COCHLEAR DEAD REGIONS IN HEARING-IMPAIRED ADULTS

A thesis submitted to the University of Manchester for the degree of

Doctor of Philosophy

in the Faculty of Medical and Human Sciences

2013

ANNA CAROLINE PEPLER

SCHOOL OF PSYCHOLOGICAL SCIENCES

CONTENTS PAGE

Word Count 49764

LIST OF TABLES

Chapter 2

Chapter 3

Chapter 4

Chapter 5

Chapter 6

LIST OF FIGURES

Chapter 2

Chapter 4

Chapter 5

Chapter 6

ABSTRACT
THE UNIVERSITY OF MANCHESTER

Anna Caroline Pepler
Doctor of Philosophy

COCHLEAR DEAD REGIONS IN HEARING-IMPAIRED ADULTS
December 2013

Cochlear dead regions (DRs) are areas in the cochlea where inner hair cells and/or neurones are functioning so poorly that a sound that causes peak basilar membrane motion in that region is more efficiently detected via off-frequency listening. The Threshold Equalising Noise (TEN) test is a clinical test procedure for detecting DRs. Psychophysical Tuning Curves (PTCs) can be used to identify the boundary frequency of the DR although the clinical importance of doing this has yet to be determined. Some studies have suggested that the reduction of amplification well inside the DR may be beneficial; however, other studies have been unable to replicate these findings in a more typical clinical population. Three studies were completed in order to:

1. determine the prevalence of DRs in a clinical sample of the UK adult population,
2. investigate repeatability, agreement and clinical feasibility of the TEN-test and fast PTCs in a clinical setting, and
3. determine the benefit of high-frequency amplification in ears with and without DRs, when listening to nonsense syllable speech material in quiet and babble.

In the first study, 343 hearing-impaired adults were tested for DRs using the TEN-test. In total, 36% (95% confidence interval 31-41) of these adults had a DR in at least one ear, but frequently at 4 kHz only. Only 3% (1-5) of participants had a DR spanning more than three consecutive frequencies. These findings suggest that DRs usually only span 1 or 2 clinically-relevant frequencies. In the second study, the TEN-test was completed on 70 ears at frequencies between 0.5 and 4 kHz. Fast PTCs were measured on 20 ears at ≥ 2 frequencies. The TEN-test and fast PTCs were highly repeatable on retest (97% and 100%, respectively). There was 87% agreement between the two procedures in terms of the presence of off-frequency listening, with the TEN-test less likely to detect a DR than fast PTCs. Compared to the TEN-test, fast PTCs had a 10% lower 'conclusive finding' rate and the test duration was typically 40 minutes longer. Therefore, the TEN-test is more clinically acceptable, but it may underestimate the extent of a DR because of its inability to precisely identify the boundary frequency. In the third study, 18 ears with a high-frequency DR and 18 matched ears without a DR were tested. Vowel-Consonant-Vowel (VCV) stimuli were presented in quiet and babble when listening with an unfiltered and three low-pass filtered hearing aid settings. Best performance was obtained in the unfiltered condition; however the DR group performed significantly poorer than the controls in babble. There was no evidence to support reducing amplification in ears with a DR. However, participants with DRs may benefit from counseling about the limitations of listening in noise. In summary, DRs are relatively prevalent in hearing-impaired adults and can be diagnosed most efficiently in a clinical setting using the TEN-test. However, DRs are often restricted to a narrow frequency range and, in the typical adult clinical population, there is no evidence to support deviating from prescription targets.

DECLARATION

No portion of the work referred to in the thesis has been submitted in support of an application for another degree or qualification of this or any other university or other institute of learning.

COPYRIGHT STATEMENT

ACKNOWLEDGEMENTS

I would like to thank Kevin Munro for the opportunity to complete this research and his academic advice and support throughout my studies. Thank you to Karolina Kluk for her excellent technical input to my research. I would like to thank Kathryn Hopkins, Piers Dawes and Rachel Ellis for providing much valued contribution to my thesis. Also thanks to Tim Wilding, Anisa Visram, Kirpa Chandan and Ann-Marie Dickinson for all their support and friendship during my time in Manchester.

I would like to thank the National Institute for Health Research and the Greater Manchester Comprehensive Local Research Network for providing the funding for this research.

Thank you to Janet Uttley for being a wonderful clinical assistant and colleague throughout my data collection, always so willing to help and discuss my PhD at length. I would like to thank Kathryn Lewis for supporting my clinical development during my PhD and for some lovely conversations about cake decorating! It was a great pleasure to work with everyone in the audiology department at Withington Community Hospital Manchester, thank you.

Thank you to all of my participants without whom I would have been unable to complete any of this research. Their commitment, enthusiasm and willingness to complete many hours of testing was really inspiring.

I would like to thank my family and friends for all their help and support throughout my time in Manchester. In particular I would like to thank my parents and Emily and James for making sure I had my priorities right by feeding the calves before working on my PhD! Thank you to Granny and Grampy for frequently checking I was working hard. Also thank you to Anne, for many helpful PhD discussions and to Claire and Rachel for just being there.

Thank you to my audiology colleagues at the Royal Surrey County Hospital, Guildford for their interest and support in my research whilst completing the final aspects of my PhD.

Finally I would like to thank Sue Robinson, without whom I would have never had a career in audiology.

PREFACE

The author obtained a BSc in Applied Biology from the University of Nottingham in 2005 and an MSc in Audiology at the University of Southampton in 2007. From 2006 to 2008 she undertook clinical training in Audiology at University Hospitals Southampton NHS Foundation Trust. In 2010 she registered as a clinical scientist in Audiology. During her PhD she was based at University Hospitals South Manchester NHS Foundation Trust. She currently works as a team leader of the adult audiology service at Royal Surrey County Hospital NHS Foundation Trust.

THESIS FORMAT

This thesis is presented in the ‘alternative’ format. The three experimental chapters are presented as journal manuscripts. The titles of each of these chapters are listed below.

Chapter 4 (Study 1): Prevalence of cochlear dead regions in new referrals and existing adult hearing aid users, Ear and Hearing, 2014.

Chapter 5 (Study 2): Repeatability, agreement and feasibility of using the threshold equalising noise test and fast psychophysical tuning curves in a clinical setting, International Journal of Audiology, In Press.

Chapter 6 (Study 3): Benefit of high-frequency amplification in ears with cochlear dead regions, Ear and Hearing, Submitted.

LIST OF ABBREVIATIONS

AoHL Action on Hearing Loss
ANOVA Analysis Of Variance
AI Articulation Index
BKB Bamford-Kowal-Bench
CASPA Computer-Assisted Speech Perception Assessment Test
dB Decibels
DR Cochlear Dead Region
DSL Desired Sensation Level
f_e DR edge frequency
GHABP Glasgow Hearing Aid Benefit Profile
GHADP Glasgow Hearing Aid Difference Profile
HL Hearing Level
IHC Inner Hair Cells
IHR Institute of Hearing Research
(k)Hz (kilo)-Hertz
MHAS Modernising Hearing Aid Services
NAL National Acoustic Laboratory
NHS National Health Service
OHC Outer Hair Cells
PTC Psychophysical Tuning Curve
QSIN Quick Speech In Noise
REIG Real Ear Insertion Gain
REM Real Ear Measurement
ROC Receiver Operator Characteristic
ROEX Rounded Exponential Function
SL Sensation Level
SII Speech Intelligibility Index
SIN Speech In Noise
SL Sensation Level
SNR Signal-To-Noise
SPL Sound Pressure Level
SSQ Speech, Spatial and Qualities of hearing scale
TEN Threshold Equalising Noise
ULL Uncomfortable Loudness Level
UK United Kingdom
USA United States of America
VCV Vowel-consonant-vowel

CHAPTER 1

INTRODUCTION

Hearing impairment is common. According to figures provided by Action on Hearing Loss, one in six adults in the United Kingdom (U.K.) have some degree of hearing impairment (AoHL 2012). It is expected that this number will rise due to increasing life expectancy and a growing population (WHO 2000). There are a wide range of acquired and congenital reasons for hearing impairment in adults and children. An abnormality of the outer or middle ear, results in a conductive hearing impairment. A sensorineural hearing impairment is associated with reduced function in the inner ear or neural pathways. Inner ear hearing impairment is often associated with damage to hair cells in the cochlea and is therefore permanent (Schuknecht & Gacek 1993). Currently the main intervention for permanent hearing impairment is a hearing aid. More than four million adults in the U.K., who currently do not have a hearing aid, would benefit from one (AoHL 2012). In addition, 0.8 million adults are believed to have a hearing aid but do not wear it (AoHL 2012). This suggests that five million adults in the UK have a hearing impairment but do not wear hearing aids. Hearing aid use improves communication which may have both psychological and cognitive benefits (Acar et al. 2011; Kricos et al. 2007). As the number of adults in the U.K. with hearing impairment rises, the need to increase the uptake, long-term adherence and benefit of hearing aids is ever more important.

Hearing aid provision in England has changed substantially over the last decade. In England and Wales, Modernising Hearing Aid Services (MHAS) were rolled out across National Health Service (NHS) audiology departments between 2001 and 2004. MHAS was funded by the Department of Health and the aim was to standardise and improve hearing aid provision across the country. This was achieved by:

a) The provision of digital hearing aids.

b) The use of real ear measurements (REMs) for verification to a prescription target.

c) Increasing rehabilitation time, including routine follow up appointments, for each patient.

d) Use of validated outcome measures such as the Glasgow Hearing Aid Benefit Profile (GHABP; Gatehouse 1999).

e) Use of a patient management system to ensure up to date and accurate information was recorded electronically during service delivery.

The addition of digital technology provides much more sophisticated programming features than available with analogue hearing aids. These features include multi-microphone technology, feedback management, noise suppression features, frequency lowering, wireless facilities and multi-programmable aids. This technology has undeniably increased the choice of hearing aid settings for audiologists and patients alike. However, we do not yet know how to personalise aspects of the fitting process to maximise patient benefit.

Hearing aids are programmed with appropriate gain, output and compression features for the patients' hearing impairment. It is known that linear output is most suitable for individuals with a conductive hearing impairment (Dillon 2012). Non-linear output is used to maintain speech intelligibility, whilst avoiding loudness discomfort in sensorineural hearing impairments (Byrne et al. 2001; Ching et al. 2001). A number of prescriptions are available which assist audiologists in fitting hearing aids to conductive (e.g. Desired Sensation Level [DSL] m[i/o]; National Acoustic Laboratory [NAL]-RP) and sensorineural hearing impairment (e.g. (DSL) 5; NAL-NL2).

A proportion of sensorineural hearing impairments can be attributed to the damage of outer or inner hair cells (Schuknecht & Gacek 1993). Outer hair cell (OHC) damage results in reduced sound detection, abnormal loudness growth and reduced frequency selectivity (Ryan & Dallos 1975; Dallos & Harris 1978). Areas in the cochlea where inner hair cells (IHCs) and/or neurones are not functioning well or even not at all

were described as cochlear dead regions (DRs; Moore 2001). However, this is incomplete because an area in the cochlea will only be defined as a DR if off-place listening occurs. This refers to an area where a tone producing peak basilar-membrane vibration is detected by off-place listening (Moore et al. 2004). DRs have been suggested to have perceptual consequences including reduced pitch detection (Huss & Moore 2005a), increased tone noisiness (Huss & Moore 2005b), increased loudness growth (McDermott et al. 1998) and reduced speech perception in quiet and noise (Vickers et al. 2001; Baer et al. 2002). These may well impact on hearing aid benefit (Hogan & Turner 1998) and potentially affect the prescription that the hearing aid is set to. This suggests audiologists may encounter a number of challenges when programming hearing aids to patients with DRs.

The prevalence of DRs has been reported for populations in India (Vinay & Moore 2007) and the United States of America (USA; Cox et al. 2011) but no study, to date, has reported DR prevalence in the U.K. It is known that the mean degree of hearing impairment varies between countries. For example, India has been reported as having twice as many adults per 1000 population with hearing impairment ≥41 dB HL than adults in the USA or U.K. (WHO 2000). It is known that DRs are more common with increasing degrees of hearing impairment (Vinay & Moore 2007). Therefore, the prevalence values measured in India cannot be used as an indicator of DR prevalence in the U.K. The study in the USA is more likely to include participants that are more comparable to those in the U.K. However, the USA study did not identify DR prevalence in new and existing hearing aid users. Audiologists need to know how prevalent DRs so that they are aware of how many of their patients are likely to have a DR. If DR prevalence is high, it may warrant audiologists routinely testing for DRs. There is an urgent clinical need to provide them with this information.

There are two masking techniques which can be used to detect the presence of a DR, the threshold equalising noise (TEN) test (Moore et al. 2000) and psychophysical tuning curve (PTC) test (Zwicker & Schorn 1978; Sek et al. 2005). Neither test is able to directly assess IHC or neurone function, but rely on off-frequency listening as an indicator of a DR. Therefore, neither is a 'gold standard' method for detecting DRs. It is important that the most accurate, repeatable and time efficient of these two tests is used in the audiology clinic. To date, no study has determined the 'best' DR detection method for use in a clinical setting.

A number of studies have suggested that DRs can impact on speech perception in quiet and in noise (Vickers et al. 2001; Baer et al. 2002; Mackersie et al. 2004). Vickers et al. (2001) and Baer et al. (2002) suggested the provision of amplification well inside the DR may have a negative effect on speech perception in quiet and noise in some patients. However, neither of these studies used audiometrically matched control participants. Therefore, it is impossible to determine whether these findings are as a result of differences in audibility or the presence of a DR. In contrast, Mackersie et al. (2004) and Cox et al. (2011, 2012) did not report any negative effect of providing amplification in the DR. In Mackersie et al. (2004) and Cox et al. (2011, 2012), participants with and without a DR were audiometrically matched, this reduced differences in audibility between the two groups. However, in order to match the groups, only participants with less extensive and limited DRs were recruited. Therefore, it is not clear whether audiologists need to take in to account the presence of DRs when fitting hearing aids. Further research is required to help audiologists fit hearing aids most appropriately for patients with DRs.

The purpose of this thesis was to be able to provide audiologists with a greater understanding of importance of detecting DRs in audiology clinics. This was achieved with three specific aims:

1) How prevalent are DRs in patients who attend a U.K. audiology clinic?
2) What test techniques should be used to detect DRs in the audiology clinic?
3) Do hearing aids need to be fitted with different gain settings for patients with DRs?

This thesis is presented using the guidelines for submission in 'alternative' format. All experimental chapters are written in the style of a journal manuscript. This format has been used as the three main areas of research are ideally suited to preparation in a manuscript layout. A brief introduction to each chapter is presented below.

Literature Review (Chapter 2)

This chapter is a critical review of current knowledge in the field of DRs. In particular, areas of limited or conflicting knowledge were identified. The chapter culminates with the aims, objectives and hypotheses of each of the experimental studies.

General Methods (Chapter 3)

This chapter provides a summary of the general methodology used in the experimental studies and includes information about the participants and test equipment. An overview of the test techniques used in each of the studies is also presented. Additional methodology that is specific to each study is presented in the relevant chapters.

Experimental study 1: Prevalence of cochlear dead regions in new referrals and existing adult hearing aid users (Chapter 4)

The first study investigated DR prevalence in a clinical sample of new referrals and existing adult hearing aid users referred to an audiology clinic in Manchester.

The data from this study has been accepted for publication in Ear and Hearing. Preliminary data from this study was presented at the British Society of Audiology

annual conference 2010 and 2011 and also the British Academy of Audiology conference 2011.

Experimental study 2: Repeatability, agreement and feasibility of using the threshold equalising noise test and fast psychophysical tuning curves in a clinical setting (Chapter 5)

The second study compared the repeatability, agreement and feasibility of the two test techniques, TEN-test and fast PTCs, at detecting DRs. The data from this study has been accepted for publication in International Journal of Audiology. Preliminary data from this study has also been presented at the British Society of Audiology annual conference 2011.

Experimental study 3: High-frequency amplification in ears with cochlear dead regions (Chapter 6)

The third study considered the effects of high-frequency amplification on consonant perception in ears with and without DRs. The data from this study has been submitted for consideration in Ear and Hearing.

General Discussion (Chapter 7)

This chapter discusses the main findings from all three experimental studies. These findings were also compared and contrasted with previous research in this area.

Conclusions and recommendations for future research (Chapter 8)

The purpose of this chapter was to consider the implications of the findings from the experimental chapters. Limitations of these studies were also discussed along with suggestions for future research in this area.

Journal Articles resulting from the thesis:

Pepler, A, Munro, K.J, Lewis, K, Kluk, K. (2014). Prevalence of cochlear dead regions in new referrals and existing adult hearing aid users, Ear and Hearing, 35, 289-386.

Pepler, A, Munro, K.J, Lewis, K, Kluk, K. Repeatability, agreement and feasibility of using the threshold equalising noise test and fast psychophysical tuning curves in a clinical setting, International Journal of Audiology. (In Press)

Pepler, A, Munro, K.J, Lewis, K, Kluk, K. Benefit of high-frequency amplification in ears with cochlear dead regions . Ear and Hearing. (Submitted)

Presentations resulting from the thesis:

Oral presentation: Prevalence of clinically significant dead regions in adult hearing aid referrals

April 2010 North West Regional Network for Adults with Complex Hearing Needs, University of Manchester

Poster presentation: Prevalence of clinically significant dead regions in adult hearing aid referrals

September 2010 British Society of Audiology Annual Conference, University of Manchester

Oral presentation: Prevalence of cochlear dead regions in adult hearing aid referrals

September 2011 British Society of Audiology Annual Conference, University of Nottingham

Poster presentation: Prevalence of cochlear dead regions in adult hearing aid referrals

September 2011 British Society of Audiology Annual Conference, University of Nottingham

Poster presentation: Comparison of test techniques for diagnosing cochlear dead regions in adults within the clinical setting

September 2011 British Society of Audiology Annual Conference, University of Nottingham

Poster presentation: Prevalence of cochlear dead regions in adult hearing aid referrals

November 2011 British Academy of Audiology Annual Conference, Llandudno

Oral presentation: Cochlear Dead Regions: Prevalence and management

March 2012 Action on Hearing Loss PhD meeting

Oral presentation: Prevalence of cochlear dead regions in adult hearing aid referrals

May 2012 British Society of Hearing Aid Audiologists Conference, Starkey Earmould Laboratory, Stockport

Poster presentation: Prevalence of cochlear dead regions in new and existing adult hearing aid users

September 2012 British Society of Audiology Annual Conference, Nottingham

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

This literature review considers DRs and their perceptual consequences. A comprehensive review of the topics related to the three aims of this thesis is also included.

2.2 Outer and Inner Hair Cells

Outer Hair Cells (OHCs) and Inner Hair Cells (IHCs) are sensory receptors, they have different physical properties associated with different roles within the auditory system.

OHCs contain contractile proteins which are able to contract and expand (Gelfand 2004). In the presence of a stimulus, OHCs rapidly convert changes in membrane potentials into mechanical energy by lengthening the cells' cytoskeleton (Brownell et al. 1985). This allows the cells to sharpen and amplify the vibrations of the basilar-membrane; therefore, they are referred to as 'mechanical amplifiers' (Raphael & Altschuler 2003).

IHCs are transducers converting vibration of the basilar-membrane into action potentials in the auditory nerve. Vibration patterns along the basilar-membrane result in the movement of a connected surface, known as the tectorial membrane. The difference in movement between the tectorial and basilar-membrane creates a shearing action, resulting in the bending of the stereocilia, (Figure 2.1). This causes transduction pores to open, with potassium and calcium ions then able to flow into the IHC, resulting in cell depolarisation, creating an action potential (Gelfand 2004). Electrochemical responses, in the form of neurotransmitters, are released at the synapses between the IHCs and innervating neurones of the auditory nerve which send impulses to higher auditory pathways. The frequency of the sound stimulus, and therefore, the location of basilar-membrane vibrations, dictates which IHCs detect the sound (Raphael &

Altschuler 2003). The frequency at which each IHC is designed to act as a transducer is referred to as its characteristic frequency (CF).

Reduced OHC and IHC function may be acquired or due to congenital abnormalities. The most common cause of reduced hair cell function is the damage of stereocilia often due to aging, excessive noise, or ototoxic exposure (Gelfand 2004).

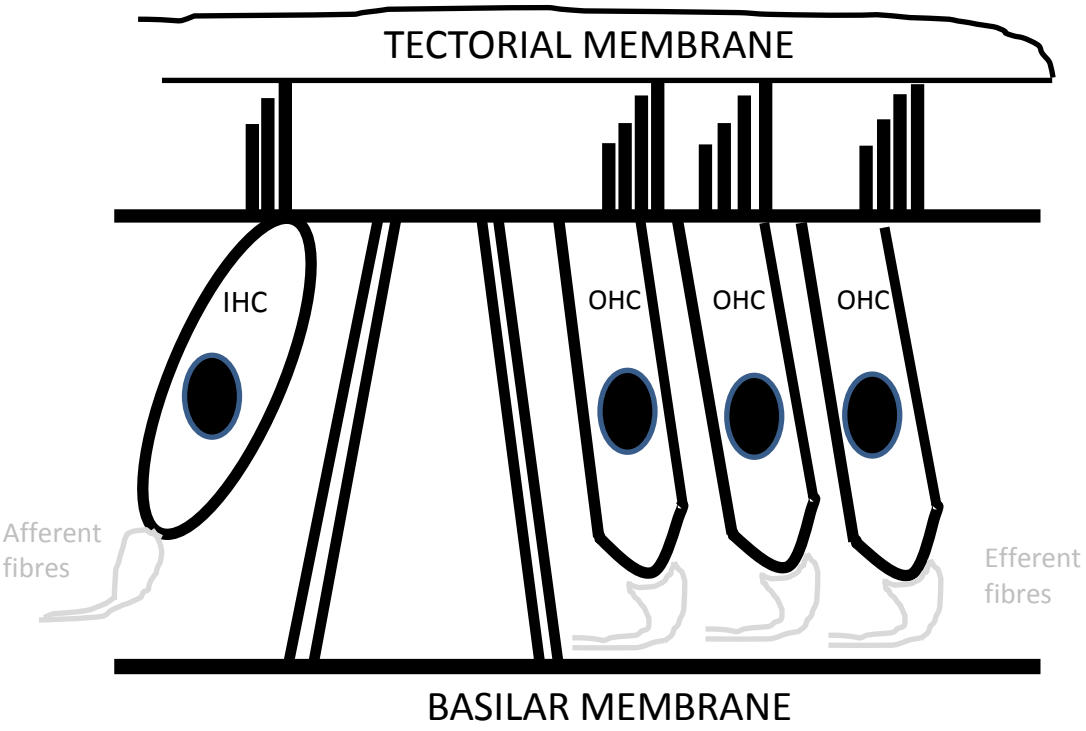

Figure 2.1. The anatomical layout of OHCs and IHCs with the basilar and tectorial membranes. Adapted from Gelfand (2004).

OHC damage results in reduced basilar-membrane vibrations at low level sounds. Therefore, sounds need to be increased in level for the basilar-membrane to produce a detectable vibration. It is thought that OHCs damage can contribute a maximum of 65 dB HL to cochlear hearing impairment (Plack 2010). OHC damage will

also reduce the peak vibration of the basilar-membrane resulting in broadening of the auditory filter, which presents as poor frequency resolution (Gelfand 2004).

IHC damage will result in reduced action potentials, particularly at low input levels (Moore 2002). In some cases an IHC will be unable to produce any detectable action potential and is classified as 'dead' (Ohlemiller 2004; Schuknecht & Gacek 1993).

2.3 Cochlear Dead Regions

Cochlear dead regions (DRs) are defined as areas in the cochlea where inner hair cells (IHCs) and/or neurones are functioning so poorly that a sound falling within that region is more efficiently detected via off-frequency listening (Moore 2001; Vestergaard 2003). Off-frequency listening enables the detection of sounds with characteristic frequencies (CFs) within a DR. This is possible as movement of the basilar-membrane does not occur solely at the position where the IHCs are tuned to process the signal frequency. Rather a process of upward or downward excitation occurs, i.e. the vibration of the basilar-membrane spreads along a considerable length (Thornton & Abbas 1980; Halpin et al. 1994). Due to the stiffness gradient of the basilar-membrane, upward spread of excitation is most likely to occur, however some individuals with hearing impairment have shown significant upward and downward spread of excitation (Glasberg & Moore 1986). Excitation levels increase with higher stimulus amplitude, likely due to a larger displacement of the basilar-membrane. In addition, OHC damage which results in the broadening of excitation patterns promotes off-frequency listening (Moore 2001).

The extent of a DR is often described based on the CFs of the damaged region. In the past DRs were often referred to as apical or basal (Alcantara et al. 2004). However, this lacks precision and DRs are now more usually defined by their edge frequency (f_e) (Moore 2004). The f_e of the DR corresponds to the CF of the IHCs or

neurones immediately adjacent to the DR. In many cases the DR extends to either the basal or apical end of the cochlea and therefore, only has one detectable f_e (Moore et al. 2000).

2.4 Clinically significant dead regions

Although the impact of off-frequency listening remains unclear, it is likely the more extensive the DR, the greater its perceptual consequences (Vickers et al. 2001; Baer et al. 2002; Mackersie et al. 2004). It has been reported that off-frequency listening affects pitch and speech perception (Huss et al. 2005a; Baer et al. 2002). It is therefore useful to be able to separate DRs according to the amount of off-frequency listening. To achieve this, the extent and continuity of DRs needs to be determined.

2.5 Dead Region Diagnosis

It is vital that the test to detect DRs is accurate, feasible and reliable, otherwise investigations in to the impact of DRs, based on the findings from these tests, will not be precise. There is no 'gold standard' method for identifying a DR because the available test techniques rely on the detection of off-frequency listening rather than detecting DRs directly. Therefore, the function of IHCs and associated neurones are not directly assessed. The only definitive method of achieving this is by opening a cochlea and visualising the damage of IHCs in the cochlea, but this is not possible in a functioning auditory system. Behavioural test methods devised to detect DRs rely on the detection of off-frequency listening which is thought to be an indicator of a DR (Moore 2001). Off-frequency listening results in a tone being masked more easily than a tone detected by an IHC with the same CF as the signal frequency (Moore 2001, 2004; Vestergaard 2003; Kluk & Moore 2006a). Thus, a markedly higher threshold, when detecting a tone in ipsilateral masking noise, suggests off-frequency listening is occurring. It is also a strong indicator that there is an area of poor functioning IHCs or

neurones at the CF of the tone (Moore et al. 2000). Two masking techniques, psychophysical tuning curves (PTCs) and threshold equalising noise (TEN), have been developed to detect the presence of off-frequency listening (Zwicker & Schorn 1978; Moore et al. 2000; Moore et al. 2004; Sek et al. 2005; Sek & Moore 2011).

2.5.1 Psychophysical Tuning Curves (PTCs)

Psychophysical tuning curves (PTCs) provide a measure of frequency selectivity, which is the ability of the auditory system to separate two sounds that are presented simultaneously (Zwicker & Schorn 1978). A PTC is a plot of the masker level needed to mask a signal, as a function of masker frequency. The tip of the PTC denotes the place where the masker is most effective i.e. the masked threshold is at its lowest point. If the signal frequency occurs within a DR, spread of excitation will result in the nearest functioning IHCs and neurones detecting and responding to the signal. Therefore, a DR is indicated when the frequency of the PTC tip is different from that of the signal (Kluk & Moore 2005; Moore 2001; Vickers et al. 2001). The frequency to which the tip of the PTC shifts is thought to be f_e (Moore & Alcantara 2001; Thornton & Abbas 1980). A high-frequency DR is indicated by a downward shift of the PTC tip, whilst an upward shift in the tip indicates a DR at a lower frequency (Moore 2001; Sek et al. 2005).

PTCs typically have a V-shape with the high-frequency slope usually much steeper than the low-frequency tail (Sek et al. 2005). A broadened PTC (shallower slopes) is indicative of reduced frequency selectivity, often associated with OHC damage. The sharpness of a PTC can be determined by calculating the bandwidth from the PTC tip to the point where the PTC is 10 dB above the tip, referred to as the Q_{10} (Moore 2001). Q_{10} = Fc / BW: where Fc is the frequency at the tip and BW is the PTC bandwidth 10 dB above the tip of the PTC. PTCs are usually broader (smaller Q_{10dB} values) than normal in cases of cochlear hearing impairment as shown in Figure 2.2.

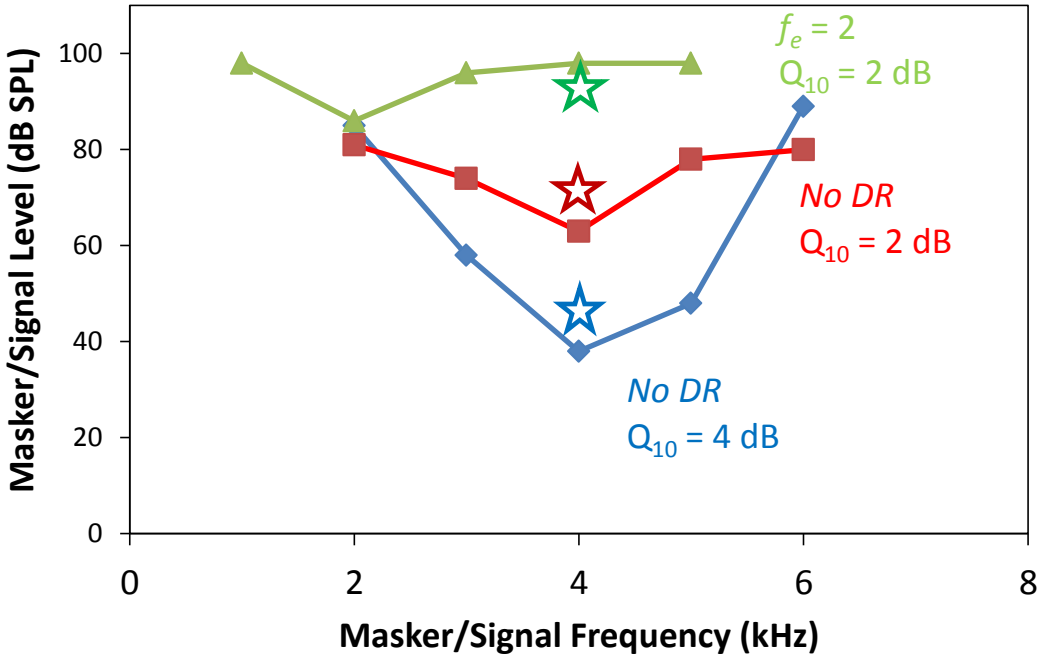

Figure 2.2. PTCs are presented for a normally-hearing ear (blue line), an ear with sensorineural hearing impairment (red line) and an ear with sensorineural hearing impairment and a DR (green line). The data presented are from a pilot study. The signal frequency and level is indicated by a star for each PTC. This figure illustrates the effects of OHC and IHC loss on reduced frequency selectivity and increased off-frequency listening respectively. The blue PTC has a Q_{10} value of 4 dB which is higher than the Q_{10} values for the red and green line PTCs. This indicates that the ear with normal hearing has a more steeply tuned PTC, which indicates good frequency selectivity. The tip of the blue and red lines is 4 kHz which for a signal frequency of 4 kHz indicates no off-frequency listening. The green line indicates a DR with f_e of 2 kHz.

PTCs are measured by presenting a signal and ipsilateral narrowband noise masker. The signal, typically a sinusoid, is presented at a low sensation level, e.g. 10 dB SL (Zwicker & Schorn 1978). The masker is generally a narrowband noise rather than a sinusoid, because it is less likely to result in beat detection (Kluk & Moore 2006a; Sek

et al. 2005; Moore 2001). Beat detection may occur as a result of the simultaneous presentation of signal and masker being more audible than the signal alone (Greenwood 1971). The signal is fixed in level and frequency, whilst the masker is presented at a range of centre frequencies. The masker level required to result in the inaudibility of the signal is measured at each masker centre frequency.

There are three possible methods of presenting the narrowband masker: simultaneously with the signal, immediately before (forward), or immediately after (backward) (Kluk & Moore 2004; Kluk & Moore 2005; Kluk & Moore, 2006a). Forward masking results in no interaction between the signal and masker; therefore, beat detection does not occur. However, in order to achieve forward masking the test time has to be increased and the results often become inconsistent (Kluk & Moore 2006b). Backward masking has resulted in variable results; therefore, it is not deemed the most suitable masking method for PTC testing (Zwicker & Fastl 1999). The simultaneous masking method has been found to be quick and reliable (Kluk & Moore 2006b). However, beat detection and combination tones occur due to the interaction of the signal and masker. Beats and combination tones can cause false positive PTCs by creating an abnormal W-shaped PTC (Kluk & Moore 2004), making tip estimation difficult. Kluk and Moore (2005) found the beats could be significantly reduced if a narrowband masker was used with a wide bandwidth such as 0.32 kHz. In addition, the presentation of a low-frequency noise in subjects with near-normal low-frequency hearing reduces combination tones (Kluk & Moore 2005). Simultaneous masking has also been found to result in suppression of the signal. However, the signal and masker are equally suppressed, therefore PTCs are still obtainable (Moore & Glasberg 1982). Simultaneous masking is a viable method of measuring a PTC as long as appropriate adjustments are made to reduce the risk of beats and combination tone detection (Sek & Moore 2011; Kluk & Moore 2006b).

In order to accurately determine the shape of the PTC, measurements at more than four different masker frequencies are required. Additionally, a PTC needs to be measured at two or more signal frequencies, to determine the extent of the DR. Each PTC can take up to 30 minutes to record (Sek et al. 2005). Therefore, PTC testing of one ear could take a number of hours to complete. This limits the application of PTC testing within the clinical setting (Kluk & Moore 2006a).

The PTC is designed to identify masked thresholds at a range of frequencies. To identify these thresholds a three-alternative, forced-choice, three up one down procedure based on the Levitt (1971) paradigm is typically used. An individual listens to three observational intervals and reports in which interval the signal is present. This can take a significant amount of test time to complete but is likely to result in an accurate masked threshold recording. A two up one down procedure was trialled by Levitt (1971) but it reduced the accuracy of the recorded masked threshold. However, Sek et al. (2005) compared these two paradigms and noted no significant effects on the results. Threshold identification can be adapted further to resemble a similar procedure to pure tone audiometry. Lutman and Wood (1984) developed a method of measuring a PTC at 2 kHz using a clinical audiometer. They reported that the results from this technique were comparable with more complex methods such as the Levitt (1971) paradigm. These findings indicate that PTC measurement may become more feasible for use in audiology clinics through adaptation of the test technique.

A limitation of 'conventional' PTCs is the length of time to complete the measurement makes them impractical for use in a clinical setting. Zwicker and Schorn (1978) and Summers et al. (2003) measured 'fast' PTCs, in normally-hearing and hearing-impaired adults. They used a Bekesy-type tracking procedure which involves the continuous adjustment of the masker level, determined by the subject, as it is swept across a set frequency range. Sek et al. (2005) reviewed this test method and

investigated the most suitable test parameters to create a reliable test. A fixed signal is presented simultaneously (and to the same ear) as a narrowband masker, which sweeps across the required frequency range. The listener then has to respond, by pressing the spacebar on the keyboard, whenever they hear the signal. When the participant pressed the spacebar, to indicate they had heard a signal, the masker level increased. Alternatively, when the participant released the spacebar, the masker level decreased. As this test technique is able to test a large range of masker frequencies during one measurement it has the potential to identify the PTC tip faster than the standard method. Using this technique, Sek and Moore (2011) have suggested, from a small sample of ears, that a tip shift of ≥10 % from the signal frequency is indicative of a DR, although test parameters will affect the tip position.

Sek et al. (2005), Kluk and Moore (2006a) and Sek and Moore (2011) tested and analysed a range of parameters and a summary of their findings is listed below:

1) Beat detection

As for conventional PTC tests, beat detection due to the simultaneous presentation of signal and noise may result in W-shaped recordings. The detection of slight differences in frequency between the masker and signal which causes these 'beats' can be significantly reduced by using a wideband masker (0.032 kHz) to sweep across the frequencies (Kluk & Moore 2005).

2) Combination tones

In patients with relatively good low-frequency hearing (40 dB HL or better at ≤ 1 kHz) and poorer high-frequency hearing, combination tones are often audible. This combination tone is centered at the difference in frequency between the signal and masker. For example if the signal frequency is 3 kHz and the center of the masker frequency is 2.5 kHz, a combination tone centered at 0.5 kHz may be produced. If the patient has good hearing at 0.5 kHz they may hear the combination tone. The

level of the combination tone is thought to be ≥40 dB below the level of the primary tone (Plomp 1965). Therefore, Sek and Moore (2011) added low-pass noise 40 dB below the signal level, in patients where their hearing was 40 dB HL or better at ≤1 kHz. The low-pass noise was set one octave below the signal frequency to avoid it having a direct masking effect on the signal (Moore & Vickers 1997).

3) Lag effect

As fast PTCs involve a masker sweeping from low to high frequencies, or vice versa, the estimable tip may be influenced by what is often referred to as the 'lag effect' (Sek et al. 2005). This occurs due to a small mismatch in time between when the patient reports the signal audibility and the change in masker level. This effect typically leads to the tip of the PTC being either slightly above the most effective masker frequency for ascending masker sweeps, or slightly below for descending masker sweeps. This lag effect means that two measurements, one ascending and one descending, need to be recorded for each signal frequency to ensure accurate tip estimation. A number of studies which have used fast PTCs have reported this effect (Sek et al. 2005; Sek & Moore 2011; Warnaar & Dreschler 2012). Sek et al. (2005) found the lag effect to be significant, but the shift for the ascending sweep (low- to high-frequency) was never more than 6% and no more than 3% for the descending sweep (high- to low-frequency). The lag effect for ascending sweeps may be higher than for descending sweeps due to the former being measured first. If this is the case the lag effect will be even smaller with practice.

4) Rate of masker level change

The rate of masker level change impacts on how accurate the recorded masked threshold is. For example a very large rate of masker change will lead to large excursions from the threshold. Sek et al. (2005) investigated the best rate of change in masker level for reliable PTC measurements. They found that a small rate of

change (<2 dB) ensured that the PTC tip could be estimated i.e. the PTC shape was well defined. It has also been reported that a rate of change as low as 0.5 or 1 dB reduces the risk of loudness discomfort (Kluk & Moore 2006a). This is because the listener has more time to react before the masker level becomes too loud. The limitation of a very low rate of masker change is that in order to measure an accurate PTC the test time needs to be lengthened. Therefore, in some cases, such as when testing patients with a short concentration span, e.g. young children, the rate of masker change may need to be increased. Malicka et al. (2009, 2010) used a 3 dB rate of masker change, avoiding loudness discomfort by stipulating a maximum output level of 80 dB SPL for the masker. In significant degrees of hearing impairment this method may not be suitable, due to effective masking not being achieved. Therefore, it is apparent that the rate of change will need to be adjusted to suit the hearing impairment and concentration span of the listener. Typically in adult listeners a rate of masker change of ≤2 dB is recommended (Sek et al. 2005, Sek & Moore 2011).

5) Masker bandwidth

When considering masker bandwidth it has to be remembered that if the masker is too narrow, beat detection becomes a problem (see point 1). However, if the bandwidth is too wide, the resultant PTC is too broad, making tip estimation difficult. Thus, Kluk and Moore (2005) suggested the following criteria: a bandwidth of one-fifth of the masker frequency ≤1.5 kHz and 0.32 kHz for frequencies >1.5 kHz. These criteria ensure the masker is as narrow as possible before beat detection results in immeasurable PTC tips.

The above five points suggest that when measuring fast PTCs there are a number of pitfalls that can be avoided if the most suitable test parameters are used. See Table

2.1 for a summary of the advantages and disadvantages of using PTCs to detect DRs in audiology clinics.

Table 2.1. A summary of the advantages and disadvantages of using PTCs to diagnose DRs.

Advantages	Disadvantages
Specific identification of f_e (Sek et al. 2005).	No criteria for the presence or absence of a DR.
Simple to set up and calibrate (Sek et al. 2005)	Test duration may still be lengthy even when using the fast PTC method (Sek & Moore 2011)
Well defined test parameters to ensure distinct PTC tips (Kluk & Moore 2005; Sek et al. 2005)	Patients with sensorineural hearing loss without DR may have a PTC with shifted tip due to broadening of the auditory filter (Sek et al. 2005)
	Fast PTCs cannot be successfully completed by some patients due to its complexity and duration (Sek et al. 2005; Malicka et al. 2009)

Sek and Moore (2011) used the settings recommended in Sek et al. (2005) to develop a PTC programme, sweeping PTC (SWPTC) for use by clinicians. This programme can be downloaded from http://hearing.psychol.cam.ac.uk and used on a standard computer with a good quality sound card. It offers the tester a number of setting adjustments including signal frequency, signal duration, signal rate, signal level, masker frequency range, masker bandwidth, noise duration (test time), sweep direction,

rate of masker level change, initial noise level and low-pass noise (level and frequency). Not only does Sek and Moore (2011) give a concise method of calibrating the equipment it also gives suggestions of the best method for tip identification. They give five different methods for identifying the PTC tip:

a) Double regression

   Two lines are fitted to the low and upper parts of the PTC which make up the V shape. The point at which the two lines intersect is used as the tip estimation.

b) Moving average

   The data are smoothed using a two or four point moving average. The frequency corresponding to the minimum of the moving average is taking as the tip estimation.

c) Quadratic function

   The data are fitted with a quadratic function line and the minimum point on the line is estimated as the PTC tip.

d) Low-pass filter

   The data are low-pass filtered and the frequency corresponding to the minimum of the result is taken as the estimated tip frequency.

e) Rounded exponential function (ROEX)

   Each side of the PTC is fitted with a ROEX (Patterson et al. 1982) and the intersection point of the two functions is taken as a tip estimate.

The software created by Sek and Moore (2011) provides an automatic tip estimation using any of these five methods. They suggest that the best method for tip estimation will depend on the number of turn points and the shape of the measured PTC.

Although fast PTC testing is now in a format that can be used in audiology clinics, no studies to date have used this test technique to detect DRs in the clinic setting.

2.5.2 Threshold Equalising Noise (TEN) Test

The threshold equalising noise (TEN) test was developed with the aim of being a more efficient method of detecting DRs than PTCs (Moore et al. 2000). Pure tones are detected in the presence of ipsilateral TEN (Moore et al. 2000). Threshold equalising noise (TEN) is spectrally-shaped broadband noise designed to create almost equal thresholds over a wide frequency range for those with and without hearing impairment. It is necessary to create this equal masking so that the masking effect is equivalent at each frequency. The level of the TEN is determined based on the level of one ERB_N, where ERB_N is the average equivalent rectangular bandwidth of an auditory filter for a particular frequency, at a moderate sound level, for young normally-hearing subjects (Moore 2001). The value of ERB_N can be calculated in kHz using the equation: 0.247(4.37F-1) where F stands for frequency in kHz (Glasberg & Moore 1986). These ERB_N calculations were used to create spectrally-shaped broadband noise (TEN). The TEN is provided on compact disk (CD) (Moore et al. 2000, 2004). The test involves the presentation of the TEN, whilst simultaneously presenting standard audiometry pure tones, either from the CD or pure tone audiometer.

The threshold equalising noise (TEN) test can be used to measure masked thresholds at half octave intervals over the 0.25-8 kHz range using the original version, which is calibrated in sound pressure level (SPL; Moore et al. 2000), or over a narrower frequency range of 0.5-4 kHz using a version calibrated in hearing level (HL; Moore et al. 2004). Although the TEN(SPL) test allows the detection of DRs across a more extensive frequency range, the reduced TEN bandwidth and low crest factor used in the

TEN(HL) implementation of the test, allow the noise to be presented at higher levels without loudness discomfort; thus, DRs can be detected when greater degrees of hearing impairment are present. The TEN-test does not accurately locate f_e (Moore & Alcantara 2001; Vestergaard 2003); however, it is thought to be sufficiently accurate to detect the presence or absence of a DR in a timely manner making them feasible for use within the clinical setting (Moore et al. 2004; Cairns et al. 2007). A summary of the advantages and disadvantages of using the TEN-test in the clinical setting is presented in Table 2.2.

If a patient with a DR detects a tone using off-frequency listening, the tone should be much easier to mask using broadband noise compared to normal-hearing or hearing-impaired listeners without DRs (Moore et al. 2000). This is because off-frequency listening results in a tone being detected away from the region of peak basilar-membrane vibration. An individual with normal hearing should have a masked threshold of about the same level as the TEN in dB/ERB$_N$. Moore et al. (2000) recorded masked thresholds, using the TEN-test, in normal-hearing listeners and on no occasion were the masked thresholds more than 7 dB above the level of the TEN. Listeners with cochlear hearing impairment, but no DR, respond to the signal using IHCs of the same CF as the sinusoid. However, the broadening of their auditory filter due to OHC damage would lead to poorer signal detection ability as a result of reduced frequency selectivity. This is likely to lead to an increased masked threshold; however in reality the change in the masked thresholds is minimal, up to 2 - 3 dB (Glasberg & Moore 1986; Moore et al. 2000). Those listening to the signal using off-frequency listening, i.e. those with DRs, will require the level of the tone to be increased significantly in the presence of noise. This is because a tone detected via off-frequency listening is not detected at peak basilar-membrane vibration reducing the temporal and amplitude information retrieved, making the tone easier to mask. Hence, the criteria for a DR, created by Moore et al.

(2000) are: the masked threshold in TEN is ≥10 dB above the TEN level/ERB_N, and is ≥10 dB above the absolute threshold.

Table 2.2. A summary of the advantages and disadvantages of using the TEN-test to diagnose DRs.

Advantages	Disadvantages
Reliable diagnosis of a DR (Moore et al. 2000).	Absolute thresholds at high frequencies immeasurable (Moore et al. 2000).
Rare occurrence of false positives (i.e. incorrectly diagnosing a DR) (Moore et al. 2000).	At high, but still measurable absolute thresholds, it may not be possible to produce intense enough TEN masking (Moore et al. 2000).
Quick to apply (Moore et al. 2000).	Loudness discomfort at high masking levels (Moore et al. 2000).
Similar to pure tone audiometry therefore a fairly easy technique for clinicians to grasp (Moore et al. 2000).	If the signal is only just inside a DR there is a risk that the DR will not be identified, especially when frequency selectivity is poor (Sek et al. 2005)
All test material saved on a CD compatible with most audiometers (Moore et al. 2004).	Auditory neuropathy or central auditory processing disorders can result in elevated thresholds and therefore false positives (Moore 2004).
Simple calibration technique (Moore et al. 2004).	Only detects DR location at half-octave level (Moore et al. 2000)
Good repeatability (Cairns et al. 2007)	

Cairns et al. (2007) calculated the test-retest ability of the TEN and found a mean difference of 0.63 dB on retest, with adults typically having a smaller masked threshold on retest. The largest variations occurred at 0.75 and 4 kHz, but even then the mean difference was below that of the 2 dB step size used. Aazh and Moore (2007) reported that some listeners with cochlear hearing impairment showed a change of up to 9 dB and although this increased elevation may be related to poor detection efficiency (Patterson et al. 1982) it is not certain that these patients do not have a DR. Therefore, the TEN-test provides a reliable method of detecting DRs in the audiology clinic.

2.5.3 TEN-test and PTC agreement

Despite its lengthy test duration, the PTC is the closest we have to a 'gold standard' test for the presence of a DR (Sek & Moore 2011). Therefore, if the TEN-test is to be used to detect DRs, it is essential that the findings agree with PTCs. Comparisons of results from these two techniques are limited and there are mixed findings. Moore et al. (2000) reported agreement between the TEN-test and conventional PTCs for 17 of 20 adult ears with hearing impairment. For the three ears where results did not agree, the TEN-test showed an elevated masked threshold, but the PTC tip was not shifted. Summers et al. (2003) compared the findings from 18 hearing-impaired ears and reported agreement for 10 ears. Again, in cases where the results did not agree, the TEN-test indicated a DR whilst conventional PTC measurements did not. Summers et al. (2003) reported that the agreement between the two tests improved to 16 of 18 ears when a stricter TEN masked threshold criterion of 14 dB above the TEN level was used. One explanation for poorer agreement could be the use of a masker with a bandwidth of 0.10 kHz, which results in beats becoming audible, resulting in the detection of combination tones, creating a 'W-shaped' PTC (Moore 2004; Kluk & Moore 2005). Kluk and Moore (2006b) completed fast PTC measurements using a

narrowband masker which was approximately equal to the bandwidth of the "normal" auditory filter (Glasberg & Moore, 1986). They found an agreement of 93% between the fast PTC and TEN-test in terms of DR presence. However, fast PTCs typically indicated the f_e to be lower than that detected by the TEN-test. Warnaar and Dreschler (2012) compared fast PTCs and TEN-test results for 10 ears of hearing-impaired adults. They used the TEN-test DR criteria proposed by Moore et al. (2004) and ≥20% of PTC tip shift as indicators of a DR. Using these criteria, the tests agreed in 80% of cases. Agreement between tests increased when using a tip shift of ≥20 % on fast PTCs and +8 dB masked threshold on the TEN-test. Only four of the 10 ears were identified as having a DR so this study provided limited data for ears with DRs. The findings from each of these studies differ substantially depending on the test set-up and DR criteria used. There is a need for further comparisons of these tests, using a larger number of ears in a clinical setting.

2.6 Prevalence of DRs

In order to determine if there is a need to develop a specific management plan for patients having a DR, it is essential to first identify its incidence within the target population, i.e. within potential hearing aid users. Incidence is a measure of the risk of a population developing a condition in a specified time frame (Martin 2007). The only way of recording DR incidence in a hearing impaired population is to test the same population for DRs over a period of time. This is unfeasible for a large clinical study where data can only be collected over a short period of time. Prevalence which is the total number of cases of a disease or condition in a given statistical population at a given time, divided by the number of individuals in the population at risk from the disease or condition (Martin 2007) is a more feasible method of obtaining population data for DRs. However, obtaining the prevalence of a DRs can be problematic due to a number of factors:

1) Random sampling error

Random sampling error will result in a representative sample of the population not being included in the study. Many of the DR studies to date have recruited participants following attendance at a hospital (Cox et al. 2011; Vinay & Moore 2007). The patients attending the hospital are likely to have noticed more difficulties with their hearing than the general population, increasing the likelihood of participants having a DR. This error can be reduced by recruiting a large sample size to the study ensuring a cross-sectional sample of the population.

2) Non-random errors

Unavailability of a subject has the potential to bias the results. It is therefore important to test all of those within the study group.

3) Observational errors

Observational errors may occur as a result of bias in data collection, such as variable test techniques. Therefore, it is vital test techniques are not varied throughout the study testing.

4) Test techniques

Ideally a test used to identify prevalence will be 100% sensitive and specific, but in reality this is never the case. A test with good sensitivity will identify most of the affected participants within the study population. In the case of DRs, all participants with DRs will be identified in a 100% sensitive test. Specificity is related to the proportion of unaffected individuals who pass the test. Therefore, no participants without DRs should be identified as having a DR if a test is 100% specific. The test also needs to be quick and easy to administer in order to maintain as high a patient catchment as possible.

Identifying DR prevalence in the general population is unnecessary as it is not important for clinicians to know how many of these people have DRs. Rather it is

important to know how many patients who turn up to audiology departments for consideration of hearing aids have DRs. The reason for this is that at the current time it is only known that DRs may impact on hearing aid benefit and this may be improved by adjusting the settings (Vickers et al. 2001; Baer et al. 2002).

DRs have been reported in hearing-impaired participants with specific audiometric configurations (Moore et al. 2000; Vickers et al. 2001; Summers et al. 2003; Simpson et al. 2005; Preminger et al. 2005; Aazh & Moore 2007; Cairns et al. 2007; Jacob et al. 2006; Cox et al. 2011). These studies do not provide prevalence estimates in hearing aid users as a whole. It is also worth noting that these studies used a range of TEN-test methodologies and participant criteria which may explain the wide range of estimates (22% to 92%). Table 2.3 provides a summary of the past studies, including their design and findings. This summary shows how varied the results from these studies are, the likely reasoning being variations in study design. Some of the studies used a final step size of 5 dB when measuring TEN masked thresholds but the most accurate results are obtained when using a 2-dB step size (Cairns et al. 2007). The studies varied in their use of the HL or SPL versions of the TEN-test. As these versions have significantly different test methods, such as test frequency range, this will have impacted on the findings. Most studies used the DR criterion suggested by Moore et al. (2000) i.e. the threshold in TEN was 10 dB or more above the TEN level / ERB_N. However, Preminger et al. (2005) used a criterion of 15 dB. This stricter criterion likely explains why they recorded a lower DR prevalence (29%).

Table 2.3. A summary of the proportion of adults with DRs in the moderate to severely hearing-impaired population.

Study Reference	Number of Participants	Age (years)	Inclusion Criteria	TEN-test technique	Frequencies (kHz)	Final Step Size (dB)	Criterion (dB)	Prevalence (Participants)
Aazh and Moore (2007)	63	> 62	60 dB HL	HL	4	2	10	23%
			65 dB HL					27%
			70 dB HL					33%
			75 dB HL					59%
			80 dB HL					57%
			85 dB HL					75%
			60 -85 dB HL					37%
Cairns et al. (2007)	20	54 – 86	Referred to audiology for a hearing test	HL	0.5-4	2	10	22%
Cox et al. (2011)	170	Adult	60 – 90 dB HL between 1 and 3 kHz and >25 dB HL below 1 kHz	HL	0.5-4	2	10	31%
Jacob et al. (2007)	43	Adult	Steeply sloping hearing loss	SPL	0.5-10	Not listed	10	92%
Markessis et al. (2006)	35	40 – 89	Moderate to severe steeply sloping hearing loss	SPL	4	2	10	87%
Moore et al. (2000)	14	Adult	Moderate to severe hearing loss	SPL	0.5-10	5	10	68%
Preminger et al. (2005)	49	21 – 75	Thresholds between 50 and 80 dB HL	SPL	0.5-10	5	15	29%
Simpson et al. (2005)	10	59 – 82	Hearing loss experienced hearing aid users	SPL	0.5-10	1	10	30%
Summers et al. (2003)	17	59 – 76	Steeply sloping high-frequency hearing loss	HL	0.5-4	1	10	33%
Vickers, et al. (2001)	10	Adult	High-frequency hearing loss	SPL	0.5-10	5	10	70%

With the exception of Cox et al. (2011), the studies presented in Table 2.3 tested between 10 and 63 participants; not substantial enough to provide an accurate sample of DRs in the hearing-impaired population. Cox et al. (2011) tested 170 (98, male and 72, female) participants for DRs in Memphis, USA and reported a DR prevalence of 31% (23% of ears). There was no significant difference in DR prevalence between men and women, 34% and 28% respectively. Age was also found to have no significant effect on

the prevalence of DRs (ages ranged from 38 to 96 years, with a mean age of 74 years). They also reported that mean hearing thresholds were significantly poorer at 2, 3, and 4 kHz in ears with DRs when compared with ears without DRs. However, they restricted participant inclusion according to degree of hearing impairment. They aimed to recruit only those participants suitable for a hearing aid fitting. This was achieved by recruiting patients with hearing impairments reaching 60 – 90 dB HL between 1 and 3 kHz and >25 dB HL below 1 kHz. However, hearing aid use was not presented in the study and therefore, hearing aid users with milder hearing impairments may have been excluded. Hence, the prevalence of DRs in new referrals or/and existing hearing aid users may be different from Cox et al. (2011).

Vinay and Moore (2007) reported the prevalence of DRs in 308 adults with sensorineural hearing impairment, who attended an audiology clinic in India. Some participants had attended the clinic previously, whilst others were attending for the first time, but most were attending for the purpose of hearing aid fitting. Participants were included in the study if they had hearing thresholds of at least 15 dB HL at any frequency between 0.25 and 8 kHz. The median hearing impairment was 50 dB HL at 0.5 kHz and 70 dB HL at 4 kHz. There was a large age range, 17 to 95 years, though the majority of the participants were within the older cohorts with a mean age of 57 years and median age of 63 years. Each participant was tested using the TEN(HL) test and the presence of a DR was determined using the standard criteria suggested by Moore et al. (2004). A TEN level of 70 dB/ERB_N was typically used, though in some cases this level had to be increased to 85 for those with severe hearing impairments. For those with mild hearing impairments, the level of the TEN was often decreased across the frequency range to avoid loudness discomfort. More than half, (57%: 95% confidence interval 52% - 64%), of participants were found to have a DR in one or both ears at one or more frequency. Of these, 51.9% had a high-frequency DR and 2.3% had a low-

frequency DR. DRs were only identified at frequencies where hearing thresholds were ≥50 dB. At 4 kHz this cut-off increased to ≥60 dB and agrees with the findings of Aazh and Moore (2007). The prevalence identified by Vinay and Moore (2007) is much higher than that found by Cox et al. (2011). A possible explanation is that Cox et al. (2011) had much stricter inclusion criteria, in terms of degree of hearing impairment however, participants still had a mean hearing impairment that was 5 dB less severe than Vinay and Moore (2007). This is consistent with previous findings where adults in India were reported to have a greater prevalence (8%) of hearing impairment ≥41 dB HL when compared to hearing-impaired adults in the USA (4%) (WHO 2000). Given these differences, the DR prevalence reported by Vinay and Moore (2007) cannot be generalised to adults in the U.K. By excluding participants according to their degree of hearing impairment, Cox et al. (2011) may have over-estimated DR prevalence in the adult hearing aid population.

Vinay and Moore (2007) suggested that the 25% of ears that met the criteria for DRs at two or more adjacent frequencies were 'clinically significant'. If an individual has a DR starting at 4 kHz, or above, it is unlikely that this will impact on hearing aid benefit, due to the limited high-frequency amplification provided by most current hearing aids. Also, an 'island' DR (i.e. occurring at one isolated frequency) is unlikely to result in a change in hearing aid management. Therefore, when estimating DR prevalence it is helpful to identify the proportion of these that are sufficiently extensive (spanning at least three consecutive frequencies) to potentially affect hearing aid management.

Vinay and Moore (2007) found no significant difference in DR prevalence between men and women, 54.4% and 58.8% respectively. Age was also found to have no significant effect on the prevalence of DRs. However, the DR location did appear to change when compared with age. It was noted that young people (18-30 years) were

more likely to present with DRs between 1-2 kHz. The eldest group aged 71-90 years presented with more DRs at low frequencies (0.5-0.75 kHz) and high frequencies (2-4 kHz). This result has to be treated with caution as there were only a small number of subjects within the younger categories. However, this trend is quite possible, as the cause of hearing impairment is likely different in the younger group to that of the older group, resulting in different hearing configurations.

In summary, none of the research to date provides a reliable estimate of DR prevalence in patients who attend U.K. audiology clinics. Cox et al. (2011) completed research in a clinical sample of adults who had similar hearing levels to those found in U.K. NHS audiology clinics. However, 63% of the population in Memphis, U.S., where Cox et al. (2011) obtained participants, are of black, African American, ethnicity (U.S. Census Bureau 2012). This is very different to the ethnic composition of the U.K. where 87.1% are of white ethnicity (United Kingdom Census Data 2011). There are suggestions that the odds of hearing impairment are greater in white than in black individuals (Lin et el. 2012). Therefore, the prevalence of DRs may well be lower in Cox et al. (2011) than in the U.K. population.

2.7 Perceptual consequences of dead regions

There is evidence that off-frequency listening in DRs can lead to increased tone noisiness (Huss & Moore 2005b), abnormal pitch perception (Huss & Moore 2005a, Moore & Carlyon 2005), rapid growth of loudness (McDermott et al. 1998) and impaired speech perception (Vickers et al. 2001; Baer et al. 2002; Mackersie et al. 2004; Preminger et al. 2005). If this is true it is vital that DRs are identified in audiology clinics and appropriate intervention derived. There are a number of reasons why DRs may result in poor speech perception. Off-frequency listening is thought to reduce the information that can be extracted from frequency components falling within the DR. Three factors that may explain this are:

1) Reduced pitch detection

   It has been suggested that tones falling in a DR are perceived to have a different pitch to that reported by normal hearing listeners (Huss & Moore 2005a). Oxenham and Shera (2004) noted the importance of the correct tonotopic organisation for complex pitch perception. Off-frequency listening has the potential to disturb this organisation, thus influencing pitch perception. However, previous research has indicated only a weak correlation between measures of frequency selectivity and frequency discrimination in hearing-impaired participants (Tyler et al. 1983; Moore & Glasberg 1986; Moore & Peters 1992).

2) Reduced sound processing

   IHCs and their afferent neurons, functioning at the boundary of a DR, will not only be detecting and processing sounds at their CF, but they will also be detecting and processing sounds in the DR. This may result in the processing of some sounds being missed or simply the processing ability reduced (Moore 2001).

3) Increased loudness growth

   DRs are often associated with steeply sloping high-frequency sensorineural hearing impairment. McDermott et al. (1998) and Moore (2002) investigated the loudness growth, also known as recruitment, in adults with hearing impairments. No specific test for the diagnosis of DRs was used. A rapid growth in loudness, was found at frequencies with hearing thresholds > 90 dB HL. Recruitment is associated with a small dynamic range which can lead to difficulties providing enough amplification, without resulting in loudness discomfort. Therefore, in these cases speech perception may be reduced, simply due to amplification having to be compromised. As no tests for DRs were used in this study, it is difficult to conclude whether recruitment is simply associated with steeply sloping impairments and OHC loss or whether it is caused by IHC loss.

Overall, there is some limited evidence that DRs may impact on the perception of sounds. However, much of this work is speculative. Therefore, it is currently not possible to say definitively that DRs have a significant effect on perception. As with any medical condition, it is not only vital to determine the prevalence of a condition, but also the effects that it has on an individual's health. It is imperative to establish how and to what extent DRs affect hearing aid benefit.

2.8 High-frequency hearing impairment and benefit of amplification

The primary aim of amplification is to restore audibility (Dillon 2012). The audibility of speech for an individual can be determined using the Speech Intelligibility Index (SII). This calculation was developed from the Articulation Index (AI) (Kryter 1962). The SII provides more flexibility in its calculation including more accountability for speech in noise levels. The SII provides a reading between 0.0 and 1.0, and is highly correlated with the intelligibility of speech (ANSI S3.5-1997). The closer the SII value to 1.0, the better the audibility of a particular sound. Importantly even if the SII has a reading of 1.0, indicating good speech audibility this does not translate in to good speech intelligibility.

The provision of hearing aid gain which is audible at high-frequencies in adults with moderate to severe high-frequency hearing impairment has sometimes been reported as providing little or no benefit for speech recognition (Murray & Byrne 1986; Hogan & Turner 1998; Ching et al. 1998; 2001; Turner & Cummings 1999; Vickers et al. 2001; Baer et al. 2002; Mackersie et al. 2004; Preminger et al. 2005; Hornsby & Ricketts 2006). Reduced frequency selectivity and temporal resolution has been suggested as a possible explanation for this lack of benefit (Moore 2002). More recently, the impact of cochlear dead regions (DRs) on speech recognition has been investigated (Vickers et al. 2001; Baer et al. 2002; Rankovic 2002; Moore 2002, 2004; Mackersie et al. 2004; Cox et al. 2011, 2012).

2.9 Dead regions and benefit of amplification

Vickers et al. (2001) and Baer et al. (2002) compared consonant recognition in quiet and noise, for different low-pass filter conditions. Adult participants with extensive, continuous DRs associated with steeply sloping hearing impairment were recruited. DRs were determined using both the TEN(SPL) test and conventional PTCs, all DRs had $f_e \leq 4$ kHz. Vowel-consonant-vowel (VCV) stimuli developed by the Institute for Hearing Research, Nottingham, UK were presented via headphones amplified using the Cambridge fitting formula (Moore & Glasberg 1998), although gain was limited in six ears with severe hearing impairments. VCV stimuli were presented unfiltered, and then low-pass filtered at f_e, half an octave, and one octave above f_e. Stimuli cut-off frequencies ranged between 0.8 and 7.5 kHz for ears without DRs. When listening in quiet, the six ears without DRs benefited from high-frequency amplification. The twelve ears with DRs only showed improved speech recognition with a low-pass filter cut off between 50 and 100% above the estimated f_e. Above this point speech recognition did not improve and in a few cases even deteriorated. More detailed trends in performance are listed below:

a) In three ears, performance above f_e increased slightly. Importantly, these three ears had the least extensive DRs ($f_e \geq 3$ kHz) of the group, potentially explaining why they had more benefit from high-frequency amplification than ears with more extensive DRs.

b) In six ears, performance reached a plateau when high-frequency amplification was provided well inside of the DR. These ears had DRs with f_e between 0.75 and 1.5 kHz and they all showed no significant increase in performance above f_e. This suggests that amplification was of no benefit in the DR. The likely explanation is that the high-frequency amplification was not audible and therefore, of no benefit. In support of this latter suggestion, amplification in

these six ears could not be matched to the chosen prescription formula. However, Vickers et al. (2001) argued that the f_e was much lower than the frequency at which the prescription targets could not be matched. In view of this, they suggested that the DR was also contributing to the plateau in performance. This argument assumes that by matching the prescription target for gain, audibility is restored. It is known that audibility relies on a number of factors beyond hearing impairment, including SNR (Hornsby 2004). Therefore, the speech intelligibility index (SII) was devised to take all of these factors in to account and provide a prediction of audibility. Without a SII value for each ear and filter setting it is impossible to say whether the high-frequency amplification was audible at f_e. Therefore, it cannot be concluded whether the plateau in performance is associated with the DR or not.

c) In the final three ears, performance declined with increasing high-frequency amplification, in one ear the decline was statistically significant. In particular Vickers et al. (2001) noted that this pattern occurred when the cut-off frequency was more than 50 to 100% above f_e. In all of these ears stimuli had been amplified to match the Cambridge prescription formula therefore, Vickers et al. (2001) suggested the decline in performance was more likely as a result of the DR than lack of audibility. However, the hearing thresholds for two of these ears at frequencies ≥2 kHz were immeasurable on the audiometer. This would suggest that even if the prescription target had been met for these two ears it was very unlikely that the sound would be audible. In neither of these ears was the decline in performance statistically significant. This would suggest that lack of audibility likely resulted in no increase in performance with increasing high-frequency amplification. This leaves one ear with f_e of 1.1 kHz, which gave a significant decline in performance between 3 and 8 kHz. Again due to the

severity of hearing impairment in the high-frequencies, audibility may be a factor. However, lack of audibility cannot explain a significant decline in speech perception. This suggests there is another factor causing speech performance to decline with increasing high-frequency amplification.

Vickers et al. (2001) concluded that for participants with high-frequency DRs, there was no benefit in providing amplification for frequencies above 1.7 times f_e.

Baer et al. (2002) completed a similar study, but this time the effect of noise on the benefits of high-frequency amplification was investigated. In total, 10 subjects were recruited; eight from the study by Vickers et al. (2001) and two were newly recruited. In total six ears with DRs and 10 ears without DRs were included in the study. An un-modulated noise was presented with the speech (SNR 0-6 dB), using a range of cut-off frequencies. All ears without DRs had improved performance in noise with increasing high-frequency amplification. Performance in ears with DRs reached a plateau when high-frequency amplification was provided well inside the DR but, no ears had worsening performance. As for Vickers et al. (2001), ears with DRs had greater degrees of hearing impairment than ears without DRs and therefore, lack of audibility may well be a factor in speech perception performance. To account for this, Baer et al. (2002) calculated the articulation index (AI) for participants with no DRs. Baer et al. created a scatter plot with VCV scores in noise as a function of the AI, for participants without DRs. VCV scores were then predicted from estimated AI values for ears with DRs. They found that the predicted and obtained scores were similar for the 10 ears without DRs. However, the predicted VCV scores in ears with DRs were higher than the obtained scores. This would suggest that amplification provided some audibility (based on the AI calculation) as this was not a limiting factor for the speech scores. Baer et al. (2002) suggested that the difference in predicted and obtained scores was related to the presence of a DR. Since this study, the AI has been adapted and renamed to the speech

intelligibility index (SII) to account for audibility for a range of speech stimuli, speech in noise levels and frequency importance functions (Hornsby 2004). Overall, it is not clear whether audibility accounted entirely for the plateau in speech perception performance with increasing high-frequency amplification or whether DRs were having an effect. Importantly, the findings from this study showed no negative effect of the provision of high-frequency amplification in ears with DRs.

The main limitation of the Vickers et al. (2001) and Baer et al. (2002) studies was that participants with DRs had a more severe hearing impairment than the control participants without DRs. Therefore, reduced audibility due to the severity of hearing impairment and restricted hearing aid gain, in the ears with a DR cannot be ruled out as impacting on performance. In order to remove this confound, Mackersie et al. (2004) matched as closely as possible (within 12 dB) the hearing thresholds of ears with and without DR. Therefore, ears with DRs were more representative of typical hearing aid users. DRs were detected using the TEN(SPL) test recommended by Moore et al. (2000). The only deviation from this test was the use of a larger than recommend final step size of 5 dB rather than 2 dB. This change will likely have resulted in the TEN-test being less repeatable (Cairns et al. 2007). In total, eight ears with DRs and eight ears without DRs were tested. A hearing aid was fitted to each participant using a soft shell mould, with no vent. The hearing aid gain was prescribed using the DSL method (Cornelisse et al. 1995) and matched within 5 dB of the REM target up to 6.3 kHz. The non-test ear was masked using a 55 dB SPL speech-shaped noise. Consonant and word recognition was assessed in quiet using VCV stimuli and low- and high-level noise using the Computer-Assisted Speech Perception Assessment Test (CASPA) monosyllabic word list (Mackersie et al. 2001). Hearing aids were fitted to the Desired Sensation Level (DSL) prescription in the test ear (Cornelisse et al. 1995); the non-test ear was plugged and muffed. The use of hearing aids set to the patient's prescription, for

the speech testing increases face validity. Speech material was presented at 65 dB SPL unfiltered or low-pass filtered at the edge, 0.5 or 1 octave above the DR. f_e was based on the lowest test frequency at which the TEN-test met the criteria for a DR. In quiet, the speech stimuli were presented at 65 dB SPL. Spectrally matched noise was added at SNR +15, +10 for the low-level noise condition and +5 and 0 dB for the high-level noise condition. Each matched participant pair listened to speech stimuli with the same cut-off frequencies. Filter cut-off frequencies in ears without DRs were matched to the DR ear they were paired with. In quiet and low-level noise there was no significant difference in mean performance between participants with and without DRs. In the high-level noise condition, participants with DRs had poorer word recognition scores than those without DRs. However, in no instance did the provision of amplification at frequencies within the DR, result in a significant worsening of word recognition, relative to a low-pass filtered condition.

No difference in speech discrimination performance was found between the matched groups when assessing consonant perception in quiet or phoneme perception in low-level noise (SNR +15 and +10 dB). Importantly ears without DRs did not obtain any additional benefit from high-frequency amplification than ears with DRs. This suggests that in quiet and low-level noise, DRs have no impact on speech perception. However, when assessing phoneme perception in high-level noise (SNR +5 and 0 dB) ears with DRs obtained less benefit from unfiltered amplification than ears without DRs. Phoneme perception in ears with and without DRs increased with increased high-frequency amplification. However, the mean scores in ears with DRs did not increase when amplification was provided beyond 1f_e (unfiltered condition). Overall, this study indicates that ears with DRs do not benefit from high-frequency amplification as much as ears without DRs.

Vestergaard (2003) investigated the benefit of high-frequency amplification in 17 hearing-impaired adults with moderate to severe hearing impairment. DANTALE monosyllabic words, created by Elberling et al. (1989) was low-pass filtered with frequencies $0.8f_e$, $1f_e$, $1.4f_e$ and $2f_e$, with f_e based on the results of the TEN(SPL) test. Each participant wore their own hearing aid, set-up using real ear measurements (REMs). Ten participants performed best in the broadband condition. For the remaining seven adults, the low-pass filter frequency which recorded the best speech perception score varied, with some above and below the f_e estimated from the TEN-test. The mixed performance on speech perception tests may have been due to inaccurate diagnosis of DRs using the TEN-test and due to the extent and continuity of DRs varying significantly. Interestingly, at higher levels of audibility the scores of ears with and without DRs were more similar. This would suggest that the provision of high-frequency amplification does not have a negative effect for ears with DRs.

Preminger et al. (2005) reported speech recognition and self-reported benefit in 49 experienced hearing aid users. All participants had hearing levels poorer than 50 dB for at least two frequencies and no audiometric thresholds poorer than 80 dB HL. The TEN(SPL) test, with a stricter DR criteria than that recommended by Moore et al. (2000), was used to detect DRs. Speech recognition was measured using the Quick signal-in-noise (SIN) test. Two versions of the Quick SIN were used, one with a standard broadband setting and one with a high-frequency emphasis, providing gain above 3 kHz. The frequency adjustment was not based on DR location. The speech material was presented unaided at SNRs between +25 and 0 dB. The speech reception threshold where the listener achieved 50% correct was recorded. To account for variations in presentation level and different configuration of hearing impairment the AI was calculated for each ear. Both groups showed benefit from increased high-frequency gain, however ears with DRs had poorer speech scores than ears without DRs, even

when the AI was accounted for. The group with DRs were not matched in any way to the group without DRs so variations in group demographics may have resulted in these data trends.

Cox et al. (2011) compared high-frequency amplification benefit in 51 ears with and 119 ears without DRs. All ears had a hearing impairment that was considered suitable for a hearing aid (60 – 90 dB HL between 1 and 3 kHz hearing and greater than 25 dB HL below 1 kHz). They detected DRs using the TEN(HL) test which was calibrated to be used with ER-3A earphones. Quick SIN speech material was presented unaided via ER-3A earphones in its broadband format and also when low-pass filtered at 2 kHz. As all ears had a different degree of hearing impairment, the SII difference between the two filter settings was calculated for each test ear. Ears without DRs gained more benefit from high-frequency amplification than ears with DRs, especially contiguous DRs at ≥2 frequencies. This difference was maintained, even when accounting for variations in the SII. This suggests that DRs have a negative effect on speech perception in noise, even when audibility was accounted for. However, this study did not identify any negative effect of high-frequency amplification on speech perception performance. Of the 307 ears tested, 72 ears were identified to have DRs only 16 of these contiguous DRs. This suggests that only a small proportion of ears with hearing impairment (5%) are going to have substantially less benefit from high-frequency amplification than ears with DRs.

Cox et al. (2012) reduced high-frequency amplification for new and experienced hearing aid users in the laboratory and real-life scenarios to assess speech recognition. Hearing aid users with and without high-frequency DRs were matched in terms of hearing levels. DRs were detected using the same TEN(HL) test method as used in Cox et al. (2011). Each participant was fitted unilaterally with a hearing aid set to the NAL linear prescription method (Byrne & Dillon 1986) and a prescription with reduced high-

frequency gain. The participants were then given two weeks to acclimatise to the hearing aids, the participant's alternated between listening in programmes 1 and 2 daily, resulting in equal amounts of experience for each programme. The participants then returned to the laboratory for speech perception testing with CASPA and BKB-SIN tests using both programme settings. For the following two weeks the participant's rated their speech understanding in a range of real-life situations switching between programmes 1 and 2. After these two weeks, the participants then returned to the laboratory for further speech perception testing. Both groups did show benefit from high-frequency amplification; however, participants with DRs obtained less benefit at high frequencies than those without DRs. In addition, the results from participant preference in daily life found no preference differences when comparing ears with or without DRs.

Malicka et al. (2013) recruited children, aged 9 to 13 years and diagnosed DRs using the TEN test and fast-PTCs. They divided ears in to groups with either a moderate (thresholds between 35 and 80 dB HL) or a severe to profound hearing impairment (thresholds between 15 and >110 dB HL). The moderate group had nine ears without DRs and three ears with restricted DRs (two consecutive frequencies). The severe to profound group had seven ears with DRs and one ear without a DR. VCV speech stimuli were low-pass filtered at a range of cut-off frequencies and presented via headphones. They found that all ears in the moderate hearing impairment group benefitted from high-frequency amplification, regardless of the presence of a DR. In the severe to profound hearing impairment group six of the seven ears with DRs and the ear without a DR showed a plateau in performance with increasing high-frequency amplification. One ear with a DR showed a significant decline in performance with increasing high-frequency amplification. These findings suggest that an extensive contiguous DR may in some cases result in reduced benefit from high-frequency

amplification. However, the ear without a DR in the severe to profound group still had hearing better than the ears with DRs, therefore differences in audibility cannot be ruled out as a factor.

The studies listed above have provided a range of findings with regard to the benefit of high-frequency amplification in ears with DRs. It was evident that different patterns in results were obtained depending on the study design and these factors are discussed below:

1) Matched control group

Cox et al. (2012) and Mackersie et al. (2004) recruited a control group with hearing impairment matched to the DR group. Conversely, Vickers et al. (2001), Baer et al. (2002), Vestergaard (2003), Preminger et al. (2005), Cox et al. (2011) and Malicka et al. (2013), recruited participants to the DR group with more severe mean hearing impairments than those in the control group. Any lack of benefit of high-frequency amplification in the DR group may be due to lack of audibility or acoustic feedback resulting in the prescribed amplification not being reached (Simpson et al. 2005). However, significant decline in performance as seen in one participant in Vickers et al. (2001) cannot be accounted for by audibility, suggesting other factors are involved.

2) DR identification technique

Vickers et al. (2001), Baer et al. (2002) and Malicka (2013) identified DRs using the TEN-test and PTCs. Vestergaard (2003), Mackersie et al. (2004), Preminger et al. (2005) and Cox et al. (2012) detected DRs based solely on the TEN-test. The TEN-test does not detect the boundaries of a DR as well as PTCs (Summers et al. 2003; Moore 2001). By not obtaining the more detailed location of the DR, using PTCs, the results may have been biased in two ways. Firstly, participants with DRs

may have been placed in the no DR group and vice versa. Secondly, the low-pass filter settings were less accurately set to the boundary of the DR. Additionally, all the studies that used the TEN-test, modified the test methodology from that suggested by Moore et al. (2000, 2004). The limitation of this is that it may reduce the test accuracy and comparison of these studies in terms of detecting DRs. Therefore, Vickers et al. (2001) and Baer et al. (2002) are the only studies to date that used the most accurate test techniques to allocate ears to a DR or no DR group.

3) Low-pass filter technique

Aside from Cox et al. (2012) all previous studies have low-pass filtered speech material. Cox et al. (2012) reduced high frequency amplification by adjusting the hearing aid settings resulting in a more clinically relevant study. However, the reduction in high frequency amplification only started to take effect at ≥2 kHz. Hirsch et al. (1954) measured the intelligibility of speech with a range of low-pass filters. They found that there was little loss of speech information with filter cutoffs as low as 1.6 kHz. When the low-pass cutoff reached 0.8 kHz the performance decreased markedly. This suggests that speech understanding is possible when frequencies up to 2 kHz are intact. Further research with more extensive low-pass filtering on hearing aids is required.

Overall, the main limitation of this past research is the variation in study design and limited comparable data. In particular no study has been completed where the main limitations are taken in to account. The limiting factors are a) Lack of accurate DR detection techniques, b) Differences in audibility between DR and no DR groups, c) Amplification cut-off frequencies in the hearing aids very limited. There is a clinical need to investigate the effects of high-frequency amplification on speech recognition in ears with DRs. It is clear from the previous studies that the inconsistent use of the TEN-

test and fast PTCs for DR detection, lack of matched groups and differing techniques of low-pass filtering speech material may have resulted in these mixed findings.

2.10 Research questions addressed in this thesis

This chapter has provided a comprehensive critical review of DR research and identified three areas that require further investigation. The three related areas investigated in this thesis are discussed below along with the aims, objectives and hypotheses of the experimental studies.

1) Prevalence of cochlear dead region in new referrals and existing hearing aid users from the UK

To our knowledge, there are no studies reporting the prevalence of DRs separately for new referrals and existing hearing aid users. Audiologists require this information when planning service provision to ensure patients with DRs are offered the most suitable management options. We identified three unanswered research questions:

- How prevalent are DRs in adults with a sensorineural hearing impairment who have, or are being assessed, for a hearing aid?
- Does the prevalence of DRs differ between new referrals and existing hearing aid users?
- How extensive are the DRs that are identified?

Aims, objectives and hypotheses

The aim of this study was to assess the prevalence and extent of DRs in a clinical sample of new referrals and existing adult hearing aid users in the U.K. It was hypothesised that the prevalence would be lower than Vinay and Moore (2007) and Cox et al. (2011), especially in the group of new referrals because the degree of hearing impairment of adults presenting to audiology clinics would likely be less. Secondary

aims include investigating the relationship between the prevalence of DRs and factors such as audiometric configuration, age and sex.

2) Repeatability, agreement and feasibility of using the threshold equalising noise test and fast psychophysical tuning curves in a clinical setting

There is a significant gap in knowledge concerning test repeatability, agreement and clinical feasibility of the TEN-test and fast PTCs. In order for audiologists to manage DRs in their audiology clinics they need an accurate and quick method of identifying DRs. There is a need for a study to compare the use of the TEN-test and fast PTC in the clinical setting. The agreement between the two tests methods needs to be considered. Also, the test repeatability and clinical feasibility of both tests needs to be investigated.

This will allow clinicians to make an informed decision as to which clinical test is most suitable for detecting DRs in the audiology clinic.

Aims, objectives and hypotheses

The aim of the second study was to investigate the test repeatability, agreement and clinical feasibility of the TEN-test and fast PTCs in a large clinical study of hearing-impaired adults with and without DRs. It was hypothesised that the TEN-test would be more feasible for use in clinic because it would be quicker and easier to complete. However, the TEN-test would be less accurate at detecting DRs than fast PTCs because of the half-octave intervals between TEN-test frequencies. Both tests were hypothesised to have good retest repeatability.

3) Benefit of high-frequency amplification in ears with cochlear dead regions

There is an urgent clinical need to investigate the effects of high-frequency amplification on speech recognition in ears with DRs. It is clear from the review of the literature that the mixed findings are due, at least in part, to inconsistent use of the TEN-test and fast PTCs and a lack of matched controls.

Aims, objectives and hypotheses

The aim of the final study was to compare the benefit of high-frequency amplification in adults with and without high-frequency DRs (diagnosed using both the TEN-test and fast PTCs). In addition, ears with DRs were audiometrically matched to ears without DRs (0.25 and 8 kHz). A secondary aim was to consider the effect of the extent of the DR on the benefit of high-frequency amplification. It was hypothesised that ears with DRs would obtain less benefit from high-frequency amplification and this would be greatest in cases where there is an extensive DRs.

CHAPTER 3

GENERAL METHODOLOGY

3.1 Introduction

This chapter provides details of the participants and procedures used in all three experiments. It also includes an overview of tests that are specific to each study, with further details regarding each one provided in the relevant chapter.

3.2 Participants

Participants were recruited from the patient database at the Audiology Department in Withington Community Hospital, a National Health Service provider of Audiology services for the South Manchester area. Adult patients attend this department for hearing assessment (typically for the consideration of hearing aid fitting) or reassessment (typically three or more years after last hearing aid fitting), hearing aid fitting, follow-up or repair. The inclusion criteria which were adhered to in each study are presented in Table 3.1. An overview of study specific criteria is provided below.

Table 3.1. Inclusion criteria for participants.

Selection Criteria	Definition
No abnormality detected on otoscopic examination	No evidence of an active outer ear infection, perforation or occluding earwax
No abnormalities of middle ear function	Normal tympanometry
Sensorineural hearing impairment	Hearing thresholds ≥ 25 dB HL at ≥1 frequencies between 0.25 and 8 kHz Air-bone gap < 15 dB at 0.5, 1, 2 and 4 kHz

Study 1: Prevalence of cochlear dead region in new referrals and existing hearing aid users from the UK

In total, 376 patients were recruited to the first study. They were required to have attended the audiology department for a hearing test either as part of an initial hearing aid assessment or as a reassessment. Patients attending for a hearing assessment did so following a referral from their general practitioner. Patients attending for a reassessment were doing so because it had been at least three years since their last hearing aid had been fitted. In total, 343 met the inclusion criteria, listed in Table 3.1, and were tested for the presence of a DR. Further details regarding the demographics of these participants are included in the methodology section of the manuscript (see Chapter 4).

When determining the sample size, the aim was to obtain a prevalence value with confidence interval of ≤ 5%. With an estimated DR prevalence of 31%, based on the findings from Cox et al. (2011), a confidence interval of ≤ 5% and a confidence level of 95%, a sample size of 320 was required. 343 participants were tested to allow for attrition.

Study 2: Repeatability, agreement and feasibility of using the threshold equalising noise test and fast psychophysical tuning curves in a clinical setting

Forty adults (30 male, 10 female) with bilateral sensorineural hearing impairment were recruited to the second study. In total, 76 ears (mean hearing impairment at 0.5, 1, 2 and 4 kHz of 51 dB HL +/- 14 SD) were tested for DRs. All participants were new or existing hearing aid users. Further details regarding the demographics of these participants are included in the methodology section of the manuscript (see Chapter 5).

Study 3: Benefit of high-frequency amplification in ears with cochlear dead regions

In total, 36 adults with high-frequency sensorineural hearing impairment were recruited to the final study. Of these, 33 had also participated in the second study. These participants were required to have native speaker level fluency in English assessed by ensuring they could repeat all sounds on the speech tests. Participants were experienced hearing aid users having worn a hearing aid in the test ear for at least one year prior to testing. Further details regarding the demographics of these participants are included in the methodology section of the manuscript (see Chapter 6).

The sample size was calculated using the predicted mean difference of 10% (± 1SD) in speech scores in ears with and ears without DRs from Mackersie et al. (2004). A sample size of 17 ears in each group was calculated; therefore 18 ears in each group met this requirement.

3.3 Ethical approval

The first study was considered by the Greater Manchester North Research Ethics Committee and the local research and development service as 'service evaluation'. This was agreed as the TEN-test is routinely used in the patient care pathway and therefore not considered as research.

The second and third studies constituted clinical research and ethical approval was granted by Greater Manchester North Research Ethics Committee on behalf of the NHS (Approval reference number: 10/H1011/62).

3.4 Test room and equipment

All testing was completed in a sound treated room, meeting ISO BS EN 6189. A Hewlett-Packard Compaq computer with flat screen was housed in this room and was used for fast PTC and speech perception testing. A Siemens Unity 2 audiometer, with

connected Siemens audiometry keyboard was attached to the computer and was used for pure tone audiometry and the TEN(HL) test. TDH49 headphones with MX41 cushions and RadioEar B-71 vibrator were also used for pure tone audiometry and the TEN(HL) test. A loudspeaker was attached for real ear measures and a NOAH (Hearing Instrument Manufacturers Software Association 1993) compatible hearing instrument programming (Hi-Pro) box was attached directly to the computer to allow for hearing aid programming and fitting.

All computer equipment was maintained by the information technology department at Withington Community Hospital. The standard audiological equipment was annually calibrated to appropriate standards by the in-house calibration team during the study on the 20/03/10, 16/03/11 and 14/03/12. All equipment met the required calibration criteria for the particular European Standard.

The research specific equipment was calibrated at the beginning and end of each study. Additionally, daily checks were routinely completed prior to each research test session for standard audiology and research specific test equipment.

An otoscope with 0.5 and 0.25 mm speculae were available within the room. An annually calibrated hand held tympanometer (otoflex 100) was available with a range of ear tips. Earmould impression facilities were also provided within the room.

Additional equipment used for this research project included:

1) Marantz CD 5000 external CD player attached to the Siemens Unity 2 for presentation of tones and masker noise in the TEN-test, used in all three studies.

2) A Creative Professional 0202 USB connected external sound card was attached directly to the computer. This was used to present stimuli via Sennheiser HD 600 headphones for fast PTC measurements used in study 2. A Fostex personal

monitor 6310B speaker was attached to the sound card when presenting speech material in study 3.

3) The sweeping fast PTC (SWPTC) software, full details of which are presented in Sek and Moore (2011) was downloaded to the computer from http://hearing.psychol.cam.ac.uk/ for fast PTC measurements in study 2 and 3.

4) Vowel-consonant-vowel (VCV) nonsense syllable software developed by the Institute of Health Research (IHR) was added to the computer for speech testing completed in study 3.

3.5 Test techniques

A brief overview of the test techniques used in each study is presented below. Full details are provided in the relevant chapters for each experimental study.

TEN-test

The TEN(HL) test was used to detect DRs in all three studies. Full details of the TEN-test methodology used for each of these studies are presented in the relevant chapters.

The TEN(HL) test calibration was conducted using the instructions supplied with the TEN-test CD (Moore et al. 2004). The calibration process was completed by inserting the CD in to a good quality CD player (Marantz 5006) to avoid electrical interference. The first track on the CD provided a calibration tone and the input sensitivity for each channel on the audiometer was adjusted to 0 dB. The TEN(HL) test could then be performed by selecting track 2, 3, 4, 5, 6, 7, or 8 which presented a 0.5, 0.75, 1, 2, 3, and 4 kHz pure tone respectively. At the start of each TEN-test the calibration tone on track 1 was played to ensure the input sensitivity was still at 0 dB.

Fast PTC

Fast PTCs were used to detect DRs in the final two studies. Full details of the fast PTC test methodology are described in each chapter.

Fast PTC calibration was completed in adherence with the recommendations in the SWPTC software. Sennheiser HD 600 headphone sensitivity of 97 dB SPL was added to the calibration adjustment, the voltage of the headphone input was then measured. This calibration was repeated twice during the study test period and the settings remained unchanged.

Speech perception tests

VCV syllable speech material was used in the final study. The methodology is described in full in chapter 6.

The VCV syllable speech stimuli were calibrated by measuring the sound pressure level at the reference test position height which was one metre in front of the speaker (at zero degrees azimuth). The programme used to administer the VCV syllables included a reference tone which was used to calibrate the presentation level of these stimuli. Presentation levels were rechecked at the start of each test session.

Head position was checked initially by ensuring the patient was looking directly at a red sticker on the loudspeaker. If the researcher noticed the participant had moved their head during testing, they would remind them to face the red sticker again. This process was repeated as many times as required to reduce head movement affecting the results.

3.6 Data Collection

All tests were carried out by the researcher. Due to the large numbers of participants to be tested in the first study on prevalence an assistant, a qualified senior audiologist, was recruited to complete some of the TEN-testing. This audiologist

followed the test protocol described in the methodology section of this study (chapter 4). All other data collecting, collating, analysis and presentation for studies 1 to 3 was completed by the researcher.

3.7 Statistical Analysis

All data in this thesis were analysed using SPSS, versions 19 and 20. The conventional 5% significant level was used throughout. Parametric statistics were used whenever the appropriate assumptions about normality were met. Data were summarised using mean and standard deviations. Data were analysed using t-tests, repeated-measures analysis of variance, correlational and regression analyses. For the repeated measures analysis of variance, where Mauchly's test of normality was significant, Greenhouse-Geisser correction was selected. When multiple paired comparisons were made the Bonferonni correction was used. Specific details relating to the analyses of results can be found in each of the experimental chapters.

CHAPTER 4

PREVALENCE OF COCHLEAR DEAD REGIONS IN NEW REFERRALS AND EXISTING ADULT HEARING AID USERS

FORMATTED TO THE EAR AND HEARING REQUIREMENTS

PREVALENCE OF COCHLEAR DEAD REGIONS IN NEW REFERRALS AND EXISTING ADULT HEARING AID USERS

Authors:

Anna Pepler, MSc, School of Psychological Sciences, University of Manchester, UK

Kevin J Munro, PhD, School of Psychological Sciences, University of Manchester, UK

Kathryn Lewis, Audiology Department, University Hospitals South Manchester NHS Foundation Trust

Karolina Kluk, PhD, School of Psychological Sciences, University of Manchester, UK

Correspondence:

Anna Pepler

School of Psychological Sciences,

Ellen Wilkinson Building,

University of Manchester,

Oxford Road,

Manchester,

M13 9PL.

Sources of funding: Research for Patient Benefit project grant from UK National Institute for Health Research (RfPB PB-PG-0408-15055)

ABSTRACT

Objectives: The primary aim of this study was to identify the prevalence of dead regions (DRs) in new adult hearing aid referrals and existing adult hearing aid users. Secondary aims included determining the effect of hearing threshold levels and slope, age and sec on the presence of DRs.

Design: Three hundred and seventy six adults were recruited from a UK National Health Service audiology clinic. Three hundred and forty three participants (674 ears) with a sensorineural hearing impairment were assessed for the presence of a DR at audiometric frequencies from 0.5 to 4 kHz using the Threshold Equalizing Noise (TEN) HL test.

Results: The overall prevalence of DRs was 36% (95% confidence interval 31 to 41). The prevalence in new referrals, and in new and existing hearing aid users was 31% (25-37), 33% (26-40) and 43% (35-51), respectively. The overall prevalence of extensive DRs, defined as spanning ≥ 3 consecutive frequencies, was 3% (1-5).

Conclusions: On the basis of the findings from the Threshold Equalizing Noise test, prevalence of DRs was relatively high in adult hearing aid users with a sensorineural hearing impairment. However, in most cases, the DR was limited to a small frequency region. This suggests that, in most cases, the presence of a DR may not be clinically significant. The difference in DR prevalence between new referrals and existing hearing aid users was not statistically significant. Hearing threshold levels, slope of hearing impairment, age and sex could not be used to reliably identify DRs.

Key Words: Adults, Cochlear dead regions, Hearing aids, Hearing impairment, Prevalence

INTRODUCTION

A cochlear dead region (DR) has been defined as, "an area in the cochlea where inner hair cells (IHCs) and/or neurons are functioning so poorly that a tone producing peak basilar-membrane vibration in that region is detected by off-place listening" (Moore 2004). Although somewhat controversial, some studies suggest that the presence of DRs may impact upon hearing aid benefit and require modified fitting practices (Vickers et al. 2001; Baer et al. 2002; Mackersie et al. 2004). There is a need to establish the prevalence of DRs in new referrals and existing hearing aid users for audiologists to know how many patients are likely to be affected. Identifying DR prevalence was the main purpose of the present study.

It is not possible to reliably detect DRs from pure-tone hearing thresholds alone (Moore 2001). DRs are common when hearing thresholds exceed 70 dB HL (Vinay & Moore 2007). Although hearing impairment with a slope of at least 20 dB/octave is suggestive of a DR (Markessis et al. 2006; Vinay & Moore 2007; Aazh & Moore 2007), this is also not a reliable indicator.

The presence of DRs can be assessed using masking techniques that identify off-frequency listening. One approach is to use psychophysical tuning curves (PTCs) which were originally developed as a way of determining frequency selectivity in the auditory system (Moore & Alcantara 2001). A PTC is a plot of the masker level needed to mask a signal, as a function of masker frequency. The tip of the PTC is the frequency where a narrowband masker is most effective at masking a signal. In cases where inner hair cells (IHC) function is normal, the tip of the PTC will occur close to the signal frequency (Moore 2001; 2002; 2004; Kluk & Moore 2004). When the tip

of the PTC is shifted, this indicates that the signal is detected at a place with a different characteristic frequency to the signal frequency: the tip frequency is assumed to be the edge frequency of the DR (Kluk & Moore 2005). Although PTCs can be used to detect the presence and boundaries of a DR, they are time consuming and considered unpractical for clinical practice.

If a patient with a DR detects a tone using off-frequency listening, the tone should be much easier to mask using broadband noise compared with normal-hearing or hearing-impaired listeners without DRs (Moore et al. 2000). This is because off-frequency listening results in a tone being detected away from the region of peak basilar-membrane vibration. The Threshold Equalizing Noise (TEN) test can be used to measure masked thresholds at half octave intervals over the 0.25 to 8 kHz range using the original version calibrated in sound pressure level (SPL) (Moore et al. 2000), or over a narrower frequency range of 0.5 to 4 kHz using a version calibrated in HL (Moore et al. 2004). Although the TEN(SPL) test allows the detection of DRs across a more extensive frequency range, the reduced TEN bandwidth and low crest factor used in the TEN(HL) implementation of the test allow the noise to be presented at higher levels without loudness discomfort; thus, DRs can be detected when greater degrees of hearing impairment are present. The TEN-test does not accurately locate the edge frequency of a DR (Moore & Alcantara 2001; Vestergaard 2003); however, it is considered to be sufficiently accurate to detect the presence or absence of a DR in a timely manner, making them feasible for use within the clinical setting (Moore et al. 2004; Cairns et al. 2007).

Although the most appropriate management for DRs is currently unclear, there are reports that DRs impact on speech, pitch and loudness perception (Vickers et al. 2001; Baer et al. 2002; Mackersie et al. 2004; Huss et al. 2005a, 2005b). DRs

spanning a number of frequencies may have a significant clinical impact (Baer et al. 2002); however, the criteria for a "clinically significant" DR are not well defined. To determine whether there is a need to develop a specific management plan for patients having a DR, it is essential to first identify its prevalence within the target population, that is, within potential hearing aid users. Prevalence is calculated as the total number of cases of a disease or condition in a given statistical population at a given time, divided by the number of individuals in the population at risk from the disease or condition (Martin 2007).

DRs have been reported in hearing-impaired participants with specific audiometric configurations (Moore et al. 2000; Vickers et al. 2001; Summers et al. 2003; Simpson et al. 2005; Preminger et al. 2005; Jacob et al. 2006; Aazh & Moore 2007; Cairns et al. 2007; Cox et al. 2011). These studies do not provide prevalence estimates in hearing aid users as a whole. It is also worth noting that these studies used a range of TEN-test methodologies and participant criteria, which may explain the wide range of estimates (22% to 92%). For example, some of the studies used a final step size of 5 dB when measuring TEN masked thresholds but the most accurate results are obtained when a 2 dB step size was used (Cairns et al. 2007). With the exception of Cox et al. (2011), these studies tested between 10 and 63 participants; not substantial enough to provide an accurate sample of DRs in the hearing-impaired population. Cox et al. (2011) tested 170 participants in total and reported a DR prevalence of 31%. However, they restricted participant inclusion according to degree of hearing impairment. They aimed to recruit only those participants suitable for a hearing aid fitting. This was achieved by recruiting patients with hearing impairments reaching 60 – 90 dB HL between 1 and 3 kHz and >25 dB HL below 1 kHz. However, hearing aid use was not presented in the study

and therefore, hearing aid users with milder hearing impairments may have been excluded. Hence, the prevalence of DRs in new referrals or in existing hearing aid users may be different from their prevalence in the study by Cox et al. (2011).

Vinay and Moore (2007) reported the prevalence of DRs in 308 hearing-impaired adults who attended an audiology clinic in India. Some participants had attended the clinic previously, whilst others were attending for the first time, but most were attending for the purpose of hearing aid fitting. Participants were included in the study if they had hearing thresholds of at least 15 dB HL at any frequency between 0.25 and 8 kHz. The median hearing impairment was 50 dB HL at 0.5 kHz and 70 dB HL at 4 kHz. Each participant was tested using the TEN(HL) test and the presence of a DR was determined using the standard criteria suggested by Moore et al. (2004). More than half of the participants (57%: 95% confidence interval 52% - 64%), were found to have a DR in one or both ears at one or more frequency; this is a much higher prevalence than identified by Cox et al. (2011). A possible explanation is that Cox et al. (2011) had much stricter inclusion criteria, in terms of degree of hearing impairment; however, participants still had a mean hearing impairment that was 5 dB less severe than Vinay and Moore (2007). This is consistent with previous findings where adults in India were reported to have a greater prevalence (8%) of hearing impairment ≥41 dB HL when compared with hearing-impaired adults in the United States (4%) (WHO 2000). Given these differences, the DR prevalence reported by Vinay and Moore may not be generalizable to adults in the United Kingdom. Although the participants in the study by Cox et al. (2011) are likely to be more comparable with the U.K. population, by excluding participants according to their degree of hearing impairment, Cox et al. may have overestimated DR prevalence in the adult hearing aid population.

Vinay and Moore (2007) suggested that the 25% of ears that met the criteria for DRs at two or more adjacent frequencies were 'clinically significant'. If an individual has a DR starting at 4 kHz, or above, it is unlikely that this will impact on hearing aid benefit, due to the limited high-frequency amplification provided by most current hearing aids. Also, an "island" DR (i.e. occurring at 1 isolated frequency) is unlikely to result in a change in hearing aid management. Therefore, when estimating DR prevalence it is helpful to identify the proportion of these that are sufficiently extensive (spanning at least 3 consecutive frequencies) to potentially affect hearing aid management. Although it is not clear how extensive a DR needs to be before it impacts on audiological management, for the purposes of the present study, it was operationally defined as a DR spanning at least three consecutive frequencies.

To our knowledge, there is no study that reports the prevalence of DRs separately for new referrals and existing hearing aid users. We identified three unanswered research questions:

- How prevalent are DRs in adults with a sensorineural hearing impairment who have, or are being assessed, for a hearing aid?
- Does the prevalence of DRs differ between new referrals and existing hearing aid users?
- How extensive are the DRs that are identified?

The aim of the present study was to assess the prevalence and extent of DRs in a clinical sample of new referrals and existing adult hearing aid users in the UK. It was hypothesized that the prevalence would be lower than in the studies by Vinay and Moore (2007) and Cox et al. (2011), especially in the group of new referrals because the degree of hearing impairment of adults presenting to audiology clinics

would likely be less. Secondary aims include investigating the relationship between the prevalence of DRs and factors such as audiometric configuration, age and sex.

MATERIALS AND METHODS

Participants

A total of 376 adult participants (752 ears) were selected from new referrals (n = 220, 436 ears) and existing hearing aid users (n=156, 308 ears) who attended the U.K. National Health Service audiology department at Withington Community Hospital, Manchester, for a hearing assessment. Participants were selected using opportunity sampling by inviting all patients who attended the clinic for hearing assessment or reassessment during the period of data collection. Participants were only included if otosocopic examination and tympanometry were normal. Pure tone audiometry (at 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, and 8 kHz) was completed in accordance with the British Society of Audiology recommended procedure (BSA 2011). Testing was carried out using the Siemens Unity 2 audiometer and TDH-39 headphones. Bone conduction testing was completed at 0.5, 1, 2 and 4 kHz using a Radio Ear B-71 earphone. All equipment was calibrated in accordance with BS EN ISO 8253-1:2010.

A total of 343 participants (674 ears) met the inclusion criteria; see Table 4.1 for the demographics of new referrals and existing hearing aid users. Of the 78 ears excluded, 25 had hearing thresholds within normal limits, 19 had a significant conductive hearing impairment, 12 had a severe hearing impairment (and it was not possible to determine masked hearing thresholds), 6 were not tested due to loudness discomfort, 4 had occluding wax and 6 participants (12 ears) gave inconsistent results on pure tone audiometry. All existing hearing aid users had been fitted with a

hearing aid at least 2 years prior to testing. Of the new referrals, 161 (83%) were offered and accepted a hearing aid, 16 (8%) were offered and declined a hearing aid and 16 (8%) were not offered a hearing aid; not being offered a hearing aid was primarily because of the mild degree of hearing impairment. The 161 new referrals who were offered and accepted a hearing aid are referred to as "new" hearing aid users.

Insert Table 4.1. about here

The TEN(HL) test, referred to as TEN-test from now on, was routinely carried out on all patients in the audiology department so it was possible to establish prevalence of DRs without the need for any additional tests. For this reason, the study was considered to be service evaluation and we were informed by the ethics committee that ethics approval was not required. Before data collection all participants were fully informed about the test procedures.

Procedure

All testing was completed in a sound-treated room in the audiology department. The TEN-test was used to detect DRs as this is currently the most feasible test for detection of DRs in the clinical setting (Moore et al. 2004). The pure-tone signal and TEN were routed from the TEN CD via a Marantz CD 5000 player through channel 1 and 2 of a Unity audiometer. The test was conducted at 0.5, 0.75, 1, 1.5, 2, 3, and 4 kHz. To determine the maximum presentation level of the TEN masker to be used with each patient, the TEN uncomfortable loudness level (ULL) was first determined using an ascending step size of 5 dB. TEN was then presented at least 2 dB below this level. The signal was adjusted in ascending and

descending step sizes of 8 dB and 4 dB respectively and a final step size of 2 dB. The presence or absence of a DR at the test frequency was determined using criteria based on those suggested by Moore et al. (2004):

- A definite DR was indicated if the masked threshold was ≥ 10 dB above the TEN level and ≥ 10 dB above the absolute threshold.
- An inconclusive DR was indicated if the masked threshold was ≥ 10 dB above the TEN level but < 10 dB above the absolute threshold.
- No DR was indicated if the TEN masked threshold was < 10 dB above the TEN level but ≥ 10 dB above the absolute threshold.

All data in this study were analyzed using SPSS, version 16. The conventional 5% significance level was used throughout. Paired *t*-tests and Chi-square tests were used to analyze within- and between-subject factors. Regression statistics were used to analyze the interactions of a number of factors. For the repeated-measures analysis of variance (ANOVA), where Mauchly's test of normality was significant, Greenhouse-Geisser correction was used. For the purposes of statistical analysis, participants' right and left ears were assumed as quasi-independent since the presence and absence of a DR at each audiometric frequency was different in 105 participants.

RESULTS

Prevalence of DRs

A summary of the prevalence data is shown in Table 4.2. When all 343 participants were included, the DR prevalence was 36% (95% CI: 31-41). Classifying by the 674 ears, the prevalence was 26% (95% CI: 23-29). Of the ears identified as having a DR, 31 (5% of total) met the criteria for a DR at one or more

frequency between 0.5 and 2 kHz, and 144 ears (21% of all ears) met the criteria for a DR at one or more frequency between 3 and 4 kHz.

Insert Table 4.2. about here

More than one-third of *participants* met the criteria for a DR. However, only 26% of *ears* met the criteria for a DR. Considering that most participants in this study had symmetrical hearing impairment, one might expect the prevalence for participants and ears to be similar. To examine this in more detail all 64 participants with a unilateral DR were selected and mean hearing impairment in the ears with and without DRs was compared. Table 4.3 shows that ears with DRs generally had a greater degree of hearing impairment. Multiple paired *t*-tests with Bonferroni post hoc correction were used to compare the hearing thresholds in ears with and without DRs. The *t*-test was significant at 3 kHz ($t[64]= 32.011$, $p = 0.004$), 4 kHz ($t[64]= 32.493$, $p = 0.001$) and 6 kHz ($t[64]=32.149$, $p = 0.003$). Therefore, although the 64 participants were classified as having symmetrical hearing impairments, the statistically significant greater hearing thresholds between 3 and 6 kHz may explain why the DR criteria were met more frequently.

Insert Table 4.3. about here

For 20 participants (38 ears), the result of the TEN-test was inconclusive at one or more frequency. For 12 participants (22 ears) this was due to insufficient tolerance of high TEN levels. In the remaining 8 participants (16 ears) this was due to the severity of the hearing impairment (> 90 dB HL). However, hearing

impairments ≥ 90 dB HL are very likely to be associated with DRs (Summers et al. 2003). When these participants (16 ears) are added to the data in Table 4.2, the overall prevalence increases to 38% (95% CI: 33-43) and 28% (95% CI: 25-31) for participant and ear, respectively.

Thirty-seven percent (95% CI: 32-42) of new and existing hearing aid wearers (n=311) met the TEN criteria for a DR: 33% (96% CI: 26-40) were new users and 43% (95% CI: 35-51) were existing users. The difference in prevalence between new and existing hearing aid users was not statistically significant ($\chi^2[2]=4.5$, p=0.106).

In terms of ears, 26% (95% CI: 23-29) of all fitted ears met the TEN criteria for a DR. The difference in prevalence between ears of new and existing users (24% and 29%, respectively) was not statistically significant (χ^2 [2]=3.8, p=0.212).

Insert Table 4.4. about here

Audiometric configuration and DRs

DR counts, according to frequency, are provided in Table 4.4. DRs are more likely to occur at high frequencies, presumably because this is where hearing impairment is greatest, see Table 4.5.

However, existing hearing aid users had a greater degree of hearing impairment than new hearing aid users (48 and 38 dB HL, respectively), see Figure 4.1. Differences in hearing impairment between the two groups were greatest between 1 and 3 kHz. The audiometric thresholds were analyzed using a mixed-model ANOVA with within-subject factor frequency [10] and between-subject factor group (new or existing hearing aid user). There was a significant effect of hearing

aid user (F[1,616]=76.3; p<0.001) and frequency (F[2.8,1721.8]=1117.4; p<0.001).There was also a statistically significant interaction (F[2.8,1721.8]=4.5; p=0.005).

Insert Table 4.5. and Figure 4.1. about here

Ears that met the TEN criteria for a DR had a greater mean hearing impairment than ears without DRs (see Table 4.6 and Figure 4.2). The greatest difference in mean hearing impairment between the two groups was at frequencies above 1 kHz. This difference in hearing impairment was analyzed using a mixed-model ANOVA with within-subject factor frequency [10] and between-subject factor group (presence of DRs). There was a significant difference between ears with and without DRs (F[1,629]=140.8; p<0.001) and a significant difference between frequencies (F[2.9,1855.0]=1118.4; p<0.001) with respect to mean hearing impairment. There was also a statistically significant interaction (F[2.9,1855.0]=38.7; p<0.001), that is, the difference between ears with and without DRs differed according to frequency.

Insert Table 4.6. and Figure 4.2. about here

To investigate the nature of the interaction between frequency and hearing threshold in more detail, the distribution of hearing threshold levels at each frequency is presented in Table 4.7 (excluding inconclusive results). The number in parenthesis indicates those ears meeting the TEN-test criteria for a DR. All hearing impairments >85 dB HL were excluded because effective masking could not be

achieved. The criteria for a DR were most commonly met when hearing thresholds were between 50 and 85 dB HL; however, TEN-test criteria were met at hearing thresholds better than this in some cases. No ears met the DR criteria at hearing thresholds less than 40 dB HL.

Insert Table 4.7. about here

The best indicator of a DR, based on hearing threshold data, was considered by calculating the "hit rate" (i.e., the ability of the chosen hearing thresholds to detect all ears with a DR) and "false alarm rate" (i.e., the ability of the chosen hearing thresholds to exclude all ears without a DR). Receiver operator characteristic (ROC) curves, in Figure 4.3, show the hit rate for a given false alarm rate at audiometric test frequencies 0.5, 1, 2, and 4 kHz. A perfect test with a 100% hit rate and a 0% false alarm would be situated in the top left-hand corner of the graph. The ROC curves, being above the diagonal 'chance' curve, show that hearing thresholds at each of these frequencies are a better indicator of a DR than chance. However, when the hit rate reached 90%, the false alarm rate increased to at least 40%. Therefore, although more ears with DRs were being correctly identified using hearing threshold level, many ears without DRs were being incorrectly identified as having a DR. The best compromise between hit rate and false alarm rate is achieved at 2 kHz. However, even here the d-prime value of 1.46 (a 100% sensitive and specific test would have a d-prime value above 6) indicates that hearing thresholds are not a sensitive and specific predictor of the outcomes of the TEN-test.

Insert Figure 4.3. about here

The slope of hearing impairment between the main audiometric frequencies (0.25 to 0.5, 0.5 to 1, 1 to 2, 2 to 4 and 4 to 8 kHz) was compared in ears with and without a DR. Ears with a DR had a greater mean slope of hearing impairment than ears without a DR, as shown in Table 4.8. The difference in slope between the two groups was greatest at 2 to 4 kHz. These data were analyzed using a mixed-model ANOVA with within-subject factor slope and between-subject factor group (ears with and without DRs). There was a significant effect of group (F[1,631]=46.7; p<0.001) and slope (F[3.4,2116.6]=100.3; p<0.001).There was also a statistically significant interaction (F[3.4,2116.6]=16.5; p<0.001).

Insert Table 4.8. about here

The association of slope and degree of hearing impairment was considered by analyzing the data using a logistic regression analysis. The Enter Method, which is a simultaneous method of inputting variables, was used as there was no evidence of one variable being more important, therefore they were all treated equally in the statistical analysis. Slope 2 to 4 kHz and 4 to 8 kHz and hearing thresholds at 4 kHz were considered as predictors of DR occurrence. Nagelkerke's R^2, a method of predicting R^2 for logistic regression analysis, of 0.466 indicated a moderate relationship between prediction and groups. Predicted overall success was 84.1% (94.8% for no DR and 56.3% for yes DR). The Wald test, the square of the *t*-test and as such can compare the effect of multiple factors, demonstrated that only hearing thresholds at 4 kHz made a significant contribution to predicted DRs (Wald = 114.565, $p < 0.001$). Slope 2–4 kHz and 4–8 kHz were not significant predictors ($p >$

0.05). Therefore, hearing thresholds at 4 kHz are primary predictors of DRs, while slope is only an indicator by being associated with increasing hearing thresholds.

Extensive DRs

Of the 343 participants who had a DR, 3% (2 to 4) met the criteria for a DR extending over at least three consecutive frequencies. Prevalence of extensive DRs was 2% (1 to 3) in the new referrals, 3% (2 to 4) in new hearing aid users and 4% (3 to 5) in existing hearing aid users. Ears that met the criteria for an extensive DR had a significantly greater hearing impairment at all frequencies compared with all other ears that met the criteria for a DR, as shown in Figure 4.4. The difference in hearing impairment between ears in the two groups of DR and no DR was analyzed using a mixed-model ANOVA with within-subject factor frequency [10] and between-subject factor group (with and without extensive DRs). There was a significant effect of group (F[1,306]=39.6; p<0.001) and frequency (F[3.3,999.1]=183.6; p<0.001).There was also a statistically significant interaction (F[3.3,999.1]=14.6; p<0.001).

Insert Figure 4.4. about here

Prevalence of DRs and predicting factors

Fifty-five women (32%) and 68 men (40%) presented with a DR in at least one ear. A Chi-square test indicated a significant effect of sex on DR prevalence, (χ^2[2] = 10.8, p=0.005). Men and women had a similar mean hearing impairment; however, their audiometric configuration differed slightly, as shown in Figure 4.5. At low frequencies, women had poorer hearing levels while at high frequencies men

had poorer hearing levels. The data were analyzed using a two-factor (group[2], frequency[10]) mixed-model ANOVA. The mean difference between groups was not statistically significant (F[1,629]=1.7; p=0.198). The mean difference between frequencies was statistically significant (F[2.9,1821.2]=1191.5; p<0.001) as was the interaction (F[2.9,1821.2]=35.2; p<0.001). Therefore, the difference in audiometric configuration between men and women was statistically significant.

Insert Figure 4.5. about here

The effect of age on prevalence of DRs was considered by separating the data into two equal groups: <73 years (n=170) and ≥ 73 years (n=173). The prevalence of DRs in the younger and older group was 25% (17-33) and 48% (40-56), respectively. A Chi-square test indicated the overall prevalence of DRs to be significantly different between the younger and older group (χ^2[2] = 32.1, p<0.001).

Mean hearing impairment was greater in the older age group (see Fig.4.6). The data were analyzed using a two-factor (group[2], frequency[10]) mixed-model ANOVA. The mean difference between groups was statistically significant (F[1,629]=66.9; p<0.001) as was the mean difference between frequencies (F[2.8,1776.2]=1142.2; p<0.001).There was also a statistically significant interaction (F[2.8,1776.2]=12.8; p<0.001).

Insert Figure 4.6. about here

The effects of age and sex on DR prevalence may be confounded by variations in hearing thresholds between groups. A logistic regression analysis, using

the Enter Method, was conducted to consider age, sex and hearing thresholds (0.5, 1, 2, 4 kHz) as predictors of DR occurrence. A test of the full model against a constant-only model was statistically significant, indicating that the group of predictors reliably distinguished between absence and presence of DRs ($\chi^2[5] = 250.281$, $p < 0.001$). Nagelkerke's R^2 of 0.472 indicated a moderate relationship between prediction and groups. Prediction success overall was 84% (94.5% for no DR and 56.6% for yes DR). The Wald criterion demonstrated that only hearing thresholds at 4 kHz made a significant contribution to prediction (Wald = 89.729, $p < 0.01$). Age, sex and hearing thresholds were not significant predictors ($p > 0.05$). EXP(B) values indicate that when hearing thresholds at 4 kHz are increased by one unit (1 dB) the odds ratio of a DR was 1.127 times as large.

Summary of findings

1) DR prevalence: 36% (95% CI: 31-41) of 343 participants, 26% (95% CI: 23-29) of 674 ears.
2) Thirty-three percent (95% CI: 26-40) of new and 43% (95% CI: 35-51), of existing hearing aid users have a DR and this difference is likely due to the greater severity of hearing impairment in the existing users.
3) Three percent of ears have an extensive DR spanning three consecutive frequencies.
4) DRs are associated with greater hearing impairment, but thresholds alone are a poor predictor.
5) DRs are associated with steeply sloping hearing impairments, in men and older participants but only because hearing impairment at 4 kHz is greater in these groups.

DISCUSSION

The main aim of the present study was to assess the prevalence and extent of DRs in a clinical sample of new referrals and existing adult hearing aid users in the United Kingdom. Secondary aims included investigating the relationship between DRs and factors such as audiometric configuration, age and sex.

DR prevalence

A substantially lower prevalence of DRs was recorded in hearing-impaired adults in the United Kingdom than reported by Vinay and Moore (2007) in India. This can be explained by Indian participants having a mean hearing impairment approximately 20 dB more severe than the participants in the present U.K. study. The prevalence estimates in the present study are similar to those reported by Cox et al. (2011; 31% [95% CI: 26-36]). To compare the estimates from the two studies, all participants in the present study who met the criteria used by Cox et al. (2011) were identified. The prevalence of DRs in this subgroup was found to be 59% (95% CI: 47-71). A Chi-Square test indicated that there was a statistically significant difference in DR prevalence between the subgroup from the present study and that from the study by Cox et al. ($\chi^2[2]=6.3$; $p<0.001$). The mean hearing impairment between the two groups was the same for ears that met the criteria for a DR (53 dB HL). One possible reason for the lower DR estimate in the study by Cox et al. (2011) is that they excluded all participants with audiometric thresholds less than 25 dB HL below 1 kHz. However, there were 222 participants in the current study with hearing thresholds better than 25 dB HL below 1 kHz. Cox et al. (2011) reported that the exclusion of patients with normal hearing in the low frequencies from their study may have increased the proportion of metabolic presbyacusis and this may have

reduced the prevalence estimate more than steeply sloping hearing impairments associated with sensory presbyacusis.

DR prevalence in new referrals and existing hearing aid users

The prevalence of DRs in new referrals and existing hearing aid users was compared. Mean hearing impairment is greatest in the existing hearing aid users and this explains the trend for the higher prevalence of DRs in this group.

Audiometric configuration and DRs

DRs were more prevalent at high frequencies where hearing impairment was greatest. As has previously been suggested, it is impossible to reliably diagnose an individual with a DR using pure tone audiometry alone (Moore 2001, 2004). ROC curves were used to assess the ability of hearing thresholds to identify a DR. A perfect test would have a hit rate of 100% and a false alarm rate of 0%. In reality, no clinical tool is perfect, but a hit rate >80% and a false alarm rate <20% is probably acceptable. Although the TEN criterion of a masked threshold being ≥10 dB HL above the masker level is commonly used to define a DR, Summers et al. (2003) and Preminger et al. (2005) suggested that a different criterion such as a masked threshold being ≥15 dB HL may be appropriate. ROC curves for 2 and 4 kHz using different criteria are presented in Figure 4.7. These show that a change in criterion does not improve test performance.

Insert Figure 4.7 about here

Vinay and Moore (2007) suggested that DRs occur at hearing thresholds ≥ 55 dB HL. In the present study, a small number of DRs were recorded at hearing thresholds ≤55 dB HL. An explanation for this difference may be that a higher proportion of individuals in the present study had a milder hearing impairment and this simply increases the chance of finding DRs at lower hearing thresholds. The recorded values may have been a result of false positives on the TEN-test; however, in two ears with DRs occurring between 40 and 45 dB HL, the DR criteria were met for both fast PTCs and the TEN-test. This would suggest that DRs do occur at hearing impairments ≤ 55 dB HL. This finding is in agreement with the finding from Hornsby and Dundas (2009) who reported DRs at hearing impairments <60 dB HL. This may be explained by variations in hearing impairment aetiology between the studies. A number of participants with moderate hearing impairment who met the criteria for a DR on the TEN-test had a congenital or acquired neurological disorder so a DR may be due to reduced or poor neural activity. However, this does not explain the wide variation in hearing thresholds associated with DRs (from 60 to 85 dB HL). It is known that outer hair cell damage can result in a hearing impairment up to around 60 dB HL (Yates 1990, 1995; Ruggero et al., 1997). An impairment greater than this is considered to be associated with some degree of IHC damage. Griffiths et al. (2001) proposed outer hair cells and IHCs damage to be disassociated in genetic hearing impairments, with different mutations resulting in varying amounts of damage in each hair cell type. Higher auditory pathways or central processes may impact on the patient's responses on pure-tone audiometry. This may result in the audiometric threshold being elevated beyond that resulting directly from hair cell damage. As the causal factors for DRs are wide and cannot be individually tested, this explains the difficulty in identifying them from hearing thresholds alone.

Previous studies have suggested that the slope of hearing impairment in those with DRs is greater (> 20 dB/octave) than in those without DRs (Preminger et al. 2005). However, Hornsby and Dundas (2009) reported that although DRs were more common in steeply sloping losses, slope is not a reliable predictor of DR presence. Vinay and Moore (2007) attempted to identify a trend in the slope of hearing impairment at the edge frequency of the DR. However, as Vinay and Moore (2007) suggested, the clinician will only have an idea of the edge frequency of the DR through use of a test which can diagnose DRs. Therefore, in the present study we compared the slope across the frequency range for ears with and without a DR. The results showed that ears with DRs have a statistically steeper slope of hearing impairment than ears without a DR, most noticeable between 2 and 4 kHz, where there was a 10 dB difference in slope between the two groups. However, slope may only be associated with greater DR prevalence due to increasing hearing impairment.

Extensive DRs

DRs are generally reported as present or absent. However, as Vinay and Moore (2007) suggested, it is more important to detect a DR that has the potential to impact on hearing aid management. Only 3% (95% CI: 2-4) of the adult hearing-impaired population in this study met our definition for an extensive DR, and these were typically adults with greater degrees of hearing impairment. However, there are no clear criteria to determine when a DR is extensive enough to impact on audiological management. Vinay and Moore (2007) suggested that only DRs occurring at ≤2 kHz are clinically significant. This was based on the findings that amplification should be provided for frequencies up to around 1.7 times the edge frequency of the DR (Vickers et al. 2001; Baer et al. 2002). This would suggest DRs,

which occur at ≥3 kHz should not be provided with amplification beyond 5 kHz. Most current hearing aids do not provide significant amplification above this frequency in the real ear. Therefore, the presence and absence of a DR at ≥3 kHz and above will make no difference to the management. However, it is not clear that amplifying 1.7 times above the edge frequency of the DR is the most suitable management plan. Because extensive DRs are often associated with greater degrees of hearing impairment, it is not clear if audibility rather than DRs impact on hearing aid benefit. Mackersie et al. (2004) accounted for audibility and reported that high-frequency amplification did not have a detrimental effect on speech perception in quiet or noise. It remains unclear whether DRs impact on hearing aid benefit, and if this impact increases with DRs spanning more frequencies.

Men were found to have a significantly higher prevalence of DRs than women. The trend of men having better hearing thresholds at low-frequency and poorer hearing thresholds at high frequencies than women has been reported previously (Davis et al., 1991; Gates and Mills, 2005). When the difference in hearing impairment configuration was accounted for, sex no longer was a predictor of DR occurrence. Participants aged ≥73 years were found to have a significantly higher prevalence of DRs than participants aged <73 years. Again, when the difference in hearing impairment was accounted for, age was no longer a predictor of DR occurrence.

CONCLUSIONS

The findings from this study show that DRs are common (1 in 3) and there is a trend for these to occur more frequently in existing, compared with new hearing aid users. However, extensive DRs were present in only 3% of hearing aid users. The

management of these individuals is currently unclear and warrants further investigation.

ACKNOWLEDGEMENTS

This paper presents independent research funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-0408-15055). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

REFERENCES

Aazh, H., Moore, B.C.J. (2007). Dead regions in the cochlea at 4 kHz in elderly adults: Relation to absolute threshold, steepness of audiogram, and pure-tone average. J Am Acad Audiol, 18, 97-106.

Baer, T., Moore, B.C.J., Kluk, K. (2002). Effects of low pass filtering on the intelligibility of speech in noise for people with and without dead regions at high frequencies. J Acoust Soc Am, 112, 1133-44.

British Society of Audiology (BSA). (2011). Recommended procedure: Pure tone air and bone conduction threshold audiometry with and without masking and determination of uncomfortable loudness levels.

Cairns, S., Frith, R., Munro, K.J., Moore, B.C.J. (2007). Repeatability of the TEN(HL) test for detecting cochlear dead regions. Int J Audiol, 46, 575-84.

Cox, R.M., Alexander, G.C., Johnson, J. et al. (2011). Cochlear dead regions in typical hearing aid candidates: Prevalence and implications for use of high-frequency speech cues. Ear Hear, 32, 339-348.

Davis, A., Ostri, B., Parving, A. (1991). Longitudinal study of hearing. Acta Otolayringol. 476S, 12-22.

Gates, G., Mills, J. (2005). Presbycusis. The Lancet, 366, 1111-1120

Griffiths, T.D., Blakemore, S., Elliott, C., et al. (2001). Psychological evaluation of cochlear hair cell damage due to the A3243G mitochondrial DNA mutation. JARO, 2, 172-179.

Hornsby, B.W.Y., Dundas, J.A. (2009). Factors affecting the outcomes on the TEN(SPL) test in adults with hearing loss. J Am Acad Audiol, 20, 251-263.

Huss, M., Moore, B.C.J., (2005a). Dead regions and pitch perception. J Acoust Soc Am, 117, 3841-3852.

Huss, M., Moore, B.C.J. (2005b). Dead regions and noisiness of pure tones. Int J Audiol, 44, 599-611.

Jacob, R.T., Fernandes, J. C., Manfrinato. J., et al. (2006). Identifying dead regions in the cochlea through the TEN Test, Rev Bras Otorrinolaringol, 72, 673-682.

Kluk, K., Moore, B.C.J. (2004). Factors affecting psychophysical tuning curves for normally hearing subjects. Hear Res, 194, 118-134.

Kluk, K., Moore, B.C.J. (2005). Factors affecting psychophysical tuning curves for hearing impaired subjects with high-frequency Dead regions. Hear Res, 200, 115-131.

Mackersie, C.L., Crocker, T.L., Davis, R.A. (2004). Limiting high-frequency hearing aid gain in listeners with and without suspected cochlear dead regions. J Am Acad Audiol, 15, 498-507.

Markessis, E., Kapadia, S., Munro, K., et al. (2006). Modification of the Threshold Equalising Noise (TEN) test for cochlear dead regions for use with steeply sloping high-frequency hearing loss. Int J Audiol, 45, 91-98.

Martin, E. (2007). Concise Medical Dictionary (7th Edition). Oxford University Press.

Moore, B.C.J. (2001). Dead regions in the cochlea: Diagnosis, perceptual consequences, and implications for the fitting of hearing aids. Trends Amplif 5, 1-34.

Moore, B.C.J. (2002). Psychoacoustics of normal and impaired hearing. British Medical Bulletin, 63, 121-34.

Moore, B.C.J. (2004). Dead regions in the cochlea: conceptual foundations, diagnosis, and clinical applications. Ear Hear 25, 98-116.

Moore, B.C.J., Alcantara, J.I. (2001). The use of psychophysical tuning curves to explore Dead regions in the cochlea. Ear Hear, 22, 268-78.

Moore, B.C.J., Huss, M., Vickers, D.A., et al. (2000). A test for the diagnosis of dead regions in the cochlea. Br J Audiol, 34, 205-24.

Moore, B.C.J., Glasberg, B.R., Stone, M.A. (2004). New version of the TEN test with calibrations in dB HL. Ear Hear 25, 478-87.

Preminger, J.E., Carpenter, R., Ziegler, C.H. (2005). A clinical perspective on cochlear dead regions: intelligibility of speech and subjective hearing aid benefit. J Am Acad Audiol 16, 600-613.

Ruggero, M.A., Rich, N.C., Recio. A., et al. (1997) Basilar-membrane responses to tones at the base of the chinchilla cochlea. J Acoust Soc Am 101, 2151-63.

Simpson, A., McDermott, H.J., Dowell, R.C. (2005). Benefits of audibility for listeners with severe high-frequency hearing loss. Hear Res, 210, 42-52.

Summers, V., Molis, M.R., Musch, H., et al. (2003). Identifying dead regions in the cochlea: psychophysical tuning curves and tone detection in threshold-equalizing noise. Ear Hear, 24, 133-142.

Vestergaard, M.D. (2003). Dead regions in the cochlea: implications for speech recognition and applicability of articulation index theory. Int J Audiol, 42, 249-61.

Vickers, D.A., Moore, B.C., Baer, T. (2001). Effects of low-pass filtering on the intelligibility of speech in quiet for people with and without dead regions at high frequencies. J Acoust Soc Am, 110, 1164-75.

Vinay, Moore, B.C.J. (2007). Prevalence of dead regions in subjects with sensorineural hearing loss. Ear Hear, 28, 231-41.

World Health Organization (WHO). (2000). Global Burden of Hearing Loss in the Year 2000. Retrieved May 15, 2012 from http://www.who.int/healthinfo/statistics/bod_hearingloss.pdf

Yates, G.K. (1990). Basilar membrane nonlinearity and its influence on auditory nerve rate-intensity functions. Hear Res, 50, 145-162.

Yates, G.K. (1995). Cochlear structure and function. In: Moore, B.C.J. ed. Hearing (1st Edition). San Diego: Academic Press, 41-73.

Zweig, M.H., Campbell, G. (1993) Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. Clin Chem, 39, 561-77.

Table 4.1. Demographics of new referrals and existing hearing aid users.

	New referrals		New hearing aid users (New referrals who obtained hearing aids)		Existing hearing aid users	
Number of participants (n)	193		161		150	
Sex (%)	96 Male 49.7	97 Female 50.3	79 Male 49.1	82 Female 50.9	74 Male 49.3	76 Female 50.7
Mean age (years) ±SD (Range)	70±10.8 (20-94)	72±11.1 (24-94)	70±11.0 (20-94)	74±10.9 (30-94)	72±11.3 (20-93)	72±11.2 (32-92)
Mean hearing impairment (0.5, 1, 2 and 4 kHz) (dB HL) ±SD (Range)	43±3.1 (8-85)	43±3.2 (6-89)	45±3.5 (15-94)	45±3.4 (21-84)	48±3.6 (18-96)	49±3.4 (16-100)

Table 4.2. Prevalence of DRs (95% confidence intervals in parenthesis). The number of DRs according and the overall number in each group is also included.

	Participants	Ears
New referrals	30.6% (25.6-35.6) 59 /193	22.7% (18.7-26.7) 86 / 378
New hearing aid users (New referrals who obtained hearing aids)	32.9% (25.9-39.9) 53 /161	24.2% (20.4-28.4) 77 / 318
Existing hearing aid users	43.3% (35.3-51.3) 65 / 150	30.0% (23.0-37.0) 89 / 296
Overall	.2% (31.2-41.2) 124 / 343	6.0% (23.0-29.0) 175 / 674

Table 4.3. Mean hearing thresholds (dB HL) in participants with unilateral DRs. The mean hearing threshold levels in ears with DRs are greater at ≥3 kHz than ears without DRs. (n=64).

		Frequency (kHz)									
		0.25	0.5	0.75	1	1.5	2	3	4	6	8	Mean
Mean hearing thresholds (dB HL)	No DR	27	28	32	35	42	45	51	60	69	72	42
	DR	29	30	32	36	43	47	56	66	76	76	44
Difference (in dB)	DR-No DR	2	2	0	1	1	2	5	6	7	4	2

Table 4.4. Percent (and number) of ears that met the TEN-test criteria for a DR according to frequency (n=175).

Test Frequency (kHz)	Percent (%) (Number)
0.5	0.9 (6)
0.75	1.2 (8)
1.0	2.3 (16)
1.5	4.1 (28)
2	4.4 (30)
3	13.2 (89)
4	14.3 (96)

Table 4.5. Mean hearing impairment, in dB HL, for new referrals and hearing aid users compared with Vinay and Moore (2007) (n=674).

		Frequency (kHz)						
		0.5	0.75	1	1.5	2	3	4
Mean hearing threshold (dB) (Range)	New referrals	24 (-2-80)	26 (-4-74)	28 (-2-72)	33 (2-72)	37 (0-100)	45 (6-100)	54 (6-100)
	New hearing aid users (New referrals who obtained hearing aids)	26 (0-80)	28 (-4-74)	30 (-2-72)	37 (4-72)	41 (10-72)	49 (22-80)	57 (0-96)
	Existing hearing aid users	35 (-4-104)	38 (0-92)	41 (0-92)	49 (4-94)	52 (6-110)	57 (16-120)	65 (22-120)
	Vinay and Moore (2007)	50	55	60	65	65	65	70

Table 4.6. Mean hearing impairment, in dB HL, for participants and ears that did and did not meet the TEN-test criteria for a DR (n=343).

			Frequency (kHz)									
			0.25	0.5	0.75	1	1.5	2	3	4	6	8
Mean hearing thresholds (dB) (Range)	Participants	No DRs	17 (0-88)	18 (-2-94)	22 (-4-78)	27 (-2-84)	35 (2-78)	40 (2-84)	49 (6-90)	56 (16-110)	65 (0-110)	67 (6-100)
		DRs	36 (0-108)	40 (0-104)	41 (0-92)	44 (0-92)	48 (2-94)	50 (6-110)	55 (18-120)	60 (30-120)	74 (28-120)	76 (20-120)
	Ears	No DRs	22 (0-70)	24 (-2-70)	28 (-4-72)	30 (-2-82)	36 (2-72)	40 (2-72)	46 (6-74)	52 (16-86)	62 (0-102)	66 (6-100)
		DRs	30 (0-108)	30 (0-104)	34 (0-92)	40 (0-92)	48 (4-94)	52 (6-110)	62 (30-120)	72 (30-120)	84 (40-120)	86 (20-120)

Table 4.7. Distribution of hearing threshold levels, between -20 and 85 dB HL, for frequencies 0.5 – 4 kHz. The number of ears meeting DR criteria is shown in parenthesis.

Hearing thresholds (dB)	Frequency (kHz)						
	0.5	0.75	1	1.5	2	3	4
5	42	35	27	14	4	1	5
10	89	62	48	35	27	8	6
15	38	36	35	16	15	0	0
20	100	94	67	28	45	24	7
25	52	49	44	48	16	17	9
30	91	91	53	27	34	41	33
35	42	57	90	82	75	29	22
40	42(1)	75(1)	90(1)	107	48	83	74(1)
45	37	44	44	44	86(1)	45(2)	34
50	41	58(1)	72(2)	86(1)	68(2)	95(2)	90
55	26	25	22	42(3)	84(1)	67(2)	70(4)
60	24	28	27(4)	39(2)	43(2)	112(20)	124(18)
65	10	9	21(3)	44(4)	29(3)	41(10)	53(10)
70	17(1)	19	19(2)	25(2)	40(4)	39(10)	59(15)
75	0	7	12(1)	9(1)	7(1)	13(8)	21(8)
80	5(3)	5(2)	3	9(2)	15(2)	22(13)	22(9)
85	1(1)	0	3(1)	3(2)	3(2)	6(4)	5(3)
Total	657(6)	694(4)	677(14)	573(17)	639(18)	643(71)	634(68)

Table 4.8. Gradient of hearing impairment, in dB, in ears that did and did not meet the TEN.

	Slope (dB difference)			
	0.5-1	1-2	2-4	4-8
Ears without DR (n=499)	5	7	12	12
Ears with DR (n=175)	7	13	20	10

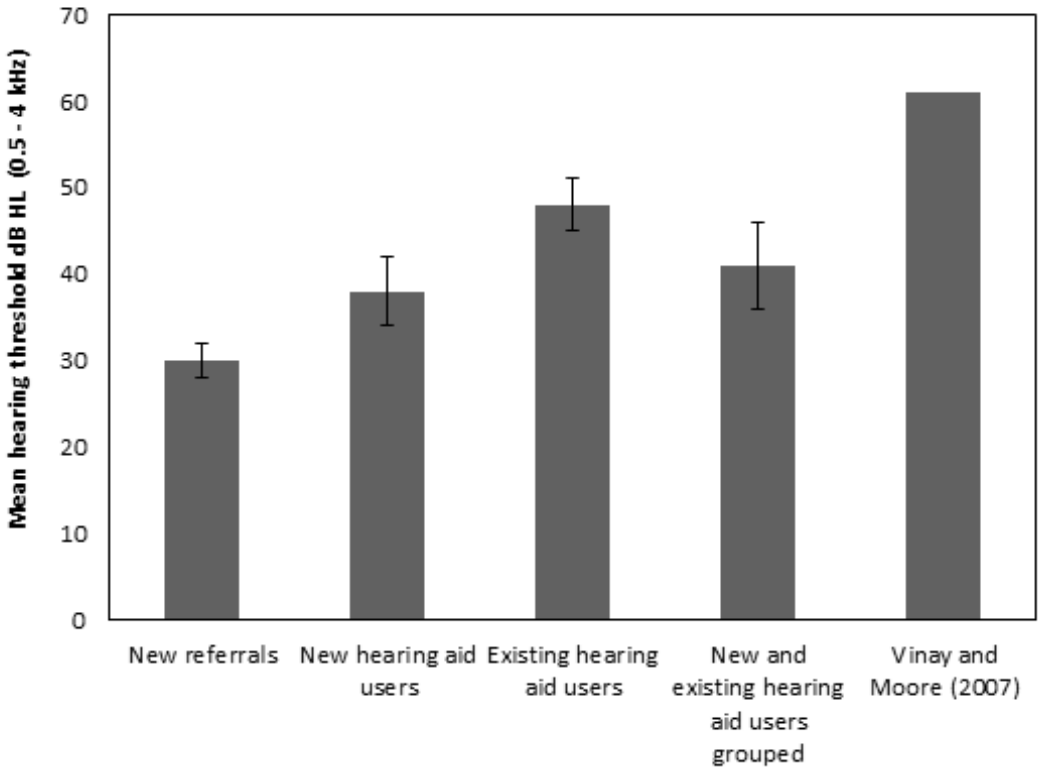

Figure 4.1. Mean hearing impairment (0.5 to 4 kHz,) in dB HL, for all 674 ears compared with Vinay and Moore (2007). Error bars show one standard error.

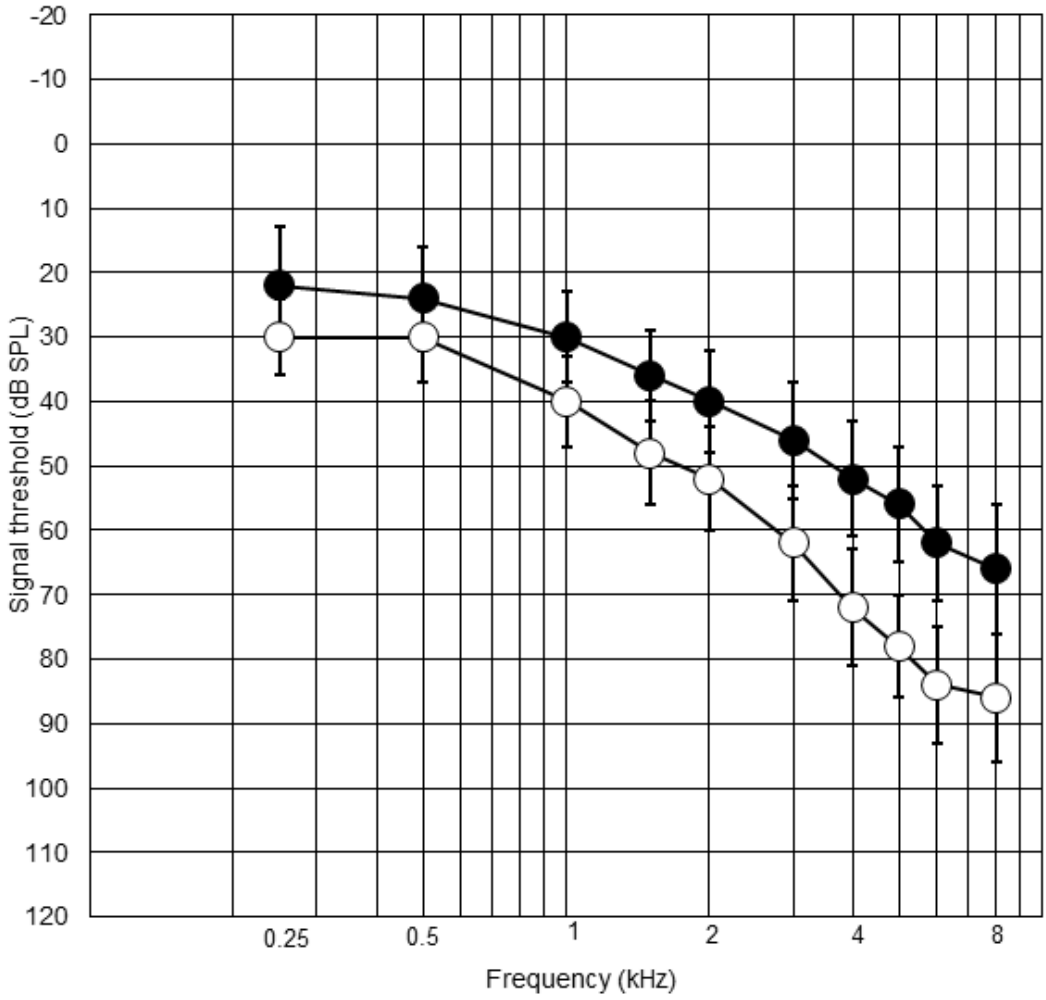

Figure 4.2. Hearing thresholds in ears with (open circles) and without (closed circles) DRs. Bars show ± one standard error.

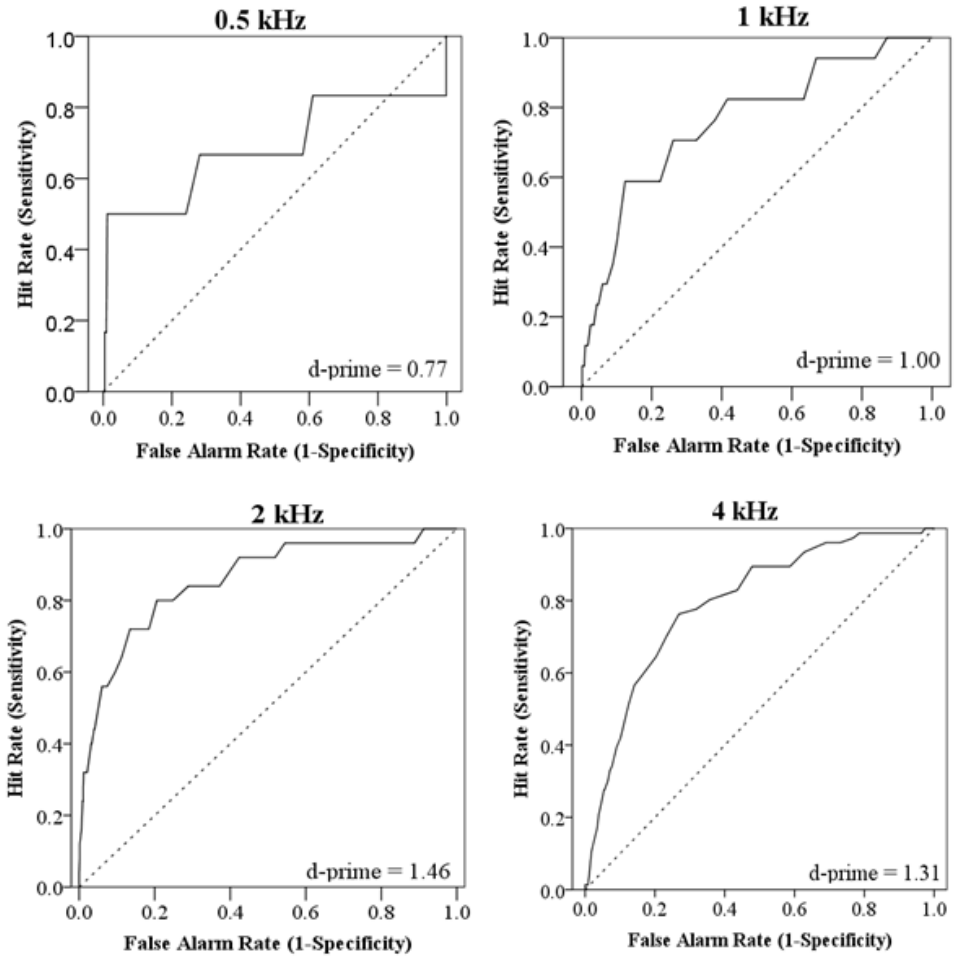

Figure 4.3. ROC curves comparing hearing thresholds with the TEN-test at test frequencies 0.5, 1, 2, and 4 kHz. The hit rate (Sensitivity) is plotted as a function of the false alarm rate (100-Specificity). The solid black line shows false alarm rate versus hit rate in percentages. Each point on the ROC curve represents a sensitivity/specificity pair corresponding to a particular decision threshold. A test with perfect discrimination has a ROC curve that passes through the upper left corner (100% sensitivity, and 100% specificity). Therefore, the closer the ROC curve is to the upper left corner, the higher the overall accuracy of the test (Zweig & Campbell, 1993). The dotted black line indicates 50%. The overall sensitivity and specificity of each test frequency is scored using a d-prime value shown in bottom right hand corner of each graph. The area under each ROC curve was statistically significant (0.69, 0.76, 0.86 and 0.75 for 0.5, 1, 2 and 4 kHz, respectively).

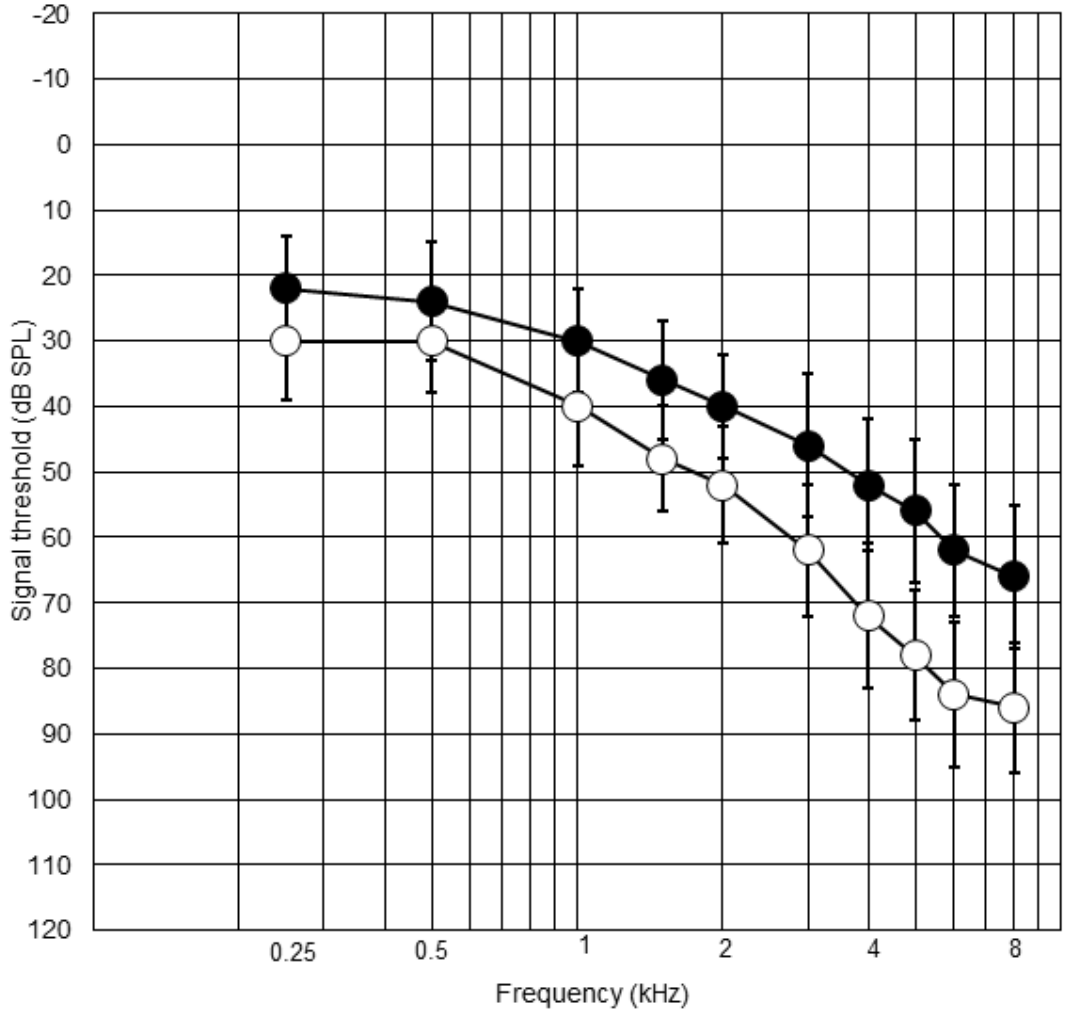

Figure 4.4. Mean hearing thresholds and standard error from frequencies 0.5 to 8 kHz for ears, which met the criteria for a DR at ≥three frequencies, extensive DRs, (closed circles) and ears, which met the criteria at <three frequencies, less extensive DRs, (open circles).

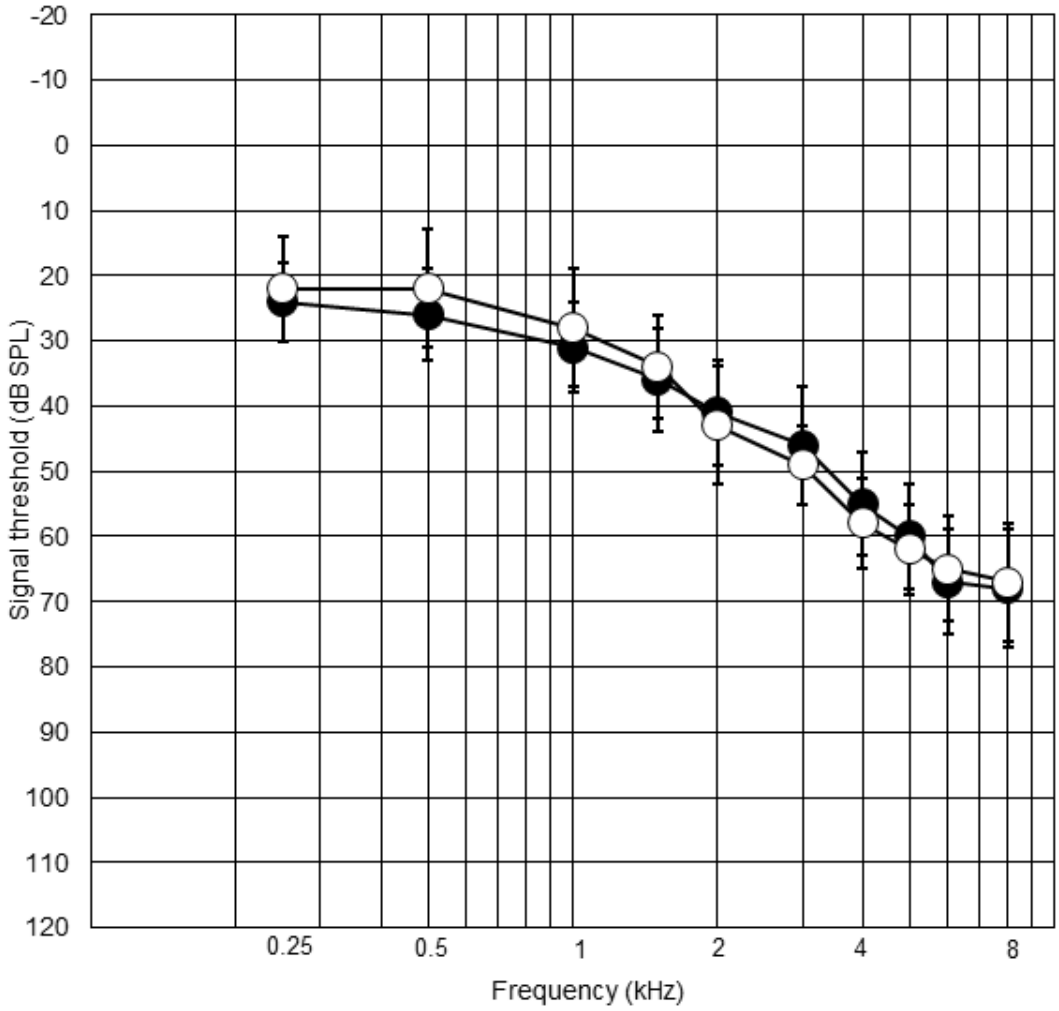

Figure 4.5. Mean hearing impairment and standard error from frequencies 0.5 to 8 kHz, for female (closed circles) and male (open circles) participants.

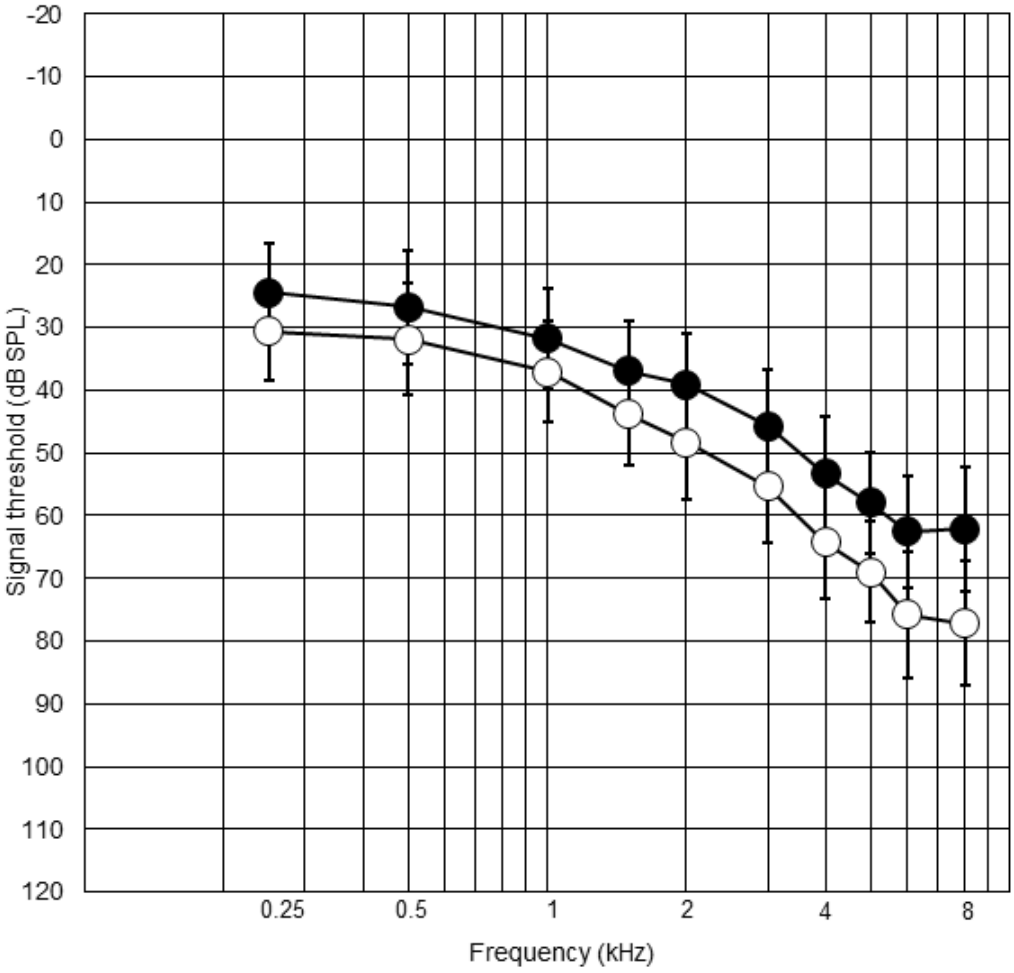

Figure 4.6. Mean hearing impairment and standard error from frequencies 0.5 to 8 kHz, for participants aged ≥73 years (open circles) and aged <73 years (closed circles).

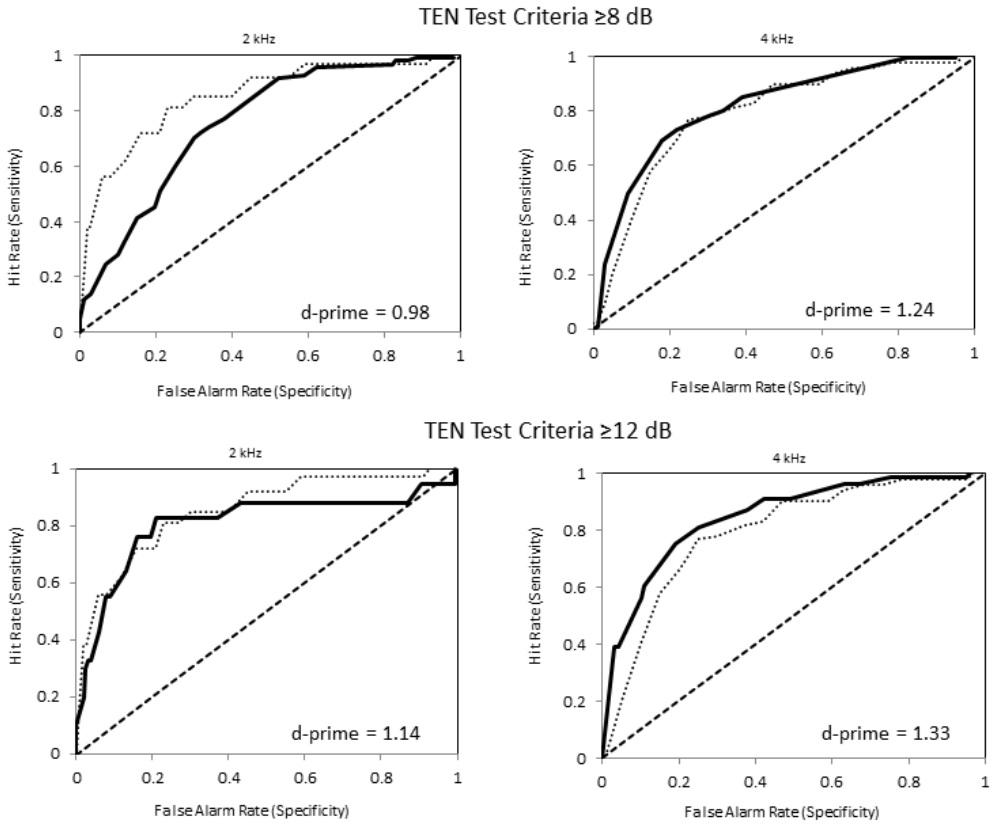

Figure 4.7. ROC curves for test frequencies 2 and 4 kHz using a less conservative TEN-test criteria, masked threshold ≥8 dB (top panels), and a more conservative masked threshold, ≥12 dB above the masker level (bottom panels). The hit rate (Sensitivity) is plotted as a function of the false alarm rate (Specificity). The solid black line shows false alarm rate versus hit rate in percentages. Each point on the ROC curve represents a sensitivity/specificity pair corresponding to a particular decision threshold. A test with perfect discrimination has a ROC curve that passes through the upper left corner (100% sensitivity, and 100% specificity). Therefore, the closer the ROC curve is to the upper left corner, the higher the overall accuracy of the test (Zweig & Campbell, 1993). The grey dotted line indicates the ROC curve for the standard TEN-test criteria of ≥10 dB. The dotted black line indicates 50%. The overall sensitivity and specificity of each test frequency is scored using a d-prime value shown in bottom right hand corner of each graph. The area under each ROC curve was statistically significant for masked threshold ≥12 dB (0.83 and 0.84 for 2 and 4 kHz, respectively).

CHAPTER 5

REPEATABILITY, AGREEMENT AND FEASIBILITY OF USING THE THRESHOLD EQUALISING NOISE TEST AND FAST PSYCHOPHYSICAL TUNING CURVES IN A CLINICAL SETTING

FORMATTED TO THE INTERNATIONAL JOURNAL OF AUDIOLOGY REQUIREMENTS

Repeatability, agreement and feasibility of using the threshold equalising noise test and fast psychophysical tuning curves in a clinical setting

Authors:

Anna Pepler[1], Kevin J Munro[1,2], Kathryn Lewis[3] and Karolina Kluk[1]

[1]School of Psychological Sciences, University of Manchester, UK

[2]Central Manchester University Hospitals NHS Foundation Trust, Manchester

Academic Health Science Centre, Oxford Road, Manchester, UK

[3]University Hospitals South Manchester NHS Foundation Trust, Manchester, UK

Correspondence: Anna Pepler, School of Psychological Sciences, Ellen Wilkinson Building,

University of Manchester, Oxford Road, Manchester, M13 9PL.

Email: apepler@nhs.net

Key words: Cochlear dead regions, threshold equalizing noise test, psychophysical tuning curves, test repeatability, agreement, feasibility.

Abbreviations:

ANOVA Analysis of Variance

DR Cochlear Dead Region

f_e DR edge frequency

IHC Inner Hair Cell

OHC Outer Hair Cell

PTC Psychophysical Tuning Curve

ROC Receiver Operator Characteristic

SL Sensation Level

SPL Sound Pressure Level

TEN Threshold Equalising Noise

Abstract

Objective: To investigate repeatability, agreement and clinical feasibility of the threshold equalising noise (TEN) test and fast psychophysical tuning curve (PTC) measurements to detect off-frequency listening, an indicator of cochlear dead regions (DRs).

Design: The TEN-test was carried out from 0.5 to 4 kHz and fast PTCs were carried out at ≥ 2 frequencies.

Study Sample: The TEN-test was completed on 70 ears whilst fast PTCs were measured on 20 ears.

Results: TEN-test findings were repeatable in terms of meeting the criteria for a DR (97%) and identifying the same edge frequency (f_e) (87%). In all cases, fast PTCs were repeatable in terms of meeting the criteria for a DRs. There was 87% agreement between the two procedures in terms of the presence of off-frequency listening and there was 73% agreement in terms of f_e. Fast PTCs had a 10% lower 'conclusive finding' rate than the TEN-test and the test duration was typically 40 minutes longer.

Conclusions: Both the TEN-test and fast PTCs have high test-retest repeatability. The TEN-test is more clinically feasible due to its shorter test duration and higher interpretation rate, but it may underestimate the extent of a DR because of its inability to precisely identify f_e.

Cochlear dead regions (DRs) are defined as areas in the cochlea where inner hair cells (IHCs) and/or neurones are functioning so poorly that a sound falling within that region is more efficiently detected via off-frequency listening (Moore et al. 2004; Vestergaard, 2003). Off-frequency listening results in a tone being detected away from the region of peak basilar-membrane vibration. DRs are common, with 36% (95% Confidence Interval: 31-41), 31% (95% CI: 26-36) and 59% (95% CI: 47-71) of adults with sensorineural hearing impairment identified as having a DR in the United Kingdom, United States and India, respectively (Pepler et al. 2014; Cox et al. 2011; Vinay & Moore 2007). There is no consensus as to the effects of DRs on speech perception and hearing aid fitting: some studies have suggested that listeners with DRs may benefit from changes to their hearing aid settings (Vickers et al. 2001; Baer et al. 2002); whilst other studies have not (Mackersie et al. 2004; Preminger et al. 2005; Cox et al. 2011, 2012). Vickers et al. (2001) and Baer et al. (2002) showed that some patients with extensive and contiguous DRs benefit from reduced amplification at frequencies within the DR. Mackersie et al. (2004), Preminger et al. (2005) and Cox et al. (2011, 2012) did not show this detrimental effect although their participants had less extensive DRs. A likely explanation for this conflict is the difference in the extent and continuity of DRs in these studies. This emphasises the importance of detecting the extent of DRs accurately in order to investigate if, and when, it is necessary to modify the amplification.

Masking techniques such as psychophysical tuning curves (PTCs) and the threshold equalising noise (TEN) test have been used successfully in the research environment to detect DRs in adults and children (Summers et al. 2003; Malicka 2009, 2010; Sek et al. 2005, Sek & Moore 2011; Warnaar & Dreschler 2012). However, there are no published reports of these techniques having been used to detect DRs in a large number of patients in the clinical environment. The purpose of the present study was to

investigate the repeatability, agreement and feasibility of the TEN-test and fast PTCs to detect DRs in a clinical setting.

PTCs provide a measure of frequency selectivity, which is the ability of the auditory system to separate two sounds that are presented simultaneously (Zwicker & Schorn 1978). The tip of the PTC occurs close to the signal frequency in listeners with normally functioning IHCs/neurones, even in the presence of reduced outer hair cell (OHC) function (Kluk & Moore 2004; Moore & Alcantara 2001; Moore 2001, 2002, 2004). In listeners where the signal frequency is presented in the DR, the PTC tip is shifted away from the signal frequency and the tip indicates the f_e of the DR (Kluk & Moore 2005). As conventional PTC measurements are very time consuming, they are unlikely to be feasible for clinical use. Therefore, Sek et al. (2005) developed an automated fast method for measuring PTCs. A fixed signal is presented simultaneously (and to the same ear) as a narrowband masker, which sweeps across the required frequency range. The listener then has to respond, by pressing the spacebar on the keyboard, whenever they hear the signal. Using this technique, Sek and Moore (2011) have suggested, from a small sample of ears, that a tip shift of ≥10 % from the signal frequency is indicative of a DR, although test parameters will affect the tip position.

The threshold equalising noise (TEN) test was developed with the aim of being a more efficient method of detecting DRs than PTCs (Moore et al. 2000). The test involves the use of spectrally-shaped broadband noise to detect the presence of off-frequency listening. Pure tones are detected in the presence of ipsilateral TEN. Masked thresholds can be measured at half octave intervals over the 0.25-8 kHz range using the original version calibrated in sound pressure level (SPL) (Moore et al. 2000), or over a narrower frequency range of 0.5-4 kHz using a version calibrated in hearing level (HL) (Moore et al. 2004). The TEN(HL) test is more commonly used as the reduced TEN bandwidth and low crest factor of the test allow the noise to be presented at higher

levels without loudness discomfort (Moore et al. 2004; Vinay & Moore 2007; Cox et al. 2011). This allows DR detection in patients with greater degrees of hearing impairment. Moore et al. (2000) evaluated the criteria for diagnosing DRs using the TEN(SPL) test and suggested if the masked threshold in the TEN is ≥10 dB above the level of the TEN and the TEN is at or above the absolute threshold, a DR is indicated. These criteria also apply to the TEN(HL) test, referred to the TEN-test from now on (Moore et al. 2004).

One characteristic of a good clinical test is that it should be accurate. Despite its lengthy test duration, the PTC is the closest we have to a 'gold standard' test for the presence of a DR (Sek & Moore 2011). Therefore, if the TEN-test is to be used to detect DRs, it is essential that the findings agree with PTCs. Comparisons of results from these two techniques are limited and there are mixed findings. Moore et al. (2000) reported agreement between the TEN-test and conventional PTCs for 17 of 20 adult ears with hearing impairment. For the three ears where results did not agree, the TEN-test showed an elevated masked threshold, but the PTC tip was not shifted. Summers et al. (2003) compared the findings from 18 hearing-impaired ears and reported agreement for 10 ears. Again, in cases where the results did not agree, the TEN-test indicated a DR whilst conventional PTC measurements did not. Summers et al. (2003) reported that the agreement between the two tests improved to 16 of 18 ears when a stricter TEN masked threshold criterion of 14 dB above the TEN level was used. One explanation for poorer agreement could be the use of a masker with a bandwidth of 0.10 kHz, which results in beats becoming audible, resulting in the detection of combination tones, creating a 'W-shaped' PTC (Moore 2004; Kluk & Moore 2005). Kluk and Moore (2006b) completed fast PTC measurements using a narrowband masker which was approximately equal to the bandwidth of the "normal" auditory filter (Glasberg & Moore, 1986). They found an agreement of 93% between the fast PTC and TEN-test in terms of DR presence. However, fast PTCs typically indicated the f_e to be lower than that detected by the TEN-

test. Warnaar and Dreschler (2012) compared fast PTCs and TEN-test results for 10 ears of hearing-impaired adults. They used the TEN-test DR criteria proposed by Moore et al. (2004) and ≥20% of PTC tip shift as indicators of a DR. Using these criteria, the tests agreed in 80% of cases. Agreement between tests increased when using a tip shift of ≥20 % on fast PTCs and +8 dB masked threshold on the TEN-test. Only four of the 10 ears were identified as having a DR so this study provided limited data for ears with DRs. The findings from each of these studies differ substantially depending on the test set-up and DR criteria used. There is an urgent clinical need for further comparisons of these tests, using a larger number of ears in a clinical setting.

A second aspect of a good clinical test is high repeatability. TEN-test-retest agreement was measured for 40 adult listeners and 35 had the same result on each test (Cairns et al. 2007). Munro et al. (2005) reported TEN-test repeatability for teenagers with longstanding hearing impairment. After an interval of 12 months, 26 of the 27 ears (that provided a conclusive finding on both test sessions) had the same interpretation. Malicka et al. (2009) measured fast PTCs on two separate occasions for five normally-hearing adults. The mean difference in tip frequency between the two measurements was 0.055 kHz and 0.186 kHz for signal frequencies of 1 and 4 kHz, respectively. No studies have investigated test-retest findings in a large clinical dataset.

It is possible that a test may be repeatable and reliable but it may not be feasible to use in a clinical setting. Previous studies have suggested that the complexity and duration of the fast PTC task means that it cannot be successfully completed by some patients (Sek & Moore 2011). Malicka et al. (2009) recorded the number of fast PTCs which resulted in a conclusive finding (interpretation rate) for 12 normally-hearing 7–10 year old children. 87% of fast PTCs produced resulted in a conclusive finding. No study has investigated the interpretation rate for hearing-impaired adults in

a clinical setting. There is a research and clinical need to compare the TEN-test and fast PTCs in terms of interpretation rate and test duration.

In summary, there is a significant gap in knowledge concerning test repeatability, agreement and clinical feasibility of the TEN-test and fast PTCs. The aim of the present study was to address this need in a large clinical study of hearing-impaired adults with and without DRs.

Method

Participants and tests conducted

This study was approved by the Greater Manchester-North ethics committee (reference number 10/H1011/62) and informed written consent was obtained from participants.

In total, 47 adult hearing aid users (76 ears) were recruited from the U.K. National Health Service audiology department at Withington Community Hospital, Manchester. The median participant age was 75 years (range 54-94). There were 35 men and 12 women. Both ears of 29 adults (58 ears) and one ear of 18 adults were tested for DRs. Reasons for testing only one ear were time constraints (13 ears), unilateral conductive hearing impairments (two ears), profound hearing-impairment (two ears) and normal hearing (one ear). Pure-tone audiometry (at 0.25, 0.5, 0.75, 1, 1.5, 2, 3, 4, 6, and 8 kHz) was completed in accordance with the British Society of Audiology recommended procedure (BSA 2011). Mean and standard deviation of hearing thresholds are presented in Figure 5.1. All testing was completed in a sound-treated booth that met the ANSI S3.1-1999 standard, using a Siemens Unity 2 audiometer and TDH-39 headphones. Bone conduction testing was completed at 0.5, 1, 2 and 4 kHz using a RadioEar B-71 vibrator.

Insert Figure 5.1 about here

The TEN-test was completed using the TEN (HL) version to keep inconclusive results and loudness discomfort to a minimum (Moore et al. 2004). Pure tones and TEN were presented via a CD player (Marantz 5000) through channels 1 and 2 of a Siemens 2 Unity audiometer. The test was conducted at 0.5, 0.75, 1, 1.5, 2, 3, and 4 kHz. Calibration was performed before and after each test session in accordance with Moore et al. (2004).

Fast PTCs were measured using software, Sweeping PTC (SWPTC), developed by Sek and Moore (2011). The software, available online at hearing.psychol.cam.ac.uk, was equipped with a 16-bit sound card (Creative Professional E-MU 0202 USB). The signal and masker were presented simultaneously with levels controlled using the computer and presented through Sennheiser HD600 headphones. Calibration of the stimuli was completed at the start and end of the study using the procedure recommended by Sek and Moore (2011).

Procedure

The pure tone signal and TEN were routed from the TEN CD via a Marantz CD 5000 player through channel 1 and 2 of a Siemens Unity 2 audiometer. The test was conducted at 0.5, 0.75, 1, 1.5, 2, 3, and 4 kHz. TEN uncomfortable loudness levels (ULLs) were identified using the British Society of Audiology ULL methodology (BSA 2011). The TEN level varied depending on the hearing threshold but was presented at least 10 dB above the hearing threshold and at least 2 dB below the participant's TEN (ULL). In most cases, the TEN level was kept the same across the frequency range; however, to increase participant comfort, it was reduced further when the hearing loss at the test frequency was mild. The same TEN level was used for test and retest. The

signal (test tone), presented to the same ear as the TEN, was adjusted in ascending and descending steps of 4 dB and 8 dB, respectively in order to determine lowest level that the participant responded >50% of presentations. A step size of 2 dB was used until the same threshold was obtained in more than 50% of responses; this was taken as the final threshold. Participants were instructed to respond, by pressing a button, when the signal was audible in the presence of the TEN. The masked thresholds were used to classify frequencies and ears with and without DRs, according to the criteria recommended by Moore et al. (2000). The TEN-test was applied on two occasions with an interval between tests of one to four weeks.

Fast PTCs were measured during the second test session with test parameters based on those suggested by Sek et al. (2005), Sek and Moore (2011) and Kluk and Moore (2005). The signal duration was 0.2 s with an interval of 0.2 s between pulses. The masker bandwidth for signal frequencies <1.6 kHz was 20% of the signal frequency. For signal frequencies ≥1.6 kHz, a masker bandwidth of 0.32 kHz was used. A masker step size of 1 dB/s was used. Although previous studies have suggested fast PTCs can be obtained using a rate of change of level of 2 dB/s (Sek & Moore 2011) a pilot study, in a group similar in demographics to the study participants, indicated a smaller step size of 1 dB/s more frequently provided PTCs with interpretable results. An ascending and descending sweep was used for each signal frequency. The masker frequency swept from at least one octave below the signal frequency to at least one octave above it, and vice-versa. For ears with DRs, the frequency range was often increased due to broadened PTCs. The test duration was between 3 and 8 minutes. A longer test time was used when participants had slow response times to ensure an increase in the number of reversals. In these cases the test duration was extended to increase the number of reversals recorded. The initial masker level was set at 40 dB SPL for mild hearing impairments and 50 dB SPL for moderate and severe hearing

impairments. The signal threshold was determined using the threshold measurement tab in the SWPTC software. Absolute hearing threshold was measured using a two alternative forced choice task. The signal level was set at 10 dB SL, although in cases where ineffective masking occurred, the level was reduced to 4 dB SL. Sek and Moore (2011) suggested a low-level low-pass noise be used to mask combination tones when hearing thresholds were better than 40 dB SPL at frequencies ≤1 kHz. The low-level noise was presented at 40 dB below the signal level at least one octave below the signal frequency using cut-off frequencies of 0.25, 0.5, 0.75, or 1 kHz.

The four-point moving average tip identification method, provided on the SWPTC software, was used. A pilot study indicated that this method provided an interpretable result in more cases than the other methods. Additionally, this method gave a tip estimate that was not statistically significantly different from the four other methods provided by the SWPTC software. When the fast PTC tip could not be interpreted, the measurement was repeated using different test parameters, e.g. if only a few reversals were recorded, the test time was increased or if the tip appeared to be missed the masker frequency range was adjusted accordingly.

The DR criterion used in the present study, based on repeatability measures reported by Sek et al. (2005), Malicka et al. (2009) and Warnaar and Dreschler (2012), was that the frequency difference between the signal and tip should be ≥10% of the signal frequency. Measurements were obtained using one signal frequency outside the DR and at least two signal frequencies inside the DR, based on initial TEN-test findings. For ears where no DR was indicated, fast PTCs were measured using one or two signal frequencies. The amount of testing depended on participant availability. To assess test-retest reliability, 10 ears with and 10 ears without DRs were tested for DRs at two frequencies using fast PTC measurement on two separate occasions. Fast PTC tip estimation was based on the mean of an ascending and descending masker sweep.

Participants were instructed to press the space bar on the keyboard when the signal was audible and to release it when the signal was inaudible. Pressing the space bar increased the masker level by 1 dB/s, depending on the chosen setting.

The number of conclusive results (i.e., the test interpretation rate) was recorded by identifying whether the measurement could be used to identify a DR. For the TEN-test, this required a masked threshold and for fast PTCs a well-defined tip. Test time was recorded in minutes, for each ear, using a digital timer that was started when the test instructions began and stopped when the last measurement was obtained. All patients took between 10 and 15 minutes break during fast PTC testing. The timer was not stopped for patient breaks as a realistic idea of the clinical time required for test completion was of interest.

Analysis

All data in this study were analysed using SPSS, version 19. Data were checked to confirm that it was appropriate to use parametric statistics. All data were summarized using mean, median, standard deviation and range. The conventional 5% significance level was used throughout. Test repeatability was analysed using Bland-Altman (1986) plots of data comparison and coefficient of repeatability which is the standard deviation of the differences between two tests multiplied by 1.96. Test agreement was analysed using Bland-Altman plots and Receiver Operator Characteristic (ROC) curves. True positive rates were calculated by dividing total true positives by the sum of true positives and false negative. True negative rates were calculated by dividing total true negatives by the sum of true negatives and false positives. Test feasibility was assessed by comparing test time (recorded, in minutes, on a digital stop watch) and test interpretation rates using *t-test* analyses and Pearson's correlation coefficient. Repeated measures analyses of variance, were used to analyse the interactions of patient-specific

factors such as age with interpretation rate. Where Mauchly's test of normality was significant, Greenhouse-Geisser correction was used.

Results

Test Repeatability

For the TEN-test, 43 (57%) ears met the criteria for a DR. The TEN-test was repeated using 70 ears. Sixty-eight (97%) ears had the same diagnostic outcome on retest. The two ears that had differing results both indicated a DR at 4 kHz on the retest session. Sixty-one (87%) ears met the criteria for a DR at the same test frequencies on both test sessions. Frequency-specific TEN-test results for the nine ears that had a different f_e on retest are shown in Table 5.1. The value of f_e differed by one half-octave for eight ears and one octave for one ear. Of these nine ears, five had mid-frequency DRs with an edge at a low and high frequencies and four had high-frequency DRs. Of the 10 masked thresholds that differed on retest, 6 and 2 changed by only 2 dB or 4 dB, respectively.

Insert Table 5.1. about here

Fast PTCs were measured for 76 ears, of which 49 (64%) showed a DR. For one ear, the tip frequency could not be estimated and was therefore excluded from further fast PTC analysis. For the 20 ears for which fast PTC measurements were repeated, all gave the same result on the two sessions, regarding the presence/absence of a DR. Data for f_e was used to derive a Bland-Altman plot (Bland & Altman 1986). This compares the mean f_e with the difference between the f_e values obtained on the test and retest sessions which gives an indicator of agreement between two test sessions. Figure

5.2 shows that the maximum variability was <0.4 kHz for all signal frequencies. The repeatability differs according to the signal frequency. The variability at 0.5 kHz was less than 0.1 kHz, whilst at 4 kHz the repeatability was less than 0.4 kHz.

Insert Figure 5.2. about here

In order to consider the test-retest variability of fast PTC measurements in more detail, a coefficient of repeatability was calculated for each signal frequency and is presented in Table 5.2. The coefficient of repeatability represents the value below which the absolute difference between two tests may be expected to lie with a probability of 95%. Coefficients of repeatability ranged from 0.075 to 0.373, indicating a maximum test-retest difference in tip frequency of 373 Hz. In order to account for differences across frequencies, the coefficient of repeatability was converted in to percentages of the signal frequency. The coefficients of repeatability were divided by the signal frequency. All coefficients of repeatability were ≤15% of the test frequency. Therefore, a tip shift of >15% is likely to be a result of more than test-retest variability. All signal frequencies ≥ 2 kHz had a repeatability coefficient <10%.

Insert Table 5.2 about here

Test Agreement

Dead region classification

The TEN-test and fast PTC results agreed that a DR was present in 65 of 75 (87%) ears. For all ten ears where the tests did not agree, the fast PTCs always met the criteria for a high-frequency DR, whereas the TEN-test results did not.

Dead region estimated f_e

The two tests agreed on the value of f_e for 55 (73%) ears. Of the 20 ears where there was disagreement, 14 DRs were more extensive and three less extensive for fast PTCs. The remaining three ears had an island DR with a high and low f_e and the TEN-test and fast PTCs did not agree for at least one f_e. Figure 5.3.shows a Bland-Altman plot which compares the f_e values estimated using the two tests. The results showed a spread in values suggesting considerable variability. The mean f_e estimated from fast PTCs, was 0.640 kHz lower than estimated from the TEN-test.

Insert Figure 5.3. about here

TEN-test specificity and sensitivity were calculated using the findings from the fast PTCs as the gold standard. Outcomes are presented in Table 5.3. This shows that the true positive rate, and the true negative rate, were 85% and 78%, respectively. The ROC in Figure 4 shows these results in more detail and confirms that the TEN-test is not an entirely sensitive and specific method of detecting DRs (assuming fast PTC measurements as a gold standard) with the best scenario as a 92% hit rate and 35% false alarm rate. Ideally the hit rate would be closer to 100% whilst maintaining a low false alarm rate.

Insert Table 5.3 about here

Insert Figure 5.4 about here

Diagnostic criteria for a dead region

The agreement between the two tests was investigated by adjusting the diagnostic criteria for each technique. Table 5.4 shows the agreement for three different criteria on fast PTC measurements: >10%, >15% and >20% of the signal frequency shift in PTC tip. The criteria used for the TEN-test were 8 dB, 10 dB and 12 dB. The agreement is presented as a percentage for both DR occurrence and f_e (in parentheses). The optimum agreement between tests (87% for occurrence, 73% for f_e) occurred with a TEN-test criterion of 10 dB and a fast PTC criterion of >10%.

Insert Table 5.4 about here

Test Feasibility

Interpretation rate

The TEN-test results could be interpreted in all 76 (100%) ears. Fast PTCs could be interpreted in all but one ear (99%). In terms of individual PTC measurements, it was possible to estimate a tip in 215 (80%) of fast PTCs measurements. Of the 55 fast PTCs which were not interpretable, 49 had too few reversals, whilst 6 were W-shaped. The fast PTC test was repeated if the initial measurement could not be interpreted. For 43 (88%) cases, it was possible to estimate the tip.

To consider factors that affect fast PTC interpretation rate, a regression analysis was completed. Fast PTCs were separated in to those that did and those that did not have tip estimates. Participant age, sex and mean hearing impairment (0.5, 1, 2, and 4 kHz) were included as independent variables. The three independent variables in combination were found to be significant predictors of interpretation rate (F[3,1563]=4.3; p = 0.004). Age was significantly correlated with interpretation rate,

(t = 2.2; p = 0.03). Sex and hearing impairment were not significantly correlated with interpretation rate, (t = 0.69; p = 0.50) and (t = 0.77; p = 0.44), respectively. This suggests that age was a significant predictor of interpretation rate.

Test time

The time to complete each test is shown in Table 5.5. The mean time to complete the TEN-test and fast PTCs for each ear was 12 and 56 minutes, respectively, and this difference was statistically significant [t = 24.8, p <0.001]. There was no statistically significant difference [t = 0.045, p = 0.964] in TEN-test time for ears with and without DRs. Fast PTC measurements took on average, 13 minutes longer to complete in ears with DRs and this difference was statistically significant [t = 4.6, p <0.001].

Insert Table 5.5. about here

Discussion

Test Repeatability

TEN-test

The TEN-test diagnostic classification was repeatable in 97% of cases. This finding shows that the TEN-test has good repeatability. In the two cases of disagreement, the test did not meet the criteria on the first test and just met the DR criteria (+10 dB masked threshold) at 4 kHz on the retest. This is consistent with a newly acquired DR since the first test; however, in both of these cases the TEN-test was carried out a third time and did not show a DR. This finding agrees with Cairns et al. (2007) who also reported that changes in diagnoses were most common when the

criteria for a DR were only just met at one or two isolated frequencies. Cairns et al. (2007) suggested that clinicians should repeat the TEN-test in cases where the criteria were only just met. The repeatability of the TEN-test in estimating f_e was 87%. For eight of the nine ears with a different f_e on retest, the difference was only one step in the available test frequencies i.e. one half-octave. In all of these cases, the results only just met the criteria for a DR on one test and not at all on the other test. Five of the nine ears with different f_e had mid-frequency DRs spanning no more than one octave, with an upper and lower f_e. This indicates that the TEN-test has good test retest repeatability in identifying the f_e as long as f_e is not located in the mid frequencies.

Fast PTCs

When using fast PTCs, DR classification was the same on test and retest for all ears. However, there was some variation in the estimated tip frequency between test and retest. Repeatability coefficients indicated that any tip shift >15% of the signal frequency is unlikely to result from test-retest variability. The repeatability coefficients did differ according to the signal frequency. The repeatability data agree with previous findings of Malicka et al. (2009), who reported a repeatability coefficient of ≤15% at 1, 2, and 4 kHz. In addition, a model created by Warnaar and Dreschler (2013) to predict PTC shift patterns suggests that a tip shift of ≤ 15% of the signal frequency may well be associated with OHC dysfunction.

Agreement across tests

There was good agreement between the two tests in terms of meeting the criteria for a DR. The 13% disagreement was due to fast PTCs meeting the criteria for a high-frequency DR, whilst the TEN-test did not. This suggests that fast PTCs are less likely to miss a DR although some of these findings may be false positives.

There was agreement between the two tests of 73% in terms of f_e. Of those cases that disagreed, 67% of fast PTCs indicated a DR f_e lower than the TEN-test and in 15% the TEN-test indicated an f_e lower than fast PTC. For the other 15%, test disagreement was associated with mid-frequency DRs which included two values of f_e. The value of f_e of a DR was typically 0.640 kHz lower when estimated using fast PTCs. Kluk and Moore (2005) also reported that the TEN-test is less likely to indicate a DR when the signal frequency is close to the f_e. In addition, the TEN-test, in its present format, can only be used at half-octave intervals. Therefore, the TEN-test will not be able to locate the f_e as accurately as fast PTCs. The implication of this is that the TEN-test may underestimate the extent of a DR. It would be possible to avoid this limitation by modifying the TEN-test to test to use smaller frequency intervals.

For three ears, the TEN-test classified a DR as present at frequencies where fast PTCs did not. Previously, Moore et al. (2004) has suggested the TEN-test may result in false positives if masking is ineffective. Therefore, the three false-positive results may have resulted from significant OHC loss resulting in a very broad auditory filter and increasing the masked threshold. To enable a better indicator of f_e, the use of fast PTCs would be advantageous.

The best agreement between the two tests was when the DR classification was based on a masked threshold being 10 dB or more above the TEN level for the TEN-test and a tip frequency 10% or more from the signal frequency for fast PTCs. These criteria do not agree with the data from the repeatability coefficients for fast PTCs, which suggested that test-retest variability may result in a tip shift of up to 15% of the signal frequency. However, agreement between the TEN-test and fast PTCs was not affected by changing the fast PTC DR criterion, as shown in Table 5.4. The 10% criterion will give higher sensitivity while the 15% criterion will provide higher specificity.

Using fast PTCs as the 'gold standard' measurement of DRs, TEN-test sensitivity and specificity were 85% and 78%, respectively. Assuming a DR prevalence of 36%, (see Pepler et al. 2014) for every 100 patients who are assessed, 17 will be classified incorrectly: five (1 in 7) patients with a DR will be missed and 14 (1 in 3) patients will be incorrectly diagnosed as having a DR. One way to address the high false positive rate is to carry out a fast PTC measurement on all those who are classified as having a DR on the TEN-test.

Test Feasibility

Interpretation Rate

All listeners were able to complete fast PTCs but the result could only be interpreted in 89% of cases. The main difficulty with interpretation was the lack of reversals. Age was found to be a significant predictor of successful tip estimation. This means that test interpretation is likely to be more difficult with older participants. As a large proportion of patients in audiology clinics are elderly, the fast PTC interpretation rate may be low in audiology clinics. It is possible that test interpretation could be improved with a different choice of test parameters. For example, the test speed or rate of masker change could be reduced to help the patient attend to the signal. Although the TEN-test does have pitfalls (Moore et al. 2000; Summers et al. 2003; Moore et al. 2004; Vinay & Moore 2007; Pepler et al. 2014) there are fewer test parameters that require adjusting. This makes the TEN-test more 'clinician friendly' and less likely to be used inappropriately.

As the time and concentration of elderly listeners are limited in audiology clinics, test duration is an important factor when deciding whether to implement a new test. The results from the present study revealed that the mean test duration of fast PTCs

was five times longer than for the TEN-test. This is a significant limitation of using fast PTCs. In particular, ears which were identified to have a DR on the TEN-test required more fast PTC measurements to establish f_e and this increases the test time further. These results suggest that greater knowledge about the importance of identifying the f_e is needed. This will allow clinicians to determine whether it is justifiable to use fast PTCs to determine f_e.

Summary and conclusions

Both the TEN-test and fast PTCs showed good test-retest reliability. The best agreement between the two procedures was obtained with the following criteria: a >10% tip shift on fast PTCs and 10 dB or more difference between the TEN level and masked threshold on the TEN-test. Fast PTCs require a longer test time than the TEN-test and cannot always be interpreted. This makes them less suitable for use in the audiology clinic.

Acknowledgements

This paper presents independent research funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-0408-15055) and facilitated by the Manchester Biomedical Research Centre and the Greater Manchester Comprehensive Clinical Research Network. The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health.

Declaration of interest: The authors report no declarations of interest.

References

ANSI S3.1-1999. Maximum permissible ambient noise levels for audiometric test rooms.

Baer, T., Moore, B.C.J. & Kluk, K. 2002. Effects of low pass filtering on the intelligibility of speech in noise for people with and without DRs at high frequencies. *J Acoust Soc Am*, 112, 1133-44.

Bland, J.M., & Altman, D.G. 1986. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet, 1*,307-10.

British Society of Audiology (BSA). 2011. Recommended procedure: Pure tone air and bone conduction threshold audiometry with and without masking and determination of uncomfortable loudness levels.

Cairns, S., Frith, R., Munro, K.J. & Moore, B.C.J. 2007. Repeatability of the TEN(HL) test for detecting cochlear DRs. *Int J Audiol*, 46, 575-84.

Cox, R.M., Alexander, G.C., Johnson. & J. Rivera, I. 2011. Cochlear dead regions in typical hearing aid candidates: Prevalence and implications for use of high-frequency speech cues. *Ear Hear*, 32, 339-348.

Cox, R.M., Alexander, G.C., Johnson. & J. Rivera, I. 2012. Implication of high-frequency cochlear dead regions for fitting hearing aids to adults with mild to moderately severe hearing loss. *Ear Hear,* 33, 573-87.

Glasberg, B.R. & Moore, B.C.J. 1986. Auditory filter shapes in subjects with unilateral and bilateral cochlear impairments. *J Acoust Soc Am*, 79, 1020-1033.

Kluk, K. & Moore, B.C.J. 2004. Factors affecting psychophysical tuning curves for normally hearing subjects. *Hear Res,* 194, 118-134.

Kluk, K. & Moore, B.C.J. 2005. Factors affecting psychophysical tuning curves for hearing impaired subjects with high-frequency DRs. *Hear Res,* 200, 115-31.

Kluk, K., Moore, B.C.J. (2006b). Detecting dead regions using psychophysical tuning curves: a comparison of simultaneous and forward masking. Int J Audiol, 45, 463-76.

Mackersie, C.L., Crocker, T.L. & Davis, R.A. 2004. Limiting high-frequency hearing aid gain in listeners with and without suspected cochlear DRs. *J Am Acad Audiol*, 15, 498-507.

Malicka, A.N., Munro, K.J. & Baker, R.J. 2009. Fast method for psychophysical tuning curve measurement in school-age children. *Int J Audiol*, 48, 546-53.

Malicka, A.N., Munro, K.J. & Baker, R.J. 2010. Diagnosing cochlear dead regions in children. *Ear Hear*, 31, 238-46.

Moore, B.C.J. & Alcantara, J.I. 2001. The use of psychophysical tuning curves to explore dead regions in the cochlea. *Ear Hear,* 22, 268-78.

Moore, B.C.J., Huss, M., Vickers, D.A., Glasberg, B.R. & Alcantara, J.I. 2000. A test for the diagnosis of dead regions in the cochlea. *Br J Audiol*, 34, 205-24.

Moore, B.C.J., Glasberg, B.R. & Stone, M.A. 2004. New version of the TEN-test with calibrations in dB HL. *Ear Hear,* 25, 478-87.

Moore, B.C.J. 2001. Dead regions in the cochlea: Diagnosis, perceptual consequences, and implications for the fitting of hearing aids. *Trends Amplif.* 5, 1-34.

Moore, B.C.J. 2002. Psychoacoustics of normal and impaired hearing. *British Medical Bulletin*, 63, 121-34.

Moore, B.C.J. 2004. DRs in the cochlea: conceptual foundations, diagnosis, and clinical applications. *Ear Hear* 25, 98-116.

Munro, K.J., Felthouse, C. & Moore, B.C.J. 2005. Reassessment of cochlear dead region in hearing-impaired teenagers with severe-to-profound hearing loss. *Int J Audiol,* 44, 8, 470-477.

Pepler, A., Munro, K.J., Lewis, K. & Kluk, K. 2014. Prevalence of new referrals and existing hearing aid users. *Ear Hear,* 35, 289-386.

Preminger, J.E., Carpenter, R., & Ziegler, C.H. 2005. A clinical perspective on cochlear dead regions: intelligibility of speech and subjective hearing aid benefit. *J Am Acad Audiol* 16, 600-613.

Sek, A., Alcantara, J., Moore, B.C.J., Kluk, K. & Wicher, A. 2005. Development of a fast method for determining psychophysical tuning curves. *Int J Audiol,* 44, 408-20.

Sek, A., & Moore, B.C.J. 2011. Implementation of a fast method for measuring psychophysical tuning curves. *Int J Audiol,* 50, 237-42.

Summers, V., Molis, M.R., Musch, H., Walden, B.E., Surr, R.K., et al. 2003. Identifying dead regions in the cochlea: psychophysical tuning curves and tone detection in threshold-equalising noise. *Ear Hear,* 24, 133-142.

Vickers, D.A., Moore, B.C.J., & Baer, T. 2001. Effects of low-pass filtering on the intelligibility of speech in quiet for people with and without dead regions at high frequencies. *J Acoust Soc Am*, 110, 1164-75.

Vestergaard, M.D. 2003. Dead regions in the cochlea: implications for speech recognition and applicability of articulation index theory. *Int J Audiol*, 42, 249-61.

Vinay, Moore, B.C.J. 2007. Prevalence of dead regions in subjects with sensorineural hearing loss. *Ear Hear*, 28, 231-41.

Warnaar, B., & Dreschler, W. 2012. Agreement between psychophysical tuning curves and the threshold equalising noise test in dead region identification. *Int J Audiol*, 51, 456-64.

Warnaar, B., & Dreschler, W. 2013. Simulating psychophysical tuning curves in listeners with dead regions. *Int J Audiol*, 52, 533-544.

Zwicker, E., & Schorn, K. 1978. Psychoacoustical tuning curves in audiology. *Audiol*, 17, 120-140.

Table 5.1. TEN-test results for the nine ears that gave a different result on retest. The values are the difference between masked threshold and TEN level (in decibels). A value of ≥10, indicates a DR. Retest values are in parentheses. Retest values are underlined where this resulted in a different diagnostic category from the initial test e.g., no DR on initial test but a DR on the retest.

Subject	Frequency (kHz)						
	0.5	0.75	1	1.5	2	3	4
5R	6 (8)	4 (8)	6 (6)	8 (8)	8 (6)	4 (6)	6 (10)
8L	6 (2)	4 (6)	8 (8)	8 (10)	8 (8)	10 (12)	14 (14)
16L	2 (4)	6 (2)	6 (6)	10 (8)	10 (8)	10 (10)	12 (14)
28R	2 (0)	0 (6)	12 (16)	8 (12)	6 (6)	14 (14)	16 (16)
28L	0 (0)	0 (6)	10 (10)	6 (14)	2 (8)	12 (20)	16 (18)
31R	2 (4)	0 (0)	4 (0)	0 (2)	6 (6)	4 (2)	8 (10)
36R	4 (2)	4 (2)	6 (6)	10 (8)	12 (10)	8 (8)	16 (12)
36L	0 (2)	0 (0)	6 (4)	6 (6)	8 (10)	12 (12)	10 (10)
42L	4 (4)	4 (0)	6 (4)	10 (12)	14 (8)	6 (8)	12 (10)

Table 5.2. The coefficient of repeatability (SD*1.96) for each test frequency. The number of repeats used to calculate each coefficient is included. For signal frequencies 1.5 to 3 kHz, ≤3 repeats were measured.

	Signal Frequency (kHz)					
	0.5	1.0	1.5	2	3	4
Number of repeats (n)	10	8	2	3	2	19
Repeatability Coefficient (kHz)	0.075	0.150	0.186	0.143	0.069	0.373
Repeatability Coefficient (%)	15.0	15.0	12.4	7.1	2.3	9.3

Table 5.3. Outcomes of the TEN-test when using fast PTCs as the gold standard test.

		PTC results		
		DR Yes	DR No	
TEN-test results	DR Yes	True Positive 47	False Positive 26	Positive Predictive Value 47/73 = 64%
	DR No	False Negative 8	True Negative 93	Negative Predictive Value 93/101 = 92%
		Sensitivity 47/55 = 85%	Specificity 93/129 = 78%	

Table 5.4. The agreement, in percent, for DR identification for the two tests using a range of criteria. Agreement on f_e is provided in parentheses.

			Fast PTC Criteria		
			(Tip estimate - Signal Frequency) / Signal Frequency x 100		
			>10%	>15%	>20%
TEN-test Criterion	Masked threshold - TEN level (dB)	+8	82% (58%)	80% (57%)	70% (53%)
		+10	87% (73%)	87% (71%)	83% (69%)
		+12	80% (60%)	81% (61%)	87% (67%)

Table 5.5. The mean time, in minutes, taken to complete the TEN-test and fast PTC measurements for ears with and without DRs (standard deviation in parentheses).

	Mean Test Time (Minutes)	
	TEN-test	Fast PTC measurements
All ears	12.4 (5.5)	55.8 (13.5)
No DR ears	12.9 (4.5)	48.1 (11.9)
DR ears	12.1 (6.2)	61.7 (11.7)

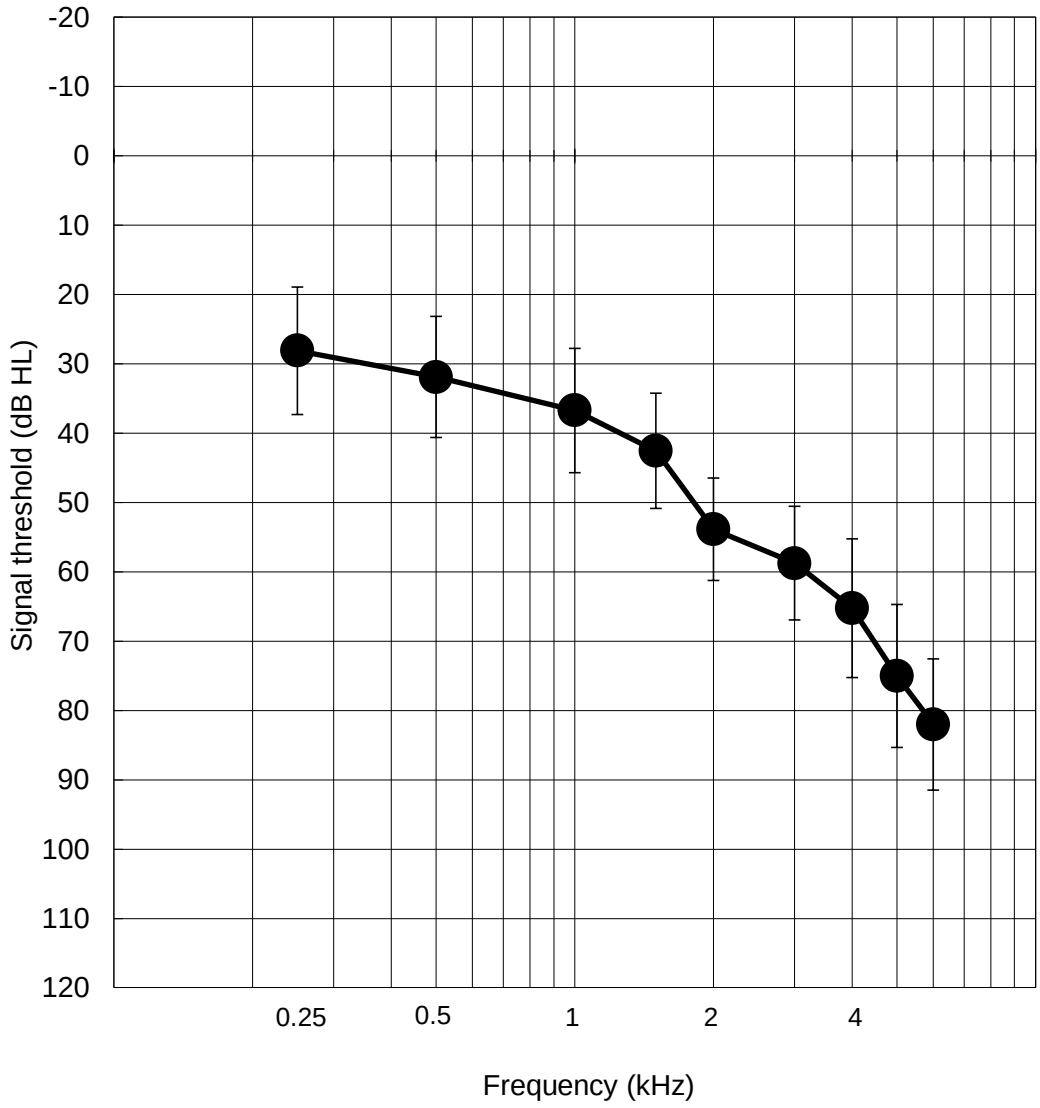

Figure 5.1. Mean hearing thresholds (0.25 to 8 kHz) for all 76 ears. Error bars show one standard error.

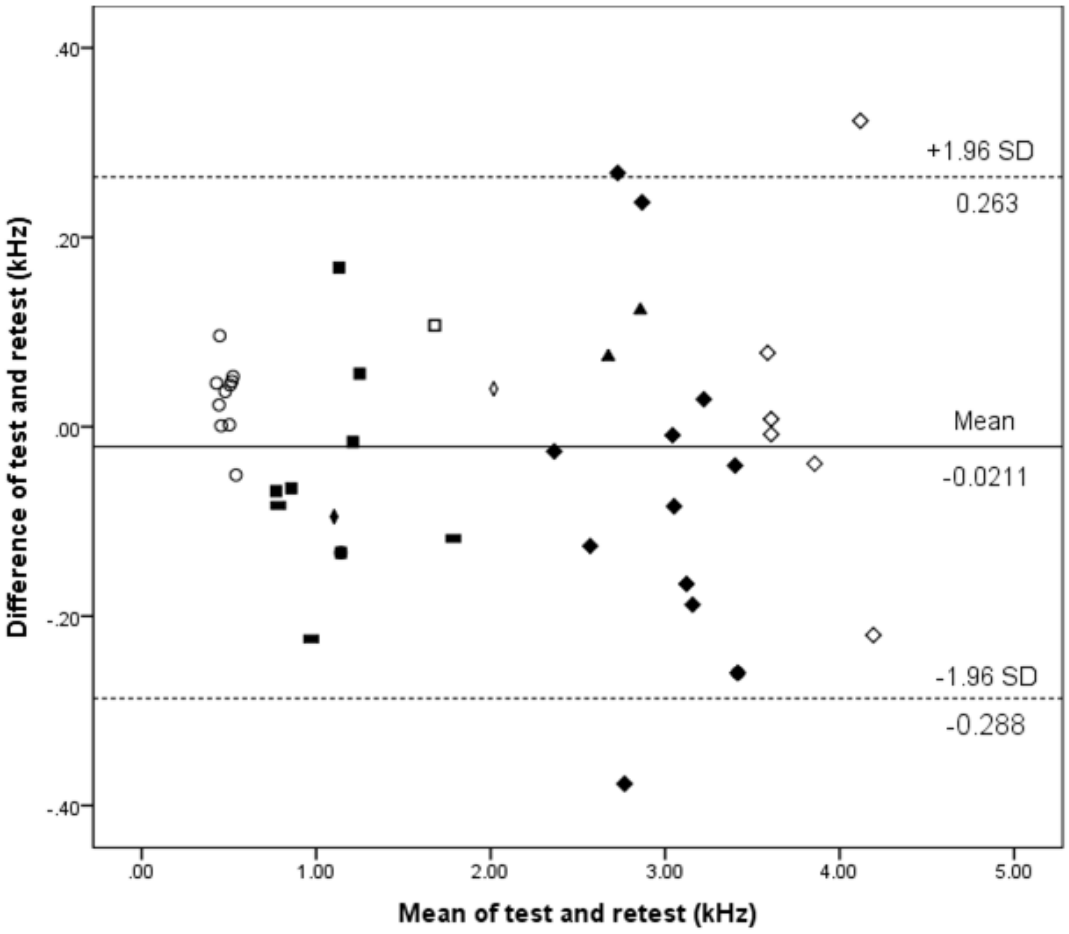

Figure 5.2. Bland-Altman plot showing the agreement of PTC tip frequency obtained on two separate occasions. The mean is presented as a solid line and ±1.96 SD is presented as a dotted line. The data for 0.5, 1, 1.5, 2, 3 and 4 kHz are shown as circles, squares, rectangles, long diamond, triangles and diamonds, respectively. The absence or presence of a DR is indicated by open and closed symbols, respectively.

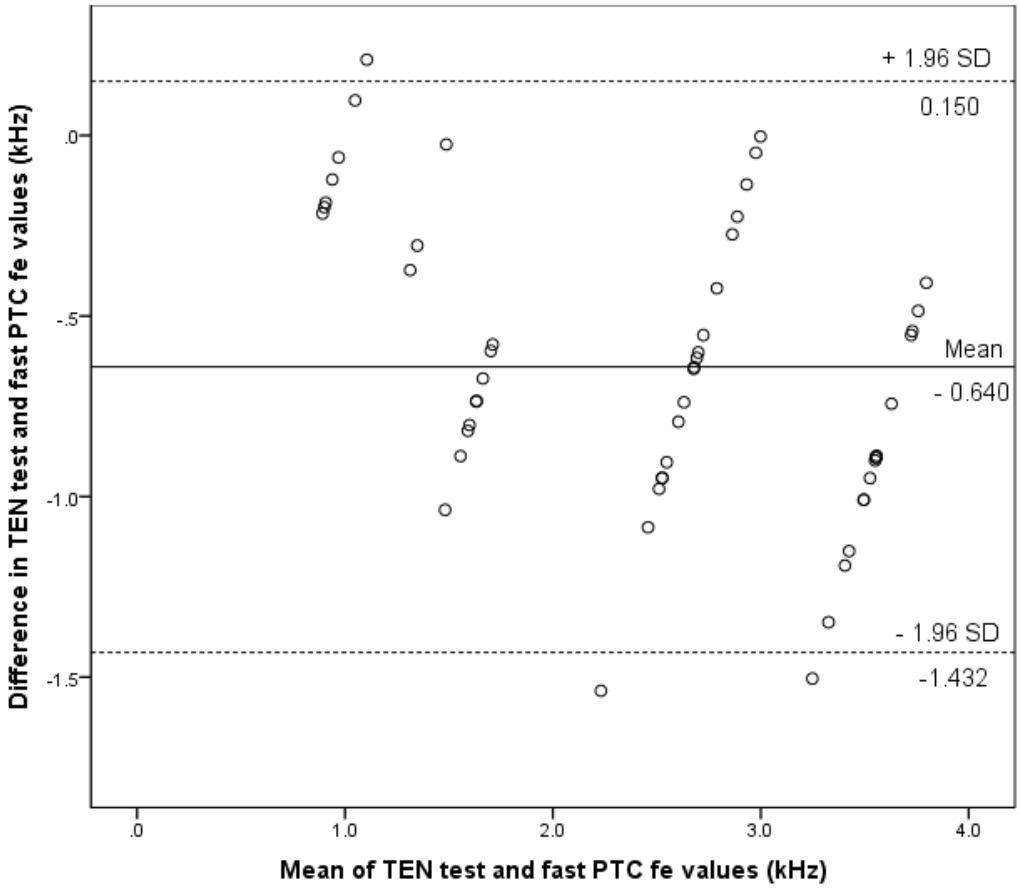

Figure 5.3. A Bland-Altman plot showing the agreement of f_e estimated from the TEN-test and fast PTCs. The mean is shown as a solid line and ± 1.96 SD is shown as a dotted line.

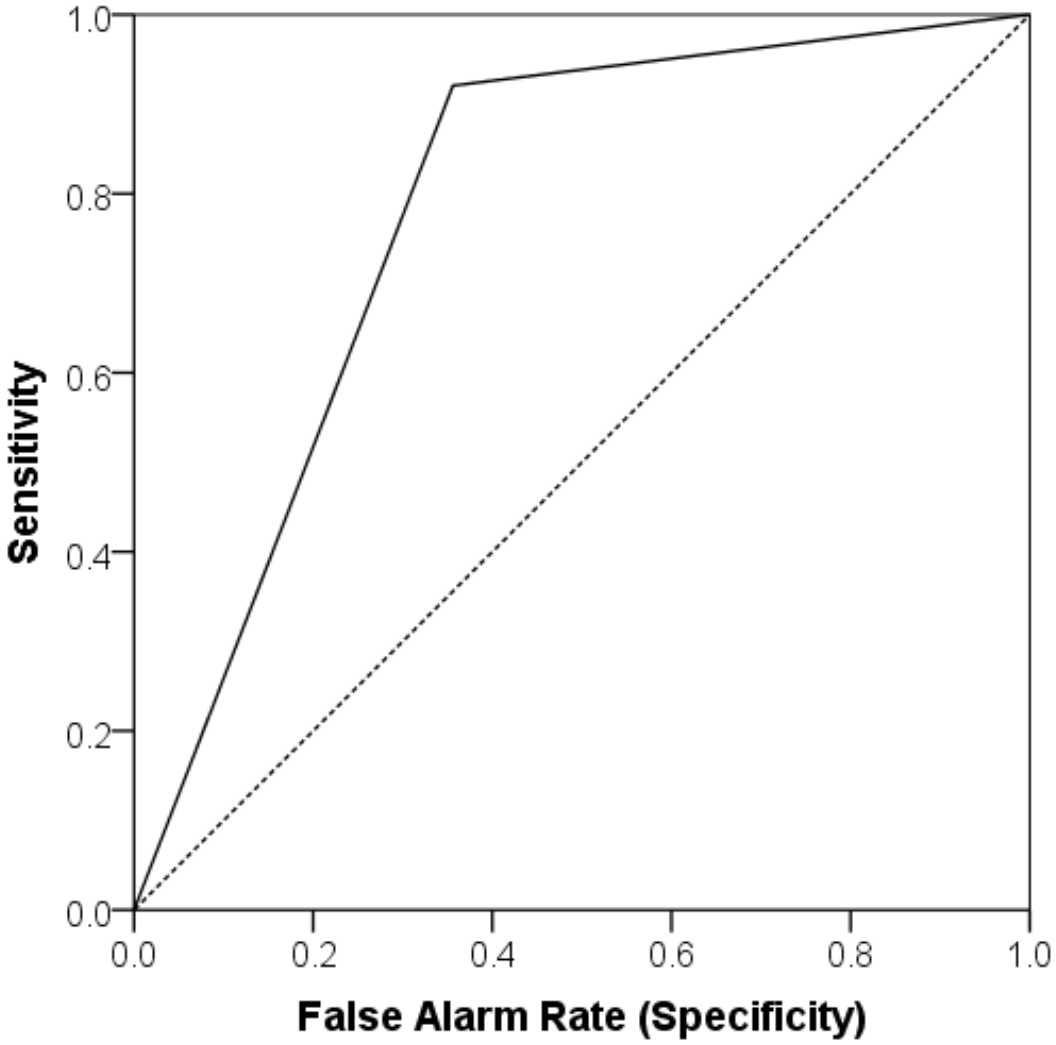

Figure 5.4. ROCs for the TEN-test. The solid black line shows the sensitivity for a given specificity and the dotted black line indicates the 50% (chance) line. Each point on the ROC represents a sensitivity/specificity pair.

CHAPTER 6

BENEFIT OF HIGH-FREQUENCY AMPLIFICATION IN EARS WITH COCHLEAR DEAD REGIONS

FORMATTED TO THE EAR AND HEARING REQUIREMENTS

Benefit of high-frequency amplification in ears with cochlear dead regions

Authors:

Anna Pepler, MSc, School of Psychological Sciences, University of Manchester, UK

Kevin J Munro, PhD, [1] School of Psychological Sciences, University of Manchester, UK, [2] Central Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Oxford Road, Manchester, M13 9WL, UK

Kathryn Lewis, University Hospitals South Manchester NHS Foundation Trust

Karolina Kluk, PhD, School of Psychological Sciences, University of Manchester, UK

Correspondence:

Anna Pepler

School of Psychological Sciences,

Ellen Wilkinson Building,

University of Manchester,

Oxford Road,

Manchester,

M13 9PL.

Sources of funding: Research for Patient Benefit project grant from UK National Institute for Health Research (RfPB PB-PG-0408-15055)

ABSTRACT

Objectives: The aim of this study was to determine the benefit of high-frequency amplification on nonsense syllable recognition, in quiet and in babble, in ears with and without a cochlear dead region (DR).

Design: A total of 36 experienced adult hearing aid users were recruited: one group of 18 with a high-frequency DR (diagnosed using the TEN-test and fast PTC measurements) and a group of 18 matched controls. Only one ear of each participant was assessed. Participants were fitted with the study hearing aid and tested under four conditions: unfiltered (NAL-NL2 prescription target) and low-pass filtered at 1.5, 2, and 3, kHz. The VCV stimuli were presented at 65 dB (A) in quiet and in 20-talker babble at a signal-to-babble ratio of 0 dB.

Results: Mean performance was best in the unfiltered condition. There was no significant difference in mean performance between the two groups when tested in quiet. However, based on the difference in performance between the unfiltered and 3 kHz filtered condition, the group with DRs obtained less benefit from unfiltered amplification than the group without DRs when listening in babble (6% and 13%, respectively).

Conclusions: Recognition of nonsense syllables was best in the unfiltered condition although performance in babble was lower in the DR group. However, performance with nonsense syllables may not be representative of all real-life listening situations, the findings in this study may be useful when counselling patients with DRs about the limitations of amplification when listening in noise.

Key Words: Cochlear dead regions, Consonant recognition, Hearing impairment

INTRODUCTION

The primary aim of amplification is to restore audibility (Dillon 2012). The provision of gain at high-frequencies in adults with moderate to severe high-frequency hearing impairment has been reported as providing little or no benefit for speech recognition (Murray & Byrne 1986; Hogan & Turner 1998; Ching et al. 1998, 2001; Turner & Cumming 1999; Vickers et al. 2001; Baer et al. 2002; Mackersie et al. 2004; Preminger et al. 2005; Hornsby & Ricketts 2006). Reduced frequency selectivity and impaired temporal resolution has been suggested as a possible explanation for this lack of benefit (Moore 2002). Reduced frequency selectivity is caused by impaired function or loss of outer hair cells (OHCs; Ryan & Dallos 1975; Dallos & Harris 1978), while dysfunction or loss of inner hair cells (IHCs) leads to impaired temporal resolution (Moore 2001, 2002). The impact of cochlear dead regions (DRs) on speech recognition remains controversial and it is unclear if individuals with a DR should be fitted with a different gain prescription to those with no DR (Vickers et al. 2001; Baer et al. 2002; Vestergaard 2003; Moore 2002, 2004; Mackersie et al. 2004; Preminger et al. 2005; Cox et al. 2011, 2012). The aim of the present study was to assess the impact of DRs on speech recognition performance in experienced adult hearing aid users using a range of hearing aid gain settings.

DRs are relatively common in the hearing-impaired population, with prevalence estimates from 36% to 59% in adults with sensorineural hearing impairment (Vinay & Moore 2007; Cox et al. 2011; Pepler et al. 2014). Although DRs are relatively common, only 3% (95% CI: 2-4) of adults in the Pepler et al. study had a DR spanning > 2 frequencies. To date, it is not clear how extensive a DR

needs to be before it may impact on clinical management. There is an urgent clinical need to determine the impact of DRs on hearing aid benefit.

Vickers et al. (2001) and Baer et al. (2002) compared consonant recognition, for different low-pass filter conditions, in 22 adult participants with and without extensive, continuous DRs associated with steeply sloping hearing impairment. DRs were determined using both the threshold equalizing noise (TEN-SPL) test (Moore et al. 2000) and psychophysical tuning curves (PTCs; Zwicker & Schorn 1978), all DRs covered the high-frequency range from below 4 kHz upwards. Vowel-consonant-vowel (VCV) stimuli developed by the Institute for Hearing Research, Nottingham, UK were presented via headphones amplified using the Cambridge fitting formula, although gain was limited in severe hearing impairments (Moore & Glasberg 1998). When listening in quiet, ears without DRs benefited from high-frequency amplification. Ears with DRs only showed improved speech recognition with a low-pass filter cut off up to 50 to 100% above the estimated edge frequency of a DR (f_e): above this point consonant recognition did not improve and in a few cases even deteriorated. Vickers et al. (2001) concluded that for participants with high-frequency DRs, there was no benefit in providing amplification for frequencies about 1.7 times f_e. Baer et al. (2002), using many of the same participants as Vickers et al, reported similar findings when testing in the presence of speech-shaped noise (signal to noise, SNR, of 0 – 6 dB).

The main limitation of the Vickers et al. (2001) and Baer et al. (2002) studies was that participants with DRs had a more severe hearing impairment than the control participants without DRs. Therefore, reduced audibility (due to the severity of hearing impairment and restricted hearing aid gain) in the ears with a DR could not be ruled out as impacting on performance. In order to remove this confound,

Mackersie et al. (2004) matched as closely as possible the hearing thresholds of ears with and without DR. DRs were detected using the TEN-SPL test (Moore et al. 2000). Consonant and word recognition was assessed in quiet, and in low and high-level noise. Hearing aids were fitted to the Desired Sensation Level (DSL) prescription in the test ear (Cornelisse et al. 1995); the non-test ear was plugged and muffed. Speech material was presented at 65 dB SPL unfiltered or low-pass filtered at f_e, 0.5 or 1 octave above the DR. In quiet and low-level noise there was no significant difference in mean performance between participants with and without DRs. In the high-level noise condition, participants with DRs had poorer word recognition scores than those without DRs. However, in no instance did the provision of amplification at frequencies within the DR result in a significant worsening of word recognition, relative to a low-pass filtered condition.

Preminger et al. (2005) investigated speech recognition and self-reported benefit in 49 experienced hearing aid users. All participants had hearing levels poorer than 50 dB for at least two frequencies and no audiometric thresholds poorer than 80 dB HL. The TEN-SPL test, with a stricter DR criteria (15 dB difference between the TEN level and masked threshold) than the 10 dB recommended by Moore et al. (2000), was used to detect DRs. Speech recognition was measured using the Quick Signal-In-Noise (SIN) test. Two versions of the Quick SIN were used unaided, one with a standard broadband setting and one with a high-frequency emphasis, providing gain above 3 kHz. Participants with DRs had poorer speech intelligibility scores and poorer subjective hearing aid benefit in noise compared to those without DRs. However, both groups showed benefit from high-frequency gain. This indicates that participants with DRs may have reduced benefit from high-frequency amplification. However, the participants with DRs were not matched in

any way to the participants without DRs so between-group differences, for example hearing level, may have led to these results.

Cox et al. (2011) compared speech recognition in noise for 307 ears with and without DRs. DRs were detected using the TEN-HL test presented via Etymotic Research (ER)-3A earphones. Quick SIN speech material was presented unaided via ER-3A earphones unfiltered and low-pass filtered at 2 kHz. Ears without DRs showed more benefit from high-frequency amplification than ears with DRs, especially contiguous DRs at ≥2 frequencies. Of the 307 ears tested, 72 ears were identified with DRs but only 16 of these were contiguous DRs. This suggests that only a small proportion of ears with hearing impairment (5%) are going to have substantially less benefit from high-frequency amplification than ears with DRs. Cox et al. (2012) reduced high-frequency amplification for new and experienced hearing aid users in the laboratory and real-life scenarios to assess speech recognition in participants with and without DRs. Hearing aid users with and without high-frequency DRs were matched in terms of hearing levels. DRs were detected using the same TEN-HL test method as used in Cox et al. (2011). Each participant was fitted unilaterally with a hearing aid set to the NAL linear prescription method (Byrne & Dillon 1986) and a prescription with reduced high-frequency gain (programme 1 and 2, respectively). The participants were then given two weeks to acclimatise to the hearing aids and allowed to alternate between the two listening programmes. The participants then returned to the laboratory for speech perception testing using BKB (Bamford-Kowal-Bench)-SIN and CASPA (Computer-Assisted Speech Perception Assessment; Mackersie et al. 2001) tests, testing using both programme settings. The participants continued to wear the hearing aids for a further two weeks, alternating between the two listening programmes. During this

period participant's rated their speech understanding in a range of real-life situations for each programme. The participants then returned to the laboratory for further speech perception testing. Both groups did show benefit from high-frequency amplification; however, participants with DRs obtained less benefit at high frequencies than those without DRs. In addition, the results from participant preference in daily life found no preference differences when comparing ears with or without DRs.

Malicka et al. (2013) recruited children, aged 9 to 13 years and diagnosed DRs using the TEN test and fast-PTCs. They divided ears in to groups of moderate (thresholds between 35 and 80 dB HL) and severe to profound hearing impairment (thresholds between 15 and >110 dB HL). The moderate group had nine ears without DRs and three ears with restricted DRs (two consecutive frequencies). The severe to profound group had seven ears with DRs and one ear without a DR. VCV speech stimuli were low-pass filtered at a range of cut-off frequencies and presented via headphones. They found that all ears in the moderate hearing impairment group benefitted from high-frequency amplification, regardless of DR presence. In the severe to profound hearing impairment group six of the seven ears with DRs and the ear without DRs showed a plateau in performance with increasing high-frequency amplification. One ear with a DR showed a significant decline in performance with increasing high-frequency amplification. These findings suggest that an extensive contiguous DR may in some cases result in reduced benefit from high-frequency amplification.

The conclusions from the studies reviewed above vary and it is not clear whether high-frequency amplification is detrimental to speech recognition in quiet and in noise. The studies described above agree that, under some circumstances

(generally high background noise), participants with DRs may not obtain as much benefit from broadband amplification as ears without DRs. There are at least two factors that may have led to this variation in outcome. Firstly, Vickers et al. (2001), Baer et al. (2002) and Malicka et al. (2013) identified DRs using both the TEN-SPL test and standard PTC measures, whilst Mackersie et al. (2004) Preminger et al. (2005) and Cox et al. (2011, 2012) used only the TEN-HL or -SPL test. Since PTCs are thought to be more accurate at determining f_e (Moore & Alcantara 2001; Kluk & Moore 2006b and Pepler et al. In Press) this suggests Mackersie et al. (2004) Preminger et al. (2005) and Cox et al. (2011, 2012) may have underestimated the extent of the DR. This may have resulted in patients with DRs being incorrectly added to the no DR group, resulting in smaller differences between the two groups. Secondly, Vickers et al. (2001) and Baer et al. (2002) used participants with more extensive DRs and greater degrees of hearing impairment. More extensive DRs are associated with more off-frequency listening and, therefore, high-frequency amplification may become detrimental in these ears. However, high-frequency amplification may not have restored audibility. This does not explain why some patients showed poorer speech recognition scores with increasingly high-frequency amplification. This would suggest the high-frequency amplification provided additional audibility that was detrimental to the listener or the amplification was accompanied by distortion or feedback. There is an urgent clinical need to investigate the effects of high-frequency amplification on speech recognition in ears with DRs. It is clear from the previous studies that the inconsistent use of the TEN-HL test and fast PTCs for DR detection and the lack of matched controls may have resulted in these mixed findings.

The aim of the present study was to compare the benefit of high-frequency amplification in adults with and without high-frequency DRs (diagnosed using both the TEN-HL test and fast PTCs). Speech recognition scores were recorded when wearing a hearing aid unilaterally, fitted to a recognised prescription target. In addition, performance was measured with an unfiltered and three low-pass filtered hearing aid gain settings. Adjustments were made via the fitting software (see below), rather than laboratory based filter techniques to give a realistic idea of what is achievable in the clinical setting. Ears with DRs were matched to ears without DRs in terms of hearing threshold levels (0.25 to 8 kHz). A secondary aim of this study was to consider the effect of the extent of the DR on the benefit of high-frequency amplification. It was hypothesized that ears with DRs would obtain less benefit from high-frequency amplification and this would be greatest in cases where there was an extensive DR when listening in quiet and babble.

MATERIALS AND METHODS

This study was approved by the Greater Manchester-North ethics committee (reference number 10/H1011/62) and informed written consent was obtained from participants.

Participants

The statistical power calculation were based on Mackersie et al. (2004), who reported a mean difference of 10% (± 10% s.d.) in speech scores in ears with and without DRs. A sample size of 17 ears was required in each group for a statistical power of 80% at a two-tailed significant level of 5% on an independent samples *t*-test.

Thirty-six adults (nine female) with high-frequency sensorineural hearing impairment, were recruited from the United Kingdom National Health Service audiology department at Withington Community Hospital, Manchester. The median participant age was 75 years (Range 59-94). Only one ear of each participant was tested. In total, eighteen ears with a DR (median age 75.5 years) and eighteen ears without a DR (median age 75 years) were tested. DRs were determined from the results of the TEN-HL test (Moore et al. 2004) and fast PTC measurements (Sek & Moore 2011). Ears that did not meet the criteria for a DR were matched to ears meeting the criteria for a DR (<10 dB difference, 0.5 to 6 kHz). The mean hearing thresholds are presented in Figure 6.1 and individual data are shown in Table 6.1.

Insert Figure 6.1 about here

Insert Table 6.1 about here

Although the ears were matched as closely as possible, ears with DRs had mean hearing thresholds poorer at 3 to 6 kHz by 5dB than ears without DRs. The hearing thresholds at 3 to 6 kHz in ears with DRs ranged from being -10 to 20 dB different to the matched ears. However the prescription target could still be met within 5 dB between 0.25 and 6 kHz for all ears. In order to avoid the need to allow a period of acclimatisation all participants were required to have worn a hearing aid, fitted to the prescription NAL-NL2, for at least one year, the mean prescription provision on participant's current hearing aid is presented in Figure 6.2

Insert Figure 6.2 about here

Threshold Equalizing Noise (TEN) test

The TEN-HL test, referred to as TEN-test from now on, was performed according to the procedure described by Moore et al. (2004). The pure tone signal and TEN were routed from the TEN CD via a Marantz CD 5000 player through channel 1 and 2 of the Unity audiometer. The signal (test tone), presented to the same ear as the TEN, was adjusted in ascending and descending steps of 8 dB and 4 dB, respectively until the participant responded at the same level for more than 50% of responses on the ascent. A final step size of 2 dB was then completed until the same threshold was obtained for more than 50% of responses and this was taken as the final threshold. Participants were instructed to respond, by pressing a button, when the signal was audible in the presence of the TEN. A DR was indicated at a specific test frequency if the masked threshold was ≥10 dB above the absolute threshold and ≥10 dB above the TEN level. The TEN-test was only completed at discrete intervals between 0.5 and 4 kHz and therefore f_e was only determined to within a half-octave range. Fast PTC testing was required to determine a more specific f_e.

Fast Psychophysical Tuning Curve (PTC) measurements

In all ears, an ascending (low to high frequency) and descending (high to low frequency) fast PTC sweep was measured at signal frequencies between 0.5 and 4 kHz. Fast PTCs were measured using a computer with external sound card (Creative Professional E-MU 0202 USB) and Sweeping PTC (SWPTC) software (Sek & Moore 2011). The test parameters were based on those suggested by Sek et al. (2005), Sek and Moore (2011) and Kluk and Moore (2005). For signal frequencies <1.6 kHz, the masker bandwidth was 20% of the signal frequency and at ≥1.6 kHz, a bandwidth of 0.320 kHz was used. A masker step size of 1 dB/s was used throughout

the test. Each test was varied in duration to suit the participant but was always between 3 and 8 minutes. The initial masker level was set at 40 dB SPL for mild hearing impairments and 50 dB SPL for moderate and severe hearing impairments. The signal threshold was determined using the threshold measurement tab in the SWPTC software. Each participant was asked to listen for a sound using a two alternative forced choice task and the absolute signal threshold was measured. The signal level was set at 10 dB SL, although in cases where ineffective masking occurred, the level was reduced to 4 dB SL. Sek and Moore (2011) suggested a low-level low-pass noise be used to mask combination tones when hearing thresholds were better than 40 dB SPL at frequencies ≤1 kHz. The low-level noise was presented at 40 dB below the signal level at least one octave below the signal frequency using cut-off frequencies of 0.25, 0.5, 0.75, or 1 kHz.

When the fast PTC tip could not be estimated, the measurement was repeated with extended test duration. The tip was determined using the Sek and Moore (2011) ROEX fitting method, provided with the SWPTC software.

The criteria, based on repeatability measures recorded by Sek et al. (2005), and Pepler et al. (In Press) were as follows: a DR is indicated if the frequency difference between the signal and tip frequencies is ≥10% of the signal frequency, when the tip frequency is averaged from ascending and descending sweeps.

For each ear, the fast PTC tip frequency is presented in Table 6.2 along with the TEN-test results. In 49 of 50 ears there was agreement in DR identification on the TEN-test and fast PTC tests. In one ear a DR was not indicated on the TEN-test, but a significant shift in the PTC tip, to the low frequencies, was recorded when using a signal frequency of 4 kHz. Both tests were repeated twice to ensure test repeatability was not affecting the results, both tests gave the same result on the

repeat. Although this indicates a discrepancy between the two tests, it has been previously suggested that the TEN-test lacks accuracy in f_e, when it is close to the signal frequency (Kluk & Moore 2005). Therefore in this case of disagreement between tests, the fast PTC DR classification was assumed as a more accurate result. If this listener had been excluded from the study this would not have changed the findings from this study.

Insert Table 6.2 about here

Hearing Aid Fitting and Verification

Each participant was an experienced hearing aid user, however for the purposes of this study they were fitted in the laboratory with a specific study hearing aid. This was to ensure that the study hearing aid had the same settings for each participant. An Oticon Spirit Zest moderate or power behind-the-ear hearing aid was fitted to the test ear. This has 12 adjustable channels and four programmable settings. The hearing aid frequency response match to the NAL-NL2 prescription target was verified using real ear measures. Real ear insertion gain was recorded on the Siemens Unity 2 using a modulated speech signal at 50, 65 and 80 dB (A). The hearing aid gain was adjusted to match the prescribed gain. Real ear insertion gain was within 5 dB of the prescribed gain from 0.25 to 6 kHz. Each hearing aid was set with noise management switched on (see discussion section for the implications of using this setting) and with tri-state directionality, as is routinely used when fitting hearing aids in this clinic. The volume control was disabled.

Filtering Conditions

The hearing aid was set with four different programmes: unfiltered (matched to the NAL-NL2 prescription target) and three low-pass filtered settings. The same filter settings (low pass filtered at 1.5, 2, and 3 kHz) were used for all participants. The mean low-pass filter settings are shown in Figure 6.2. These filter settings were chosen as the hearing aid software provided adjustment at these frequencies that were in the region of the DR f_e. The Speech Intelligibility Index (Hornsby 2004; ANSI S3.5-1997; Kryter 1962) values for ears with and without DRs for all four filter conditions is presented in Table 6.2.

Insert Figure 6.2 about here

Speech stimuli and procedure

Consonant identification was assessed using vowel-consonant-vowel nonsense syllables in quiet and in 20-talker babble. This test material was selected in order to reduce the influence of context to assess true speech recognition. It comprised the use of one vowel /a/ with one of 20 consonants /b/, /tʃ/, /d/, /f/, /g/, /dʒ/, /k/, /l/, /m/, /n/, /p/, /r/, /s/, /ʃ/, /t/, /θ/, /v/, /w/, / j/, and /z/. Three recordings of each VCV combination spoken by a female were played back from a CD ROM produced by the Institute of Hearing Research (IHR), Nottingham, UK. The stimuli were presented at 65 dB(A) i.e. the level of the low-pass filtered stimuli was increased to preserve the overall level of 65 dB(A). This was to ensure speech perception was not influenced by significant changes in stimuli loudness. There were four test sessions in total with four lists (160 stimuli) presented in each filter and listening condition (quiet and babble). Testing in quiet was completed in the first and

third test sessions and testing in babble completed in the second and fourth test sessions. The order of hearing aid settings was counterbalanced across participants and test sessions. The time lapse between the first and fourth test session was never more than 6 weeks. Pure tone audiometry was completed at the first and last test session. In no instance did the hearing thresholds change by more than 5 dB at any frequency.

The stimuli were presented from a loudspeaker positioned one metre in front of the participant at head height and at 0^{o} azimuth. The non-test ear was plugged and muffed throughout testing. A pilot study on twelve participants with and without DRs was completed to determine optimum signal-to-noise ratios i.e. to avoid floor and ceiling effects. In all twelve participants, mean scores between 40 and 80% were achieved for 0 dB SNR. For each test, the participant was given a list of the 20 possible consonant sounds, e.g. T, SH, B. Each participant was asked to indicate which consonant they had heard by repeating and pointing to the letter. The researcher then recorded this response on the computer and another VCV was presented. No feedback was provided. There was a practice session at the start of each session in quiet and in babble, consisting of one list using the hearing aid in the unfiltered condition. This may have resulted in the participants being more acclimatized to the unfiltered setting than the low-pass filter settings, see the discussion for more details.

The data were analyzed using SPSS, version 16. The conventional 5% significant level was used throughout. The data demonstrated a normal distribution therefore parametric statistical tests were used. Data have been summarised using mean with standard deviation. Analyses consisted primarily of repeated-measures analysis of variance (ANOVA) when comparing speech recognition scores across

different test conditions. Where Mauchly's test of normality was significant, the Greenhouse-Geisser correction was used.

RESULTS

Consonant recognition

Mean performance for ears with and without DRs are shown in Figure 6.3. Best performance, in quiet and babble, for ears without DRs was obtained in the unfiltered condition. The unfiltered mean score for ears with DRs was 84 and 59% and for ears without DRs was 86 and 67% in quiet and babble, respectively. Performance progressively decreased with increasing low-pass filtering, with the scores reducing by up to 22% and 19% in ears with and without DRs in babble, respectively. The mean consonant recognition scores in babble, for both groups, were >10% poorer for all filter conditions than in quiet.

The data were analysed using a three-factor (two within-factors of filter[4] and listening condition [2] and one between-factor of group [2]) repeated measure ANOVA. There was a significant effect of filtering (F[2.4,82.3] =93.5, $p < 0.001$) and a significant effect of babble (F[2.4,82.3] = 93.5, $p< 0.001$) . There was no significant difference between the scores for the two groups (F[1,35] = 2.197, $p > 0.05$).

Insert Figure 6.3 about here

The data were analysed using a two-factor (filter setting, group) repeated measure ANOVA for quiet and babble conditions. In quiet, there was a significant effect of filtering (F[1.86,55.8] =57.4, $p < 0.001$). There was no significant

difference between the scores for the two groups (F[1,30]=0.41, p > 0.05) and no significant interaction between the two factors (F[1.86,55.8]=1.344, p > 0.05). In babble, there was a significant effect of filtering (F[2.45,73.6] =92.9, p < 0.001) and, importantly, a significant difference between the scores for the two groups (F[1,30]=4.356, p = 0.045). There was also a borderline significant interaction between the two factors (F[2.45,73.6]=2.954, p = 0.048). Four one-way ANOVAs were completed comparing the two groups for each of the four filter conditions in babble separately. This indicated a significant difference between group scores for the unfiltered condition (F[1,30]=13.1, p = 0.001). However, no significant difference in group scores was identified for any of the three low-pass filtered conditions even before (p > 0.05) correction for multiple paired comparisons.

In summary, these results indicate no significant difference in mean performance between groups when tested in quiet. There was a significant difference in mean performance between groups when tested in babble: ears with DRs performed significantly poorer in the unfiltered condition.

Filtering effect

In order to consider in more detail the benefit of high-frequency amplification in ears with and without DRs, the same comparison method as Mackersie et al. (2004) was used. This approach compares the difference in scores between the unfiltered and 3 kHz filtered condition (see Figure 6.4). Ears that benefitted from high-frequency amplification will give a positive score i.e. the unfiltered score will be higher than the filtered score. The mean benefit of unfiltered amplification (5%) was similar for both groups in the quiet condition. In babble, ears

with and without DRs had a 6% and 13% difference in scores between the 3 kHz filtered condition and unfiltered condition, respectively.

This data were analysed using a two-factor (listening condition, group) repeated measure ANOVA. There was a significant effect of listening condition (F[1,321] =10, p = 0.003). There was no significant difference between the scores for the two groups (F[1,34] = 2.091, p > 0.05). Importantly, there was a significant interaction between the two factors (F[1,34]=6.39, p = 0.016). A one-way ANOVA was completed for each listening condition. In quiet, there was no significant difference between the two groups (F[1,30] = 0.185, p >0.05). In the 20-talker babble condition, there was a significant difference in benefit between the two groups (F[1,30] =9.0, p = 0.005), even when corrected for multiple comparison (p < 0.025).

In summary, ears with DRs benefitted from broadband amplification to the same extent as ears without DRs when tested in the quiet but obtained less benefit in babble.

Insert Figure 6.4 about here

Extensive DRs

In order to determine whether participants with extensive DRs benefit from broadband amplification, DRs with f_e commencing <3 kHz (n=9) were identified. The mean hearing thresholds of each of the ears with and without DRs is shown in Figure 6.5. The ears with DRs have greater mean hearing threshold levels above 2 kHz thus, further analysis of these data, includes hearing threshold as a covariate.

Insert Figure 6.5 about here

The mean scores in quiet and in babble for ears with and without extensive DRs are shown in Figure 6.6. Best performance was obtained in the quiet, unfiltered condition. Performance progressively decreased with increasing low-pass filtering. Ears with extensive DRs had poorer mean scores for all four conditions. The greatest difference in scores was in the unfiltered condition.

Insert Figure 6.6 about here

The data were analysed using a three-factor, (two within-factors of filter [4] and listening condition [2] and one between-factor of group [2]) repeated measure ANOVA with mean hearing threshold added as a covariate. There was a significant effect of filtering (F[2.1,33.3] = 63.2, $p < 0.001$) and a significant effect of listening condition (F[1,16] = 88.7, $p < 0.001$) . There was no significant difference between the scores for the two groups (F[1,15] = 2.197, $p > 0.05$). There was a significant effect of hearing impairment (F[1,15] = 5.508, $p = 0.033$).

This data were analysed using a two-factor (filter, group) repeated measure ANOVA and hearing impairment as covariate. In quiet, there was no significant effect of group (F[1,15]=1.349, p>0.05) or filter (F[1.8,27.2] =0.782, $p > 0.05$) and there was no significant interaction (F[1.8,27.2] = 2.056, $p > 0.05$). There was also no significant effect of hearing impairment (F[1,15] = 3.141, $p > 0.05$). Therefore, DRs with f_e <3 kHz did not have a significant impact on speech scores in quiet, even when accounting for variations in hearing thresholds. In babble, there was no significant effect of group (F[1,15] =2.135, p > 0.05) or filter (F[2.1,32.1) = 0.098, p

> 0.05) and no significant interaction between the two factors (F[2.1,32.1) = 1.713, p > 0.05). There was a significant effect of hearing impairment (F[1,15] = 8.34, p = 0.011). Therefore, there was not a significant difference in scores in babble, when accounting for variations in hearing thresholds.

The benefit from unfiltered amplification was calculated by subtracting the filtered at 3 kHz score from the unfiltered score; the results are shown in Figure 6.7. The pattern of benefit differs between ears with and without DRs. Ears without DRs benefitted from high-frequency amplification, especially in babble. As the sample size was halved in this analysis, the standard error increased. These data were analysed using a two-factor (listening condition, group) repeated measure ANOVA. There was no significant effect of listening condition (F[1,1.15] =1.174, p > 0.05), no significant difference between the scores for the two groups (F[1,15] = 3.066, p > 0.05) and there was no significant interaction between the two factors (F[1,15] = 1.57, p > 0.05).

Insert Figure 6.7 about here

Amplification and f_e

The amplification cut-off frequency was considered for each ear in terms of the f_e. In order to do this, the low-pass filter frequency (unfiltered, 3, 2 and 1.5 kHz) was divided by the estimated f_e. Therefore, the smaller the value, the greater the low-pass filtering. The unfiltered frequency was taken as 6 kHz, based on the results of real ear measurements. For ears without DRs, the estimated f_e of the audiometrically matched pair was used. Amplification bandwidth divided by f_e was plotted against consonant scores in quiet and babble, and is presented in Figure 6.8.

In quiet, scores in ears with (filled circles) and without DRs (open squares) increased with greater provision of amplification in the DR. A univariate ANOVA was completed with dependent variable, consonant correct score, and fixed factor, DR group. Amplification bandwidth, according to f_e, was included as a covariate. DR group had no significant effect (F[629,1] = 3.6, p = 0.058). Amplification bandwidth had a significant effect on consonant recognition (F[4340,1] = 25.3, p < 0.001). Therefore, provision of wide-band amplification is beneficial to ears with and without DRs when listening to speech in quiet. Additionally, the provision of increasing amplification in the DR is of no disadvantage when listening in quiet situations.

In babble, scores in ears with (full circles) and without DRs (open squares) increased with greater provision of amplification in the DR. However, ears with DRs, had, on average 5% poorer consonant recognition scores than ears without DRs. Amplification bandwidth, according to f_e, does not appear to affect this trend. A univariate analysis of variance was completed with dependent variable, consonant correct score and fixed factor, DR group. Amplification bandwidth, according to the f_e, was added as a covariate. DR group (F[1173,1] = 6.8, p = 0.010) and amplification bandwidth had a significant effect (F[5977,1] = 35.1), p < 0.001). These results suggest that provision of high-frequency amplification is beneficial to ears with and without DRs when listening to speech in babble. However, ears without DRs obtain more benefit from high-frequency amplification than ears with DRs, regardless of the cut-off frequency.

Insert Figure 6.8 about here

DISCUSSION

The aim of the present study was to compare the benefit of high-frequency amplification in ears with and without DRs using VCV nonsense syllables. In the present study all ears were tested for DRs with both the TEN-test and fast PTCs and ears with and without DRs were matched in terms of hearing level.

Mean performance in quiet was best with the unfiltered condition and there was no difference between ears with and without a DR. This finding is in agreement with Mackersie et al. (2004) and Cox et al. (2012). A possible explanation for the discrepancy with Vickers et al. (2001) and Baer et al. (2002) is that they did not have a matched control group: the controls had better hearing at the high frequencies. It is likely that greater hearing impairment resulted in less audibility, and hence poorer performance, in the DR group. To match the hearing impairments of ears with and without DRs, the present study (and Cox et al. 2012; Mackersie et al. 2004) included less extensive DRs than those in Vickers et al. (2001). This suggests that participants with more extensive DRs may benefit less from high-frequency amplification. However, this is not easy to determine as DRs are associated with increasing hearing thresholds. Therefore, an ear with an extensive DR is impossible to match with an ear without a DR. This means that audibility can never be ruled out as a factor in amplification benefit.

When listening to VCV in 20-speaker babble, both participants with and without DRs performed best in the unfiltered condition. However, participants with DRs consistently performed more poorly than participants without DRs regardless of whether the amplified speech was filtered or not. This suggests that it may not be the provision of amplification in the DR that is having a negative effect. Rather, an ear with a DR has poorer function across the frequency range. Only ears with less

extensive DRs were recruited to the present study, suggesting that these ears may not be dependent on off-frequency listening. It is possible the participants in the Vickers et al. (2001) and Baer et al. (2002) studies with more contiguous and extensive DRs than presented here, relied much more on off-frequency listening resulting in amplification having a negative effect. To investigate further how extensive a DR needs to become in order to benefit from reduced amplification further studies are required. It may well be possible to audiometrically match ears with less contiguous DRs to ears with more contiguous DRs. This may allow the effect of DR extent on high-frequency amplification benefit to be determined.

In the present study the nine ears with relatively more extensive DRs (f_e < 3kHz), were analysed separately. Again these ears showed no significant difference in performance when listening in quiet. There was no significant difference in performance between these two smaller groups when listening in quiet. There was a significant difference between groups when listening in background babble; however, amplification was never detrimental. This analysis included only a small number of ears reducing the effect size. In addition, the most extensive DR in the present study was still not as extensive as those in Vickers et al. (2001) and Baer et al. (2002).

There are a number of potential limitations to the present study. Firstly, by ensuring that ears with and without DRs matched as closely as possible in terms of hearing impairment, other factors that may differ between the groups were not considered. For example, age, sex and aetiology of hearing impairment were not closely monitored when matching the groups. Any of these factors could have resulted in increased variables in the groups. However, it has to be remembered that avoiding these variables in addition to the degree of hearing impairment would have

made the aim of this study implausible. Secondly, low-pass filtering was achieved using the hearing aids to ensure a more clinically relevant outcome. Previous studies have suggested that reducing amplification 1.7 times above f_e is the most desirable setting for ears with DRs. However, hearing aids with this channel flexibility were not readily available on the U.K. NHS when this study began, limiting the clinical ability to meet this requirement. Thirdly, participants were not given time to acclimatize to the low-pass filtered conditions. Practice was provided with the unfiltered settings to allow for task learning, in order to reduce the effect of practice. This may have resulted in participants being more acclimatized to the unfiltered condition than the low-pass filter conditions, increasing the difference between scores in the unfiltered and filtered conditions. However, Dawes et al. (2013a,b) have suggested that the effects of auditory acclimatization may be negligible. It would be helpful to complete a further study with participants wearing the hearing aid in the unfiltered and filtered conditions for a period of time prior to testing, to account for any acclimatization effect. Fourthly, this study only considered speech recognition scores for nonsense syllables. It is important to consider performance when using speech material with greater context, as well as self-reported benefit. Fifthly, the hearing aid settings used in this study included the digital noise reduction being switched on. The primary reason for doing so was to ensure the settings on the hearing aid were as similar to those set by audiologists. However, as the speech material was presented in babble, the noise reduction feature may have reduced the impact of the noise. As the test environment and hearing aid settings were the same in all cases, this feature should have had a similar effect on ears with and without DRs and the various filter settings.

It is important to consider how the findings in the present study impact on clinical decisions. It is known that DRs are relatively common, with 33% of UK adults hearing aid referrals having a DR on the TEN-test at one, or more, frequencies (Pepler et al. 2014). However, only 3% of DRs occurred at two or more adjacent frequencies. The present study suggests that provision of high-frequency amplification, although less beneficial for ears with DRs, is still useful. At the current time, the evidence would suggest that it is not advisable for clinicians to reduce high-frequency amplification for patients with less extensive DRs (spanning <3 consecutive frequencies). Further research is needed to consider whether given acclimatisation time, participants obtain more benefit from the low-pass filter settings. The findings from the present study only relate to less extensive DRs associated with moderate hearing impairment. More extensive DRs were not considered in this study as it was impossible to match audiometrically these to ears without DRs. There is evidence, based on the previous findings of Vickers et al. (2001), Baer et al. (2002) and Malicka et al. (2013) that listeners with an extensive contiguous DR may in some cases benefit from reduced high-frequency amplification. Therefore clinicians should still consider a different approach for amplification in patients with more extensive DRs than considered in the present study.

CONCLUSIONS

1) Mean performance on speech perception tasks using VCV nonsense syllables in quiet was not significantly different in ears with and without limited DRs associated with mild-to-moderate high-frequency sensorineural hearing loss.
2) Ears with DRs obtained less benefit from high-frequency amplification than ears without DRs, when listening in noise. However, these results should be

interpreted with caution because performance with low-pass filtered conditions could be different after a period of acclimatization.

3) Unfiltered broadband amplification was not detrimental in listeners with restricted high-frequency DRs.

ACKNOWLEDGEMENTS

This paper presents independent research funded by the National Institute for Health Research (NIHR) under its Research for Patient Benefit (RfPB) Programme (Grant Reference Number PB-PG-0408-15055). The views expressed are those of the author(s) and not necessarily those of the NHS, the NIHR or the Department of Health. This research was facilitated by the Manchester Biomedical Research Centre.

REFERENCES

ANSI (1997) ANSI S3.5-1997. Methods for Calculation of the Speech Intelligibility Index. New York, American National Standards Institute.

Baer, T., Moore, B.C.J., Kluk, K., (2002). Effects of low pass filtering on the intelligibility of speech in noise for people with and without DRs at high frequencies. J Acoust Soc Am, 112, 1133-44.

Byrne, D, Dillon, H, (1986). The National Acoustic Laboratories (NAL) New Procedure for Selecting the Gain and Frequency Response of a Hearing Aid. Ear Hear, 7, 207-82.

Ching, T.Y.C., Dillon, H., Byrne, D. (1998). Speech perception of hearing-impaired listeners: Predictions from audibility and the limited role of high-frequency amplification. J Acoust Soc Am, 103, 1128-40.

Ching, T.Y.C., Dillon, H., Katsch, R. et al. (2001). Maximizing effective audibility in hearing aid fitting. Ear Hear, 22, 212-24.

Cornelisse, L.E., Seewald R.C., Jamieson, D.G. (1995). The input/output (i/o) formula: A theoretical approach to the fitting of personal amplification devices. J Acoust Soc Am, 97, 1854-64.

Cox, R.M., Alexander, G.C., Johnson, J. et al. (2011). Cochlear dead regions in typical hearing aid candidates: Prevalence and implications for use of high-frequency speech cues. Ear Hear, 32, 339-48.

Cox, R.M., Alexander, G.C., Johnson, J. Rivera, I. (2012). Implication of high-frequency cochlear dead regions for fitting hearing aids to adults with mild to moderately severe hearing loss. Ear Hear, 33, 573-87.

Dallos, P., Harris, D. (1978). Properties of auditory-nerve responses in absence of outer hair cells. J Neurophys, 41, 365-83.

Dawes, P., Munro, K.J., Kalluri, S., Edwards, B. (2013a). Brainstem processing following unilateral and bilateral hearing-aid amplification. Neuroreport, 24, 271-75.

Dawes, P., Munro, K.J., Kalluri, S., Edwards, B. (2013b). Unilateral and bilateral hearing aids, spatial release from masking and auditory acclimatization. J Acoust Soc Am, 134, 596-606.

Dillon, H. (2012). Hearing Aids. 2nd Edition, Thime Publishers.

Hogan, C.A., Turner, C.W. (1998). High-frequency audibility: benefits for hearing-impaired listeners. J Acoust Soc Am, 104, 432-41.

Hornsby, B.W.Y. (2004). The Speech Intelligibility Index: What is it and what's it good for? Hearing, 57, 10-17.

Hornsby, B., and Ricketts, T. (2006). The effects of hearing loss on the contribution of high- and low- frequency speech information to speech understanding II. Sloping Hearing Losses. J Acoust Soc Am, 199, 1752-63.

Kluk, K., Moore, B.C.J. (2005). Factors affecting psychophysical tuning curves for hearing impaired subjects with high-frequency DRs. Hear Res, 200, 115-31.

Kluk, K., Moore, B.C.J. (2006b). Detecting dead regions using psychophysical tuning curves: a comparison of simultaneous and forward masking. Int J Audiol, 45, 463-76.

Kryter, K. D. (1962). "Methods for the calculation and use of the articulation index," J Acoust Soc Am, 34, 1689-97.

Mackersie, C.L., Crocker, T.L., Davis, R.A. (2004). Limiting high-frequency hearing aid gain in participants with and without suspected cochlear DRs. J Am Acad Audiol, 15, 498-507.

Malicka, A., Munro, K., Baer, T., Baker, R. & Moore, B (2013). The Effect of Low-Pass Filtering on Identification of Nonsense Syllables in Quiet by School-Age Children With and Without Cochlear Dead Regions. Ear Hear 34(4), 458-69.

Moore, B.C., Alcantara, J.I. (2001). The use of psychophysical tuning curves to explore DRs in the cochlea. Ear Hear, 22, 268-78.

Moore, B.C.J., Glasberg, B. R. (1998). Use of a loudness model for hearing-aid fitting. 1. Linear hearing aids. Br J Audiol, 32, 317-35.

Moore, B.C., Huss, M., Vickers, D.A., et al. (2000). A test for the diagnosis of DRs in the cochlea. Br J Audiol, 34, 205-24.

Moore, B.C.J., Glasberg, B.R., Stone, M.A. (2004). New version of the TEN-test with calibrations in dB HL. Ear Hear, 25, 478-87.

Moore, B.C.J. (2001). DRs in the cochlea: Diagnosis, perceptual consequences, and implications for the fitting of hearing aids. Trends Amplif, 5, 1-34.

Moore, B.C.J. (2002). Psychoacoustics of normal and impaired hearing. British Medical Bulletin, 63, 121-34.

Moore, B.C.J. (2004). DRs in the cochlea: conceptual foundations, diagnosis, and clinical applications. Ear Hear, 25, 98-116.

Murray, N., Byrne, D. (1986). Performance of hearing-impaired and normal hearing listeners with various high-frequency cut-offs in hearing aids. Aus J Audiol 8, 21-28.

Pepler, A., Munro, K.J., Lewis, K., Kluk, K. (2014). Prevalence of new referrals and existing hearing aid users. Ear Hear, 35, 289-386.

Pepler, A., Munro, K.J., Lewis, K., Kluk, K. Repeatability, agreement and feasibility of using the threshold equalising noise test and fast psychophysical tuning curves in a clinical setting Int J Aud, (In Press).

Preminger, J.E., Carpenter, R., Ziegler, C.H. (2005). A clinical perspective on cochlear DRs: intelligibility of speech and subjective hearing aid benefit. J Am Acad Audiol 16, 600-13.

Ryan, A., Dallos. P. (1975). Effect of absence of cochlear outer hair cells on behavioural auditory threshold. Nature, 253, 44-6.

Sek, A., Alcantara, J., Moore, B.C.J., et al. (2005). Development of a fast method for determining psychophysical tuning curves. Int J Aud, 44, 408-20.

Sek, A., Moore, B.C.J. (2011). Implementation of a fast method for measuring psychophysical tuning curves. Int J Audiol, 50, 237-42.

Turner, C. W., Cummings, K. J. (1999). Speech audibility for listeners with high-frequency hearing loss. American J Audiol, 8, 47-56.

Vestergaard, M.D. (2003). DRs in the cochlea: implications for speech perception and applicability of articulation index theory. Int J Audiol, 42, 249-61.

Vickers, D.A., Moore, B.C., Baer, T. (2001). Effects of low-pass filtering on the intelligibility of speech in quiet for people with and without DRs at high frequencies. J Acoust Soc Am, 110, 1164-75.

Vinay, Moore, B.C.J. (2007). Prevalence of DRs in subjects with sensorineural hearing loss. Ear Hear, 28, 231-41.

Zwicker, E., Schorn, K. (1978). Psychoacoustical tuning curves in audiology. Audiol, 17, 120-40.

Table 6.1. Hearing levels, in dB, for ears with and without DRs. The * symbol indicates frequencies falling within the estimated DR. C=control; DR=dead region.

Subject	Frequency (kHz)							Speech Intelligibility Index for each filter condition			
	0.25	0.5	0.75	1	2	3	4	Unfiltered	3 kHz	2 kHz	1.5 kHz
1C	10	15	25	30	45	45	60	0.80	0.77	0.72	0.65
1DR	15	20	30	35	50	50*	60*	0.79	0.74	0.70	0.63
2C	25	25	30	35	45	50	65	0.79	0.77	0.74	0.67
2DR	20	25	30	35	40	50	70*	0.79	0.77	0.72	0.65
3C	25	30	30	50	60	60	70	0.75	0.73	0.70	0.67
3DR	25	35	40	50	65	65	75*	0.72	0.7	0.68	0.65
4C	20	30	40	50	55	65	80	0.74	0.71	0.67	0.60
4DR	25	25	35	50	55	65	80*	0.78	0.74	0.67	0.60
5C	50	65	70	65	70	55	70	0.71	0.68	0.64	0.55
5DR	65	70	75	70	60	60	75*	0.72	0.68	0.64	0.55
6C	40	55	55	60	60	60	65	0.76	0.72	0.68	0.57
6DR	40	40	50	70	60	60	65*	0.74	0.71	0.68	0.59
7C	30	40	50	70	65	60	65	0.69	0.67	0.64	0.61
7DR	40	35	40	65	60	60	65*	0.72	0.69	0.65	0.62
8C	30	40	35	40	50	60	75	0.70	0.67	0.63	0.56
8DR	10	20	30	50	60	65*	80*	0.72	0.70	0.64	0.54
9C	10	20	25	35	45	70	75	0.66	0.64	0.61	0.59
9DR	30	30	30	50	60	70*	80*	0.63	0.61	0.60	0.58
10C	40	50	55	60	65	70	80	0.68	0.65	0.62	0.59
10DR	35	50	50	50	50	70*	90*	0.71	0.66	0.63	0.56
11C	30	40	45	55	65	70	70	0.77	0.73	0.69	0.62
11DR	20	40	40	55	65	75*	80*	0.74	0.71	0.68	0.59
12C	30	45	50	55	60	65	70	0.75	0.72	0.67	0.59
12DR	40	40	45	55	60	70*	75*	0.76	0.74	0.69	0.62
13C	20	30	40	50	60	65	70	0.77	0.74	0.68	0.64
13DR	20	20	30	50	60	60*	70*	0.74	0.71	0.68	0.64
14C	30	40	40	40	40	60	65	0.75	0.73	0.70	0.63
14DR	35	40	40	40	40	60	70*	0.73	0.72	0.67	0.65
15C	10	20	30	40	40	60	70	0.81	0.76	0.72	0.69
15DR	20	25	30	45	50	65*	70*	0.83	0.78	0.75	0.71
16C	40	50	50	70	70	70	80	0.70	0.67	0.64	0.60
16DR	30	40	50	55	60*	70*	85*	0.69	0.67	0.63	0.59
17C	40	50	50	60	70	75	80	0.65	0.63	0.61	0.54
17DR	50	55	60	65	70	70	75*	0.67	0.62	0.60	0.53
18C	10	20	20	35	45	70	70	0.78	0.76	0.73	0.70
18DR	20	30	30	40	50	70	70*	0.80	0.77	0.74	0.70
MEAN C	27	37	41	50	56	63	71	0.74	0.71	0.67	0.62
MEAN DR	30	36	41	52	56	64	74	0.74	0.71	0.67	0.61

Table 6.2. The location of DRs estimated using the TEN-test and fast PTC measures.

Subject	DR estimated boundary (KHz)	
	TEN-Test	Fast PTC
1 DR	4	2.9
2 DR	4	3.2
3 DR	4	3.5
4 DR	4	3.2
5 DR	4	3.4
6 DR	4	3.4
7 DR	4	3.1
8 DR	3	2.4
9 DR	3	2.8
10 DR	3	2.6
11 DR	3	2.3
12 DR	3	3.0
13 DR	3	2.9
14 DR	N	3.3
15 DR	2	2.7
16 DR	1.5	1.8
17 DR	3	3.2
18 DR	4	3.4

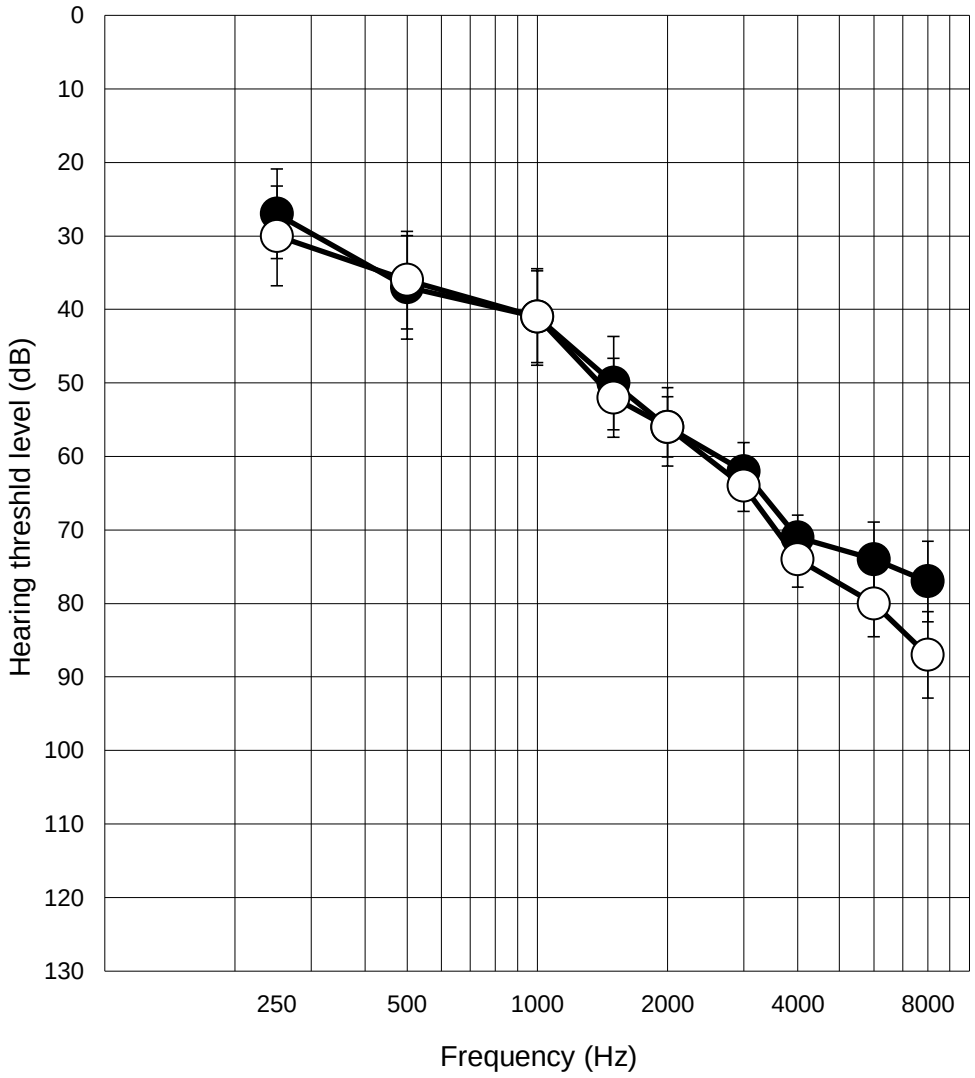

Figure 6.1. Mean hearing thresholds for ears with (open circles) and without DRs (closed circles). Error bars ± 1 standard error (n=36).

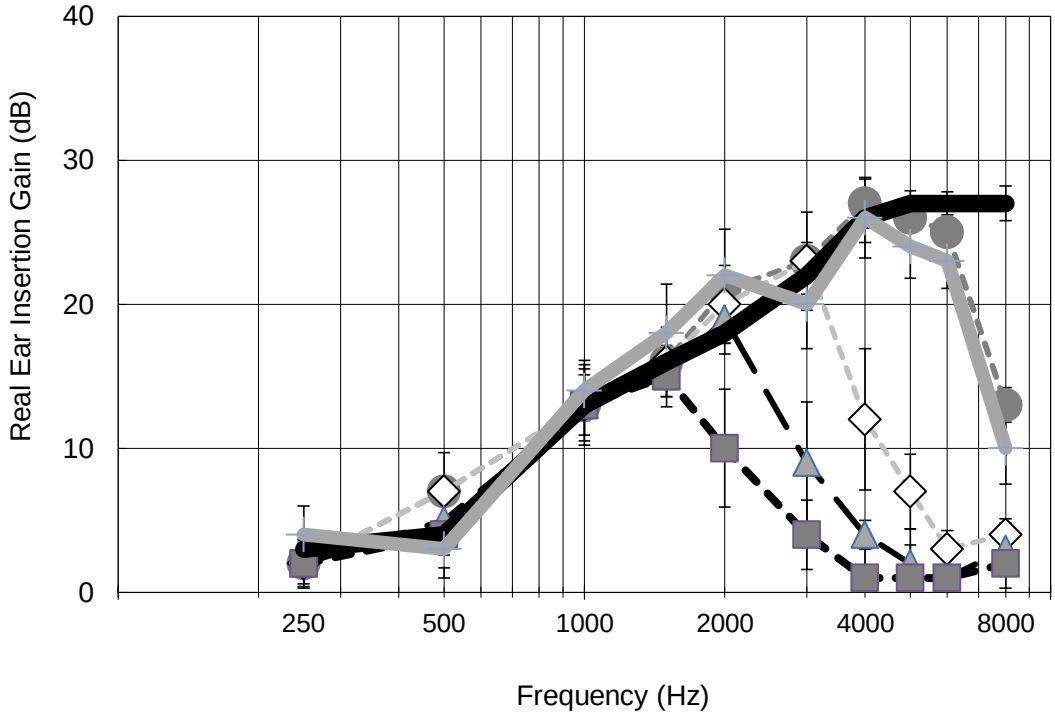

Figure 6.2. Mean (± 1 standard error) real ear insertion gain, for the four test conditions. The dark solid line shows the mean NAL-NL2 prescription target for an input of 65 dB SPL. The light solid line represents the mean gain for the participants own hearing aid. For the test hearing aid, the unfiltered condition is represented by closed circles, 3 kHz filtered condition open diamonds, 2 kHz filtered condition closed triangles and 1.5 kHz filtered condition closed squares.

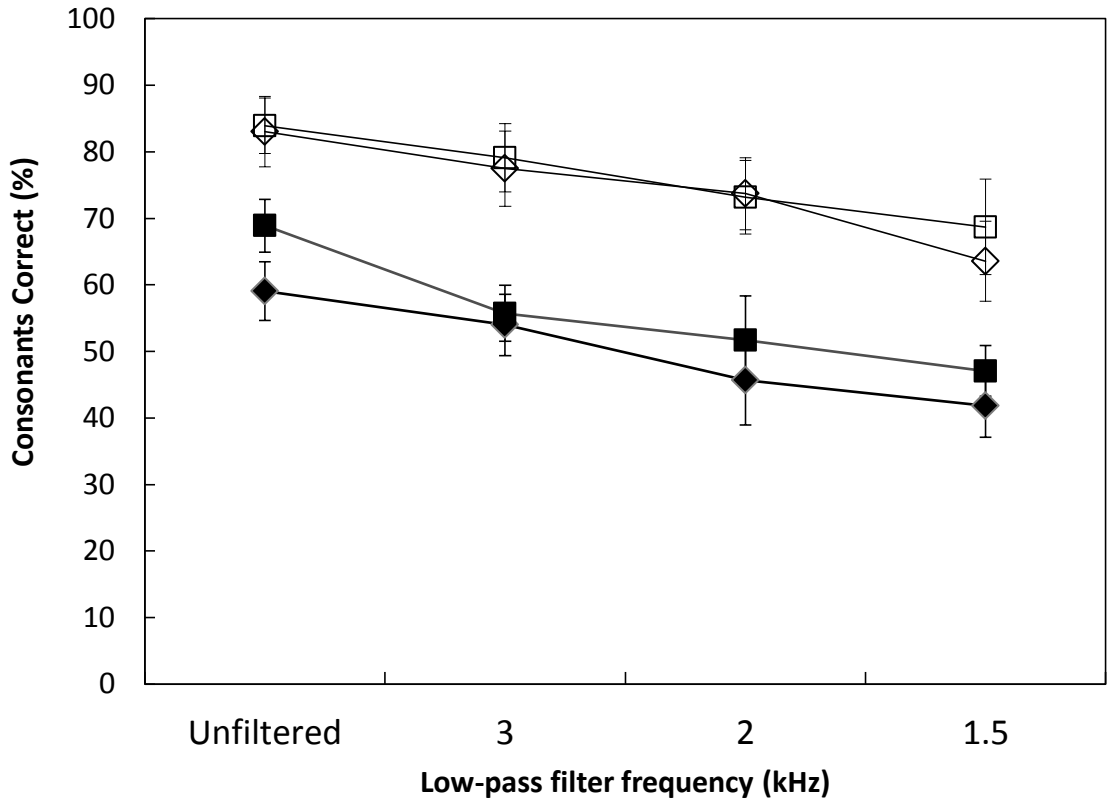

Figure 6.3. Mean consonant scores in ears with (diamond symbols) and without DRs (square symbols) in quiet (open symbols) and in noise (closed symbols). Error bars show ± 1 standard error (n=36).

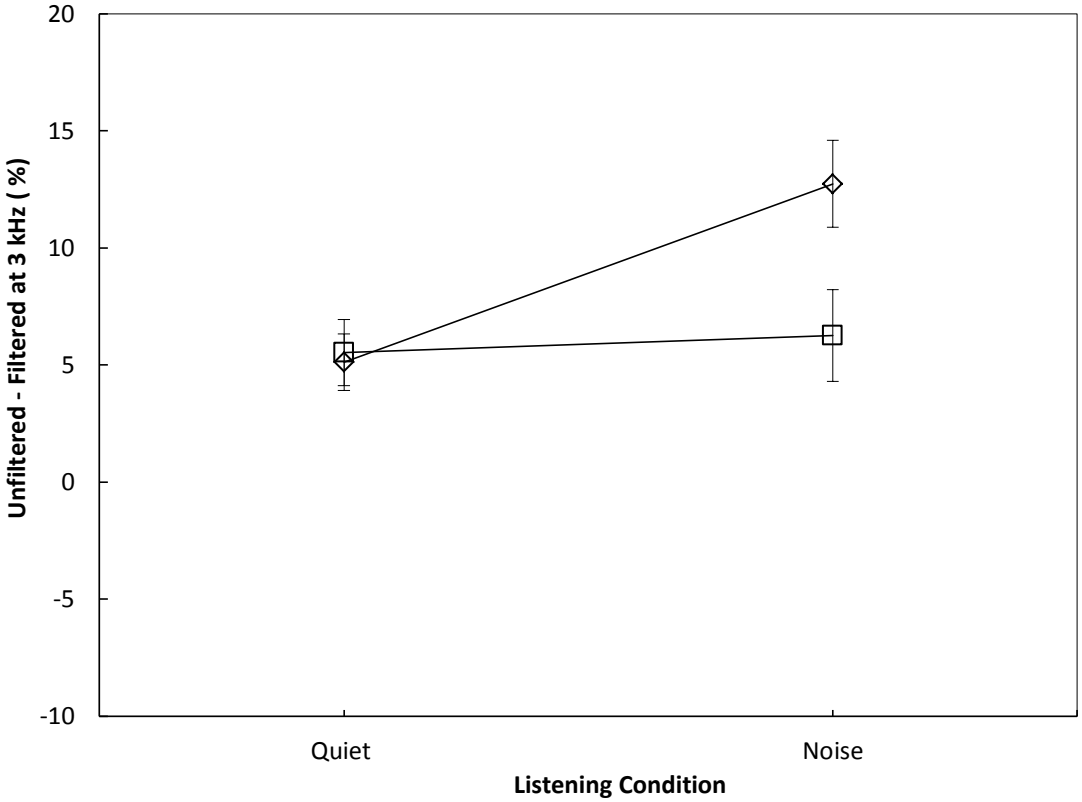

Figure 6.4. Mean difference in consonant scores between the unfiltered and 3 kHz condition in quiet and noise for ears with (square symbols) and without DRs (diamond symbols). Error bars show ± 1 standard error (n=36).

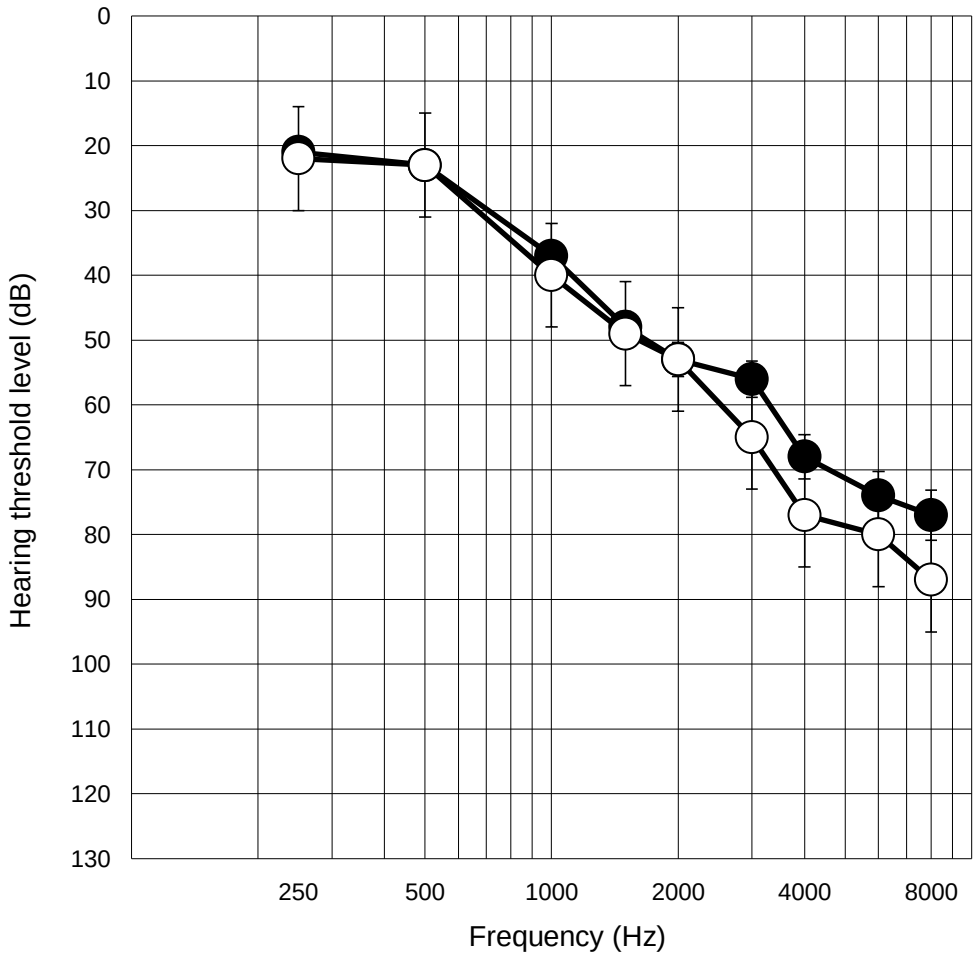

Figure 6.5. Mean hearing thresholds for ears with DRs with edge frequency ≤ 3 kHz (open circles) and without DRs (closed circles). Error bars show ± 1 standard error (n=18).

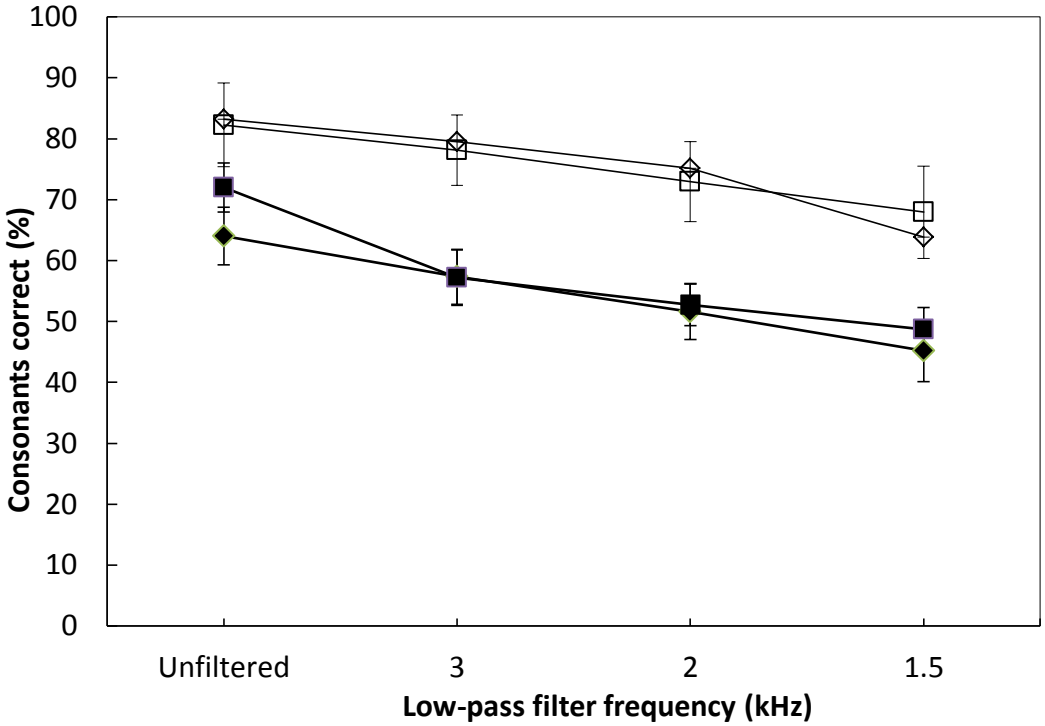

Figure 6.6. Mean consonant scores in ears with a DR < 3 kHz (diamond symbols) and without DRs (square symbols) in quiet (open symbols) and noise (closed symbols). Error bars show ± 1 standard error (n=18).

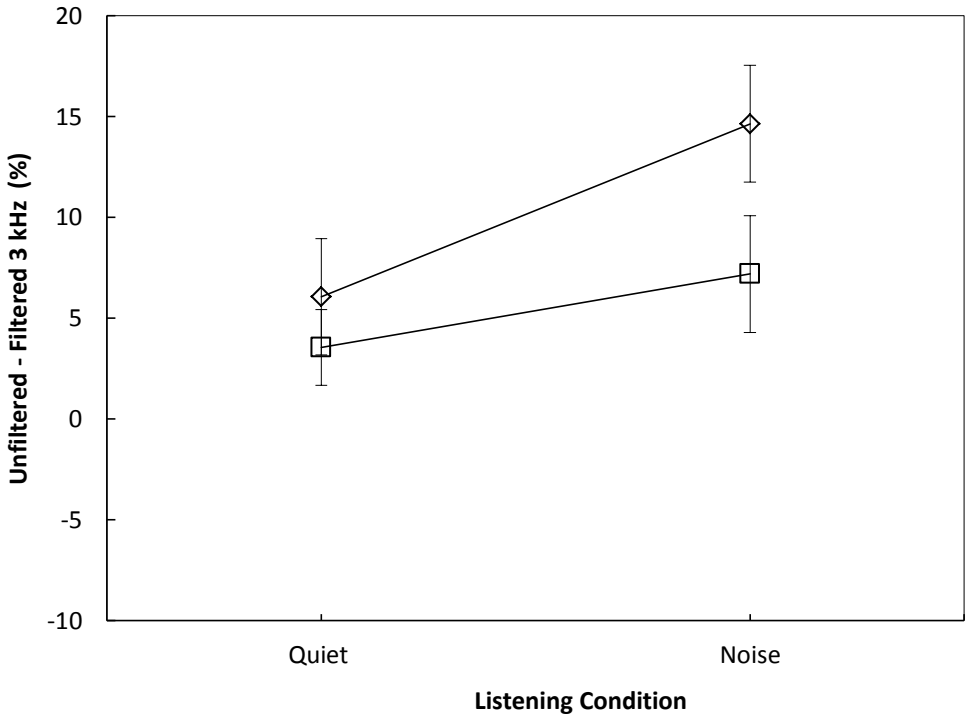

Figure 6.7. The mean difference between the unfiltered and filtered at 3 kHz condition in quiet and noise for ears with DR edge frequency <3 kHz and ears without DRs. Error bars show ± 1 standard error (n=18).

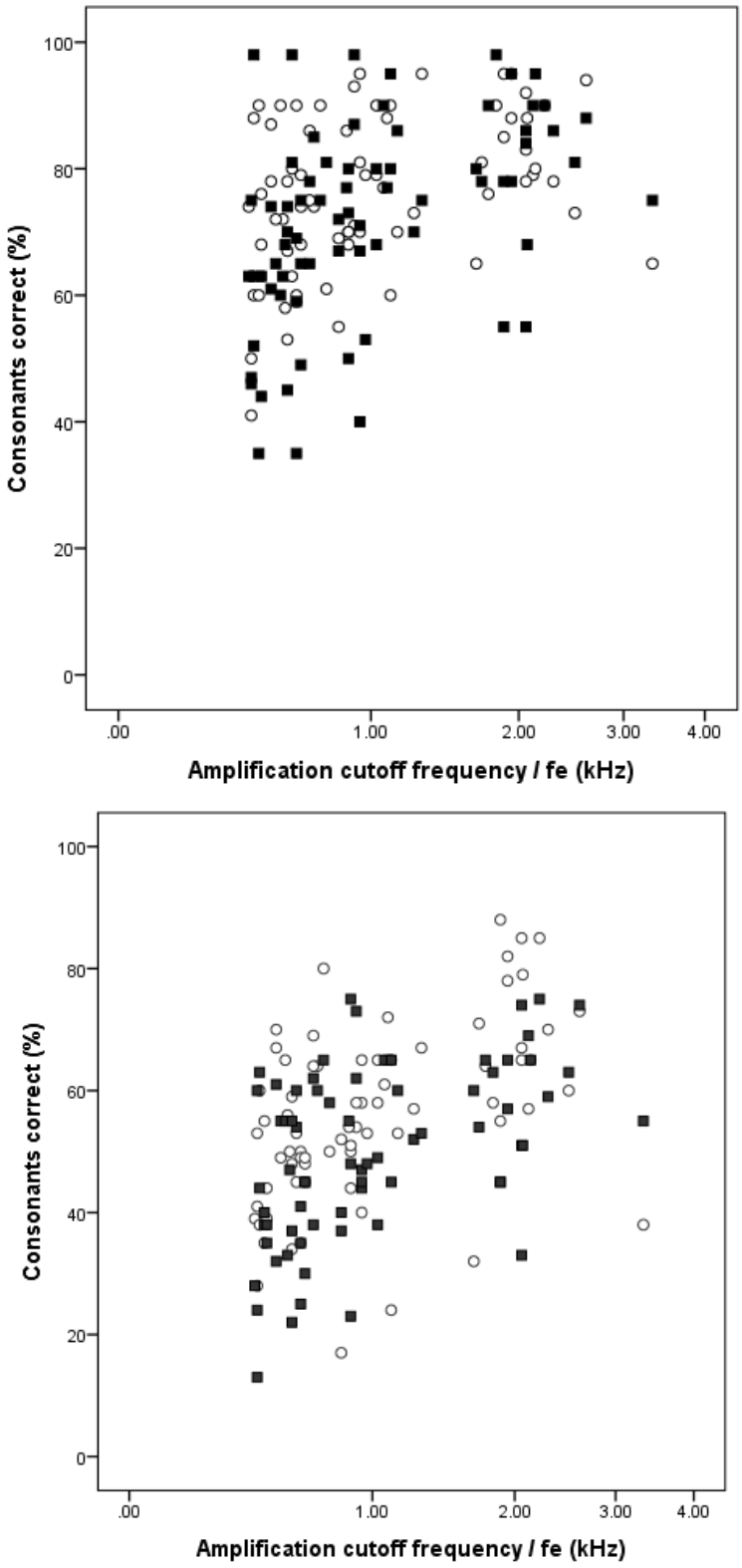

Figure 6.8. The relationship between amplification cut-off according to f_e and VCV performance (Filled squares, DR; open circles, no DR). The top panel represents speech in quiet and the bottom panel speech in babble.

CHAPTER 7

GENERAL DISCUSSION

The main aims, hypotheses, findings and clinical implications of the experimental studies in this thesis are presented in this chapter. Recommendations for the audiologists are also provided based on the findings from this thesis.

STUDY ONE

Prevalence of cochlear dead regions in new referrals and existing adult hearing aid users (Ear and Hearing, 2014)

AIM

The aim of the first study was to determine the prevalence of DRs in a clinical sample of the UK adult population of new audiology referrals and existing hearing aid users. It was hypothesised that the prevalence would be lower than that reported by Vinay and Moore (2007) and Cox et al. (2011), especially in the group of new referrals because the degree of hearing impairment of adults presenting to audiology clinics would probably be less. Secondary aims included investigating the relationship between the prevalence of DRs and factors such as audiometric configuration, age and sex.

MAIN FINDINGS

1) DR prevalence was 36% (95% CI: 31-41)
2) The difference in DR prevalence between new referrals 31% (95% CI: 25-37) and existing hearing aid users 43% (95% CI: 35-51) was not statistically significant.
3) DRs are less prevalent in the U.K. than in India where Vinay and Moore (2007) recorded a prevalence of 59% (95% CI: 52-64) in hearing-impaired

adults. This was expected as mean hearing impairment is lower in the U.K. population.

4) DR prevalence was similar to that observed by Cox et al. (2011); 31% (95% CI: 26-36) in an adult population in the USA, where mean hearing impairments were similar to the U.K. population.
5) Only 3% of DRs spanned more than three consecutive test frequencies.

DISCUSSION

As DR prevalence was significantly lower in the U.K. clinical sample than the Indian sample, the hypothesis for this study could be accepted. This difference is likely due to a greater degree of hearing impairment in the Indian populations, possible reasons for this difference include:

1) Only 50-79% of children are immunised against measles and rubella compared to over 90% in the U.K. It is known that measles and rubella can result in sensorineural hearing impairment (WHO 2000).
2) The WHO (2000) presented data that noise exposure, resulting in hearing impairment, was five times greater in South East Asia compared to high income countries such as the U.K.

The prevalence estimates in the present study were similar to those reported by Cox et al. (2011). However, when the prevalence of DRs between these two studies were compared using the same inclusion criteria, the prevalence in the U.K. population was significantly higher. The degree of hearing impairment for ears with DRs was not significantly different between these two populations, suggesting that DRs are not found at better hearing thresholds in the U.K., rather hearing impairment

is greater in the U.K. population. This may well be explained by the differences in ethnicity between the two populations. According to the USA census, 62.7% of the population in Memphis are of Black American origin. There is evidence that people of black ethnicity are less likely to have hearing impairment (Lin et al. 2012).

In this study, the aetiology of patients hearing impairment was not recorded. The primary reason for this is that it was not feasible to complete tests such as auditory brainstem responses (ABR) or otoacoustic emissions (OAEs) which may have helped distinguish sensory and neural hearing impairment on such a large clinical dataset. Questioning of patients with regards noise exposure and duration of hearing impairment was attempted, but it soon became apparent this was too subjective to use reliably as a tool to determine hearing impairment aetiology. However, the pattern of DR occurrence according to degree of hearing impairment is an important discussion as this may well indicate a link between DR prevalence and hearing impairment aetiology. Vinay and Moore (2007) suggested that DRs occur at hearing thresholds ≥ 55 dB HL. In the present study, a small number of DRs were recorded at hearing thresholds ≤55 dB HL. An explanation for this difference may be that a higher proportion of individuals in the present study had a milder hearing impairment and this simply increases the chance of finding DRs at lower hearing thresholds. The recorded values may have been as a result of false positives on the TEN-test; however, in two ears with DRs occurring between 40 and 45 dB HL, the DR criteria were met for both fast PTCs and the TEN-test. This would suggest that DRs do occur at hearing impairments ≤ 55 dB HL. This finding is in agreement with the finding from Hornsby and Dundas (2009) who reported DRs at hearing impairments <60 dB HL. This may be explained by variations in hearing impairment aetiology between the studies. A number of participants with moderate hearing

impairment who met the criteria for a DR on the TEN-test had a congenital or acquired neurological disorder so a DR may be due to reduced or poor neural activity. However, this does not explain the wide variation in hearing thresholds associated with DRs (from 60 to 85 dB HL). It is known that OHC damage can result in a hearing impairment up to around 60 dB HL (Yates 1990, 1995; Ruggero et al., 1997). An impairment greater than this is considered to be associated with some degree of IHC damage. Griffiths et al. (2001) proposed OHC and IHC damage to be disassociated in genetic hearing impairments, with different mutations resulting in varying amounts of damage in each hair cell type. Higher auditory pathways or central processes may impact on the patient's responses on pure-tone audiometry. This may result in the audiometric threshold being elevated beyond that resulting directly from hair cell damage. As the causal factors for DRs are wide and cannot be individually tested, this explains the difficulty in identifying them from hearing thresholds alone.

Even though degree of hearing impairment is associated with DRs, sensitivity and specificity data from the present study revealed that there is a high risk of false positives or negatives when using the pure tone audiogram to predict DRs. These findings are in agreement with those from Vinay and Moore (2007) and Cox et al. (2011) suggesting that hearing thresholds are not a reliable DR indicator.

Age was found to be significantly associated with higher prevalence of DRs. This would suggest that with the increasing ageing population, DRs will have an greater effect. However, it was found that it is unlikely age itself results in greater DR prevalence, rather greater degree of hearing impairment is associated with increasing age.

Only a small number of DRs were found to be extensive and contiguous. This would suggest that only a small number of patients attending U.K. audiology clinics will have DRs extensive enough to result in substantial perceptual consequences. However, there is no conclusive data indicating how many frequencies a DR has to span to impact on a patient's hearing aid benefit. Therefore, it is not possible to accurately determine how many of these DRs were "clinically significant".

These findings have three relevant clinical implications. Firstly, as DRs are prevalent in a sample within the U.K. there is clinical importance of investigating the impact of DRs further. Secondly, as DRs cannot be determined from hearing thresholds alone, it is crucial that a reliable, accurate and feasible test is identified. Therefore, the next study in this thesis was designed to investigate the tests available to diagnose DRs in the audiology clinic. Thirdly, to have a greater understanding of the clinical significance of DRs, it is important to determine hearing aid benefit. Therefore, the third and final study in the thesis was designed to compare hearing aid benefit in ears with and without DRs.

STUDY TWO

Repeatability, agreement and feasibility of using the threshold equalising noise test and fast psychophysical tuning curves in a clinical setting (International Journal of Audiology, In Press)

AIM

The aim of the second study was to investigate the test repeatability, agreement and clinical feasibility of the TEN-test and fast PTCs in a large clinical population of hearing-impaired adults with and without DRs. It was hypothesised that the TEN-test would be more feasible for use in clinic because it would be quicker and easier to complete than fast PTCs. However, the TEN-test would be less accurate at detecting DRs than fast PTCs because of the half-octave intervals between TEN-test frequencies. Both tests were hypothesised to have good retest repeatability.

MAIN FINDINGS

1) The TEN-test and fast PTC measurements were repeatable in terms of meeting the criteria for a DR.
2) The TEN-test gives a more repeatable f_e than fast PTCs on test-retest comparison. However, this is likely due to fast PTCs being able to provide an exact location f_e increasing the risk of variability in the outcome.
3) A fast PTC tip shift >15 % of the signal frequency is significant because this cannot be explained in terms of test-retest repeatability.
4) The TEN-test was more likely to result in conclusive results than fast PTCs, in typical patient groups that attend audiology clinics because the test was quicker and easier for patients to complete.
5) On average, fast PTC measurements took five times longer to complete than the TEN-test.

6) The TEN-test is less likely to identify extensive DRs than fast PTCs because it can only detect DRs at half-octave intervals. This suggests that fast PTCs are more sensitive at identifying DRs.
7) The agreement of the TEN-test and fast PTCs in terms of DR diagnosis was greatest (87%) when the following test criteria were used:
    - For fast PTCs, a DR is indicated if the difference in tip frequency and signal frequency is greater than 10% of the signal frequency in Hz. For example, for a signal frequency of 4000 Hz, the difference between tip frequency and signal frequency needs to be >400 Hz for a DR to be indicated.
    - For the TEN-test, a DR is indicated if the masked threshold is ≥10 dB above the TEN level and absolute threshold. For example, if the absolute threshold is 70 dB and the presented TEN level is 76 dB, the masked threshold needs to be ≥86 dB to indicate a DR.

CLINICAL IMPLICATIONS

The findings revealed that the TEN-test is the most feasible test in terms of detecting DRs in the clinic. The limitation of the TEN-test is that it may underestimate the extent of a DR because it only tests at half-octave intervals. Therefore, the hypothesis that fast PTCs are more accurate at detecting DRs but less feasible for use in audiology clinics can be accepted. As a result the TEN-test should be used to detect the presence of a DR in patients; however, if it is crucial that the f_e is identified accurately, then fast PTCs should be used. Both tests were repeatable and therefore the hypothesis that both tests would be repeatable can be accepted. The TEN-test was generally more repeatable than fast PTCs, likely due to the limited test frequencies used that reduced the likelihood of variability.

In order for audiologists to know whether it is necessary for the DR to be accurately located, knowledge of the implications of a DR in terms of hearing aid benefit is vital. This was the motivation for the third and final study, which investigated the impact of DRs on the benefit of different amplification settings.

STUDY THREE

Benefit of high-frequency amplification in ears with cochlear dead regions

AIM

The aim of the final study was to compare the benefit of high-frequency amplification in adults with and without high-frequency DRs (diagnosed using both the TEN-test and fast PTCs). In addition, ears with DRs were audiometrically matched to ears without DRs (0.25 and 8 kHz). A secondary aim was to consider the effect of the extent of the DR on the benefit of high-frequency amplification. It was hypothesised that ears with DRs would obtain less benefit from high-frequency amplification and this would be greatest in cases where there is an extensive DRs.

MAIN FINDINGS

1) Provision of amplification well inside a DR has no negative effect on speech perception for the population used in this thesis.
2) Listeners with DRs obtained less benefit from amplification than listeners without DRs when completing speech perception tests in noisy conditions.

CLINICAL IMPLICATIONS

It is important to consider two aspects of this study which limit its relevance to the hearing aid population as a whole. Firstly, it was impossible to match the hearing impairments of ears with more extensive contiguous DRs to ears without DRs. This resulted in the participants in this study having DRs that spanned less than 3 frequencies. Therefore, the results of this study can only be used to consider the impact of hearing aid benefit in ears with less extensive DRs. In addition by matching as closely as possible the degree of hearing impairment in ears with and without DRs, other variables such as age, sex and aetiology of hearing impairment were not considered and matched. These unmatched factors may have caused bias in each group thus influencing the results. Secondly, low-pass filtering was achieved by adjusting hearing aid frequency response to ensure a more clinically relevant outcome. Previous studies have suggested that reducing amplification 1.7 times above f_e is the most desirable setting for ears with DRs. However, at the time when this research began hearing aids with this channel flexibility were not available limiting the clinical ability to meet this requirement. However, hearing aid gain channels availability has increased substantially since then and now it may be possible to achieve the 1.7 times f_e cut-off.

These results suggest that audiologists should continue to provide high-frequency amplification using a recognised prescriptive fitting method, within the limits of auditory feedback, as they currently do at least for ears with less extensive DRs. However, audiologists should provide further counselling for patients with DRs, with the knowledge that speech perception performance in noise may be lower, than the hearing impairment would suggest, for these patients. Further research is

required to investigate if acclimatisation in real-world situations to low-pass filter settings changes the outcomes.

CLINICAL RECOMMENDATIONS FOR AUDIOLOGISTS

The primary aim of this thesis was to provide the audiologist with a greater understanding of how to detect and manage DRs in the clinical setting. A flowchart of recommendations is provided in Appendix A which the audiologist can refer to. The text below explains the reasoning for the flowchart layout.

Although DRs were identified as being prevalent (36% of patients) only a small proportion of patients (3%) were found to have extensive DRs, spanning three or more consecutive frequencies (Pepler et al. 2014). The findings from study 3 demonstrated that in patients with less extensive DRs there is currently no evidence to adjust the hearing aid settings. Therefore it is unlikely that routinely testing each patient that attends the audiology clinic for a DR is going to be a worthwhile use of very limited clinical time. However, there is also evidence that patients with DRs, of any extent, are likely to have more difficulty in noisy situations. In this instance the patient may well benefit from 'realistic expectations' counselling. Therefore, the flowchart shows that any patient that reports distortion and/or difficulty in noise beyond that expected for their degree of hearing impairment should be referred to the a dedicated clinic for more complex cases. This is a very subjective referral criterion and many patients report some degree of difficulty hearing in noise likely associated with the limitations of the hearing aid sound processing features. The audiologist should use their own experience and knowledge to determine whether the patient is likely to benefit from additional testing. Although the TEN test may not be as sensitive as fast PTCs at identifying extensive DRs, it is more feasible for clinical

use (Pepler et al. In Press). Therefore, when the patient is seen in the complex case clinic the TEN test should be used as a screening tool for DRs. If no DR is identified, further testing should be completed to identify why the patient is having significant difficulty in noise. If the TEN test identifies a DR that spans ≤2 consecutive frequencies this suggests that the patient is very unlikely to benefit from reduced high-frequency amplification. In these patients it will be important to counsel them with regards to DRs being associated with greater difficulties hearing in noisy situations. If the TEN test identifies a DR that spans ≥3 consecutive frequencies the evidence from previous research is that some patients may benefit from reduced amplification. At present it is not clear what causes a patient not to benefit from amplification. However, the reduction of high-frequency amplification is unlikely to be detrimental to this group of patients, as performance in this group typically plateaus with increasing high-frequency amplification. If the audiologists were to trial reduced amplification it would be beneficial to complete fast PTC measurements using a signal frequency inside of the DR to determine f_e. This is due to the findings in the second study showing that the TEN test results underestimated the DR f_e which may result in amplification being low-pass filtered too conservatively.

The overall aim of this flowchart is to avoid excessive testing of DRs in clinical situations where time is limited but at the same time ensuring that patients with DRs are managed effectively. The recommendations to audiologists will inevitably become clearer as more research is completed in this area.

CHAPTER 8

CONCLUSIONS AND RECOMMENDATIONS FOR FURTHER RESEARCH

This chapter considers the main clinical and research implications for each of the key research findings and also recommendations for potential future research.

Prevalence of DRs

At least 1 in 3 hearing-impaired adults, attending an audiology clinic with a sensorineural hearing impairment in the UK, met the TEN-test criteria for a DR. This indicates that DRs are sufficiently common to warrant further research studies investigating hearing aid benefit. These findings indicate a number of further research opportunities which would be beneficial to the clinician:

1) Does the prevalence of DRs differ in different geographical locations in the UK?

This is an important question as it is possible that DR prevalence is particularly high or low in Manchester. If DR prevalence was particularly high or low in Manchester compared to other parts of the UK, the importance of investigating DR management options may have been misleadingly increased or decreased, respectively. Manchester has been traditionally known as an industrial and urban area (Davis et al. 1991). It would be valuable to recruit and test a large clinical sample of patients for DRs in other areas in the UK, with different socioeconomic status. Locations which may be considered include Bournemouth, a more elderly population with little history of industrial labour or Mid Wales or the South West of England which is considered a more rural population (Davis et al. 2001).

2) Does the prevalence of DRs differ according to the aetiology of hearing impairment?

It is valuable for clinicians to know in what patient group DRs are most prevalent. This will allow DR tests and management plans to be targeted to most at risk groups, reducing the costs of testing all patient groups. It has been suggested that DRs may be more prevalent in patients with significant noise exposure. However, this is difficult to quantify. The main difficulty in answering this question is defining the aetiology of hearing impairment, as noise exposure is based on subjective reports from the patient. Therefore, DR prevalence would need to be measured in groups with relatively well determined hearing aetiology. Data may be analysed by considering the prevalence of DRs in each group. In addition, each risk factor may be considered independently using logistic regression analysis. Problems such as multiple risk factors and a significant time lapse since the onset of hearing impairment may all result in difficulties in completing a non-biased study.

3) Can an association between hearing impairment and DR occurrence be identified using mathematical modelling?

Although DRs are associated with greater degrees of hearing impairment, it was not possible to identify a sensitive yet specific method of identifying DRs from hearing thresholds alone (Vinay & Moore 2007; Cox et al. 2011; Pepler et al. 2014). If it were possible to identify a DR using the pure tone audiogram this would increase the likelihood of clinicians considering DRs when fitting hearing aids. The data analysis in this thesis considered individual characteristics of hearing impairment such as hearing thresholds and gradient of hearing impairment. However, combining these characteristics using statistical modelling, may provide a

more sensitive and specific method of identifying DRs from the pure tone audiogram.

4) Is the prevalence of DRs different in hearing-impaired children and adults?

It is important to know if the paediatric population is as likely to have DRs as the adult population. If DRs are less prevalent in the paediatric population this may suggest that routine testing for DRs is not warranted in this group. Neither the TEN-test nor fast PTCs can be used until a child is able to complete a behavioural test. Malicka et al. (2009) found that children from the age of eight were able to complete fast PTCs, although the mean tip shifts were typically greater than that recorded in adults. The study should be completed in the same geographical location and with the same sample size as used in the adult prevalence study. Ideally the hearing impairment of the paediatric population would be matched to the adult population to ensure hearing impairment was not a factor in DR prevalence. The findings will provide audiologists with useful information as to whether a specialist rehabilitation service for children with DRs is required within their departments.

Diagnostic test methods

The TEN-test has shorter test duration and higher interpretation rate than fast PTCs. However, the TEN-test may underestimate the extent of a DR because of its inability to precisely identify f_e. If a large number of patients need to be tested for DRs, the TEN-test provides a reasonably repeatable and very efficient method of detection. If the accuracy of DR location is paramount and it is vital that all DRs are detected, fast PTC measurements should be obtained. These findings indicate a number of further research opportunities which would be beneficial to the clinician:

1) Assessing the use of the TEN-test at smaller frequency intervals

Currently one of the limitations of the TEN-test is that it is only completed at half-octave intervals. This limits its ability to accurately diagnose f_e (Pepler et al. In Press). However, if the TEN-test could be used at smaller intervals, such as 0.1 kHz this would increase test accuracy. As the TEN-test has not been completed at such small intervals it would be important to evaluate the implications of extra test frequencies on test duration and accuracy.

2) Investigating methods of reducing fast PTC test time

The lengthy test time of fast PTCs makes it unfeasible for clinical use even though it is the most accurate test for detecting DRs (Pepler et al. In Press). Therefore it is important to consider ways to increase the feasibility of testing fast PTCs in clinical settings. The lag effect, which results from the PTC tip being shifted in the direction of the masker sweep, means that ascending and descending sweep measurements are required. However, if the mean tip shift of ascending and descending sweeps, in ears without DRs, was measured at a range of signal frequencies it may be possible to account for the lag effect. If this could be achieved, either the ascending or descending sweep may no longer be required. This would halve the number of recordings, significantly reducing the test time thus increasing the clinical feasibility of the test.

Outcome when a DR is present

Ears with and without DRs, benefit from high-frequency amplification. However, ears with DRs obtain less benefit from high-frequency amplification than ears without DRs in noise. There is little evidence to support the need to use a

different prescription approach when a DR is present in a typical NHS hearing aid user. However, there is evidence that DRs are associated with reduced speech perception in noise, at least when listing to nonsense syllables in the laboratory. Therefore audiologists should be aware of this and provide suitable rehabilitation for patients with DRs. The findings from this study indicate a number of further research opportunities which would be beneficial to the clinician:

1) Does the extent of a DR impact on hearing aid benefit?

It is important to know whether the extent of a DR has an impact on hearing aid benefit as the most appropriate management plans may differ depending on the extent of the DR. Two groups would be identified, one with contiguous DRs with $f_e \leq 2$ kHz and one with contiguous DRs with $f_e > 2$ kHz. Each of these groups would be matched for hearing impairment, age, education level and socioeconomic status as closely as possible. One limitation of this study would be its reliance on the accuracy of fast PTCs locating f_e. In addition the difference in extent of DRs between groups may be so small that it will be difficult to assess effect. Therefore, when pairing ears it will be necessary to ensure that f_e is sufficiently different.

2) Does the provision of a different signal processing strategy effect hearing aid benefit in listeners with DRs?

Numerous hearing aids with a range of processing strategies are available to audiologists. Therefore it is important to identify which are the best signal processing strategies for patients with DRs. One signal processing strategy of particular interest is frequency lowering, which allows sounds presented within a DR to be compressed in to a frequency region on the edge or outside of the DR. To

consider whether frequency lowering is beneficial to listeners with DRs, ears with and without DRs need to be audiometrically matched. It would be crucial to allow the patients' time to acclimatise to the hearing aid settings with and without frequency lowering switched on. This is due to the significant difference in signal processing strategies from typical NHS hearing aids. Speech perception scores in quiet and babble would be measured with and without frequency lowering switched on. This will help audiologists determine the most suitable hearing aid processing technology for patients with DRs.

3) Do DRs have an impact on hearing aid benefit in real-world situations following acclimatisation?

The third study in this thesis considered the benefits of low-pass filtering hearing aid amplification in the laboratory. However, it is equally important to identify which amplification is preferred and most suitable for patients in real-world situations, after a period of acclimatisation. Cox et al. (2012) completed a study considering these questions, but further research is required to gain a better understanding of the most suitable amplification for patients with more extensive DRs in real-world situations.

REFERENCES

Aazh, H., Moore, B.C.J. (2007). Dead regions in the cochlea at 4 kHz in elderly adults: Relation to absolute threshold, steepness of audiogram, and pure-tone average. J Am Acad Audiol, 18, 97-106.

Acar, B., Yurekli, M.F., Babademez, M.A. et al. (2011). Effects of hearing aids on cognitive functions and depressive signs in elderly people. Arch Gerontology Geriatrics, 52, 250-52.

Action on Hearing Loss (AoHL), (2012). Retrieved May 15, 2012 from http://www.actiononhearingloss.org.uk/your-hearing/about-deafness-and-hearing-loss/statistics.aspx

Alcantara, J.I., Moore, B.C.J., Marriage, J. (2004). Comparison of three procedures for initial fitting of compression hearing aids. II. Experienced users, fitted unilaterally. Int J Audiol, 43, 3-14.

ANSI (1999). ANSI S3.1-1999. Maximum permissible ambient noise levels for audiometric test rooms. New York, American National Standards Institute.

ANSI (1997) ANSI S3.5-1997. Methods for Calculation of the Speech Intelligibility Index. New York, American National Standards Institute.

Ashmore, J. (2008). Cochlear outer hair cell motility. Physiological Reviews, 88, 173-210.

Baer, T., Moore, B.C.J., Kluk, K. (2002). Effects of low pass filtering on the intelligibility of speech in noise for people with and without DRs at high frequencies. J Acoust Soc Am, 112, 1133-44.

Bland, J.M., Altman, D.G. (1986). Statistical methods for assessing agreement between two methods of clinical measurement. Lancet, 1 (8476) 307-10.

British Society of Audiology (BSA). (2011). Recommended procedure: Pure tone air and bone conduction threshold audiometry with and without masking and determination of uncomfortable loudness levels.

Brownell, W.E., Bader, C.R., Bertrand, D., Deribaupierre, Y. (1985). Evoked Mechanical Responses of Isolated Cochlear Outer Hair-Cells. Science, 227, 194-196.

Byrne, D, Dillon, H, (1986). The National Acoustic Laboratories (NAL) New Procedure for Selecting the Gain and Frequency Response of a Hearing Aid. Ear Hear, 7, 207-282.

Byrne, D., Dillon, H., Ching, T., et al. (2001). NAL-NL1 procedure for fitting nonlinear hearing aids: characteristics and comparisons with other procedures. J Am Acad Audiol, 12, 37-51.

Cairns, S., Frith, R., Munro, K.J., Moore, B.C.J. (2007). Repeatability of the TEN(HL) test for detecting cochlear DRs. Int J Audiol, 46, 575-84.

Ching, T.Y.C., Dillon, H., Byrne, D. (1998). Speech perception of hearing-impaired listeners: Predictions from audibility and the limited role of high-frequency amplification. J Acoust Soc Am, 103, 1128-40.

Ching, T.Y.C., Dillon, H., Katsch, R. et al. (2001). Maximizing effective audibility in hearing aid fitting. Ear Hear, 22, 212-24.

Cornelisse, L.E., Seewald R.C., Jamieson, D.G. (1995). The input/output (i/o) formula: A theoretical approach to the fitting of personal amplification devices. J Acoust Soc Am, 97, 1854-64.

Cox, R.M., Alexander, G.C., Johnson, J. et al. (2011). Cochlear dead regions in typical hearing aid candidates: Prevalence and implications for use of high-frequency speech cues. Ear Hear, 32, 339-348.

Cox, R.M., Alexander, G.C., Johnson, J. Rivera, I. (2012). Implication of high-frequency cochlear dead regions for fitting hearing aids to adults with mild to moderately severe hearing loss. Ear Hear, 33, 573-87.

Dallos, P., Harris, D. (1978). Properties of auditory-nerve responses in absence of outer hair cells. J Neurophys, 41, 365-83.

Davis, A., Ostri, B., Parving. A. (1991). Longitudinal study of hearing. Acta Otolayringol. 476S, 12-22.

Dawes, P., Munro, K.J., Kalluri, S., Edwards, B. (2013a). Brainstem processing following unilateral and bilateral hearing-aid amplification. Neuroreport, 24, 271-75.

Dawes, P., Munro, K.J., Kalluri, S., Edwards, B. (2013b). Unilateral and bilateral hearing aids, spatial release from masking and auditory acclimatization. J Acoust Soc Am, 134, 596-606.

Dillon, H. (2012). Hearing Aids. 2nd Edition, Thime Publishers.

Elberling, C., Ludvigsen, C., Lyregaard, P.E. (1989). DANTALE: A new Danish speech material, Scand Audiol, 18, 169–176.

Etymotic Research (2001). “QuickSIN Speech-in-Noise Test, Version 1.3.” (Compact Disk).

Gatehouse, S., (1999). A self-report outcome measure for the evaluation of hearing aid fittings and services. Health Bulletin, 57, 424-36.

Gates, G., Mills, J. (2005). Presbycusis. Lancet, 366, 1111-20.

Gelfand, S (2004), Hearing - An introduction to psychological and physiological acoustics. 4th Edition. Marcel Decker.

Glasberg, B.R., Moore, B.C.J. (1986). Auditory filter shapes in subjects with unilateral and bilateral cochlear impairments. J Acoust Soc Am, 79, 1020-1033.

Greenwood, D.D. (1971). "Aural combination tones and auditory masking". J Acoust Soc Am, 50, 502-543.

Griffiths, T.D., Blakemore, S., Elliott, C., et al. (2001). Psychological evaluation of cochlear hair cell damage due to the A3243G mitochondrial DNA mutation. JARO, 2, 172-179.

Halpin, C., Thornton, A., Hasso, M. (1994). Low-frequency sensorineural loss - Clinical-evaluation and implication for hearing-aid fitting. Ear Hear, 15, 71-81.

Hirsh, I.J., Reynolds, E.G., Joseph, M., (1954), "The intelligibility of different speech materials", J Acoust Soc Am, 26, 530-538.

Hogan, C.A., Turner, C.W. (1998). High-frequency audibility: benefits for hearing-impaired listeners. J Acoust Soc Am, 104, 432-41.

Hornsby, B.W.Y. (2004). The Speech Intelligibility Index: What is it and what’s it good for? Hearing, 57, 10-17.

Hornsby, B., and Ricketts, T. (2006). The effects of hearing loss on the contribution of high- and low- frequency speech information to speech understanding II. Sloping Hearing Losses. J Acoust Soc Am, 199, 1752-1763.

Hornsby, B.W.Y., Dundas, J.A. (2009). Factors affecting the outcomes on the on the TEN(SPL) test in adults with hearing loss. J Am Acad Audiol, 20, 251-263.

Huss, M., Moore, B.C.J. (2005a). Dead regions and pitch perception. J Acoust Soc Am, 117, 3841-3852.

Huss, M., Moore, B.C.J. (2005b). Dead regions and noisiness of pure tones. Int J Audiol, 44, 599-611.

Jacob, R.T., Fernandes, J. C., Manfrinato. J., et al. (2006). Identifying dead regions in the cochlea through the TEN-test, Rev Bras Otorrinolaringol, 72, 673-682.

Kricos, P.B., Erdman, S., Bratt, G.W., et al. (2007). Psychosocial correlates of hearing aid adjustment. J Am Acad Audiol, 18, 304-22.

Kluk, K., Moore, B.C.J. (2004). Factors affecting psychophysical tuning curves for normally hearing subjects. Hear Res, 194, 118-134.

Kluk, K., Moore, B.C.J. (2005). Factors affecting psychophysical tuning curves for hearing impaired subjects with high-frequency dead regions. Hear Res, 200, 115-131.

Kluk, K., Moore, B.C.J. (2006a). Dead regions in the cochlea and enhancement of frequency discrimination: Effects of audiogram slope, unilateral versus bilateral loss, and hearing-aid use. Hear Res, 222, 1-15.

Kluk, K., Moore, B.C.J. (2006b). Detecting dead regions using psychophysical tuning curves: a comparison of simultaneous and forward masking. Int J Audiol, 45, 463-76.

Kryter, K. D. (1962). "Methods for the calculation and use of the articulation index," J Acoust Soc Am, 34, 1689–1697.

Levitt. (1971). Transformed up-down methods in psychoacoustics. J Acoust Soc Am, 49, 467-477.

Lin, F.R., Maas, P., Chien, W., Carey, J.P., et al. (2012). Association of skin color, race/ethnicity, and hearing loss among adults in the USA. J Assoc Res Otolaryngol, 13, 109-117.

Lutman, M.E., Wood E. (1984). A simple clinical measure of frequency resolution. Br J Audiol, 19, 1-8.

Mackersie, C., Boothroyd, A., Minniear, D. (2001). Evaluation of the Computer-Assisted Speech Perception Assessment Test (CASPA). J Am Acad Audiol, 12, 390-396.

Mackersie, C.L., Crocker, T.L., Davis, R.A. (2004). Limiting high-frequency hearing aid gain in listeners with and without suspected cochlear DRs. J Am Acad Audiol, 15, 498-507.

Markessis, E., Kapadia, S., Munro, K., et al. (2006). Modification of the Threshold Equalising Noise (TEN) test for cochlear DRs for use with steeply sloping high-frequency hearing loss. Int J Audiol, 45, 91-98.

Malicka, A.N., Munro, K.J., Baker, R.J. (2009). Fast method for psychophysical tuning curve measurement in school-age children. Int J Audiol, 48, 546-53.

Malicka, A.N., Munro, K.J., Baker, R.J. (2010). Diagnosing cochlear dead regions in children. Ear Hear, 31, 238-46.

Malicka, A., Munro, K., Baer, T., Baker, R. & Moore, B (2013). The Effect of Low-Pass Filtering on Identification of Nonsense Syllables in Quiet by School-Age Children With and Without Cochlear Dead Regions. Ear Hear 34(4), 458-69.

Martin, E. (2007). Concise Medical Dictionary (7th Edition). Oxford University Press.

McDermott, H.J., Lech, M., Kornblum, M.S., Irvine, D.R. (1998). Loudness perception and frequency discrimination in subjects with steeply sloping hearing loss: possible correlates of neural plasticity. J Acoust Soc Am, 104, 2314-25.

Moore, B.C.J. (2001). Dead regions in the cochlea: Diagnosis, perceptual consequences, and implications for the fitting of hearing aids. Trends Amplif, 5, 1-34.

Moore, B.C.J. (2002). Psychoacoustics of normal and impaired hearing. British Medical Bulletin, 63, 121-34.

Moore, B.C.J. (2004). Dead regions in the cochlea: conceptual foundations, diagnosis, and clinical applications. Ear Hear 25, 98-116.

Moore, B.C.J., Glasberg, B.R. (1982). Interpreting the role of suppression in psychophysical tuning curves. J Acoustic Soc Am, 72, 1374-79.

Moore, B.C.J., Glasberg, B. R. (1986). The role of frequency selectivity in the perception of loudness, pitch and time, in Frequency Selectivity in Hearing, edited by Moore B.C.J. (Academic, London), 251-308.

Moore, B.C.J., Peters, W.P. (1992). Pitch discrimination and phase sensitivity in young and elderly subjects and its relationship to frequency selectivity. J Acoust Soc Am, 91, 2881-93.

Moore, B.C.J., Vickers, D.A. (1997). The role of spread excitation and suppression in simultaneous masking. J Acoust Soc Am, 102, 2284-90.

Moore, B.C.J., Glasberg, B. R. (1998). Use of a loudness model for hearing-aid fitting. 1. Linear hearing aids. Br J Audiol, 32, 317-35.

Moore, B.C.J., Huss, M., Vickers, D.A., et al. (2000). A test for the diagnosis of dead regions in the cochlea. Br J Audiol, 34, 205-24.

Moore, B.C.J., Alcantara, J.I. (2001). The use of psychophysical tuning curves to explore dead regions in the cochlea. Ear Hear, 22, 268-78.

Moore, B.C.J., Glasberg, B.R., Stone, M.A. (2004). New version of the TEN-test with calibrations in dB HL. Ear Hear, 25, 478-87.

Moore, B.C.J., Carlyon, R.P. (2005). Perception of pitch by people with cochlear hearing loss and by cochlear implant users. Pitch: Neural, coding and perception. Springer Handbook of Auditory Research, 24, 234-77.

Munro, K.J., Felthouse, C., Moore, B.C.J. (2005). Reassessment of cochlear dead region in hearing-impaired teenagers with severe-to-profound hearing loss. Int J Audiol, 44, 8, 470-477.

Murray, N., Byrne, D. (1986). Performance of hearing-impaired and normal hearing listeners with various high-frequency cut-offs in hearing aids. Aus J Audiol 8, 21-28.

Ohlemiller, K.K. (2004). Age-related hearing loss: the status of Schuknecht's typology. Current Opinions in Otolaryngology, Head and Neck Surgery 12, 439-43.

Oxenham, A.J., Shera, C.A. (2004).Estimates of human cochlear tuning at low levels using forward and simultaneous masking. Journal of the Association for Research in Otolaryngology 5, 459-459.

Patterson, R.D., Milroy, R., Lutfi, R.A. (1982). The deterioration of hearing with age – frequency selectivity, the critical ratio, the audiogram and speech threshold. J Acoust Soc Am, 72, 1788-03.

Pepler, A., Munro, K.J., Lewis, K., Kluk, K. (2014). Prevalence of cochlear dead regions in new referrals and existing hearing aid users. Ear Hear, 35, 289-386.

Pepler, A., Munro, K.J., Lewis, K., Kluk, K. Repeatability, agreement and feasibility of using the threshold equalising noise test and fast psychophysical tuning curves in a clinical setting Int J Aud. (In Press).

Plack, C.J. (Ed.) (2010). Hearing, Oxford: Oxford University Press.

Plomp, R. (1965). Detectability threshold for combination tones. J Acoust Soc Am, 37, 1110-16.

Preminger, J.E., Carpenter, R., Ziegler, C.H. (2005). A clinical perspective on cochlear DRs: intelligibility of speech and subjective hearing aid benefit. J Am Acad Audiol, 16, 600-13.

Rankovic, CM., (2002). Articulation index prediction for hearing-impaired listeners with and without cochlear dead region. J Acoust Soc. Am.111, 2549-50.

Raphael, Y., Altschuler, R.A. (2003). Structure and innervation of the cochlea. Brain Research Bulletin, 60, 397-422.

Ruggero, M.A., Rich, N.C., Recio. A., et al. (1997). Basilar-membrane responses to tones at the base of the chinchilla cochlea. J Acoust Soc Am, 101, 2151-63.

Ryan, A., Dallos. P. (1975). Effect of absence of cochlear outer hair cells on behavioural auditory threshold. Nature, 253, 44-6.

Schuknecht, H.F., Gacek, M.R. (1993). Cochlear pathology in presbycusis. Annals of Otology Rhinology and Laryngology, 102, 1-16.

Sek, A., Alcantara, J., Moore, B.C.J., et al. (2005). Development of a fast method for determining psychophysical tuning curves. Int J Audiol, 44, 408-20.

Sek, A., Moore, B.C.J. (2011). Implementation of a fast method for measuring psychophysical tuning curves. Int J Audiol, 50, 237-42.

Simpson, A., McDermott, H.J., Dowell, R.C. (2005). Benefits of audibility for listeners with severe high-frequency hearing loss. Hear Res, 210, 42-52.

Summers, V., Molis, M.R., Musch, H., et al. (2003). Identifying DRs in the cochlea: psychophysical tuning curves and tone detection in threshold-equalizing noise. Ear Hear, 24, 133-42.

Thornton, A.R., Abbas, P.J. (1980). Low frequency hearing loss - Perception of filtered speech, psychophysical tuning curves and masking. J Acoust Soc Am, 67, 638-643.

Turner, C. W., Cummings, K. J. (1999). Speech audibility for listeners with high-frequency hearing loss. Am J of Audiol, 8, 47-56.

Tyler, R. S., Wood, E. J., and Fernandes, M. (1983). Frequency resolution and discrimination of constant and dynamic tones in normal and hearing-impaired listeners. J Acoust Soc Am, 74, 1190-99.

United Kingdom Census Data (2011). Retrieved May 1, 2014 from http://www.ons.gov.uk/ons/datasets-and-tables/index.html?pageSize=50&sortBy=none&sortDirection=none&newquery=ethnicity

United States Census Bureau, Memphis statistics. (2012). Retrieved April 11, 2014 from http://quickfacts.census.gov/qfd/states/47/4748000.html

Vestergaard, M.D. (2003). DRs in the cochlea: implications for speech perception and applicability of articulation index theory. Int J Audiol, 42, 249-61.

Vickers, D.A., Moore, B.C., Baer, T. (2001). Effects of low-pass filtering on the intelligibility of speech in quiet for people with and without dead regions at high frequencies. J Acoust Soc Am, 110, 1164-75.

Vinay, Moore, B.C.J. (2007). Prevalence of dead regions in subjects with sensorineural hearing loss. Ear Hear, 28, 231-41.

Warnaar, B., Dreschler, W. (2012). Agreement between psychophysical tuning curves and the threshold equalizing noise test in dead region identification. Int J Audiol, 51, 456-64.

Warnaar, B., Dreschler, W. (2013). Simulating psychophysical tuning curves in listeners with dead regions. Int J Audiol, 52, 533-544.

World Health Organization (WHO). (2000). Global Burden of Hearing Loss in the Year 2000. Retrieved May 15, 2012 from http://www.who.int/healthinfo/statistics/bod_hearingloss.pdf

Yates, G.K. (1990). Basilar membrane nonlinearity and its influence on auditory nerve rate-intensity functions. Hear Res, 50, 145-162.

Yates, G.K. (1995). Cochlear structure and function. In: Moore, B.C.J. ed. Hearing (1st Edition). San Diego: Academic Press, 41-73.

Zweig, M.H., Campbell, G. (1993) Receiver-operating characteristic (ROC) plots: a fundamental evaluation tool in clinical medicine. Clin Chem, 39, 561-77.

Zwicker, E., Schorn, K. (1978). Psychoacoustical tuning curves in audiology. Audiol, 17, 120-140.

Zwicker, E., Fastl, H. (1999). Psychoacoustics - Facts and Models, (1st Edition) Springer-Verlag, Berlin.

Appendix A: Flowchart of Audiology Recommendations for Cochlear Dead Regions