is damaged the higher frequencies of hearing tend to be affected more easily. These frequencies are above the frequency levels that we usually test but the audiology department is able to test these frequencies with special equipment.

Our department is very interested in studying the effect of surgery on all frequencies of hearing (that measured and those high frequencies not commonly measured). This will give us good information into whether inner ear function is affected after middle ear surgery and also help us plan for future studies into possible intervention to minimize the effect of surgery on the ear if indeed surgery does cause change to inner ear function.

We are hoping that you may want to take part in our study.

What does the study involve for you?

All that will be different for you is that you have an extra audiogram (ten minutes) performed after the standard audiogram before your surgery and then at your post-operative visits when you would be having an audiogram anyway. The hearing results will be freely available to you after the study.

The study will in no way affect the success of your surgery or affect healing. You can pull out of the study at anytime and this will have no effect on your care after surgery. Your General Practitioner will be informed that you are in the study. At the end of the study if you wish you will be sent the results of all of the study.

If you take part in the study your privacy and confidentiality will be protected and there will be no information shown to people outside the medical study staff that could be identified to you. No material that could personally identify you will be used in any reports on this study.

If you have any questions or would like any extra information please feel free to ask.

If you have any queries or concerns regarding your rights as a participant in this study, you may wish to contact an independent health and disability advocate:
Free phone: 0800 555 050
Free fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

This study has received ethical approval from the Upper South B Ethics Committee, ethics reference number URB/09/07/029/AM01

Please feel free to contact the researcher if you have any questions about this study.

Canterbury
District Health Board
Te Poari Hauora ō Waitaha

Study assessing inner ear function after ear surgery

Patient Consent Form

An interpreter is not readily available, if you would like an interpreter we will endeavour to find one:

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai
Samoan	Ou te mana'o ia i ai se fa'amatala upu.	Ioe	Leai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai

Yes No

Please read and tick the appropriate box:

I have read and <u>understood</u> the information sheet "Research assessing inner ear function after middle ear surgery" ☐ ☐

◦ I have had the opportunity to use whanau support or a friend to help me ask questions and understand the study. I am satisfied with the answers given to me. ☐ ☐

◦ I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time and this will in no way affect my future health care ☐ ☐

◦ I understand that taking part in this study is confidential and no material that could identify me will be used in any reports of this study. ☐ ☐

◦ I have had time to consider whether to take part in this study. ☐ ☐

I, _____[insert your full name]

Hereby consent to taking part in this study. I understand that this will involve having an extra audiogram before my surgery and at follow-up appointments.

Signed:_____ Date (day/month/year): ___/___/___

Project explained by:_____ Signed:_____

At the end of the study I would like a copy of the results to be sent to me ☐ Yes ☐No

Thank you, for your assistance.

Melissa Babbage
Audiologist/PhD student
Department of Communication Disorders
University of Canterbury
Private Bag 4800
Christchurch 8140
03 364 2431

Mr Phil Bird
Consultant Otologist
Department of Otolaryngology
Christchurch Public Hospital
2 Riccarton Avenue
Christchurch

Dr Greg O'Beirne
Lecturer in Audiology
Department of Communication Disorders
University of Canterbury
Private Bag 4800
Christchurch 8140
03 364 2431

Investigators:
Sarah Gray, Master of Audiology student
Department of Communication Disorders
Ph: 0276505055
Email: seg60@uclive.ac.nz

Melissa Babbage, PhD student
Department of Communication Disorders
Email: melissa.babbage@pg.canterbury.ac.nz

Dr Greg O'Beirne, Lecturer in Audiology
Department of Communication Disorders
Tel: + 64 3 364 2987 ext. 7085
Email: gregory.obeirne@canterbury.ac.nz

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

Project Information

Study assessing localisation ability of people with an extended high frequency hearing loss

You are invited to take part in a study assessing the effect of extended high frequency hearing loss on localisation ability. Your participation is entirely voluntary (your choice). If you decide to participate, all testing will take place at the University of Canterbury Speech and Hearing Clinic. If you decide not to participate, this will in no way affect any further audiological assessments or treatment that you may require.

Background information

The auditory function of localisation provides humans with an awareness of the position of sounds in their environment. Studies up to now have mainly compared localisation ability of normal to hearing impaired listeners using the typically measured hearing thresholds of 250 Hz to 8 kHz. However, it has been found in some instances that simulated hearing loss in the extended high frequencies above 8 kHz (above the frequency range assessed in a standard hearing test) can have an impact on the ability to localize.

It has also been noticed that after ear surgery, although hearing often improves in the range of frequencies most important for understanding speech in quiet environments, there may be subtle decreases of hearing in the extended higher frequencies because of very subtle trauma during surgery to the inner ear or cochlea.

The purpose of this Masters study is to establish whether a hearing loss in the extended high frequencies does have an impact on the function of localisation. By obtaining further information about whether the extended high frequencies are utilized, it will help in the

planning for future studies about minimizing the effects of surgery on high frequency hearing and may provide information about whether providing amplification (e.g. hearing aids) at these frequencies would be beneficial.

What does the study involve for you?

The first part of the study will involve measuring your hearing sensitivity at the typical frequencies, in addition to the extended high frequencies. This should take approximately half an hour. If your results indicate that you are suitable for part two of the study you will be asked if you would like to participate.

Part two of the study involves sitting in a chair either facing or positioned side on to a group of covered speakers. Some noises and speech will be played and you will be required to point in the direction that you hear the sound or speech stimuli. This will take approximately one hour.

The results of the tests you perform will be used in the current study, as well as possibly being used in future studies within the University of Canterbury. If you agree to participate, all identifying information, such as your name and address, will be kept confidential. At the end of the study, if you wish, you will be sent the results of all of the study.

If you have any questions or would like any extra information please feel free to ask.

This project has been given ethical approval by the University of Canterbury Human Ethics Committee. The tests will in no way cause you any discomfort or harm. Nonetheless, you may end the tests at any time and are free to discontinue participation in this study, including withdrawal of any information you may have provided.

If you have any queries or concerns regarding your rights as a participant in this study, you may wish to contact an independent health and disability advocate:
Free phone: 0800 555 050
Free fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

Study assessing localisation ability of people with an extended high frequency hearing loss

Participant Consent Form

An interpreter is not readily available, if you would like an interpreter we will endeavour to find one:

English	I wish to have an interpreter.	Yes	No
Maori	E hiahia ana ahau ki tetahi kaiwhakamaori/kaiwhaka pakeha korero.	Ae	Kao
Cook Island	Ka inangaro au i tetai tangata uri reo.	Ae	Kare
Fijian	Au gadreva me dua e vakadewa vosa vei au	Io	Sega
Niuean	Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu.	E	Nakai
Samoan	Ou te mana'o ia i ai se fa'amatala upu.	Ioe	Leai
Tokelaun	Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika	Ioe	Leai
Tongan	Oku ou fiema'u ha fakatonulea.	Io	Ikai

Please read and tick the appropriate box:

I have read and understood the project information sheet "Study assessing localisation ability of people with an extended high frequency hearing loss" ☐ ☐

◦ I have had the opportunity to ask questions about the study, and am satisfied with the answers I have been given.

◦ I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time. ☐ ☐

◦ I understand that taking part in this study is confidential and no material that could identify me will be used in any reports of this study. ☐ ☐

◦ I have had time to consider whether to take part in this study. ☐ ☐

I, _____[insert your full name]

Hereby consent to taking part in this study. I understand that this will involve having a typical and extended high frequency audiogram and if suitable further localisation testing.

Signed:_____ Date (day/month/year): ___/___/___

Project explained by:_____ Signed:_____

At the end of the study I would like a copy of the results to be sent to me Yes ☐ No ☐

Thank you, for your assistance.
Sarah Gray
Masters of Audiology Student

Dr Greg O'Beirne
Lecturer in Audiology

Melissa Babbage
PhD Student

Appendix B: Hearing outcomes according to surgical variables

Stapedectomy

Type of laser:

	Approximate time since surgery					
	Preop	1 week	1 month	3 months	6 months	12 months
Argon						
n	31	27	30	26	25	24
AC PTA						
Mean *(SD)*	59.6 *(11.9)*	42.7 *(17.1)*	32.9 *(11.7)*	30.0 *(12.1)*	29.8 *(11.8)*	32.0 *(16.8)*
HF BC PTA						
Mean *(SD)*	25.9 *(11.3)*	29.4 *(11.2)*	24.6 *(12.0)*	21.7 *(10.8)*	21.9 *(11.4)*	22.6 *(11.1)*
Air-bone gap						
Mean *(SD)*	32.4 *(11.1)*	14.1 *(10.8)*	8.4 *(6.7)*	7.1 *(6.7)*	7.3 *(7.8)*	9.2 *(11.7)*
≤ 10 dB	3.2%	51.9%	70.0%	80.8%	80.0%	75.0%
≤ 20 dB	16.1%	74.1%	93.3%	96.2%	92.0%	87.5%
CO_2						
n	12	11	11	9	9	9
AC PTA						
Mean *(SD)*	51.1 *(10.3)*	35.2 *(13.8)*	25.7 *(8.9)*	25.1 *(5.0)*	21.8 *(4.2)*	21.8 *(3.7)*
HF BC PTA						
Mean *(SD)*	20.8 *(6.5)*	23.8 *(9.6)*	18.0 *(11.1)*	18.0 *(7.3)*	15.0 *(6.1)*	15.2 *(6.1)*
Air-bone gap						
Mean *(SD)*	28.8 *(9.0)*	10.9 *(9.1)*	7.7 *(4.5)*	6.0 *(3.6)*	5.8 *(2.5)*	5.6 *(3.4)*
≤ 10 dB	0.0%	45.5%	72.7%	100.0%	100.0%	88.9%
≤ 20 dB	25.0%	81.8%	100.0%	100.0%	100.0%	100.0%

Primary vs. revision:

	Approximate time since surgery					
	Preop	1 week	1 month	3 months	6 months	12 months
Primary						
n	31	28	29	25	23	23
AC PTA						
Mean *(SD)*	57.5 *(11.7)*	41.5 *(17.4)*	30.9 *(12.4)*	29.8 *(11.6)*	28.8 *(12.0)*	31.1 *(16.7)*
HF BC PTA						
Mean *(SD)*	25.3 *(10.6)*	27.7 *(10.5)*	23.2 *(12.4)*	21.8 *(9.5)*	20.5 *(11.2)*	21.2 *(10.9)*
Air-bone gap						
Mean *(SD)*	30.7 *(10.1)*	14.2 *(11.0)*	7.8 *(5.7)*	7.2 *(6.7)*	7.9 *(7.9)*	9.5 *(11.8)*
≤ 10 dB	3.2%	46.4%	79.3%	80.0%	73.9%	69.6%
≤ 20 dB	19.4%	75.0%	96.6%	96.0%	91.3%	87.0%
Revision						
n	13	11	13	11	12	11
AC PTA						
Mean *(SD)*	56.2 *(12.5)*	38.3 *(13.1)*	30.7 *(8.8)*	26.1 *(8.6)*	25.2 *(7.8)*	25.2 *(9.3)*
HF BC PTA						
Mean *(SD)*	23.2 *(9.9)*	24.5 *(12.0)*	21.8 *(10.9)*	17.9 *(10.8)*	19.0 *(9.2)*	19.4 *(9.3)*
Air-bone gap						
Mean *(SD)*	32.7 *(11.8)*	10.9 *(7.8)*	9.2 *(7.0)*	6.9 *(5.2)*	5.4 *(3.6)*	5.6 *(3.7)*
≤ 10 dB	0.0%	54.5%	53.8%	90.9%	100.0%	100.0%
≤ 20 dB	15.4%	81.8%	92.3%	100.0%	100.0%	100.0%

Tympanoplasty

Cholesteatoma presence:

	Approximate time since surgery					
	Preop	1 week	1 month	3 months	6 months	12 months
Cholesteatoma						
n	6	4	5	5	4	4
AC PTA						
Mean *(SD)*	34.0 *(13.3)*	41.3 *(11.1)*	33.5 *(8.5)*	30.0 *(5.8)*	30.3 *(8.3)*	32.5 *(6.7)*
HF BC PTA						
Mean *(SD)*	17.5 *(9.5)*	21.3 *(8.9)*	19.3 *(9.1)*	15.3 *(10.0)*	20.0 *(10.5)*	20.8 *(7.5)*
Air-bone gap						
Mean *(SD)*	16.3 *(13.2)*	22.5 *(13.8)*	16.8 *(7.9)*	14.3 *(3.8)*	11.9 *(3.9)*	14.4 *(2.2)*
≤ 10 dB	50.0%	25.0%	20.0%	20.0%	50.0%	0.0%
≤ 20 dB	66.7%	50.0%	80.0%	100.0%	100.0%	100.0%
No cholesteatoma						
n	21	12	12	16	9	15
AC PTA						
Mean *(SD)*	37.4 *(16.0)*	49.2 *(16.7)*	38.4 *(17.1)*	33.8 *(16.3)*	21.9 *(11.2)*	36.4 *(18.1)*
HF BC PTA						
Mean *(SD)*	17.4 *(13.8)*	22.1 *(15.2)*	17.1 *(13.1)*	16.4 *(13.3)*	10.2 *(7.0)*	16.8 *(10.8)*
Air-bone gap						
Mean *(SD)*	19.3 *(10.6)*	27.9 *(9.3)*	22.1 *(11.1)*	16.6 *(10.5)*	11.4 *(9.9)*	18.1 *(11.7)*
≤ 10 dB	19.0%	0.0%	8.3%	43.8%	66.7%	26.7%
≤ 20 dB	57.1%	25.0%	41.7%	68.8%	77.8%	60.0%

Primary vs. revision:

	Approximate time since surgery					
	Preop	1 week	1 month	3 months	6 months	12 months
Primary						
n	17	10	11	13	9	11
AC PTA						
Mean *(SD)*	36.0 *(17.0)*	48.9 *(16.0)*	35.0 *(16.4)*	30.0 *(15.5)*	22.4 *(10.1)*	33.6 *(17.8)*
HF BC PTA						
Mean *(SD)*	14.9 *(12.5)*	20.0 *(14.2)*	15.9 *(11.7)*	13.3 *(12.3)*	11.7 *(10.3)*	15.9 *(9.7)*
Air-bone gap						
Mean *(SD)*	20.1 *(12.6)*	24.8 *(11.3)*	20.6 *(10.1)*	15.1 *(9.3)*	9.7 *(4.3)*	17.2 *(11.3)*
≤ 10 dB	29.4%	10.0%	9.1%	38.5%	66.7%	18.2%
≤ 20 dB	52.9%	40.0%	54.5%	84.6%	100.0%	72.7%
Revision						
n	10	6	6	8	4	8
AC PTA						
Mean *(SD)*	37.8 *(13.9)*	52.7 *(14.4)*	40.6 *(12.6)*	37.5 *(12.0)*	29.4 *(12.4)*	38.3 *(14.6)*
HF BC PTA						
Mean *(SD)*	21.8 *(12.8)*	25.0 *(13.4)*	21.1 *(12.4)*	20.6 *(11.9)*	16.7 *(4.9)*	20.0 *(11.0)*
Air-bone gap						
Mean *(SD)*	16.1 *(7.8)*	29.58 *(8.6)*	20.1 *(11.8)*	17.7 *(9.6)*	15.6 *(14.0)*	17.5 *(10.0)*
≤ 10 dB	20.0%	0.0%	16.7%	37.5%	50.0%	25.0%
≤ 20 dB	70.0%	16.7%	50.0%	62.5%	50.0%	62.5%

Ossiculoplasty

Primary vs. second stage vs. revision:

	Approximate time since surgery					
	Preop	1 week	1 month	3 months	6 months	12 months
Primary						
n	5	4	4	4	5	4
AC PTA						
Mean *(SD)*	51.8 *(7.1)*	61.6 *(17.7)*	36.6 *(9.6)*	35.0 *(10.3)*	38.3 *(12.1)*	36.3 *(11.4)*
HF BC PTA						
Mean *(SD)*	18.7 *(13.8)*	25.8 *(12.2)*	11.3 *(6.0)*	14.2 *(14.5)*	15.3 *(14.0)*	16.3 *(17.9)*
Air-bone gap						
Mean *(SD)*	31.0 *(10.0)*	36.3 *(6.8)*	23.4 *(6.6)*	19.4 *(1.6)*	21.0 *(6.7)*	19.4 *(4.6)*
≤ 10 dB	0.0%	0.0%	0.0%	0.0%	0.0%	0.0%
≤ 20 dB	20.0%	0.0%	50.0%	75.0%	60.0%	50.0%
Revision						
n	7	4	6	2	4	4
AC PTA						
Mean *(SD)*	48.9 *(12.9)*	40.0 *(23.0)*	32.3 *(11.0)*	40.6 *(0.9)*	39.4 *(8.8)*	41.3 *(8.7)*
HF BC PTA						
Mean *(SD)*	20.2 *(12.8)*	15.4 *(13.6)*	11.9 *(8.9)*	21.7 *(4.7)*	20.0 *(12.1)*	16.7 *(13.6)*
Air-bone gap						
Mean *(SD)*	30.3 *(14.9)*	22.8 *(17.8)*	20.0 *(14.1)*	16.3 *(1.8)*	19.7 *(9.1)*	28.1 *(13.6)*
≤ 10 dB	14.3%	50.0%	33.3%	0.0%	25.0%	0.0%
≤ 20 dB	28.6%	50.0%	50.0%	100.0%	50.0%	25.0%
Second stage						
n	16	13	10	10	13	12
AC PTA						
Mean *(SD)*	46.7 *(11.6)*	36.8 *(10.0)*	41.4 *(9.9)*	38.0 *(19.8)*	38.0 *(12.4)*	39.6 *(16.2)*
HF BC PTA						
Mean *(SD)*	16.9 *(9.0)*	15.5 *(8.1)*	14.8 *(7.0)*	17.7 *(10.3)*	14.9 *(6.0)*	17.2 *(9.0)*
Air-bone gap						
Mean *(SD)*	29.2 *(12.6)*	22.1 *(6.2)*	26.4 *(9.4)*	20.1 *(12.6)*	23.8 *(12.5)*	21.6 *(10.5)*
≤ 10 dB	6.3%	0.0%	0.0%	20.0%	15.4%	16.7%
≤ 20 dB	25.0%	46.2%	30.0%	50.0%	38.5%	50.0%

PORPs vs. TORPs:

	Approximate time since surgery					
	Preop	1 week	1 month	3 months	6 months	12 months
PORP						
n	19	15	14	10	14	13
AC PTA						
Mean *(SD)*	47.9 *(11.7)*	46.8 *(17.2)*	37.5 *(10.1)*	36.3 *(11.3)*	39.7 *(8.6)*	38.7 *(8.8)*
HF BC PTA						
Mean *(SD)*	19.8 *(10.6)*	20.3 *(10.4)*	14.9 *(7.1)*	19.5 *(7.1)*	18.8 *(9.2)*	16.9 *(10.6)*
Air-bone gap						
Mean *(SD)*	28.1 *(12.5)*	26.4 *(11.9)*	22.0 *(10.4)*	17.0 *(9.6)*	21.1 *(8.4)*	22.2 *(9.4)*
≤ 10 dB	5.3%	13.3%	14.3%	20.0%	14.3%	7.7%
≤ 20 dB	31.6%	33.3%	42.9%	80.0%	42.9%	53.8%
TORP						
n	9	6	6	6	8	7
AC PTA						
Mean *(SD)*	48.8 *(10.4)*	30.6 *(8.3)*	38.1 *(12.2)*	39.2 *(23.4)*	35.8 *(15.3)*	40.4 *(20.8)*
HF BC PTA						
Mean *(SD)*	14.3 *(10.1)*	10.3 *(6.2)*	9.4 *(6.6)*	13.6 *(14.9)*	10.8 *(6.8)*	16.9 *(13.2)*
Air-bone gap						
Mean *(SD)*	33.5 *(12.6)*	21.3 *(4.5)*	28.3 *(10.1)*	23.5 *(9.8)*	24.7 *(14.1)*	22.9 *(12.6)*
≤ 10 dB	11.1%	0.0%	0.0%	0.0%	12.5%	14.3%
≤ 20 dB	11.1%	50.0%	33.3%	33.3%	50.0%	28.6%

Who can participate?

We are looking for people who are likely to have an extended high-frequency hearing loss.

People who fit this category may already have a high-frequency hearing loss that they know about, or they may be unaware of it. In some cases they may have had ear surgery, cancer treatment, or exposure to excessive noise.

You will receive a free hearing test and participate in a localisation experiment at the University of Canterbury. This involves listening to sounds and pointing to their perceived location.

It will take approximately 2 hours. The first visit involves around 30 minutes for a hearing test and the second visit takes 90 minutes for the localization testing.

Please contact :

University of Canterbury

Department of Communication Disorders

Sarah Gray

Masters of Audiology student

Ph: 0276505055

Email: seg60 @uclive.ac.nz

Dr. Greg O' Beirne

Audiology Lecturer

Ph: + 64 3 364 2987 ext. 7085

Email: gregory.obeirne@canterbury.ac.nz

Melissa Babbage

PhD student

Ph: 021 172 2992

Email: melissa.babbage@pg.canterbury.ac.nz

University of Canterbury

UC UNIVERSITY OF CANTERBURY
Te Whare Wānanga o Waitaha
CHRISTCHURCH NEW ZEALAND

The Effects of Extended High Frequency Hearing Loss on the Ability to Localise Sound