5-2019

Comparison of Automated Hearing Testing Approaches for Outpatients Receiving Ototoxic Chemotherapy

Ashley Stumpf

UNIVERSITY OF NORTHERN COLORADO

Greeley, Colorado

The Graduate School

COMPARISON OF AUTOMATED HEARING TESTING APPROACHES FOR OUTPATIENTS RECEIVING OTOTOXIC CHEMOTHERAPY

A Capstone Research Project Submitted in Partial Fulfillment
of the Requirements for the Degree of
Doctor of Audiology

Ashley Stumpf

College of Natural and Health Sciences
School of Audiology & Speech-Language Sciences
Audiology

May 2019

This Capstone Project by: Ashley Stumpf

Entitled: *Comparison of Automated Hearing Testing Approaches for Outpatients Receiving Ototoxic Chemotherapy*

has been approved as meeting the requirement for the Degree of Doctor of Audiology in the College of Natural and Health Sciences in the Department of Audiology and Speech-Language Sciences, Program of Audiology

Accepted by the Capstone Research Committee

_____

Deanna K. Meinke, Ph.D., Research Advisor

_____

Jennifer E. Weber, Au.D., Committee Member

_____

Kathryn Bright, Ph.D., Committee Member

Accepted by the Graduate School

_____

Linda L. Black, Ed.D.
Associate Provost and Dean
Graduate School and International Admissions
Research and Sponsored Programs

ABSTRACT

Stumpf, Ashley. *Comparison of Automated Hearing Testing Approaches for Outpatients Receiving Ototoxic Chemotherapy.* Unpublished Doctor of Audiology Capstone Research Project, University of Northern Colorado, 2019.

Detection of the highest audible frequency of hearing is used to monitor patients undergoing chemotherapy for ototoxic effects of pharmaceuticals. The current study evaluated the feasibility of utilizing Creare's (2016) wireless attenuated hearing test system (WAHTS) in two outpatient cancer treatment centers to administer automated hearing tests for the identification of the highest audible frequency. Twenty cancer patients being treated with carboplatin and cisplatin were recruited for hearing testing and eight untrained nurses were recruited to operate the WAHTS. Ambient noise measurements were taken in each treatment center before and after hearing testing and supported the validity of threshold measurements. Listener participants completed two automated hearing tests: conventional high-frequency audiometry typically used to identify the sensitive region for ototoxicity (SRO) and a newly proposed fixed-level frequency test (FLFT; Fausti et al., 1999; Rieke et al., 2017). The highest audible frequency (HAF) identified by each test method was compared using a 2-tailed Wilcoxon signed ranks test. The HAF identified by each hearing test method (automated high frequency audiometry [AHFA] vs. FLFT) was not significantly different from each other. The FLFT was completed much faster (24.78 minutes for the AHFA versus 2.4 minutes for the FLFT). Administering the FLFT during outpatient cancer treatment therapy

appeared to be a promising test method to potentially overcome current barriers in ototoxicity monitoring. Future research should implement the WAHTS (Creare, 2016) technology in a more diverse assortment of chemotherapy treatment centers with a larger population of participants. Use of the FLFT and AHFA would need to be evaluated as part of a clinical research study that would implement a full ototoxicity monitoring program.

ACKNOWLEDGMENTS

I wish to express my sincere gratitude to my research advisors for their continuous support throughout the process of my research. With their help, I have grown as a scholar and have a newfound respect for research and its importance in all professions.

This project would not have been possible without the help from the research staff at the outpatient cancer centers. Their involvement in the completion of data collection was vital. I have the deepest appreciation for all the work they put in on my project and so many others in order to advance science.

I would also like to sincerely thank my family for their unending support throughout my educational pursuits. Without their extra encouragement to go outside my comfort zone, I would not have been able to take on such an in-depth project.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF FIGURES

LIST OF ABBREVIATIONS

ANSI	American National Standards Institute
AHFA	Automated High Frequency Audiometry
CNC	Could Not Calculate
dB	Decibel
DFMO	Difluoromethylornithine
DNA	Deoxyribonucleic acid
FFA	Fixed Frequency Audiometry
FLFT	Fixed-Level Frequency Threshold
HAF	Highest Audible Frequency
HFA	High Frequency Audiometry
HHI-E	Hearing Handicap Inventory for the Elderly
HL	Hearing Level
Hz	Hertz
HVAC	Heating, Ventilation, and Air Conditioning
IEC	International Electrotechnical Commission
IRB	Institutional Review Board
ISO	International Organization for Standardization
IV	Intravenous
MPANL	Maximum Permissible Ambient Noise Level

OB	Octave Band
SD	Standard Deviation
SLM	Sound Level Meter
SPL	Sound Pressure Level
SRO	Sensitive Region for Ototoxicity
USA	United States of America
WAHTS	Wireless Automated Hearing Test System

CHAPTER I

STATEMENT OF THE PROBLEM

Ototoxic hearing loss can occur when drugs or chemicals negatively interact with the structures in the auditory system, primarily in the cochlea. This interaction causes damage that presents itself in the form of a hearing loss. Certain pharmaceuticals have been documented to cause hearing loss. Commonly prescribed ototoxic pharmaceuticals are aminoglycosides and platinum-based chemotherapeutics (Hawkins, 1976; Neuwelt et al., 1998). Ototoxic hearing loss is a hearing loss that is potentially preventable with early detection and intervention.

A high frequency hearing loss is most commonly associated with ototoxic exposure, although not necessarily limited to that frequency alone. With increased dosage and exposure, hearing loss is more likely to become more severe and affect lower frequency hearing abilities (Kopelman, Budnick, Sessions, Kramer, & Wong, 1988). When hearing loss begins to impact frequencies responsible for coding speech sounds, patients report social isolation, depression, and a reduced quality of life (Arlinger, 2003). Hearing loss has also been linked to cognitive decline in the elderly population (Lin et al., 2013). Prevention or rehabilitation of hearing loss due to ototoxicity is becoming a greater concern with the increased numbers of cancer survivors attributed to advances in medicine.

The American Academy of Audiology (2009) recommended patients exposed to ototoxic pharmaceuticals be monitored for ototoxicity. By monitoring for ototoxicity, more severe hearing loss might be prevented by modification of treatment regimens implemented by the physician. If changes in treatment cannot be made, the patient might be referred for audiological intervention during the early stages of hearing loss. Several approaches are accepted as effective ways of monitoring hearing changes but no matter the method, early detection is key in preventing a more severe hearing loss.

One approach accepted by the American Academy of Audiology (2009) relies upon high frequency audiometry. This testing evaluates hearing thresholds at the frequency region most commonly affected by ototoxicity over time. When hearing sensitivity decreases and meets certain criteria, an ototoxic shift in hearing is documented. At this time, the physician can make an adjustment to treatment if indicated. To reduce audiometric testing time, Fausti et al. (1999) determined a sensitive region for ototoxicity (SRO) worthy of focus. The SRO approach monitors the highest frequency where a patient can hear at 100 dB SPL and the six adjacent frequencies as opposed to finding hearing thresholds at all frequencies from 250-20,000 Hz. This shortens the test time and makes the monitoring potentially more cost efficient and efficient. To calculate the SRO, baseline testing is obtained at all available test frequencies. Moving forward, only the SRO is monitored.

Monitoring ceases to occur in many patients even though the implementation is well documented along with the negative effects of hearing loss. The National Comprehensive Cancer Network's (2003) guidelines, which are commonly followed by oncologists, do not suggest ototoxic monitoring, implying that many patients are not

receiving any audiologic treatment/management while receiving known ototoxic pharmaceuticals. Possible reasons for why patients are not receiving audiologic services are related to patient and physician factors. Patients are managing multiple appointments and potentially have reduced physical well-being due to the severity of the disease. Adding audiologic evaluations, which might add to the scheduling, transportation, and cost burdens, might not be a healthcare priority for the patient. Physicians might be unaware of the importance of preventing hearing loss and preserving their patient's communication abilities. Therefore, patients are either not being referred for audiologic services or patients might be unable/unwilling to follow-up in a timely manner.

The purpose of the current study was to determine whether newly developed wireless automated hearing test system (WAHTS; Creare Inc., 2016) would make it possible for patients undergoing platinum-based cancer treatments to have their hearing status evaluated at the time of their chemotherapeutic treatment session. The study also aimed to compare two audiometric testing procedures in terms of outcomes and time savings. The first method was based upon the SRO approach implemented with Békésy (1947) method-of-adjustment threshold testing. The second, newer method uses a Békésy-like approach to quickly determine the highest audible frequency by sweeping pure-tones at 80 dB SPL; it is termed the fixed-level frequency test (FLFT). Implementation of this new technology and test protocols might potentially eliminate the need for patients to make multiple audiological appointments and coordinate schedules. It might also reduce the test time for patients who are easily fatigued due to disease and treatment demands. If the research protocol was successful, it might be possible for more

patients to receive audiologic monitoring and prevention or rehabilitation of hearing loss due to ototoxicity.

The following research questions and hypotheses guided this study:

Q1 Is it feasible to implement the WAHTS (Creare Inc., 2016) technology in an outpatient cancer treatment center when operated by nurses?

Q2 What are the ambient noise levels during chemotherapy in outpatient cancer centers? Is the attenuation of the WAHTS sufficient to allow for valid threshold testing in this environment?

Q3 Is there a difference between the highest audible frequency identified using the FLFT test method compared to the automated high frequency audiometry (AHFA) obtained with the WAHTS?

Q4 Is there a difference in test duration for the FLFT as compared to the AHFA test?

$H_0 1$ There will be no significant difference between the highest audible frequency detected when using the FLFT vs. the AHFA.

H1 The FLFT test method will have significantly reduced test time when compared to the AHFA approach.

CHAPTER II

REVIEW OF THE LITERATURE

Introduction

Individuals diagnosed with cancer are often treated with chemotherapeutic drugs to save or prolong their lives. When receiving these drugs, the body undergoes physiologic changes that are not isolated to the area affected by cancer. The inner ear is an area commonly affected by these drugs and the pharmaceuticals are classified as ototoxic. When inner ear structures are damaged due to the drug, hearing loss might occur, commonly in the high frequencies.

Hearing loss has been documented to cause social isolation, depression, and reduce the quality of life of the person directly affected and also negatively impacts communication partners (Arlinger, 2003). Hearing loss is also linked to cognitive decline in the elderly population (Lin et al., 2013). Individuals receiving chemotherapeutics are at an increased risk of hearing loss. Therefore, it is important to provide an early detection and monitoring system to identify and track the progression of hearing loss. Once a hearing loss is detected, physicians might have options to adjust the administration or type of chemotherapy to help prevent further hearing loss. It is often a delicate balance between the treatment needed for the life-threatening illness and the ototoxic dosage. The American Speech-Language-Hearing Association (ASHA; 1994) and the American Academy of Audiology (2009) provided position statements on

ototoxic monitoring. There are different modes of delivery of the monitoring programs. The following literature review explains the physiologic effects of chemotherapeutics on the ear, ototoxic monitoring using high frequency audiometry, and challenges present when implementing an ototoxic monitoring program.

Auditory System Overview

Normal Anatomy/Physiology

The auditory system is comprised of the outer ear, middle ear, inner ear, auditory nerve, auditory brainstem, and auditory cortex. The outer ear collects acoustic energy, which is transferred to the tympanic membrane. The tympanic membrane separates the outer ear from the middle ear. Vibration of the tympanic membrane forces the ossicles in the middle ear to vibrate. In this process, acoustical energy is transformed into mechanical energy. The most medial ossicle, the stapes, pushes on the round window of the cochlea in response to vibration. The cochlea is located in the inner ear. Pressure on the oval window causes movement of the fluid in the cochlea. This fluid is produced by a structure in the cochlea called the stria vascularis. This fluid movement causes the basilar membrane to be set into motion. On top of the basilar membrane are the sensory cells of the cochlea, which is located in the organ of Corti. These sensory cells are the inner and outer hair cells--one row of inner hair cells and three rows of outer hair cells. Located on top of the hair cells are stereocilia. The outer hair cell's main function is to amplify sound, whereas the inner hair cell's function is to transmit the amplified signal electrochemically to the auditory nerve. The basilar membrane is tonotopically organized. The basal end of the cochlea codes high frequency information whereas the apex of the basilar membrane codes for low frequency information. When the basilar

membrane is set into motion, the stereocilia shear causes an influx of calcium and potassium into the hair cell. This influx of calcium and potassium allows for a neurotransmitter to be released into the synaptic junction, thus causing a signal to be sent along the auditory nerve and brainstem. The signal makes its way to the auditory cortex where the brain can interpret it.

Hearing Loss

To have normal hearing, all of the structures in the auditory pathway need to be functioning properly. Normal hearing ranges from -10 dB HL to 20 dB hearing level (HL) for adults in the conventional audiometric frequency range of 250-8000 Hz. When hearing is within this range, the human cochlea has the ability to hear frequencies in human speech. This allows for successful verbal communication. When hearing thresholds are poorer than 20 dB HL, hearing at a distance, hearing soft sounds, or understanding speech in the presence of background noise becomes difficult. The more severe the hearing loss, the greater the spoken communication difficulties.

In the higher frequencies, thresholds are considered abnormal if they fall outside the -10-20 dB HL range as well. Frank (1990) conducted a study with the main objective of determining high-frequency (8,000-16,000 Hz) thresholds (reference equivalent threshold sound pressure levels [RETSPLs]). The second objective was to evaluate intra-subject threshold variability at these frequencies. Threshold testing was completed on 100 individuals with normal hearing between 250 and 8,000Hz with an equal number of males and females. Sennheiser HDA 200 circumaural earphones were used. High frequency thresholds were subject to a three-factor analysis of variance. The factors were test ear, test session, and gender. No significance was shown for any factor. The median

thresholds for each test session were similar across all frequencies. As frequency increased, so did threshold. Median threshold at 8,000 Hz was 18.2 dB sound pressure level (SPL); whereas at 16,000 Hz, the median threshold was 57.7 dB SPL. Standard deviation also increased from 6.6 dB SPL at 8,000 Hz to 17.5 dB SPL at 16,000 Hz. An analysis of variance (ANOVA) in R showed no significant difference in terms of the repeatability of high frequency thresholds. Frank concluded that even though there was high intersubject variability for high frequency thresholds, RETSPLs could be used to set the output of the audiometers to 0 dB HL. It was also important to note that between test sessions, there was minimal variation in threshold, signifying the successful application for serial monitoring of the high frequency thresholds (Frank, 1990). At frequencies above 8,000 Hz, age affects thresholds (Osterhammel, 1977). However, high frequencies in older adults can be used to obtain serial audiograms and monitor for changes even if thresholds are outside of the normal reference levels compared to young adults. These outcomes are important since high-frequency audiometry might be useful to detect and monitor damage to the auditory system.

Damage or malfunction in different areas of the auditory system accounts for different types of hearing loss. If a problem exists in the outer or middle ear, acoustic energy might not be able to reach the sensory cells in the cochlea. A hearing loss present due to outer or middle ear dysfunction is considered a conductive hearing loss. In this case, the sensory cells of the auditory system are functioning properly but sound is reduced upon reaching the cochlea. When damage occurs in the inner ear, it results in a sensory hearing loss. This type of hearing loss is usually rehabilitated with hearing aids or cochlear implants and cannot be medically corrected in most cases. If there is a

problem in the outer or middle ear and the inner ear, this is termed a mixed hearing loss. If the outer, middle, and inner ear are functioning normally, there could be a problem in the transmission of sound past the cochlea in the auditory nerve, brainstem, central auditory pathway, or cortex, causing a hearing loss termed "neural" hearing loss or "central" hearing loss. Many factors could contribute to hearing loss including genetics, age, infection, and systematic disease. Exposure to ototoxins such as noise, chemicals, and pharmaceuticals could also cause hearing loss.

Ototoxicity

Ototoxicity is a common side effect of some medications. These pharmaceuticals cause damage in the cochlea, which results in a hearing loss. For some medications, damage initially occurs in the basal end of the cochlea, causing hearing threshold shifts in the high frequency range. However, damage is not limited to that cochlear location. Over time, auditory damage can progress toward the apical region of the cochlea, causing impairment of hearing in the mid-frequencies. Ototoxic effects are not confined to the cochlea. In some cases, ototoxicity can affect the vestibular system. For the purposes of this manuscript, vestibulotoxicity is not discussed in detail.

Multiple sources of ototoxic exposures can affect the cochlea, vestibular system, or both. Due to life threatening conditions, patients must sometimes receive treatment through ototoxic sources. Different classes of drugs and chemicals cause different symptoms from the ototoxicity. A common source of ototoxicity is from chemotherapeutic drug exposure (chemotherapeutics). This class of drugs is discussed in length in a later section. Aminoglycosides are another well-documented class of medications known to be ototoxic. Aminoglycosides were first found effective in

treating tuberculosis (Schatz & Waksman, 1944). Due to low cost, aminoglycosides are the most common antibiotic used around the world (Schacht, 2007). Aminoglycosides primarily affect outer hair cells, starting at the base of the cochlea and progressing to the apex with continued administration (Hawkins, 1976).

Loop diuretics have also been shown to have ototoxic effects; these drugs include ethacrynic acid, furosemide, bumetanide, and torsemide (Rybak, 2007). Several loop diuretic studies conducted on rodents have shown ototoxic effects that were generally reversible (Green & Mirkin, 1981; Klinke & Mertens, 1988; Rybak, 1993).

Commonly prescribed pharmaceutical agents can also be a source of ototoxicity including aspirin, anti-inflammatory drugs, quinine, and macrolides. This class of drugs can cause a high frequency hearing loss along with tinnitus. However, following cessation of the drug, the symptoms usually cease and no structural damage is done to the cochlea (Lonsbury-Martin, Martin, & Pettis, 2007).

Chemical exposure can also cause ototoxic effects and make the hearing organ more susceptible to noise-induced hearing loss (Pouyatos & Pettis, 2007). Carbon monoxide, cyanide, lead, mercury, manganese, ethyl benzene, xylene, trichloroethylene, and acrylonitrile are considered ototoxic chemicals. Chemical solvents such as styrene and toluene are also ototoxic chemicals (Pouyatos & Pettis, 2007). This manuscript focused on chemotherapeutics in terms of early detection of hearing loss and intervention to prevent hearing loss.

Chemotherapeutics

Overview of Cancer Treatment

Cancer is often treated using chemotherapeutics. In many patients diagnosed with cancer, the ototoxicity of the drug they are receiving is of minor concern in the context of life-threatening health issues. In many cases, the only choice of treatment is an ototoxic drug. Different dosages and types of chemotherapeutics are used to treat different cancers and different cancer stages. However, not all chemotherapy drugs are known to cause hearing loss.

The purpose of chemotherapeutic drug therapy is to prevent cancer cells from proliferating, invading, and metastasizing (Rybak, Huang, & Campbell, 2007). Chemotherapeutics are classified based on their effect on the phases in the cell cycle (Skeel, 1999). Phase-specific drugs are chemotherapeutics that are active against cells in a specific phase of the cell cycle including drugs that inhibit deoxyribonucleic acid synthesis. There are also cell cycle-specific drugs that are only active when the cell is in cycle but are independent of the cell cycle's phase. The last classification is cell-cycle non-specific drugs. In this classification, the drugs are effective whether the cells are in cycle or not. Many chemotherapeutics are not bound to one classification; rather, multiple mechanisms are involved, causing multiple intracellular sites to be implicated (Rybak et al., 2007).

Chemotherapeutic Agents and Associated Hearing Loss

Cisplatin. Cisplatin is a type of chemotherapy drug that was introduced in the 1970s. Some of the cancers commonly treated with cisplatin include germ cell, ovarian, endometrial, cervical, urothelial, head and neck, lung, and brain cancers (Boulikas &

Vougiouka, 2004; Sturgeon, 2004). Cisplatin is systemically toxic (Hartmann & Lipp, 2003), meaning its effects are not isolated to one area. This leads to a potential for ototoxicity. In fact, cisplatin is the most ototoxic platinum compound and the most ototoxic drug in clinical use (Hartmann & Lipp, 2003).

Incidence of cisplatin ototoxicity varied within the research literature. The range for ototoxicity from cisplatin is 40% to 60% (Bokemeyer et al., 1998; de Jongh et al., 2003; Li, Womer, & Silber, 2004). Different factors influence the risk for ototoxicity including dose regimen, administration, and location of cancer (Blakley, Gupta, Myers, & Schwan, 1994; Kopelman et al., 1988; Vermorken, Kapteijn, Hart, & Pinedo, 1983).

Kopelman and colleagues (1988) monitored patients with advanced cancers receiving a high dosage of cisplatin (150 to 225 mg) by bolus administration. A common dose is 50 mg (Rybak et al., 2007). After one of two doses, all patients who previously had normal hearing failed to respond at 9,000 Hz and above (Kopelman et al., 1988), indicating the higher dosage of cisplatin dramatically increased the incidence of ototoxicity in these patients.

Laurell and Jungnelius (1990) found the risk of ototoxicity was greater based on the amount of a single dose and not the cumulative dose. Conversely, other researchers found the best predictor of ototoxic risk was more related to cumulative dose (Bokemeyer et al., 1998; Klis et al., 2002; Li et al., 2004). Li et al. (2004) reported that when the cumulative dose reached 400 mg/m^2, the risk of ototoxicity increased dramatically. Laurell and Jungnelius also found pre-existing hearing loss did not have an effect on ototoxic risk. However, advanced age did increase the risk for ototoxicity with cisplatin.

Blakley et al. (1994) found the incidence of ototoxicity due to cisplatin increased when patients had decreased levels of red blood cells, hemoglobin, and serum albumin as a result of poor overall health. Ototoxic risk was shown to be increased in guinea pigs when animals were exposed to high levels of noise 30 minutes prior to cisplatin (Laurell, 1992).

Hearing loss due to cisplatin ototoxicity initially occurs in frequencies higher than those traditionally tested in pure tone audiometry (250 Hz-8,000 Hz). Kopelman and colleagues (1988) discovered the first signs of hearing loss occurred at 9,000 Hz and above. After administration of a second high dose cisplatin (150-225 mg), hearing loss progressed into the lower frequencies (2,000 to 8,000 Hz). However, the hearing loss did plateau at a moderate level hearing loss of 40 to 60 dB HL. All participants also reported tinnitus (Kopelman et al., 1988).

Laurell and Jungnelius (1990) monitored 54 patients receiving high dosages of cisplatin (100-120 mg). Eighty-one percent of patients had at least 15 dB elevations in air conduction thresholds at one threshold and 10 dB shifts at three or more frequencies. Forty-one percent of these patients had deterioration of hearing in the speech frequencies (Laurell & Jungnelius, 1990). Hearing loss associated with cisplatin ototoxicity is usually symmetric, bilateral, and permanent, especially when the hearing loss is in the profound range (Kopelman et al., 1988; Vermorken, Mangioni, & Van Oosterom, 1983). The hearing loss might also be progressive or sudden (Blakley & Myers, 1993).

Structural changes have also been noted in the cochlea due to cisplatin therapy. Marco-Algarra, Basterra, and Marco (1985) observed in guinea pigs that the outer hair cells in the cochlea were more susceptible to damage compared to the inner hair cells.

Estrem, Babin, Ryu, and Moore (1981) also found that damage to the supporting and pillar cells occurred in guinea pig cochleas following cisplatin treatment. Strauss et al. (1983) noted degeneration of spiral ganglion cells as well as cochlear neurons after examining the temporal bones of a patient with documented hearing loss who had frontal lobe astrocytoma and was treated with cisplatin.

Carboplatin. Carboplatin is another platinum compound commonly used to treat small cell lung, ovarian, head, and neck cancers (Bauer, Westhofen, & Kehrl, 1992; Gatzemeier et al., 1991; Gordon et al., 2002). The greatest benefit of carboplatin over cisplatin is the overall lower neurotoxic effects (Cavaletti et al., 1997).

Forty-four percent of pediatric patients receiving carboplatin along with hematopoietic stem cell transplantation expressed hearing loss (Punnett et al., 2004). Neuwelt and colleagues (1998) found 79% of patients had hearing loss due to ototoxicity when they were treated with carboplatin in combination with mannitol. Contrarily, in the same study, Neuwelt and colleagues observed very little hearing loss when patients were treated with sodium thiosulfate following carboplatin treatment.

By using animal subjects, morphological changes in the cochlea were visible. Saito et al. (1989) found carboplatin-induced hearing loss caused damage to the outer hair cells; however, the inner hair cells remained undamaged in guinea pigs. Wake, Takeno, Ibrahim, Harrison, and Mount (1993) found that in a chinchilla, the inner hair cells were preferentially damaged. Therefore, pathophysiological differences across animal species might exist.

Vinka alkaloids. Vinka alkaloids make up a group of products: vinblastine, vincristine, and vinorelbine. Vinblastine and vincristine are natural products derived from the periwinkle plant (Rybak et al., 2007).

Vinblastine blocks mitosis while also altering amino acid metabolism (Rybak et al., 2007). Vinblastine is a cell cycle-specific drug for the M phase. Vinblastine is used to treat breast carcinoma, choriocarcinoma, testicular germ cell carcinomas, bladder carcinoma, non-small cell lung carcinoma, carcinomas of the kidney, Hodgkin's and non-Hodgkin's lymphomas, Kaposi's sarcoma, Letterer-Wiew disease, mycosis fungoides, metastatic malignant melanoma, and germ cell ovarian tumors (Rybak et al., 2007).

In rabbits, vinblastine was reported to destroy hair cells without having an effect on nerve fibers or spiral ganglion (Serafi & Hashash, 1982). There has been only one human case where ototoxicity was reported with vinblastine (Moss, Hickman, & Harrison, 1999). The patient was also receiving doxorubicin, bleomycin, and dacarbazine. After each session, the patient reported tinnitus, which lasted 7-10 days. A mild high-frequency hearing loss occurred in the patient but speech frequencies were not affected (Moss et al., 1999)

Vincristine is similar to vinblastine. Vincristine treats various types of cancer. However, contrary to vinblastine, vincristine was shown to destroy sensory cells, spiral ganglion neurons, and their fibers in rabbits (Serafy & Hashash 1982). Some cases reported hearing loss after receiving vincristine therapy. Mahajan, Ikeda, Myers, and Baldini (1981) reported a case where a woman experienced two separate cases of temporary bilateral, severe (60 dB HL), sudden sensorineural hearing loss across all

conventional test frequencies following vincristine treatment. After two months, hearing was restored in both cases following treatment with prednisone and cytosine arabinoside.

Vinorelbine is also a vinca alkaloid derived from vinblastine. Non-small cell lung carcinoma and breast carcinoma are cancers vinorelbine has been used to treat. Hearing loss was not a common side effect of vinorelbine (Rybak et al., 2007).

Difluoromethylornithine. Difluoromethylornithine (DFMO) is derived from the amino acid ornithine and is used for prevention and treatment of cancers and parasitic diseases (Rybak et al., 2007). Meyskens and Gerner (1999) reported DFMO caused not only cochlear ototoxicity but the vestibular system could also be affected. Creaven, Pendyala, and Petrelli (1993) as well as Horn, Schechter, and Marton (1987) found DFMO caused high frequency hearing loss but symptoms were reversible in most cases. However, Croghan, Aickin, and Meyskens (1991) reported hearing loss following DFMO therapy at 500, 1,000, 2,000, 4,000, and 8,000 Hz, while Meyskens, Kingsley, Glattke Loescher, and Booth (1986) reported a flat configuration hearing loss (all conventional test frequencies). Patients undergoing DFMO treatment might present with atypical audiograms typically associated with ototoxicity. Tinnitus was also a reported symptom (Creaven et al., 1993).

Position Statements on Ototoxicity

The American Speech-Language-Hearing Association (1994) released a position statement titled *Audiologic Management of Individuals Receiving Cochleotoxic Drug Therapy*. According to this statement, testing higher frequencies above the conventional limit of 8,000 Hz allowed for earlier detection of ototoxic frequency shift. It was recommended that patients be counseled on the potential ototoxic effects before

treatment, baseline testing be completed before drug administration, and follow-up monitoring sessions be completed as soon as possible following treatment. Testing of fewer frequencies on patients who were too ill to complete an entire test was acceptable.

The American Academy of Audiology (2009) released a position statement on ototoxic monitoring. In this statement, the following two main goals of a program were stated:

> 1. Early detection of changes to hearing status presumably attributed to a drug/treatment regime so that changes in the drug regimen may be considered, and 2. Audiologic intervention when handicapping hearing impairment has occurred). (p. 3)

This type of program potentially provided prevention of hearing loss in frequencies essential to communication. When a hearing loss affected frequencies where speech sounds occurred, the correct intervention could be made so communication abilities remained successful. This intervention included counseling on communication strategies, amplification, and assistive listening devices.

Ototoxicity Monitoring

The American Academy of Audiology (2009) recognized conventional and high frequency audiometry (HFA) as a successful approach to ototoxic monitoring. Other methods discussed as successful approaches were conventional audiometry and otoacoustic emissions. With each approach to ototoxicity monitoring, a baseline assessment needed to be obtained for comparison to follow-up evaluations. Ideally, the baseline assessment included not only air-conducted, pure tone thresholds but also tympanometry and word recognition testing.

Fautsi et al. (1984) demonstrated the success of HFA in a study of 77 males receiving ototoxic medication. Hearing threshold shifts were detected sooner using HFA when compared to conventional audiometry. In HFA, a Hughson-Westlake (Hughson & Westlake, 1944) method is used in non-conventional audiometry test frequencies of 9,000-20,000 Hz (Carhart & Jerger, 1959). High frequency testing is a concern in non-sound treated environments due to the increased interference of ambient noise. However, Gordon, Phillips, Helt, Konrad-Martin, and Fausti (2005) demonstrated HFA was reliable in a hospital ward.

Fausti et al. (1999) identified a sensitive region in the cochlea (SRO), which was essential to establish HFA monitoring. The SRO was unique to each patient. The researchers discovered five thresholds specific for each participant's hearing capabilities that were most sensitive to changes in hearing due to ototoxicity. In this method, the highest audible frequency where patient's thresholds were ≤ 100 dB SPL was labeled as the reference frequency. The only frequencies that needed to be tested to have a 94% detection rate were the reference frequency and the next four frequencies below it in $1/6^{th}$-octave steps. With this method, there was a 94% detection rate when monitoring cisplatin-induced ototoxicity. Obtaining conventional and high frequency thresholds was reported to take 20 to 25 minutes, whereas using the SRO method only took six to eight minutes. By only using these five high frequency thresholds, time of testing was cut to less than one-third of the time used when conducting full-frequency testing. This protocol could alleviate some of the time demands and cost barriers that prevented the acceptance of ototoxic monitoring programs (Fausti et al., 1999). To increase reliability

and sensitivity, Fausti et al. (2003) proposed using the same reference frequency as used in the previous study along with the six lower, adjacent frequencies in 1/6th-octave steps.

According to the American Academy of Audiology (2009), one of the main benefits of HFA in an ototoxic monitoring program is use of accepted criteria for an ototoxic shift in hearing loss. The American Academy of Audiology referenced ASHA's (1994) criteria for detecting an ototoxic shift when using HFA. The American Speech-Language-Hearing Association identified the criteria for a confirmed ototoxic shift in hearing sensitivity including a 10 dB shift in hearing sensitivity in two or more adjacent frequencies, a 20 dB shift at any one frequency, and a consecutive failure to respond at three adjacent frequencies where a response was present at baseline testing (this was included for HFA where thresholds might be approaching the limits of the equipment). After a shift is initially detected, it must be proven repeatable.

Challenges in Ototoxicity

Not all cancer centers have ototoxic monitoring programs in place and audiologists frequently encounter challenges when attempting to implement an ototoxic monitoring program. Current National Comprehensive Cancer Network (2003) guidelines, which are followed by oncologists, do not include any form of ototoxic monitoring, suggesting many patients are not receiving any monitoring or management (Dille, McMillan, Helt, Konrad-Martin, & Jacobs, 2015). Reasons for this did not appear to be addressed formally in the literature. It appeared patient and physician factors made ototoxic monitoring programming challenging to implement.

Patients receiving ototoxic treatments are undergoing those treatments because they have been diagnosed with a life-threatening disease, which negatively impacts their

physical well-being. Cancer can be an overwhelming diagnosis and patients are often busy with multiple medical appointments required for ongoing treatment of the primary disorder and side effects of the chemotherapy treatment. Requiring audiology appointments at a different clinical site might add to the scheduling, transportation, and cost burdens; a hearing evaluation might not be a top healthcare priority for the patient.

Physicians might not see hearing monitoring as a healthcare priority or be familiar with the importance of auditory rehabilitation strategies and timelines. Consequently, patients are not always informed of the potential for a hearing loss, not given the opportunity to have their hearing monitored, and indirectly are denied the potential benefits of early identification and intervention. To have a successful program, the physician needs to believe in the importance of hearing health care and integrate hearing health care. Another potential problem with the implementation of an ototoxic monitoring program is coordinating with primary care physicians. The success of an ototoxic program relies on referrals from the primary care physician. A baseline test needs to be obtained before the patient's first treatment. The audiologist and the physician need to have a good relationship in order to make appropriate decisions with regard to the patient.

Currently, ototoxic monitoring programs are yet to be mandated even though there is a wealth of information regarding their importance. Financing these programs could also create a barrier for program implementation. Ototoxic monitoring requires patient enrollment, patient and professional appointment time, and proper equipment to complete the specialized audiologic testing. Recruiting physicians and finding funding for these services might be a challenge. In cases of established ototoxic monitoring

programs, it appeared the medical, pharmacy and audiology staff worked together (usually within a hospital) to establish ototoxic monitoring protocols.

Hearing Testing

Ambient Noise

To obtain a hearing threshold, a person has to respond to the softest level of sound he/she can perceive 50% of the time. To accomplish this, the ambient noise (background noise) in the test environment must not interfere with or mask the test signal to obtain accurate results. When ambient noise masks the test signal, elevated thresholds are recorded.

The International Organization for Standardization (ISO; 2019) developed a series of standards in order to ensure that reliable hearing thresholds are obtained. In ISO's (2009) ISO 8252: *Acoustics: Audiometric test methods, Part 1*, maximum permissible ambient sound pressure levels were provided. The American National Standards Institute's (ANSI; 2013) ANSI S3.1-R2013 also specified the maximum permissible ambient sound levels for audiometric testing using supra-aural earphones, insert phones, and bone conductors. It was recommended when measuring these levels that a type 1 sound level meter with octave bands be used. The maximum permissible ambient noise levels (MPANLs) for each organization are illustrated in Table 1. Maximum permissible levels of ambient noise were not included above 8,000 Hz due to the lack of information of attenuation of ear phones at frequencies above 8,000 Hz and the effects of upward spread of masking on these frequencies (ANSI, 2013). No ambient noise levels for inter-octave frequencies were published in the literature.

Table 1

Maximum Permissible Ambient Sound Levels in Decibels Sound Pressure Level

	Octave Band Center Frequency				
Standard	500 Hz	1,000 Hz	2,000 Hz	4,000 Hz	8,000 Hz
ISO 8253	18	20	27	34	33
ANSI S3.1-R2013 Supra-Aural	16	21	29	32	32
ANSI S3.1-R2013 Insert earphones	45	42	44	45	51

Automated Audiometry

Georg von Békésy first introduced automated audiometry into the field of audiology in 1947. Békésy created a method that used a self-recording threshold audiometer, which required the patient to hold a button down when they heard a signal and release it when they lost the perception of the signal. This method of finding threshold was referred to as method of adjustment. Today, automated audiometers are typically programmed to use the Hughson-Westlake threshold-seeking method (Hughson & Westlake, 1944). In this method, the audiometer or computerized audiometer makes adjustments based on whether the patient correctly responds to a stimulus or lacks a response to a stimulus. This method of limits hearing threshold approach can be accomplished by the patient pressing the appropriate button or tapping on a touchscreen device (Margolis & Morgan, 2008).

Automated or computerized audiometry has been used to provide hearing screening, diagnostic, and intervention services at locations where access to hearing specialists are limited. In a report by Windmill and Freeman (2013), the global shortage

of audiological services was emphasized with shortages not only occurring in low and middle-income countries. The computer-based approach allows for many people to receive services who typically would not. One healthcare provider could oversee more people when automated audiometry is utilized. Automated audiometry has typically been used to aid in mass industrial hearing screenings and in research (Margolis & Morgan, 2008).

The validity of automated audiometry was assessed by Mahomed, Swanepoel, Eikelboom, and Soer (2013) in a systematic review and meta-analysis. Twenty-nine reports comparing automated audiometry to manual audiometry were analyzed to determine the validity of automated audiometry. The researchers concluded no significant differences were seen in test-retest reliability between manual audiometry and automated audiometry. Test-retest variability for automated audiometry was also within normal limits compared to the manual audiometry's test-retest variability. Researchers did note limited data were available on difficult-to-test populations such as children and individuals who are mentally handicapped; many studies only tested people with normal hearing.

Brennan-Jones, Eikelboom, Swanepoel, Friedland, and Atlas (2016) tested 42 participants using manual and automated audiometry. The aim of this study was to eliminate bias and include participants with a range of hearing thresholds. Participants were tested manually in a sound isolated room and then with the KUDU wave automated audiometry system in a non-sound-isolated environment. Participants in this study presented diverse clinical conditions including sensorineural hearing loss, tinnitus, conductive hearing loss, otosclerosis, otitis media, acoustic neuromas, Ménière's disease,

benign paroxysmal positional vertigo, perforated tympanic membrane, Eustachian tube dysfunction, ototoxic hearing loss, skull base fracture, and unilateral hearing loss. The researchers found the difference in threshold between the two situations was low with 86.5% of four frequency averages within 10 dB and 94.8% within 15 dB.

Hearing Testing Outside a Sound Booth.

Audiometric testing is completed in a sound isolated room in order to obtain valid thresholds in normal hearing individuals. The sound booth helps to control for ambient noise levels. However, new technology has recently allowed for audiometric testing outside of a sound-isolated room. Williams (2010) found it was possible to conduct hearing testing in environments where ambient noise levels were not adequate by testing with the use of noise-excluding headsets. However, an audiometer that is used with the headset needs to be calibrated to the noise-excluding headset and proper placement of the headset is important.

Gordon et al. (2005) conducted a study to evaluate whether extended high frequency monitoring could be accomplished outside of a sound isolated room when using insert earphones. Hearing thresholds obtained in a double walled sound booth using Koss circum-aural earphones were compared to thresholds obtained at bedside in a hospital ward. The thresholds from the sound booth were used to identify the SRO (the highest frequency where a threshold was ≥100 dB SPL and the six adjacent lower frequencies in 1/6th-octave steps). This SRO was used for comparisons of thresholds obtained outside of the sound booth. Hearing testing was then repeated outside of the sound booth at the test frequencies in the SRO and at 2,000 Hz due to the increased risk of interfering ambient noise at that level. A second test session was then completed two

hours to three days after completion of the first test session. During the second session, the order of testing was reversed--hearing testing was first completed outside of the sound booth and then followed by testing in the sound booth at the SRO and 2,000 Hz. Researchers found no significant differences in high frequency thresholds obtained in the booth and in the ward. Researchers noted the results indicated good test-retest reliability when obtaining serial audiograms in the same setting with the same transducer. However, if setting and transducer were changed, results needed to be interpreted with caution. During each test outside of the sound booth, ambient noise levels were recorded using the A-weighted filter in the octave band range of 125-16,000 Hz. The mean ambient noise levels from the test sessions are illustrated in Figure 1.

Typically, octave band measurements are not A-weighted and cannot be directly compared to maximum permissible ambient noise measurements (MPANLs). Konrad-Martin, Reavis, McMillan, Helt, and Dille (2014) reported ambient noise levels in dB SPL for hearing testing conducted in Veterans' Administration (VA) hospital wards. Table 2 extrapolates the values from Figure 7 of that publication (Konrad-Martin et al., 2014).

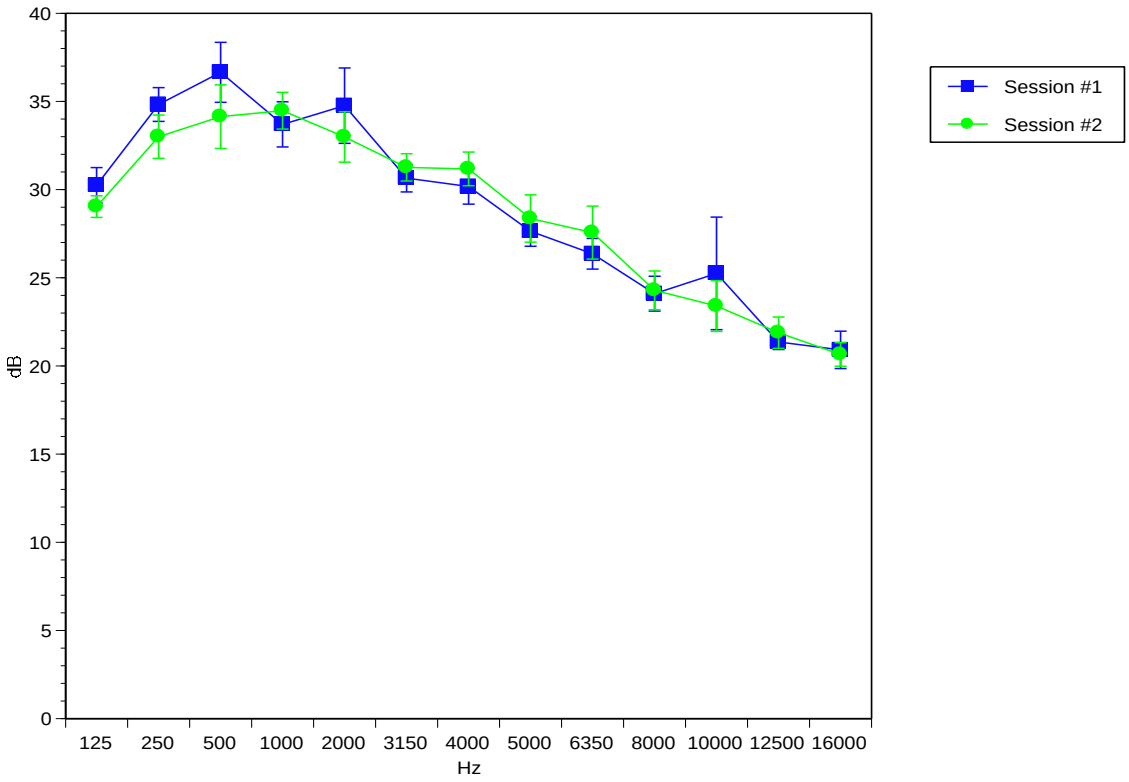

Figure 1. Mean ambient noise levels (dBA) reported in Gordon et al. (2005). Graphic provided courtesy of Jane Gordon (personal correspondence).

Table 2

Extrapolated Mean Ambient Noise Levels in Decibels Sound Pressure Level Reported from Veterans' Administration Hospital Ward Measurements

	Ambient Noise Levels							
	125	250	500	750	1,000	1,500	2,000	3,250
Frequency Band (Hz)	46	43	40.0	36	34	34	36	29
	Ambient Noise Levels							
	4,000	5,000	6,350	8,000	10,000	12,500	16,000	
Frequency Band (Hz)	29	28	26	25	27	28	28	

Note. Extrapolated from Konrad-Martin et al. (2014), Figure 7. Original data values are archived and unavailable (personal communication).

Creare Wireless Automated

Hearing test system. Engineers at Creare Inc. (2016) recently developed a wireless automated hearing test system (WAHTS; see Figure 2). This system was developed to permit audiometric threshold testing in atypical settings outside of a conventional sound booth (Meinke, Norris, Flynn, & Clavier, 2017). This system was developed to

> (1) maximize passive attenuation, while keeping the headset comfortable enough to wear for the duration of a typical hearing exam, (2) leverage mobile technologies and eliminate cables, and (3) meet ANSI S3.6 and IEC 60645-1 standards for audiometers. (Meinke et al., 2017, Instrumentation)

The system includes a supra-aural headset that is operated in congruence with a tablet. The ear cups on the headset are lined with polyurethane foam. The right ear cup contains a wireless audiometer circuit and the left ear cup contains a rechargeable lithium ion battery. A speaker is mounted in a plastic faceplate covered in fabric. This allows for the stimulus to be presented. Overall, the headset is relatively large, stiff, and somewhat heavy in order to provide passive attenuation. The headband in the system uses frictionless fit to enable quick placement of the WAHTS. The frictionless fit also allows the WAHTS to hold its position on the listener's ears. The WAHTS supports a 4.0+ Bluetooth Low Energy interface. This allows the device to be connected to a computerized tablet, which initiates the automated threshold test and receives the results through an application called TabSINT. This application allows for customized tests and questionnaires to be administered on an array of mobile devices.

Figure 2. Creare wireless automated hearing test system including iPad.

Meinke et al. (2017) conducted a study to characterize the Creare (2016) WAHTS performance in an occupational setting when administered by untrained personnel. A within-subject repeated measures design study was completed to compare air-conducted threshold testing (500 to 8,000 Hz) obtained by untrained operators using the WAHTS in worksite conference rooms to test results obtained using computerized CCA-200 audiometers in a mobile trailer sound booth by a trained tester. Twenty workers were tested twice with the WAHTS in the conference room and once with the CCA-200 in the mobile trailer. Mean thresholds obtained with the WAHTS were equivalent to mean thresholds obtained from the mobile trailer at 1,000, 2,000, and 3,000 Hz. Thresholds were within 5 dB at 500, 4,000, 6,000, and 8,000 Hz. Test-retest reliability results showed the Creare wireless headset system was equivalent to or better than previously reported ranges obtained by traditional equipment. The ambient noise levels recorded in the rooms outside of the sound booth did not meet the ANSI (2013) standard for maximum permissible ambient noise for audiometric testing. However, test-retest

average differences at frequencies up to 8,000 Hz were less than 1 dB and 1.1 dB at 8,000 Hz. It was important to note this was better than what was obtained in a sound booth with insert or TDH-39 supra-aural earphones (Swanepoel, Mngemane, Molemong, Mkwanazi, & Tutshini, 2010).

Meinke et al. (2017) also found the Creare (2016) wireless headset provided attenuation to low frequency ambient noise equivalent to a "mini" single-walled sound booth. These results suggested the WAHTS is a useful device for obtaining valid thresholds in diverse test locations without the use of a sound isolated test room and hearing thresholds could be obtained by an untrained operator.

At the completion of the audiometric testing (Meinke et al., 2017), the WAHTS (Creare Inc., 2016) operator and the listener both took a survey on the tablets in order for the researchers to gain subjective data on the overall experience and usability of the device. The operator survey included 18 statements that required a 7-point Likert-type scale response (1 = *Strongly Disagree,* 2 = *Disagree,* 3 =*Somewhat Disagree,* 4 = *Neither Agree or Disagree,* 5 =*Somewhat Agree,* 6 = *Agree,* and 7=*Strongly Agree*). One open-ended question was also included for additional comments related to the WAHTS. Listeners responded to eight statements on the same Likert-type scale listed for the operators. Listeners also had the chance to provide additional opinions on the WAHTS. Overall, operators who were unfamiliar with the technology felt the device was easy to use, intuitive, did not require practice to operate it, and they said they would use this device if they had access to it. Similarly, listeners also had an overall positive response to the device. Listeners felt subjectively that the testing with the WAHTS was just as accurate as the test in the trailer with the sound treated booths. However, some listeners

commented they needed eyeglasses to view the tablet and one listener said he/she could not close his/her eyes during testing, which resulted with him/her being visually distracted. Some listeners felt the test took longer with the WAHTS than in the mobile trailer, which was most likely due to the multiple tests on each ear being conducted to assess the reliability of the WAHTS (Meinke et al., 2017).

Recent Advances in Ototoxicity Monitoring

Rieke et al. (2017) proposed a new method for evaluating ototoxicity--a Békésy (1947)-style fixed-level frequency-threshold (FLFT). This approach allows the listener to vary frequency at a fixed presentation level rather than having the listener vary the sound level. By quickly sweeping through the frequencies at 80 dB SPL, the highest audible frequency is quickly determined. Rieke and colleagues compared the FLFT to a modified SRO (limited output at 80 dB SPL), which was the commonly accepted method used to monitor ototoxicity. Participants in the study had to have normal hearing in the conventional frequency range. All patients were between the ages of 23 and 35 years. Each subject attended at least four different sessions. During the first session, all subjects were trained on the Békésy tracking procedure. Hearing thresholds were obtained at 0.5, 1, 2, 3, 4, 6, 8, 9, 10, 11.2, 12.5, 14, 16, 18, and 20,000 Hz. The stimulus was a pulsed pure tone that would start at 40 dB SPL and decrease in 4 dB step sizes. Subjects would hold a response button until they no longer heard the tone. The tone intensity would then increase again. After the second reversal, the step size decreased to 2 dB. The Békésy-style fixed frequency audiometry (FFA) was then used to find the threshold at each frequency. The SRO FFA frequencies were calculated by determining the uppermost frequency at which the subject had a valid threshold and the six adjacent lower

frequencies in 1/6th-octave steps. The upper SPL limit was not set in advance for this study in order to determine the highest frequency in the SRO. Any threshold within the allowable limits of the hardware was accepted (up to 111 dB SPL). In all subsequent test sessions, thresholds were only obtained in the individualized SRO using FFA. The FLFT was also obtained at each session.

The FLFT method was adapted from Békésy's (1947) method of adjustment threshold testing. Contrary to Békésy's original method, the FLFT stayed at the same intensity level and switched frequencies. Listeners pressed a button when they could hear the frequency and released it when they could no longer detect the frequency. The frequency level then decreased to lower frequencies until listeners pressed the button, again signaling they could detect a sound again. The highest audible frequency was then labeled as the average over a certain amount of reversals. In the current study, the average of the last six reversals was averaged with the first two being excluded. Stimulus presentations started at 80 dB SPL at 8,000 Hz with pulsed tones extending up to 20,000 Hz. The initial frequency step-size was 1/6th-octave steps. At the first reversal, the frequency step-size changed to 1/12th-octave steps. Figure 3 is the trace of an FLFT test obtained during the present study.

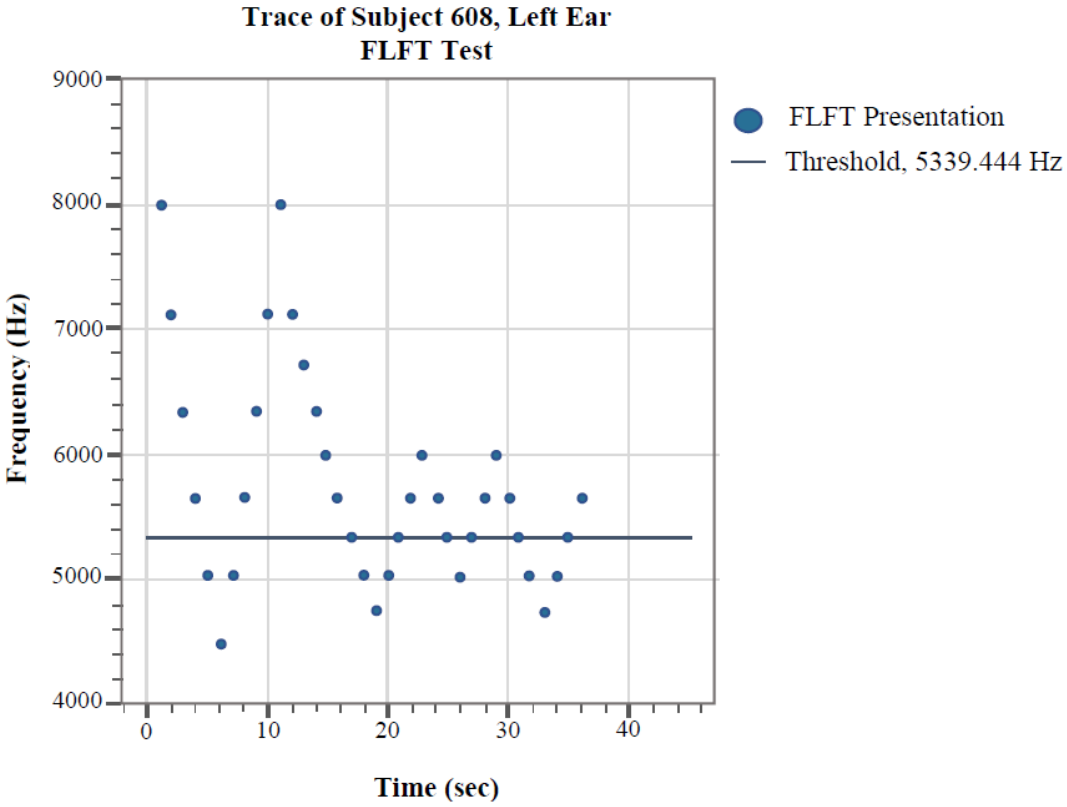

Figure 3. Sample fixed-level frequency test tracing for Subject 608.

The FLFT was evaluated in terms of repeatability, timing, and accuracy compared to the SRO. It was concluded the FLFT and the FFA SRO were both highly repeatable, fast, and accurate. Subjects served as their own controls because thresholds were compared to baseline. Subjects were not expected to have any hearing changes so this study did not look at sensitivity of the FLFT. To evaluate reliability, intra- and intersession variability was calculated using the root mean square difference from the baseline SRO thresholds and FLFT. To evaluate the repeatability, a single factor repeated measures ANOVA was used to evaluate learning effects over time. After analysis, no learning effects were shown. The SRO FFA took approximately 4.5 minutes and the FLFT took approximately 30 seconds to complete--a drastic decrease in test time

when compared to conventional audiometry (a reduction of 98%). The FLFT directly translated to the SRO, suggesting the FLFT could be used to evaluate ototoxicity in patients. Due to the suprathreshold testing, an additional benefit to the FLFT was the practicality of testing outside of a sound isolated room. These advances might afford an opportunity to overcome the challenges that currently limit the implementation of ototoxicity monitoring programs and create an opportunity for more cancer patients to reap the benefits of early detection and intervention for ototoxicity.

The Value of Ototoxic Monitoring

Due to advances in science, survival rates have improved for people diagnosed with cancer. More people are living in remission, which has led to an increased number of people who are living with the long-term side effects of the treatment they received. In many cases, the hearing loss acquired due to ototoxicity of various forms of cancer treatment lasted past the final treatment. It was important to understand what effect living with an acquired hearing loss could have on a person in remission. In general, hearing loss could have negative effects on people beyond the sensory deficit. Uncorrected hearing loss could potentially lead to reduced quality of life and social activity along with increased isolation and depression (Arlinger, 2003). Lin et al. (2013) found hearing loss accelerated cognitive decline and incidence of cognitive impairment in elderly adults.

Chia et al. (2007) assessed quality of life in relation to hearing loss. Participants were given the Short Form Health Survey (SF-36; Ware, Kosinski, & Keller, 1994), which is a quality of life assessment that has eight subscales that represent dimensions of health and well-being: physical functioning, role limitations due to physical problems,

bodily pain, general health perceptions, vitality, social functioning, role limitations due to emotional problems, and mental health. Participants received a hearing assessment, which included an interview about perceived hearing loss, and air and bone conduction threshold testing at traditional test frequencies. Factor analysis, Australian normalized scores, Mantel-Henzsel chi-square statistic with 1 degree of freedom, *t*-tests, and *F*-statistic were used to analyze the data in this study. Participants with bilateral hearing loss scored lower on the SF-36 in comparison to participants with unilateral hearing loss. People with mild bilateral hearing loss scored lower on the SF-36 than those with normal hearing (Chia et al., 2007).

Similar findings in older adults were reported by Dalton et al. (2002) who conducted a study comparing quality of life to hearing loss. Dalton et al. used the Hearing Handicap Inventory for the Elderly-Screening (Ventry & Weinstein, 1982) along with additional hearing related communication difficulty questions to assess quality of life. People with hearing loss had decreased scores in every domain of the Hearing Handicap Inventory for the Elderly-Screening version. Severity of hearing loss was directly related to self-reported communication difficulties as well as lower scores on both the Mental Component Summary score and the Physical Component Summary score of the SF-36 (Dalton et al., 2002).

People who have a close relationship with a person with a hearing loss might also be negatively affected. In a study conducted by the National Council on Aging in the United States (Seniors Research Group, 1999), the researchers compared people with longstanding hearing loss who wore hearing aids and those who did not in relation to quality of life. The researchers also gave the participants' significant others a

questionnaire to assess the significant other's well-being. People with untreated hearing loss reported feeling sad or depressed more often as well as worried and paranoid. People with untreated hearing loss also took part in less social activity and had more emotional turmoil. This also corresponded with the spouse's response. When comparing the results of the people who wore amplification, their significant others often reported even more benefit than the person with the hearing loss in terms of the relationship at home, confidence, and other relationships (Seniors Research Group, 1999).

Gruney et al. (2007) evaluated quality of life in relation to hearing loss caused by drug treatment in children who had neuroblastoma. One objective of Gruney et al. was to assess hearing loss and parent-reported psychosocial difficulties for the child after treatment. The Pediatric Quality of Life Inventory 4.0 (Varni, 2019) was used to assess quality of life in the children. Neuroblastoma survivors with hearing loss had a mean score of 10-points lower on the Pediatric Quality of Life Inventory 4.0. Researchers concluded neuroblastoma survivors with hearing loss had an elevated risk for psychosocial difficulties (Gruney et al., 2007)

When hearing loss is rehabilitated through amplification, there are potential improvements to quality of life. Chia et al. (2007) found people who habitually wore hearing aids had better physical functioning on average. In a meta-analysis, Chisolm et al. (2007) analyzed 16 studies where the researchers looked at quality of life in relation to hearing loss rehabilitation with hearing aids. Research included in this study had information on non-acoustic benefits from amplification such as emotional well-being, stress levels, relationships, loneliness, and self-efficacy (Chisolm et al., 2007). Chisolm et al. also concluded that hearing aids decreased negative psychosocial, social, and

emotional effects in people with hearing loss. The authors also reported hearing loss could be a "potentially devastating chronic health condition if left unmanaged" (Chisolm et al., 2007, p. 169).

Properly informing patients about the possibility of hearing loss as a side effect of the drug they are being exposed to could potentially reduce the negative impacts hearing loss has on quality of life if they are identified and treated early. If patients are made aware of the possibility of side effects, they would potentially realize the hearing loss earlier by having their hearing status evaluated and be able to seek rehabilitation, thus retaining a better quality of life. If the patient is receiving audiological services, a shift in hearing might be noticed before the negative effects of a hearing loss are noticed by the patient. When this occurs, the physician might be contacted and a different drug regimen might be suggested to reduce the drug's impact on the auditory system.

Rationale for Study

Hospital-based cancer care centers in northern Colorado administer chemotherapeutics to patients that have the potential to be ototoxic. These hospitals do not currently have an ototoxic monitoring program due to the lack of audiological test facilities and personnel. The hospital-based cancer treatment setting presents a unique opportunity to implement novel hearing testing technology and test protocols that might provide earlier identification of hearing loss or reinforce the need for audiological rehabilitation in cancer patients. This study evaluated the use of the WAHTS (Creare, 2016) to test the hearing of patients when operated by nursing staff at two hospital-based cancer treatment centers in northern Colorado.

CHAPTER III

METHODS

This study was designed to evaluate the use of Creare Inc.'s (2016) wireless automated hearing test system (WAHTS) in two cancer treatment centers when operated by untrained nursing staff. In addition, the study compared the hearing test outcomes for the fixed-level frequency test (FFLT) and automated high frequency audiometry (AHFA) in terms of the identification of the highest audible frequency (HAF).

Participants

Participants in this study consisted of listeners who were undergoing cancer treatment and untrained nurse operators who administered the hearing testing. Listeners and operators were recruited from two outpatient cancer treatment centers. The study exclusion criterion included the following: formally trained in audiometry. The research was conducted under the University of Northern Colorado's Institutional Review Board's (IRB) protocol (see Appendix A for approval).

Listeners

Study inclusion criteria included the following:

- Be an adult over the age of 18 years
- Be receiving chemotherapy with either carboplatin or cisplatin
- Understand, speak, and read English
- Have sufficient vision to view the tablet computer

- Have sufficient dexterity to be able to tap on the on-screen box displayed on the tablet computer.

Study exclusion criteria included the following:

- Have a cochlear implant
- Have any medical condition of the ear that prevents use of the wireless headset such as a draining ear
- Have any head injuries, surgical incisions or wounds
- Are too febrile to participate in the hearing testing per nursing judgment.

Operators

Study inclusion criteria included the following:

- Be employed as hospital/cancer center nursing staff
- Understand, speak, and read English
- Have sufficient vision to view the tablet computer
- Have sufficient dexterity to be able to follow on-screen instructions to operate the computer tablet and place the wireless earphones on the listener.

Instrumentation

Creare Wireless Automated Hearing Test System

Creare Inc.'s (2016) wireless automated hearing test system (WAHTS) was used to obtain hearing sensitivity information. The WAHTS was used to obtain the AHFA and the FLFT. Both audiological tests determined the highest audible frequency a person could hear. To measure hearing responses for AHFA, the WAHTS used an algorithm based on a modified version of the Hughson-Westlake procedure (Carhart & Jerger,

1959). The WAHTS also used an algorithm to perform a Békésy-like (Békésy, 1947) FLFT technique.

Order of administration of the AHFA and the FLFT was counter-balanced along with the starting test ear. For AHFA, thresholds were identified at each test frequency (1,000, 2,000, 3,000, 4,000, 6,000, 8,000, 9,000, 10,000, 11,200, 12,500, 14,000, 16,000, 18,000, 20,000). The HAF was selected based on the highest audible frequency for which a person had a measurable threshold. Thresholds could be as high as the output of the WAHTS at each frequency.

For the FLFT testing, a tone was presented at 80 dB SPL at 8,000 Hz. The frequency of the tone gradually increased in $1/6^{th}$-octaves until the patient could no longer detect the tone. The frequency then decreased until the patient detected the tone. After the first reversal, the step size was $1/12^{th}$-octave. The highest audible frequency was calculated based on the average of the last six reversals, ignoring the first two reversals. This was the same FLFT method used by Rieke et al. (2017).

Tablet

The WAHTS (Creare Inc., 2016) system supported a Bluetooth low energy (4.0+) interface, which allowed it to be connected to a tablet. The tablet initiated the testing using an application (app) developed by Creare Inc. (2016) called TabSINT (v1.7.4). The TabSINT allowed the researcher to administer customized tests and questionnaires. This app allowed the WAHTS to be connected to the tablet (Shapiro & Galloza, 2016). Subject identifiers were inputted into the app. After data import was complete, the researcher was instructed to give the tablet to the hearing test operator. The operator was instructed to place the WAHTS on the listener's head and hand the iPad to the listener.

The app screen then displayed a large touchscreen box the listener touched to respond to the stimulus for each test.

Sound Level Meter

A Quest Type 2 SLM, Model 2700 (serial # HU2040042; Pine Environmental, 2019a) with an OB-300 octave band analyzer (serial # HW3050014; Multimedia, n.d.) was used to obtain pre- and post-test ambient noise measurements. Prior to each pre-test measurement, the SLM was calibrated using a Quest Model QC-10/QC-20 Acoustic Calibrator (serial # QIE010076; Lesman Instrument Co., 2019) to assure the SLM was in accordance with ANSI's (1983) specifications for sound level meters.

Survey Instrument

Operators and listeners each completed a survey created in Qualtrics. A 7-point Likert-type response was used in both the operator and listener survey: (1 = *Strongly Disagree*, 2 = *Disagree*, 3 = *Somewhat Disagree*, 4 =*Neither Agree or Disagree*, 5 = *Somewhat Agree*, 6 = *Agree*, 7 = *Strongly Agree*). The operator survey consisted of 17 statements previously used in WAHTS studies related to operator characteristics and settings (see Appendix B). The listener survey included 12 statements previously used in WAHTS studies as well as the inclusion of new statements specific to this population's characteristics. An additional open-ended question for comments related to usability and the experience with the WAHTS was also included at the conclusion of both operator and listener surveys. Operator and listener surveys were completed on a Google Nexus 7 Tablet (Asus, Taiwan). Results were uploaded to a password-protected webserver.

Experimental Procedures

Following proper calibration of equipment and informed consent, pre-test ambient noise was measured using a Quest Type 2 SLM, Model 2900 (serial # HU2040042; Pine Environmental, 2019b). Ambient noise measurements were obtained at 31.5, 63, 125, 250, 500, 1,000, 2,000, 4,000, 8,000, and 16,000 Hz. Measurements took place within a two-foot circumference of the listener's head. Measurements were completed before and after the audiometric testing.

After the completion of data entry of alpha-numerical subject numbers and demographic details (age and gender), the tablet was handed to the nurse operator. The operator followed on-screen directions to prep the listener and place the WAHTS (Creare Inc., 2016) on the listener's head and handed the tablet to the listener. The listener was instructed by the researcher and by reading text on the tablet regarding the steps to complete the AHFA and FLFT hearing tests in each ear. Each test was timed through the TabSint (Creare Inc., 2016) app. Post-test ambient noise levels were measured and data entered in the same method as pre-test ambient noise levels. At the completion of the testing, the operator and listener took the usability survey.

Data Analysis

To determine if the WAHTS (Creare Inc., 2016) could feasibly be implemented into outpatient cancer centers, user/operator surveys were descriptively analyzed (see Appendices B and C). Mean pre- and post-test ambient noise levels were analyzed and compared for the two test sites. Attenuation of the WAHTS in relation to the average ambient noise level was compared at each frequency band. Listener/operator surveys and ambient noise levels were imported from the database into Excel. All data were analyzed

in Excel. A Wilcoxon (1945) signed ranks test was used to evaluate differences between the highest audible frequency identified by the FLFT and the AHFA. A Student's *t*-test was used to evaluate the testing time differences between the AHFA and the FLFT audiological tests.

.

CHAPTER IV

RESULTS

Participants were recruited and data were collected in accordance with an approved IRB executed by the University of Northern Colorado (see Appendix A) and a reciprocal agreement from Banner Health's IRB (see Appendix D).

Test Environments

Data collection took place in two outpatient cancer treatment centers in northern Colorado. The chemotherapy clinics were set up to have multiple patients treated simultaneously in the same room. Site 1 was set up in a "pod" design with a ratio of one nursing station to four patient chairs. There were half walls separating patients from one another and from other "pods" (see Figure 4). Site 2 was one large room with leather recliners lined up beside each other around the perimeter of the room. There were no dividers between patients at Site 2 (see Figure 5). A single nursing station was positioned so all patient chairs could be sight monitored. The area where audiometric testing took place in each cancer center was based on where the listener subject was receiving treatment and locations were not pre-selected on the basis of room acoustics. Listener and operator participants were recruited from the staff and patient populations at each test site as previously described in the methods section of Chapter III.

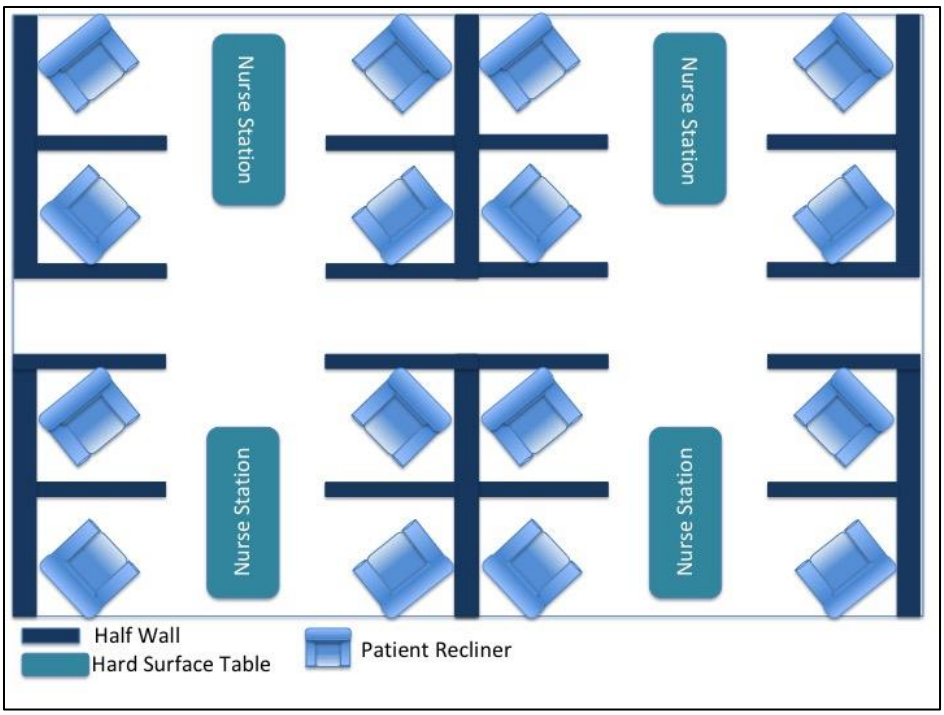

Figure 4. Aerial diagram of chemotherapy treatment area at Site 1.

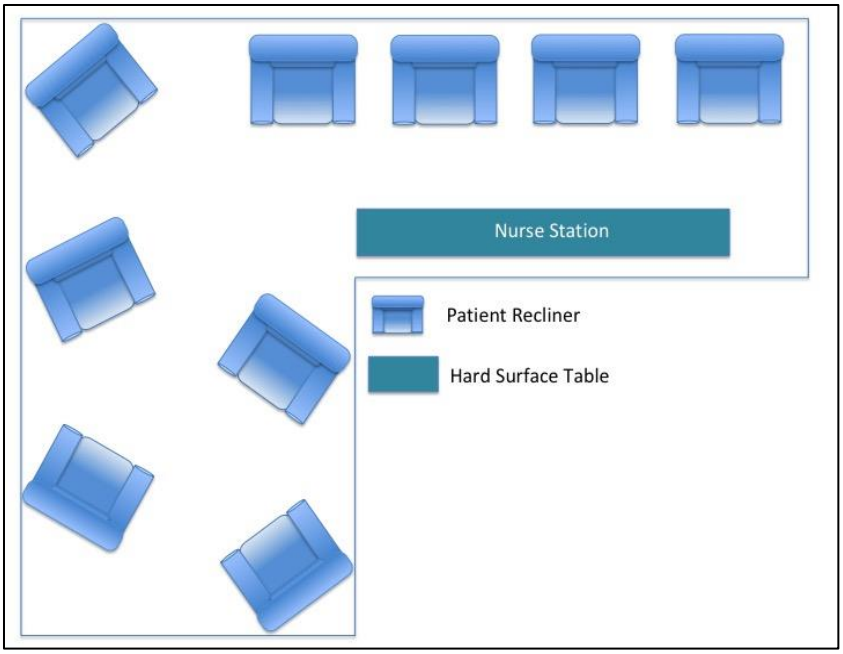

Figure 5. Aerial diagram of the chemotherapy treatment area at Site 2.

Participants

Study participants were comprised of both hearing test listeners (*n* = 21) and operators (*n* = 8).

Listeners

Listener participants included 21 patients being treated in one of two outpatient cancer treatment facilities. There were 9 males and 12 females. The ages of listener participants ranged from 36 to 76 years with an average age of 60.2 years. Seven participants were being treated with cisplatin and 14 were being treated with carboplatin. The most common cancer diagnosis being treated was ovarian (*n* = 5), followed by lung (*n* = 3), breast (*n* = 2), esophageal (*n* = 2), bladder (*n* = 1), endometrial (*n* = 1), endometrial/uterine (*n* = 1), kidney (*n* = 1), ovarian/colon (*n* = 1), pharynx (*n* = 1), and throat (*n* = 1). Treatment cycles ranged from cycle 1 to cycle 22 with the majority falling within cycles 2-5. Table 3 provides a summary of listener participants' demographic and treatment information.

Hearing testing occurred simultaneously while listeners were receiving chemotherapy or outpatient services such as fluid replacement due to cancer treatment. Eleven listeners were tested at Site 1 and 10 listeners were tested at Site 2. All hearing tests were completed during routine operating hours of the clinics.

Table 3

Demographic and Treatment Characteristics of Listener Participants

Subject	Sex	Age (yrs.)	Cancer Diagnosis	Treatment	Cycle
Site 1					
1	M	56	Throat	Cisplatin	2
2	F	67	Ovarian	Carboplatin	22
3	F	58	Breast	Carboplatin	5
4	M	56	Bladder	Cisplatin	2
5	M	70	Esophageal	Cisplatin	4
6	M	56	Esophageal	Carboplatin	3
7	F	46	Breast	Carboplatin	5
8	M	76	Liver	Cisplatin	2
9	F	50	Breast	Carboplatin	1
10	M	76	Lung	Carboplatin	2
11	M	60	Kidney	Cisplatin	2
Site 2					
12	F	56	Ovarian/Colon	Carboplatin	4
13	M	63	Lung	Carboplatin	3
14	F	68	Lung	Carboplatin	3
15	F	36	Ovarian	Carboplatin	4
16	F	65	Ovarian	Cisplatin	2
17	F	63	Ovarian	Carboplatin	9
18	F	53	Endometrial	Carboplatin	3
19	F	61	Endometrial/uterine	Carboplatin	4
20	F	78	Ovarian	Carboplatin	4
21	M	51	Pharynx	Cisplatin	2
M (SD)	60.2(10.4)				

Operators

Eight registered nurses from Site 1 and Site 2 participated in this study as "operators" of the hearing test equipment. All operators reported they had not given hearing tests before. Operators were able to test multiple listener participants if the listener subject was on their caseload for chemotherapy treatment at the time of listener

recruitment. Table 4 provides a summary of operators and number of hearing tests given per operator.

Table 4

Operator Testing Session Summary

Operator Subject Number	Number of Listeners Tested
Site 1	
1	1
2	3
3	2
4	2
5	3
Site 2	
6	4
7	2
8	4

Ambient Noise Levels

One-third octave-band ambient noise level measurements were taken before and after hearing test data collection and are summarized in Table 5.

Table 5

Ambient Noise Level Measurements Taken Before and After Hearing Test Data Collection

	Overall Ambient Noise	Octave Bands (Hz) (dB SPL)									
	dBA	31.5	63	125	250	500	1,000	2,000	4,000	8,000	16,000
1 Pre	42	64	61	51	45	48	32[b,c]	30[b]	34[b,c]	25[a,b,c]	27
1 Post	46	64	61	51	46	43[b]	44	46	39[b,c]	33[b,c]	28
2 Pre	47	62	56	50	46	43[b]	43	39[b]	33[b,c]	35[b,c]	27
2 Post	44	62	57	50	45	42[b]	38[b]	37[b]	39[b,c]	32[a,b,c]	28
3 Pre	46	60	52	50	46	42[b]	33[b,c]	34[b,c]	36[b,c]	28[a,b,c]	28
3 Post	54	61	55	52	48	41[b]	44	39[b]	32[a,b,c]	28[a,b,c]	27
4 Pre	45	63	57	52	41	36[b,c]	35[b,c]	35[b,c]	38[b,c]	26[a,b,c]	29
4 Post	45	64	56	54	48	47	35[b,c]	34[b,c]	30[a,b,c]	26[a,b,c]	27
5 Pre	52	64	57	49	47	41[b]	37[b,c]	32[b,c]	27[a,b,c]	26[a,b,c]	27
5 Post	54	64	57	50	45	40[b]	34[b,c]	38[b]	37[b,c]	29[a,b,c]	28
6 Pre	58	60	63	54	50	43[b]	42[b]	34[b,c]	33[b,c]	29[a,b,c]	28
6 Post	46	60	62	48	50	42[b]	34[b,c]	40[b]	39[b,c]	28[a,b,c]	27
7 Pre	48	67	58	50	47	50	48	44[b]	44[b,c]	32[a,b,c]	27
7 Post	43	66	59	50	46	39[b]	40[b]	33[b,c]	33[b,c]	28[a,b,c]	27
8 Pre	49	64	57	49	49	39[b]	35[b,c]	35[b,c]	44[b,c]	32[a,b,c]	28
8 Post	47	65	58	51	56	44[b]	38[b]	41[b]	39[b,c]	34[b,c]	27
9 Pre	49	62	56	49	48	49	29[b,c]	31[b,c]	26[a,b,c]	25[a,b,c]	27

Table 5 Continued

	Overall Ambient Noise	Octave Bands (Hz) (dB SPL)									
	dBA	31.5	63	125	250	500	1,000	2,000	4,000	8,000	16,000
9 Post	47	66	58	49	49	37[b,c]	46	43[b]	34[b,c]	28[a,b,c]	28
10 Pre	46	66	60	50	49	44[b]	38[b]	35[b,c]	38[b,c]	33[b,c]	28
10 Post	60	67	61	51	45	42[b]	40[b]	37[b]	39[b,c]	31[a,b,c]	28
11 Pre	39	64	46	49	40	34[b]	30[b,c]	39[b]	27[a,b,c]	25[a,b,c]	27
11 Post	39	64	55	49	40	39	36[b,c]	30[b]	24[a,b,c]	25[a,b,c]	27
12 Pre	45	60	49	47	47	43[b]	48	36[b,c]	35[b,c]	26[a,b,c]	27
12 Post	49	56	45	46	47	41[b]	38[b]	37[b]	36[b,c]	25[a,b,c]	27
13 Pre	54	58	50	59	57	54	55	44[b]	40[b,c]	32[a,b,c]	28
13 Post	57	57	48	55	53	47	40[b]	49	36[b,c]	30[a,b,c]	28
14Pre	48	51	48	53	50	50	38[b]	35[b,c]	41[b,c]	27[a,b,c]	29
14 Post	49	50	49	46	48	43[b]	51	38[b]	35[b,c]	40[b,c]	28
15 Pre	57	55	47	49	53	55	45	47	46	38[b,c]	28
15 Post	52	58	50	48	51	66	49	56	39[b,c]	41[b,c]	28
16 Pre	60	55	50	54	49	48	49	44[b]	53	37[b,c]	29
16 Post	54	57	50	50	49	49	48	47	48[b]	42[b,c]	31
17 Pre	45	56	53	48	50	44[b]	39[b]	36[b,c]	34[b,c]	25[a,b,c]	27
17 Post	50	57	53	48	55	45[b]	46	47	40[b,c]	35[b,c]	28

Table 5 Continued

	Overall Ambient Noise	Octave Bands (Hz) (dB SPL)								
	dBA	31.5	63	125	250	500	1,000	2,000	4,000	8,000	16,000
18 Pre	46	52	48	46	44	45[b]	41[b]	42[b]	39[b,c]	27[a,b,c]	27
18 Post	46	53	50	44	46	43[b]	43	41[b]	33[b,c]	26[a,b,c]	27
19 Pre	43	50	48	46	44	43[b]	37[b,c]	38[b]	35[b,c]	27[a,b,c]	27
19 Post	44	55	49	43	45	40[b]	40[b]	34[b,c]	33[b,c]	27[a,b,c]	27
20 Pre	49	52	47	51	48	49	45	41[b]	34[b,c]	30[a,b,c]	27
20 Post	52	54	48	48	49	48	43	40[b]	37[b,c]	33[b,c]	29
21 Pre	59	56	47	49	52	52	46	39[b]	35[b,c]	36[b,c]	28
21 Post	53	57	48	49	49	46	48	43[b]	36[b,c]	27[a,b,c]	28
M	49	59	53	50	48	45[b]	41[b]	39[b]	36[b,c]	30[b,c]	28
SD	5	5	5	3	4	6	6	6	6	5	1
Range	39-60	50-67	45-62	43-59	38-57	34-66	29-55	30-56	24-53	25-42	27-31

[a]Level meets ANSI S3.1-1999 (R2013) criteria for testing from 250 to 8000 Hz with supra-aural earphones
[b]Level meets ANSI S3.1-1999 (R2013) criteria for testing from 250 to 8000 Hz with insert earphones
[c]Level meets the average attenuation values for WAHTS (Meinke, Norris, Flynn, & Clavier, 2017)

A Student's *t*-test (paired, two-tailed) was utilized to compare pre- and post-ambient noise measurements at each octave band. Using an alpha value of $p = .05$, there were significant differences between ambient noise levels at 63 Hz at Site 1 and 125 Hz at Site 2. All other pre- and post-ambient noise levels were not significantly different. Because hearing test frequencies in this study were 1,000 to 20,000, the significantly different ambient noise levels at 63 and 125 Hz were not critical to analysis or practical in terms of determining the validity of hearing thresholds. Therefore, pre- and post-test noise level measurements between the two sites were averaged together and mean values were used to compare the two test locations using a two-tailed unpaired Student's *t*-test with an alpha value of $p = .05$. There was a significant difference in the overall dBA value and for the octave-bands of 125, 8,000, and 16,000 Hz. Table 6 provides all *p*-values for ambient noise measurement comparisons.

Table 6

Statistical Significance for Ambient Noise Measurement Comparisons

	Site 1 Pre- and Post-Comparison	Site 2 Pre- and Post-Comparison	Site Combined Comparison
Octave Band	*p*-value	*p*-value	*p*-value
dB C	0.10	0.26	0.00
dB A	0.87	0.44	**0.10**
31.5	0.07	0.40	0.00
63	**0.04**	0.58	0.00
125	0.71	**0.01**	**0.18**
250	0.34	0.74	0.01
500	0.57	0.41	0.00
1,000	0.32	0.92	0.00
2,000	0.25	0.09	0.00
4,000	0.83	0.23	0.04
8,000	0.65	0.36	**0.09**
16,000	0.47	0.46	**0.18**

Note: Significantly different ($p > 0.05$) ambient noise measurements are in boldface.

Ambient noise levels were compared to ANSI (2013) maximum permissible ambient noise levels (MPANLs) for supra-aural and insert earphones when testing to 0 dB HL. The octave-band noise levels from both sites exceeded MPANLs throughout the frequency range for testing with supra-aural earphones. For insert earphones, the MPANLs were exceeded at 125-2,000 Hz. However, ambient noise levels at 4,000 and

8,000 Hz were below specified maximum decibel levels. ANSI did not provide maximum permissible ambient noise levels for frequencies above 8,000 but recommended using the values for 8,000 Hz when considering higher test frequencies. Following this recommendation; all ambient noise measurements at 16,000 Hz were within the maximum permissible ambient noise levels for insert earphones. Compliance with ANSI MPANLs were summarized in Table 5.

Ambient noise measurements were below the average attenuation levels for the WAHTS (Creare, 2016) for frequencies of 4,000 and above, permitting testing to 0 dB HL (Meinke et al., 2017). Ambient noise was <5 dB above tolerances at 1,000-3,000 Hz, permitting testing to 5 dB HL. The highest audible frequency data from both the AHFA and FLFT were all above 4,000 Hz. Therefore, all thresholds used for analysis of highest audible frequency were valid.

Figure 6 is an illustration of the mean ambient noise levels obtained at both research sites compared to attenuation of the WAHTS (Creare, 2016; Meinke et al., 2017), ambient noise levels for VA hospital wards (Konrad-Martin et al., 2014) and MPANLs for supra-aural headphones according to ANSI (2013) criteria.

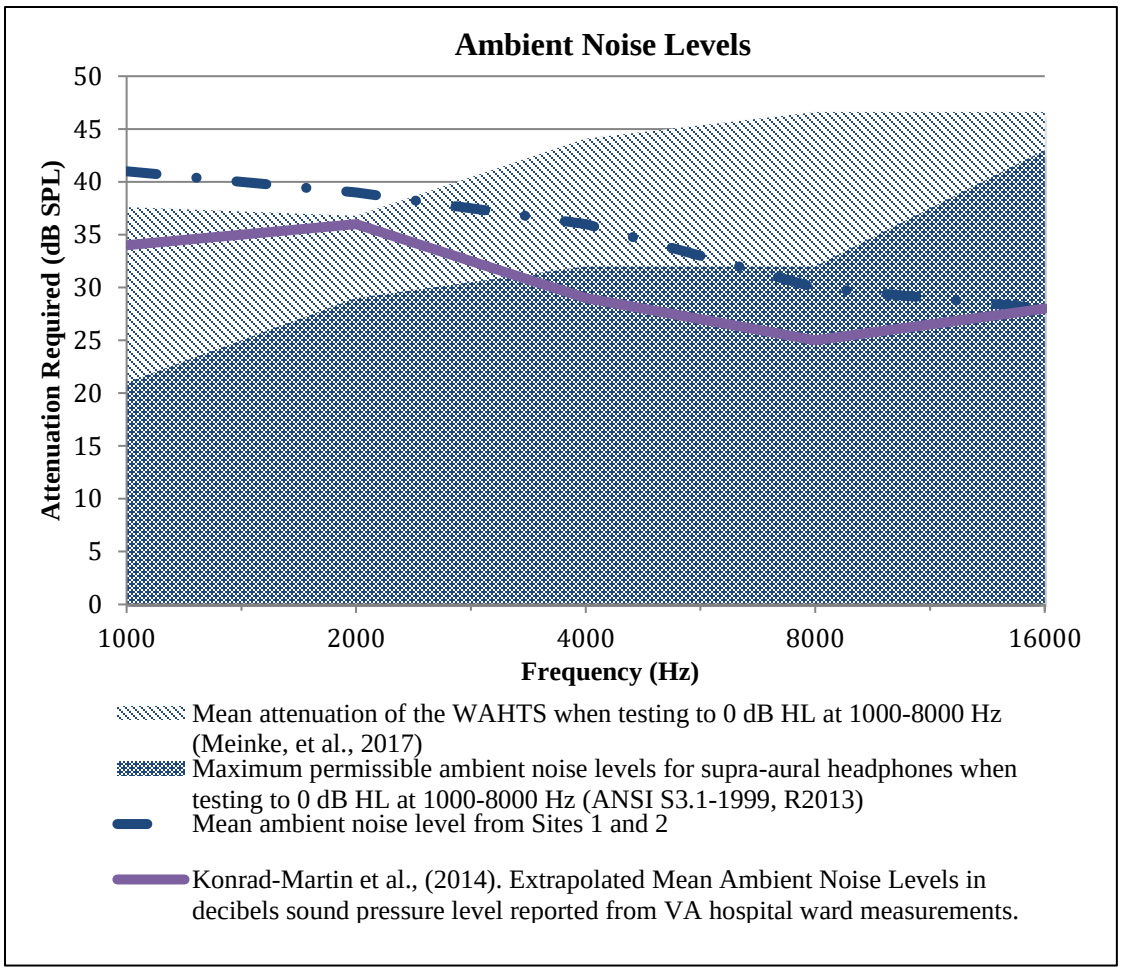

Figure 6. Comparison of the wireless automated hearing tests system attenuation values for various test locations.

Outcomes for Highest Audible Frequency

The WAHTS (Creare, 2016) was used to perform automated high frequency audiometry (AHFA) and the fixed-level frequency testing (FLFT). The AHFA test yielded hearing thresholds measured at 1,000 to 20,000 Hz for 20 of the 21 listeners recruited for the study. Subject 9 was unable to follow test instructions, which was most likely attributed to low cognitive ability reported by the nurse operator after the testing session. Therefore, this subject was omitted from data analysis and outcomes were based

upon 20 listeners. The highest audible frequency (HAF) used in analysis was the highest test frequency at which a valid hearing threshold could be measured using the two audiological test methods (AHFA and FLFT). The highest audible hearing threshold obtained with AHFA was converted from dB HL to dB SPL for data analysis and test comparisons. The FLFT measurement yielded a single frequency value, representing the highest audible frequency reported in Hz. This frequency value was used for data analysis. All thresholds for the highest audible frequency measured with FLFT were at 80 dB SPL. Table 7 includes summary data for both the AHFA and FLFT outcomes. Highest audible frequency differences were reported as AHFA minus FLFT.

Table 7

Automated High Frequency Audiometry and Fixed-Level Frequency Testing Outcome Summary

		Automated High Frequency Audiometry			Fixed-Level Frequency Threshold			Difference (AHFA-FLFT)		
Subject	Ear	dB SPL	HAF (Hz)	Test Time (sec)	dB SPL	HAF (Hz)	Test Time (sec)	dB	Hz	Time (sec)
1	R	90	4000	CNC	80	3175	142	10	825	CNC
	L	95	8000		80	5138		15	2862	
2	R	70	11200	1192	80	12457	123	-10	1257	1069
	L	80	10000		80	11533		0	1533	
3	R	70	10000	1339	80	13325	122	-10	3325	1217
	L	65	10000		80	13982		-15	3982	
4	R	80	12500	1479	80	12699	152	0	199	1327
	L	80	12500		80	13584		0	1084	
5	R	90	9000	1909	80	7266	108	10	1734	1801
	L	75	6000		80	6727		-5	727	
6	R	75	14000	1230	80	14814	181	-5	814	1049
	L	75	12500		80	14945		-20	2445	
7	R	60	12500	1274	80	14672	211	-20	2172	1063
	L	55	12500		80	14117		-25	1617	
8	R	80	10000	1116	80	8156	241	0	1844	875
	L	70	10000		80	8894		-10	1106	

Table 7 Continued

		Automated High Frequency Audiometry			Fixed-Level Frequency Threshold			Difference (AHFA-FLFT)		
Subject	Ear	dB SPL	HAF (Hz)	Test Time (sec)	dB SPL	HAF (Hz)	Test Time (sec)	dB	Hz	Time (sec)
10	R	75	10000	1386	80	5237	124	-5	4763	1262
	L	95	9000		80	5288		15	3712	
11	R	75	10000	2475	80	11423	76	-5	1423	2399
	L	70	10000		80	11986		-10	1986	
12	R	75	14000	1891	80	14254	138	-5	254	1753
	L	75	12500		80	14957		-5	2457	
13	R	75	10000	1429	80	10679	293*	-5	679	1136
	L	65	10000		80	11758		-15	1758	
14	R	80	10000	1514	80	6051	303	0	3949	1211
	L	90	9000		80	5879		10	3121	
15	R	75	14000	1207	80	15844	99	-5	1844	1108
	L	45	14000		80	13070		-35	930	
16	R	75	10000	1386	80	11533	100	-5	1533	1286
	L	95	8000		80	5391		15	2609	
17	R	80	10000	1424	80	10991	88	0	991	1336
	L	80	10000		80	9514		0	486	

Table 7 Continued

		Automated High Frequency Audiometry			Fixed-Level Frequency Threshold			Difference (AHFA-FLFT)		
Subject	Ear	dB SPL	HAF (Hz)	Test Time (sec)	dB SPL	HAF (Hz)	Test Time (sec)	dB	Hz	Time (sec)
18	R	75	12500	1371	80	13982	158	-5	1482	1213
	L	75	12500		80	14672		-5	2172	
19	R	85	12500	1375	80	10177	166	5	2323	1209
	L	80	12500		80	9514		0	2986	
20	R	95	9000	1746	80	6303**	127	20	1449	1619
	L	95	9000		80	5339		15	3661	
21	R	70	12500	1513	80	13505	88	-10	1005	1425
	L	80	12500		80	13716		0	1216	
M			10705	1487		10695	144.6	-3	1886.7	1335
SD			1916	323		3600	57.3	11.5	1086.2	350
Min			4000	1116		3175	76	-35	199	875
Max			14000	2475		15844	303	20	4763	2399

**Highest audible frequency was manually calculated with five frequency reversals instead of six due to software error on last reversal.

FLFT was higher than AHFA

Highest Audible Frequency Comparison

The range of frequency differences between the AHFA and FLFT was 199-4,763 Hz. The mean difference in the highest audible frequency identified by each hearing test was 1,886.7 Hz with neither the AHFA nor FLFT consistently identifying the highest audible frequency higher or lower than the other. Figure 7 provides a graphic illustration of the highest audible frequency identified by both test methods for each subject.

A 2-tailed Wilcoxon signed ranks test was completed to compare the highest audible frequency identified by AHFA and FLFT automated test procedures. There was no significant difference between the two test methods ($p = 0.995$). Therefore, the highest audible frequency elicited from the FLFT and AHFA is not statistically nor significantly different. A Wilcoxon signed-ranks test was also utilized to further analyze ear differences in highest audible frequency. In right ears, the difference in highest audible frequency was not statistically nor significantly different ($p = 0.926$). The previous statement was also true for left ears ($p = 0.911$).

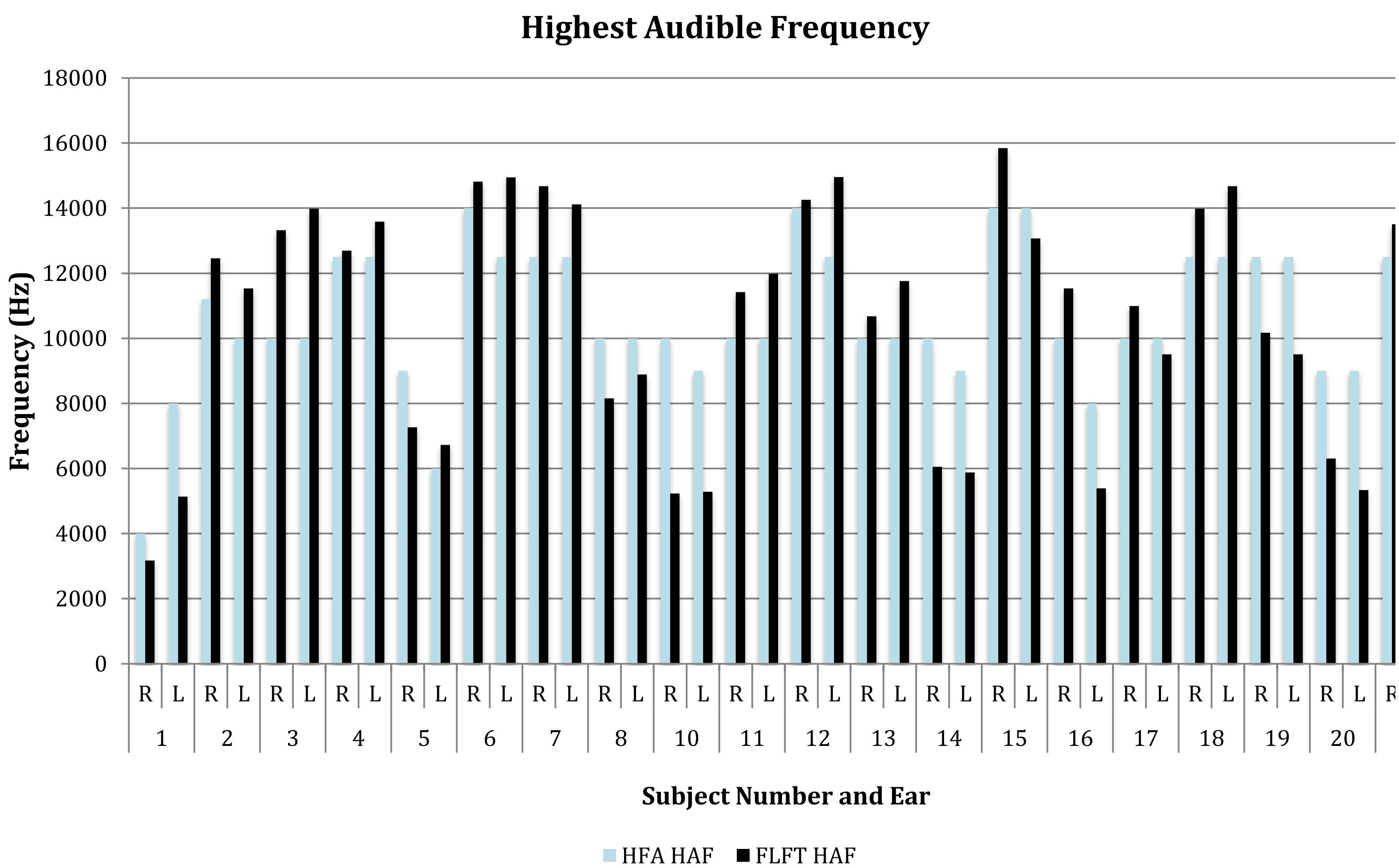

Figure 7. Comparison of highest audible frequencies identified by fixed-level frequency testing and automated high frequency audiometry.

Influence of Stimulus Levels

The single stimulus level during the FLFT (80 dB SPL) and variable stimulus levels available for measuring the highest audible frequency using AHFA likely contributed to some discrepancies between the highest audible frequencies identified between the two test methods. In some test frequencies (125-9,000; 12,500; 16,000-20000), output limits of the WAHTS (Creare, 2016) was ≥5 dB than the 80 dB SPL used in FLFT testing. Therefore, a hearing threshold measured during AHFA could be higher than 80 dB SPL at these frequencies. This could result in an over-estimation of highest audible frequency being reported for AHFA in comparison to the FLFT. Contrarily, patients could also have an actual hearing threshold at the highest audible frequency during the AHFA testing that is below 80 dB SPL. This could lead to the AHFA under-estimating the HAF compared to the FLFT administered above the actual hearing threshold. The majority of these discrepancies occurred between 75 and 80 dB SPL and likely reflected the test-retest variability (±5 dB) when measuring hearing thresholds in adults (Swanepoel et al., 2010). Figure 8 illustrates the trends of over- and under-estimating the highest audible frequency identified by each test method when referencing the threshold level for AHFA.

In 100% of AHFA tests, where the hearing threshold level was 85-90 dB SPL, the HAF was an over-estimation of HAF identified in comparison to the FLFT. When AHFA thresholds were between 45-75 dB SPL, the AHFA audiometry underestimated the HAF in 86% of tests.

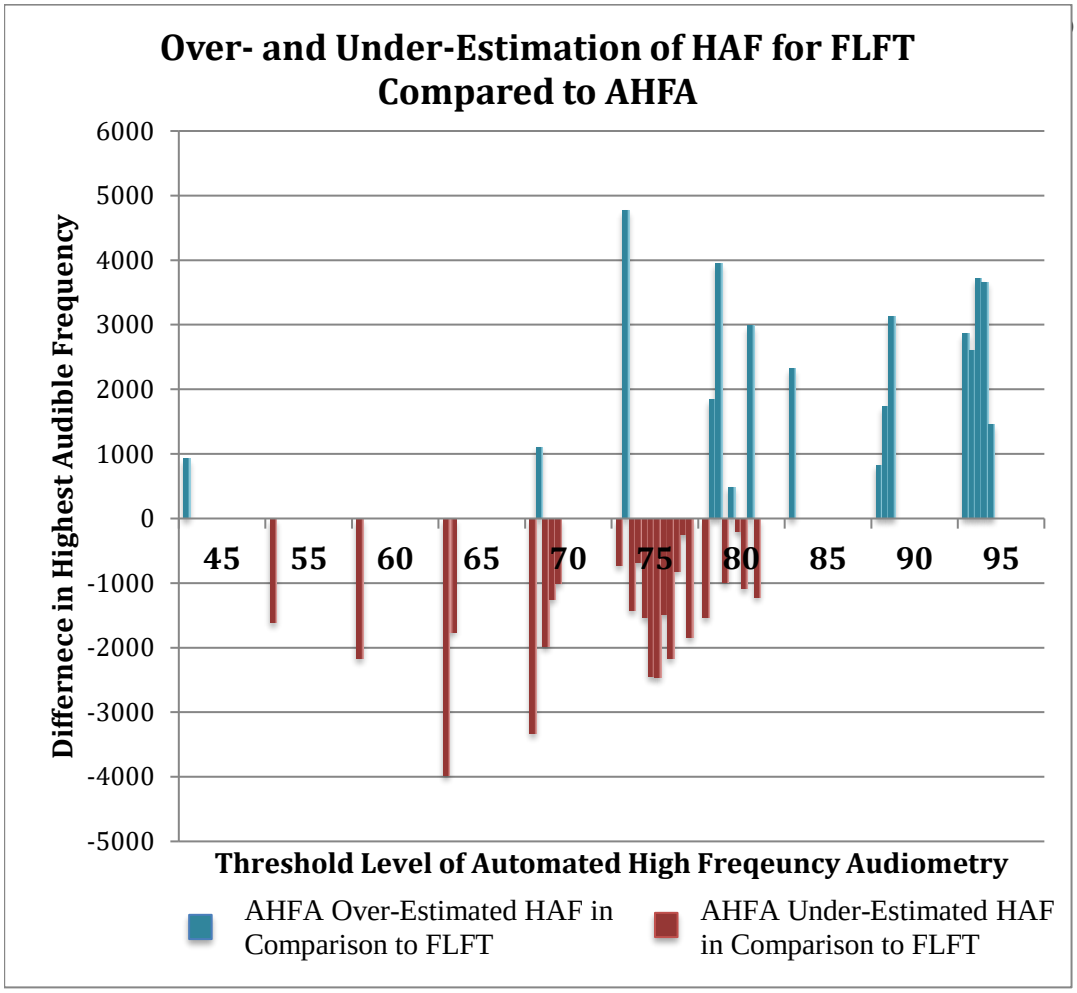

Figure 8. Trend in over- and under-estimation of highest audible frequency.
Note. Formula used to calculate difference in HAF was AHFA HAF-FLFT HAF.

Test Time Comparison

Time was reported as the average time in seconds it took to complete the test. The mean test time for the automated AHFA was 1,487 seconds (24 minutes, 46.8 seconds) and the mean test time for the FLFT was 144.6 seconds (2 minutes, 24.6 seconds). The mean difference in time was 1,317 seconds or 21 minutes, 57 seconds. A one-tailed paired Student's *t*-test was utilized to compare timing differences between

AHFA and FLFT test time. Utilizing a 95% confidence interval, the FLFT test time was significantly faster than the AHFA (p = 1.09414E-13).

Survey Outcomes

Listeners

Twenty-one listener survey responses were collected at the conclusion of the audiometric testing and 20 were considered valid (Subject 9 omitted). Listeners responded to twelve 7-point Likert scale statements. A summary of survey responses is provided in Figure 9.

The listeners provided 11 additional open-ended comments and feedback (see Table 8). Overall, listener responses had a positive trend. The mean Likert score was 6.2 out of seven. Listeners thought the headset fit appropriately and comfortably and the tablet was easy to use. Listeners also responded that having their hearing monitored during treatment was somewhat important (Likert = 5) to them and scheduling/traveling to multiple hearing appointments would be problematic for them (5.95 and 6.96, respectively). The mean Likert score from listeners was a 4.9 on the statement related to being aware of the risk of hearing loss before treatment. This value corresponded with the "somewhat agree" rating. This was the lowest ranked statement for the listeners. Optional feedback provided by the listeners commonly reported that using the WAHTS was a more convenient option to have hearing monitored when compared to traditional ototoxic monitoring practices. Some listeners were concerned about external noise and felt they might have confused IV pump beeps with presented beeps on the tablet.

Figure 9. Listener survey responses (n = 20

Table 8

Listener Additional Feedback and Comments

Listener	Comment
1.	Differentiating real life beeps from computer beeps was difficult at times. It was often difficult for me to actually differentiate between phantom beeps in my head. Either because I was hearing actual beeps or phantom beeps was hard to tell. On FLFT I know that often I still had my thumb on trigger when sound went out and I left it on the trigger for just a split second more just to make sure but in actuality my finger was on the trigger when I no longer could hear the sound.
2.	Neuropathy in the fingers had a slight affect on the touch pad.
3.	It's a noisy environment. I'd like to have a comparative test at the end of chemo.
4.	This was much more convenient than going to another appointment and the test was simple to take.
5.	This was much more convenient than going to another appointment and the test was simple to take.
6.	Some of the tones were similar to the tones of the infusion machines, which could distract.
7.	The background noise made it a little difficult. I felt like I would have done better had it been quiet.
8.	It was very convenient to have it done here at the hospital.
9.	It was very easy and the headphones were comfy.
10.	It was a painless test. It was good because I knew I was going to have to get my hearing tested anyway and I think it would be beneficial for those of us getting this chemotherapy to know the amount of hearing loss and to see if there is someway to help prevent it in the future.

Operators

Twenty-one operator surveys were completed by eight different operators. Two statements were reverse coded for consistency in directionality. Figure 10 summarizes the tabulated scores. In three surveys, operators left additional comments or feedback (see Table 9).

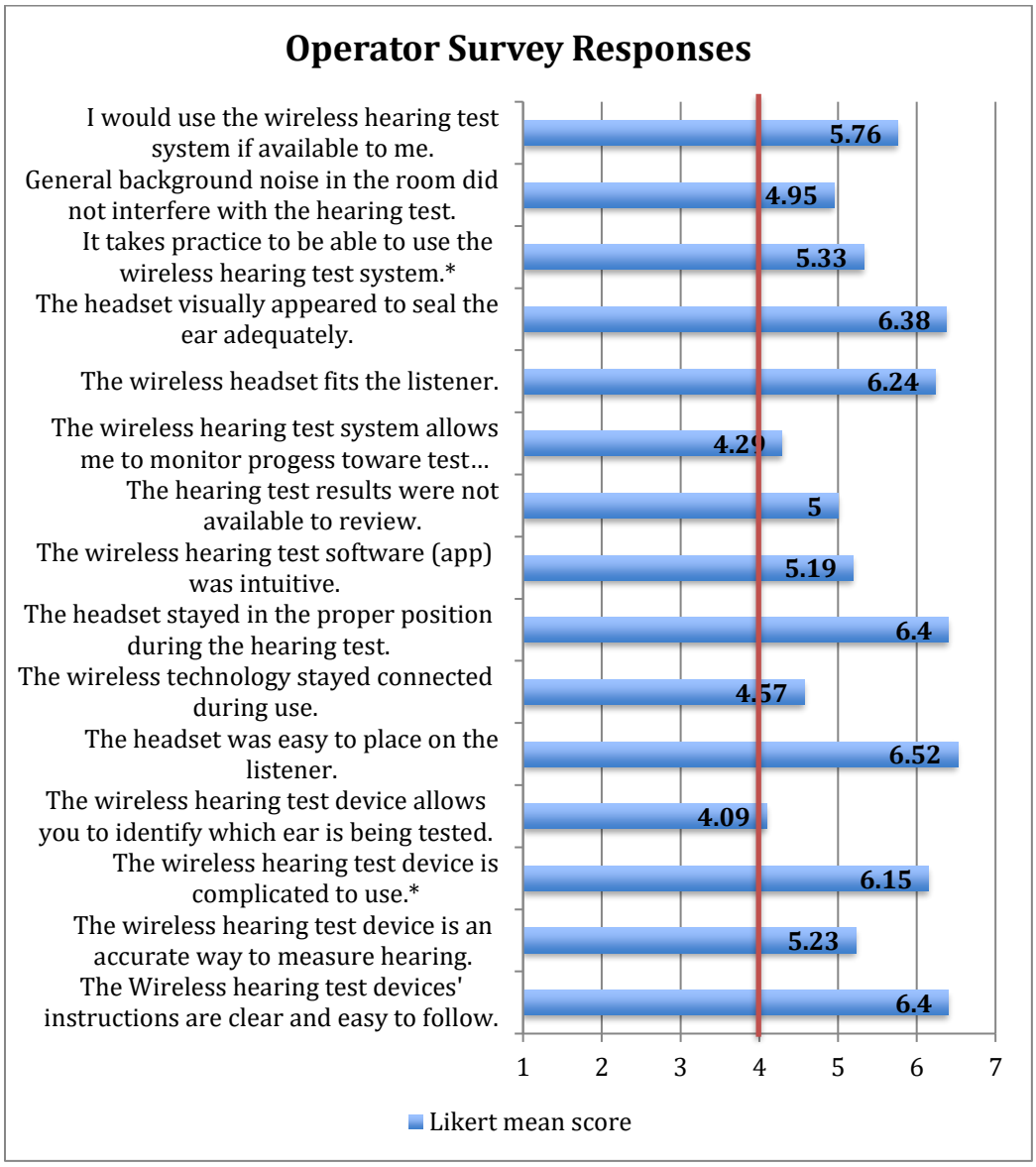

Figure 10. Operator survey response tabulated scores (n = 21).

Table 9

Operator Additional Feedback and Comments

Operator	Comments
1.	Worried about the external noise that I was creating during the test for the patient.
2.	Hard to keep noise limited in the testing area.
3.	Patient reported the headset was a little too tight.

Overall, operator responses showed a positive trend with mean Likert score of 5.5 out of seven. Operators reported the WAHTS (Creare, 2016) was easy to use, appeared to fit the listener well, and they would use the device if it was available to them. In this study, operators did not manage the tablet throughout the duration of the testing due to other work responsibilities so responses to statements related to tablet functioning tended to indicate that operators neither agreed nor disagreed. Additional feedback from nurses was commonly related to not being able to control the external noise.

Summary of Outcomes

The WAHTS (Creare, 2016) provided sufficient attenuation for ambient noise levels to permit valid hearing threshold testing in two outpatient chemotherapy centers that differed in room design and layout. The highest audible frequencies obtained with the automated AHFA and FLFT tests were statistically compared and found to be comparable. In terms of mean test time, the FLFT was significantly faster (1,868.9 seconds or 31 minutes and 15 seconds faster) in comparison to the AHFA. The operators and listeners responded favorably to the WAHTS technology when used in the outpatient chemotherapy settings. Both AHFA and FLFT appeared to be valid test methods for

identifying the highest audible frequency by nursing staff for patients being treated in outpatient cancer treatment centers. The FLFT might be preferable as a screening protocol due to the significantly faster test administration.

CHAPTER V

DISCUSSION

Ambient Noise

Ambient noise was measured at two outpatient cancer treatment centers with different floor plans. Site 1 was in 'pod' design where half walls surrounded the patient and Site 2 had an open layout with chairs lined up beside each other. Sources of ambient noise were other patients talking nearby, nurses working in surrounding spaces, and IV pump alarms. No heating, ventilation, and air conditioning systems were audible by the researcher but might have contributed to differences in low frequency ambient noise (63- and 125 Hz).

Due to the level of ambient noise in the treatment centers, hearing thresholds could not be measured accurately to 0 dB HL across all test frequencies (250-20,000) with all transducers (insert earphones, supra-aural headphones, WAHTS; ANSI, 2013; Meinke et al., 2017). Ambient noise has a greater effect on lower test frequencies. However, lower frequencies were not as critical for testing patients exposed to ototoxic chemotherapeutics. This was due to the initial onset of the hearing loss typically beginning in the higher frequencies (Kopelman et al., 1988; Punnett et al., 2004). Therefore, in the limited sample of two out-patient centers, the attenuation of the WAHTS (Creare, 2016) allowed for accurate testing of thresholds down to 0 dB HL at 4,000 Hz and above. Thresholds were obtained at 5 dB HL for the test frequencies of

250-3,000 when using the WAHTS. This was still sufficient for identifying an ototoxic threshold shift of 15 dB at a single frequency or 10 dB at adjacent frequencies as specified by ASHA (1994), especially since changes in threshold typically influence the higher test frequencies and older adults seldom have thresholds at 0 dB HL at all test frequencies.

Testing could potentially be completed in exam rooms before chemotherapy treatment, especially if using the short-duration FLFT approach. This would be of benefit to patients who have tinnitus or who are too distracted in the treatment environment and prefer a quieter listening environment. Ambient noise levels in the exam rooms were not measured but were presumed to be lower in level due to isolation from other noise sources (patients, nursing staff, and medical equipment). Patients were often seen in exam rooms prior to being moved to the treatment area so it would be feasible to have them take the hearing test at that time. However, it would be important to have ambient noise measured before selecting which rooms would be best for audiological testing to take place and reconcile those levels with the WAHTS (Creare, 2016) attenuation values.

Extrapolated mean ambient noise levels from research at a VA hospital ward (Konrad-Martin et al., 2014) were lower in all frequencies in comparison to ambient noise levels from Site 1 and 2 in the current research. Attenuation of the WAHTS (Creare, 2016) would allow for testing to 0 dB HL at 1,000-16,000 Hz in the VA hospital ward. Potential causes of the lower mean ambient noise levels in the VA hospital ward were the testing being conducted in a room secluded from other patients and their families as well as nurses working on nearby patients. However, specific test

environment information was not included in the methodology of the Konrad-Martin et al. (2014) study.

One common concern voiced in the listener survey was interference between the IV pump monitors' alarm tones with test stimuli presentations. After becoming aware of this concern, the alert tones on the IV pumps were measured with a sound level meter. Thirty-second averages were sampled using dBA. Ten measurements (five by each ear) were taken in the approximate location of where the patient's ears would be during chemotherapy treatment. The measurements were recorded as the "near ear" and the "far ear" with regard to physical placement of the IV equipment. The maximum sound level for each sample was averaged to calculate the sound pressure level for the IV pump alarm. This approach allowed for a more accurate representation of the alarm level because the breaks in between the alarm beeps would artificially reduce the average sound level of the alarm. The average maximum sound level for the ear closest to the IV pump was 78.4 dBA and 77.0 dBA for the "far" ear. Intermittent beeps of 77.0-78.4 dBA could have potentially artificially elevated thresholds and interfered with listener attention. A trained operator or listener could pause the WAHTS (Creare, 2016) pending silencing the alarm. Another potential solution to relieve this problem, which is currently being investigated by Creare (2016), would be to implement a sound level meter built into the headset that continually sampled ambient noise and automated software that temporarily paused testing when MPANLS were exceeded.

Technology Implementation

Implementing the technology into the outpatient cancer centers presented certain challenges due to the characteristics of the environment as well as characteristics of the

test populations. At both test locations, the tablet and headset dropped Bluetooth connection on multiple occasions and, occasionally, multiple times during a test session. Throughout testing, the tablet had to be reconnected to the headset at least one time for 14 of the 20 participants and had to be reconnected five times for one participant. Due to this technological difficulty, the researcher had to remain close to the subject during testing to be ready to troubleshoot connection issues. Recently, Creare (2016) determined the dropped Bluetooth issue was a hardware bug for the Nexus tablet computer model used in this study and has been resolved with newer hardware releases by Nexus.

Chemotherapy Patient Factors

Written instructions were on the tablet for the listener subjects to follow. However, they often had to put on eyeglasses to be able to read the small print. Ramsdale and Charman (1989) reported the static response of the eye begins to decline at age 45; thus, the incidence of presbyopia increases after age 45 and the need of reading glasses increases. The mean age of participants in the current capstone was 60 years so consequently, it was common for participants to require reading glasses to read the written instructions on the tablet. This led to the headset having to be placed on participants' heads multiple times throughout testing. Testing would have been more seamless if recorded test instructions were built into the device in addition to the written instructions.

No patient was too ill to complete testing. Overall, patients had a very positive response to the testing based on survey responses. Patients who were being administered carboplatin were also commonly receiving taxol. Benadryl could be effective in

counteracting the negative physical reactions from taxol (Carretta, Eisenhauer, & Rozencweig, 1997). Depending on site protocol, patients either received Benadryl through an IV or took it orally at the time of treatment. Patients and nurses often reported they would be unable to continue testing when the Benadryl began to take effect because of extreme drowsiness and being unable to stay awake for the testing. On one occasion, a nurse had to delay the start of Benadryl administration so the participant could finish the hearing testing. This situation would further justify the use of the FLFT method in terms of speed of testing.

Peripheral neuropathy is another side effect of taxol. Carretta et al. (1997) reported 80 of 151 patients being treated with taxol experienced neuropathy. Peripheral neuropathy is also a side effect from cisplatin and carboplatin (Go & Adjei, 1999). Peripheral neuropathy could become an issue if patients were unable to feel if they were touching the tablet screen due to decreased tactile perception. A physical button might be more appropriate in allowing biofeedback for patients with peripheral neuropathy symptoms in their fingers. One subject in the current study verbally reported taxol-induced peripheral neuropathy made it difficult to monitor how lightly or strongly to tap the screen when the sound was heard. This subject completed the study without problem in spite of their concern.

Listener usability and comfort survey responses were in agreement with responses from Meinke et al. (2017). This was an indication that patients undergoing cancer treatments did not have increased difficulty completing the hearing testing in comparison to people taking the hearing test in an occupational setting.

Implementing Fixed-Level Frequency Test and Automated High Frequency Audiometry in Ototoxicity Monitoring

A Wilcoxon signed ranks analysis demonstrated no statistical difference between the highest audible frequency measured by the AHFA and FLFT. This result was in agreement with findings from Rieke and colleagues (2017) who tested the method on normal hearing younger adults. Just as the highest audible frequency identified by FLFT directly translated to the SRO fixed frequency audiometry (FFA) in Rieke et al.'s research, there was no statistical difference between highest audible frequency identified by the AHFA and FLFT in the current study. This study further extended the applicability of the FLFT administered with the WAHTS (Creare, 2016) outside of a sound-booth and demonstrated the practicality of administering the exam in two chemotherapy treatment centers.

Ototoxicity monitoring relies upon the establishment of a sensitive region of ototoxicity as defined on a baseline audiogram and monitored throughout chemotherapy treatment. Typically, the highest audible frequency at 100 dB HL and six lower frequencies are targeted for audiometric monitoring (Fausti et al., 1999). The sensitivity and specificity of the FLFT for identifying a change in hearing status due to ototoxicity is unknown at this time. The mean difference between the highest audible frequencies (HAF) identified between the AHFA (SRO approach) and the FLFT test methods was 1,886.7 Hz, and the standard deviation was 1,086.2 Hz. The clinical implication of an approximately 2,000 Hz error is most critical for the lower/speech frequencies when communication starts to be negatively impacted by chemotherapeutics. If the FLFT under-estimated the highest audible frequency, which was used to define the SRO for

ototoxicity monitoring, the earliest shift in hearing status would potentially be missed or delayed in time. If the FLFT over-estimated the highest audible frequency, it would fail to detect ototoxic effects occurring at lower frequencies. It might be worthwhile to consider a higher output level (test level) for the FLFT that is more consistent with current audiometer output levels. This would likely eliminate errors caused by the lower output limit of 80 dB HL implemented in the current version of the FLFT.

The FLFT was found to be much faster than the AHFA. The mean time it took for the FLFT to be completed was 144.6 seconds (2 minutes, 24.6 seconds). This was slower than the reported FLFT test time of ~30 seconds by Rieke et al. (2017). This was possibly due to the testing taking place in a more distracting test environment, which might require more time to obtain six reversals on the Bekesy (1947) tracking. The current study also evaluated the FLFT on subjects without normal hearing and receiving medication treatment, which might have influenced their level of alertness. Nonetheless, the decreased test time in comparison to the AHFA has an advantage for patients and examiners. Patients would spend less time testing so they would not need to schedule extra time for appointments or worry about the length of testing being challenging due to increased fatigue from side effects of the chemotherapy. Examiners would spend less time administering the testing so more patients could be seen with no need for additional equipment or personnel to operate equipment. In the current version, the FLFT might be well-suited as a quick ototoxicity screener, which might then be followed up with more extensive threshold testing in a controlled test environment if a shift in the highest audible frequency was detected.

Potential to Increase Patient Access to Ototoxicity Monitoring

Operator Training

Nurse operators who have had no specialized training in hearing testing could administer testing. However, if nurses would be the only ones there to administer the testing, they would need more training on troubleshooting the device with regard to connection drops. A mechanism would also have to be developed to transfer the test results to the audiologist for review, interpretation, and follow-up. Training could be completed in one session held by the hearing healthcare professional who organized the program. Nurses would be given an overview of the device and training on the software.

Survey responses obtained by nurses included concerns about outside noise in the cancer centers interfering with the hearing test. In order to have nurses' concerns be addressed, data would need to be presented to the nurses showing ambient noise levels were acceptable to produce valid hearing thresholds. Nurse operator survey responses were also similar to operator survey responses from research in occupational hearing testing (Meinke et al., 2017). Both groups of operators felt the device fit the listener's ears well and would use it if available to them. Therefore, the WAHTS (Creare, 2016) would likely be accepted in other treatment centers.

Benefits of Ototoxicity Monitoring with the Wireless Automated Hearing Test System

Utilizing the WAHTS (Creare, 2016) to implement the FLFT has the potential to overcome barriers currently preventing the implementation of ototoxicity monitoring programs in the classic manner as reported by Konrad-Martin et al. (2017). Because the WAHTS could be utilized in an outpatient treatment center, the hassle of scheduling

multiple appointments for the patient would be eliminated. Consequentially, it would also require less time commitment. Operators would not need to be trained in hearing testing so current staff could administer the testing with just one hearing healthcare provider reviewing the testing at an on-site or off-site location. Nurses were used in the current study to administer the hearing testing but because operating the device did not require formal training, less highly paid support staff might be able to administer the testing. The implementation of the WAHTS to administer the FLFT and/or the AHFA was feasible for both test sites. No barriers were identified during the research study and both nurses and patients were supportive of its use. Either the AHFA or the FLFT approach was feasible to implement using the WAHTS. The advantage of the AHFA was the more detailed threshold data obtained with the testing and more information regarding ototoxic changes. The disadvantage was the substantially longer test time. As mentioned previously, the FLFT might be a useful screening tool to implement for ototoxicity monitoring. To get an ototoxicity monitoring program functioning with the WAHTS in these settings, operating staff would need to complete a training session on the device and a plan would need to be developed with oncologists with regard to test choice, test protocol, and report/communication preferences with the audiologist.

Strengths and Limitations

Testing was only completed in two outpatient cancer treatment centers. However, the test environments were designed very differently from each other, which might permit generalization to a large number of outpatient chemotherapy centers. The current study had a relatively small number of participants and was slightly lower in number to the Rieke et al. (2017) study (n = 29). Recruiting patients was difficult because patients

were not receiving hearing results due to the experimental nature of the technology and test protocol. Future studies that could actually implement an ototoxicity monitoring program and inform the patients of their hearing status would likely gain greater participation.

Ambient noise measurements were not done continuously throughout testing so they might not have captured when ambient noise levels were above the attenuation of the WAHTS (Creare, 2016) at specific test frequencies. Meinke et al. (2017) recommended further research to implement and evaluate accuracy of in-ear microphones continuously measuring ambient noise levels and pausing testing when levels were too high to produce valid thresholds. Additionally, the highest audible frequency using AHFA and FLFT was not compared to a gold-standard hearing test in a sound booth, which would have been ideal but impractical for this capstone research project.

Future Research

Future research should implement the WAHTS (Creare, 2016) technology in a more diverse assortment of chemotherapy treatment centers with a larger population of participants. Use of the FLFT and AHFA would need to be evaluated as part of a clinical research study that would implement a full ototoxicity monitoring program. Future studies should also investigate whether the test needed to be nurse administered, support staff administered, or if the patient could self- administer the exam. In this model, only one audiology professional would be required to supervise the program and review/interpret the test results. Additionally, the audiologist would also be trained in troubleshooting the device and be on call for technology issues, similar to the way newborn hearing screening programs are implemented in hospital nurseries.

Conclusions

The WAHTS (Creare, 2016) provided sufficient attenuation of ambient noise and enabled valid hearing threshold measurements to 5 dB HL for 250-20,000 Hz in two outpatient chemotherapy treatment settings in northern Colorado. There was no statistical difference in the highest audible frequency measured by the AHFA and FLFT test methods. The FLFT required substantially shorter test times on average (24.78 minutes versus 2.4 minutes). Both the FLFT and AHFA administered via the WAHTS would be useful means of performing ototoxicity monitoring for patients receiving cisplatin and carboplatin treatments onsite in outpatient cancer treatment centers by untrained nursing staff.

REFERENCES

American Academy of Audiology. (2009). *Position statement and clinical practice guidelines: Ototoxic monitoring*. Retrieved from http://audiology-web.s3.amazonaws.com/migrated/OtoMonGuidelines.pdf_539974c40999c1.58842217.pdf

American Speech-Language-Hearing Association. (1994). *Guidelines for the audiologic management of individuals receiving cochleotoxic drug therapy*. *American Speech-Language-Hearing Association, 36* (Suppl 12), 11-19.

American National Standards Institute. (1983). *Specifications for sound level meters.* New York: Author.

American National Standards Institute. (2013). *Maximum permissible ambient noise levels.* New York: Author.

Arlinger, S. (2003). Negative consequences of uncorrected hearing loss- A review. *International Journal of Audiology, 42(*2), 17-20. doi:10.3109/14992020309074639

Bauer, F. P., Westhofen, M., & Kehrl, W. (1992). The ototoxicity of the cytostatic drug carboplatin in patients with head-neck tumors. *Laryngo-rhino-otologie, 71*(8), 412-415. Retrieved from http://europepmc.org/abstract/med/1388466

Békésy, G. V. (1947). A new audiometer. *Acta Oto-Laryngologica, 35*(5-6), 411-422. doi:10.3109/00016484709123756

Blakley, B. W., Gupta, A. K., Myers, S. F., & Schwan, S. (1994). Risk factors for ototoxicity due to cisplatin. *Archives of Otolaryngology–Head & Neck Surgery*, *120*(5), 541-546. doi:10.1001/archotol.1994.01880290051009

Blakley, B. W., & Myers, S. F. (1993). Patterns of hearing loss resulting from cis-platinum therapy. *Otolaryngology--Head and Neck Surgery*, *109*(3), 385-391. doi:10.1177/019459989310900302

Bokemeyer, C., Berger, C. C., Hartmann, J. T., Kollmannsberger, C., Schmoll, H. J., Kuczyk, M. A., & Kanz, L. (1998). Analysis of risk factors for cisplatin-induced ototoxicity inpatients with testicular cancer. *British Journal of Cancer*, *77*(8), 1355-1362. doi:10.1038/bjc.1998.226

Boulikas, T., & Vougiouka, M. (2004). Recent clinical trials using cisplatin, carboplatin and their combination chemotherapy drugs (Review). *Oncology Reports*, *11*(3), 559-595. doi:10.3892/or.11.3.559

Brennan-Jones, C. G., Eikelboom, R. H., Swanepoel, D., Friedland, P. L., & Atlas, M. D. (2016). Clinical validation of automated audiometry with continuous noise-monitoring in clinically heterogeneous population outside a sound-treated environment. *International Journal of Audiology*, *55*(9), 507-513. doi:10.1080/14992027.2016.1178858

Carhart, R., & Jerger, J. (1959). Preferred method for clinical determination of pure-tone thresholds. *Journal of Speech & Hearing Disorders*, *24*, 330-345. doi:10.1037/e539802008-001

Carretta, R. M., Eisenhauer, E., & Rozencweig, M. (1997). *Methods for administration of taxol.* Washington, DC: U.S. Patent and Trademark Office.

Cavaletti, G., Bogliun, G., Zincone, A., Marzorati, L., Melzi, P., Frattola, L., ...Galli, A. (1997). Neuro-and ototoxicity of high-dose carboplatin treatment in poor prognosis ovarian cancer patients. *Anticancer Research, 18*(5B), 3797-3802. Retrieved from http://europepmc.org/abstract/med/9854499

Chia, E., Wang, J., Rochtchina, E., Cumming, R. R., Newall, P., & Mitchell, P. (2007). Hearing impairment and health-related quality of life: The blue mountains hearing study. *Ear & Hearing, 28*(2), 187-195. doi:10.1097/AUD.0b013e31803126b6

Chisolm, T. H., Johnson, C. E., Danhauer, J. L., Portz, L. J. P., Abrams, H. B., Lesner, S., …Newman, C. W. (2007). A systematic review of health-related quality of life and hearing aids: Final report of the American Academy of Audiology task force on the health-related quality of life benefits of amplification in adults. *Journal of the American Academy of Audiology*, *18*(2), 151-183. doi:10.3766/jaaa.18.2.7

Creare. (2016). *Hearing assessment*. Hanover, NH: Creare Research and Development.

Creaven, P. J., Pendyala, L., & Petrelli, N. J. (1993). Evaluation of alpha-difluoromethylornithine as a potential chemopreventive agent: Tolerance to daily oral administration in humans. *Cancer Epidemiology Biomarkers & Prevention*, *2*(3), 243-247.

Croghan, M. K., Aickin, M. G., & Meyskens, F. L. (1991). Dose-related alpha-difluoromethylornithine ototoxicity. *American Journal of Clinical Oncology*, *14*(4), 331-335. doi:10.1097/00000421-199108000-00012

Dalton, D. S., Cruickshanks, K. J., Klein, B. E. K., Klein, R., Wiley, T. L., & Nondahl, D. M. (2002). The impact of hearing loss on quality of life in older adults. *The Gerontologist, 43*(5), 661-668. doi:10.1093/geront/43.5.661

de Jongh, F. E., Van Veen, R. N., Veltman, S. J., de Wit, R., Van der Burg, M. E. L., Van den Bent, M. J., ...Verweij, J. (2003). Weekly high-dose cisplatin is a feasible treatment option: Analysis on prognostic factors for toxicity in 400 patients. *British Journal of Cancer*, *88*(8), 1199-1206. doi:10.1038/sj.bjc.6600884

Dille, M. F., McMillan, G. P., Helt, W. J., Konrad-Martin, D., & Jacobs, P. (2015). A store-and-forward tele-audiology solution to promote efficient screenings for ototoxicity during cisplatin cancer treatment. *Journal of the American Academy of Audiology*, *26*(9), 750-760. doi:10.3766/jaaa.15028

Estrem, S. A., Babin, R. W., Ryu, J. H., & Moore, K. C. (1981). Cis-diamminedichloro-platinum (II) ototoxicity in the guinea pig. *Otolaryngology--Head and Neck Surgery*, *89*(4), 638-645.

Fausti, S. A., Helt, W. J., Phillips, D. S., Gordon, J. S., Bratt, G. W., Sugiura, K. M., & Noffsinger, D. (2003). Early detection of ototoxicity using 1/6th-octave steps. *Journal of the American Academy of Audiology*, *14*(8), 444-450. Retrieved from http://www.ingentaconnect.com.unco.idm.oclc.org/contentone/aaa/jaaa/2003/00000014/00000008/art00006

Fausti, S. A., Henry, J. A., Helt, W. J., Phillips, D. S., Frey, R. H., Noffsinger, D., …Fowler, C. G. (1999) An individualized, sensitive frequency range for early detection of ototoxicity. *Ear & Hearing*, *20*(6), 497-505. doi:10.1097/00003446-199912000-00005

Fausti, S. A., Rappaport, B. Z., Schechter, M. A., Frey, R. H., Ward, T. T., & Brummett, R. E. (1984). Detection of aminoglycoside ototoxicity by high-frequency auditory evaluation: Selected case studies. *American Journal of Otolaryngology*, *5*(3), 177-182.

Frank, T. (1990). High-frequency hearing thresholds in young adults using a commercially available audiometer. *Ear and Hearing*, *11*(6), 450-454. doi:10.1097/00003446-199012000-00007

Gatzemeier, U., Hossfeld, D. K., Neuhauss, R., Reck, M., Achterrath, W., & Lenaz, L. (1991). Carboplatin in small cell lung cancer. *The Oncologist*, *3*(3), 145-154. doi:10.1016/0169-5002(91)90055-B

Go, R. S., & Adjei, A. A. (1999). Review of the comparative pharmacology and clinical activity of cisplatin and carboplatin. *Journal of Clinical Oncology*, *17*(1), 409-409.

Gordon, A. N., Hancock, K. C., Matthews, C. M., Messing, M., Stringer, C. A., Doherty M. G., & Teneriello, M. (2002). Phase I study of alternating doublets of topotecan/carboplatin and paclitaxel/carboplatin in patients with newly diagnosed, advanced ovarian cancer. *Gynecologic Oncology*, *85*(1), 129-135. doi:10.1006/gyno.2001.6581

Gordon, J. S., Phillips, D. S., Helt, W. J., Konrad-Martin, D., & Fausti, S. A. (2005). Evaluation of insert earphones for high-frequency bedside ototoxicity monitoring. *Journal of Rehabilitation Research and Development*, *42*(3), 353-361. doi:10.1682/jrrd.2004.06.0093

Green, T. P., & Mirkin, B. L. (1981). Furosemide disposition in normal and proteinuric rats: Urinary drug-protein binding as a determinant of drug excretion. *Journal of Pharmacology and Experimental Therapeutics*, *218*(1), 122-127. doi:10.1016/0024-3205(80)90238-6

Gruney, J. G., Tersak, J. M., Ness, K. K., Landier, W., Matthay, K. K., & Schmidt, M. (2007). Hearing loss, quality of life, and academic problems in long-term neuroblastoma survivors: A report from the children's oncology group. *Pediatrics*, *120*(5), 1229-1236. doi:10.1542/peds.2007-0178

Hartmann, J. T., & Lipp, H. P. (2003). Toxicity of platinum compounds. *Expert Opinion on Pharmacotherapy*, *4*(6), 889-901. doi:10.1517/14656566.4.6.889

Hawkins, Jr., J. E. (1976). Drug ototoxicity. In *Auditory system* (pp. 707-748). Berlin Heidelberg: Springer.

Horn, Y., Schechter, P. J., & Marton, L. J. (1987). Phase I–II clinical trial with alpha-difluoromethylornithine: An inhibitor of polyamine biosynthesis. *European Journal of Cancer and Clinical Oncology*, *23*(8), 1103-1107. doi:10.1016/0277-5379(87)90141-6

Hughson, W., & Westlake, H. D. (1944). *Manual for program outline for rehabilitation of aural casualties both military and civilian*. Omaha, NE: Douglas Print Co.

International Organization for Standardization. (2009). *ISO 8252: Acoustics-- Audiometric test methods, Part 1*. Retrieved from https://www.iso.org/standard/43601.html

Klinke, R., & Mertens, M. (1988). Quantitative assessment of torasemide ototoxicity. *Arzneimittel-Forschung, 38*(1A), 153-155.

Klis, S. F., O'Leary, S. J., Wijbenga, J., de Groot, J. C., Hamers, F. P., & Smoorenburg, G. F. (2002). Partial recovery of cisplatin-induced hearing loss in the albino guinea pig in relation to cisplatin dose. *Hearing Research*, *164*(1), 138-146. doi:10.1016/s0378-5955(01)00425-7

Konrad-Martin, D., Reavis, K. M., McMillan, G., Helt, W. J., & Dille, M. (2014). Proposed comprehensive ototoxicity monitoring program for VA healthcare (COMP-VA). *Journal of Rehabilitation Research and Development, 51*(1), 81.

Konrad-Martin, D., Poling, G. L., Garinis, A. C., Ortiz, C. E., Hopper, J., O'Connell-Bennett, K., & Dille, M. F. (2017). Applying US national guidelines for ototoxicity monitoring in adult patients: perspectives on patient populations, service gaps, barriers and solutions. *International Journal of Audiology*, *57*(sup4), 1-16.

Kopelman, J., Budnick, A. S., Sessions, R. B., Kramer, M. B., & Wong, G. Y. (1988). Ototoxicity of high-dose cisplatin by bolus administration in patients with advanced cancers and normal hearing. *The Laryngoscope*, *98*(8), 858-864. doi:10.1288/00005537-198808000-00014

Laurell, G. F. (1992). Combined effects of noise and cisplatin: short-and long-term follow-up. *The Annals of Otology, Rhinology, and Laryngology, 101*(12), 969-976.

Laurell, G., & Jungnelius, U. (1990). High-dose cisplatin treatment: Hearing loss and plasma concentrations. *The Laryngoscope*, *100*(7), 724-734. doi:10.1288/00005537-199007000-00008

Lesman Instrument Co. (2019). *Quest Model QC-10/QC-20 acoustic calibrator.* Retrieved from http://www.raeco.com/products/noise/quest_qc10sound calibrator.html

Li, Y., Womer, R. B., & Silber, J. H. (2004). Predicting cisplatin ototoxicity in children: The influence of age and the cumulative dose. *European Journal of Cancer, 40*(16), 2445-2451. doi:10.1016/j.ejca.2003.08.009

Lin, F. R., Yaffe, K., Xia, J., Xue, Q. L., Harris, T. B., Purchase-Helzner, E., …Simonsick, E. M. (2013). Hearing loss and cognitive decline in older adults. *Journal of American Medical Assotiation, 173*(4), 293-299. doi:10.1001/jamainternmed.2013.1868.

Lonsbury-Martin, B. L., Martin, G. K., & Pettis, J. (2007). Other ototoxins: Aspirin and other nonsteroidal anti-inflammatory drugs, quinine, and macrolides. In K. C. M. Campbell (Ed.), *Pharmacology and ototoxicity for audiologists* (pp. 187-196). Clifton Park, NY: Delmar Cengage Learning.

Mahajan, S. L., Ikeda, Y., Myers, T. J., & Baldini, M. G. (1981). Acute acoustic nerve palsy associated with vincristine therapy. *Cancer*, *47*(10), 2404-2406. doi:10.1002/1097-0142(19810515)47:10%3C2404::aid-cncr2820471014%3E3.0.co;2-2

Mahomed, F., Swanepoel, D., Eikelboom, R. H., & Soer, M. (2013). Validity of automated threshold audiometry: A systematic review and meta-analysis. *Ear and Hearing*, *34*(6), 745-752. doi:10.1097/aud.0b013e3182944bdf

Marco-Algarra, J., Basterra, J., & Marco, J. (1985). cis-Diaminedichloro platinum ototoxicity: An experimental study. *Acta oto-laryngologica*, *99*(3-4), 343-347. doi:10.3109/00016488509108921

Margolis, R. H., & Morgan, D. E. (2008). Automated pure-tone audiometry: An analysis of capacity, need and benefit. *American Journal of Audiology*, *18*, 78-89. doi:10.1044/1059-0889(2008/07-0047

Meinke, D. K., Norris, J. A., Flynn, B. P., & Clavier, O. H. (2017). Going wireless and booth-less for hearing testing in industry. *International Journal of Audiology*, *56*(sup1), 41-51.

Meyskens, F. L., & Gerner, E. W. (1999). Development of difluoromethylornithine (DFMO) as a chemoprevention agent. *Clinical Cancer Research*, *5*(5), 945-951. doi:10.1002/jcb.240590816

Meyskens, F. L., Kingsley, E. M., Glattke, T., Loescher, L., & Booth, A. (1986). A phase II study of α-difluoromethylornithine (DFMO) for the treatment of metastatic melanoma. *Investigational New Drugs*, *4*(3), 257-262.

Moss, P. E., Hickman, S., & Harrison, B. R. (1999). Ototoxicity associated with vinblastine. *Annals of Pharmacotherapy, 33*(4), 423-425. doi:10.1345/aph.18288

Multimedia. (n.d.). *OB-300 octave band analyzer*. Retrieved from http://multimedia.3m.com/mws/media/760877O/1700-2700-sound-level-meter-user-manual.pdf

National Comprehensive Cancer Network. (2003). *Clinical practice guidelines in oncology*. Retrieved from https://www.nccn.org/professionals/physician_gls/default.aspx

Neuwelt, E. A., Brummett, R. E., Doolittle, D. N., Muldoon, L. L., Kroll, R. A., Pagel. M. A, …Bubalo, J. S. (1998). First evidence of otoprotection against carboplatin-induced hearing loss with a two- compartment system in patients with central nervous system malignancy using sodium thiosulfate. *The Journal of Pharmacology, 286*(1), 77-84. Retrieved from http://jpet.aspetjournals.org/content/286/1/77.short

Osterhammel, D. (1978). High-frequency thresholds using a quasi-free-field technique. *Scandinavian Audiology*, *7*(1), 27-30. doi:10.3109/01050397809043128

Pine Environmental. (2019a*.). Quest Type 2 SLM, Model 2700*. Retrieved from http://www.pine-environmental.com/products/detail/10775/quest-model-2700-impulse-sound-level-meter/

Pine Environmental. (2019b). *Quest Type 2 SLM, Model 2900*. Retrieved from http://www.pine-environmental.com/products/detail/10219/quest-2900-type-2-w-calibrator/

Pouyatos, B., & Pettis, J. (2007). Industrial chemicals and solvents affecting the auditory system. In K. C. M. Campbell (Ed.), *Pharmacology and ototoxicity for audiologists* (pp. 197-215). Clifton Park, NY: Delmar Cengage Learning.

Punnett, A., Bliss, B., Dupuis, L. L., Abdolell, M., Doyle, J., & Sung, L. (2004). Ototoxicity following pediatric hematopoietic stem cell transplantation: A prospective cohort study. *Pediatric Blood & Cancer, 42*(7), 598-603. doi:10.1002/pbv.20036

Ramsdale, C., & Charman, W. N. (1989). A longitudinal study of the changes in the static accommodation response. *Ophthalmic and Physiological Optics, 9*(3), 255-263.

Rieke, C. C., Clavier, O. H., Allen, L. V., Anderson, A. P., Brooks, C. A., Fellows, A. M., ...Buckey, J. C. (2017). Fixed-level frequency threshold testing for ototoxicity monitoring. *Ear and Hearing*, *38*(6), e369-e375.

Rybak, L. P. (1993). Ototoxicity of loop diuretics. *Otolaryngologic Clinics of North America*, *26*(5), 829-844. doi:10. 1016/s0030-6665(06)00098-3

Rybak, L. P. (2007). Renal function and ototoxicity of loop diuretics. In K. C. M. Campbell (Ed.), *Pharmacology and ototoxicity for audiologists* (pp. 177-186). Clifton Park, NY: Delmar Cengage Learning.

Rybak, L. P., Huang, X., & Campbell, K. C. M. (2007). Cancer and ototoxicity of chemotherapeutics. In K. C. M. Campbell (Ed.), *Pharmacology and ototoxicity for audiologists* (pp. 139-162). Clifton Park, NY: Delmar Cengage Learning.

Saito, T., Saito, H., Saito, K., Wakui, S., Manabe, Y., & Tsuda, G. (1989). Ototoxicity of carboplatin in guinea pigs. *Auris Nasus Larynx, 16*(1), 13-21. doi:10.1016/s0385-8146(89)80003-3

Schacht, J. (2007). Aminoglycoside antibiotics. In K. C. M. Campbell (Ed.), *Pharmacology and ototoxicity for audiologists* (pp. 163-176). Clifton Park, NY: Delmar Cengage Learning.

Schatz, A., & Waksman, S. A. (1944). Effect of streptomycin and other antibiotic substances upon mycobacterium tuberculosis and related organisms. *Experimental Biology and Medicine, 57*(2), 244-248. doi:10. 3181/00379727-57-14769

Seniors Research Group. 1999. *The consequences of untreated hearing loss in older persons*. Washington, DC: National Council on the Aging.

Serafy, A., & Hashash, M. (1982). The effect of vinblastine sulphate on the neurological elements of the rabbit cochlea. *The Journal of Laryngology & Otology*, *96*(11), 975-979. doi:10.1017/s0022215100093385

Shapiro, M., & Galloza, H. (2016). *Open source mobile software platform for distributed studies of hearing*. Presented at the American Auditory Society Conference, Scottsdale, AZ. Also available http://creare-com.github.io/tabstint/

Skeel, R. T. (1999). Biologic and pharmacologic basis of cancer chemotherapy. In *Handbook of cancer and chemotherapy* (5th ed., pp. 3-19). Philadelphia: Lippincott.

Strauss, M., Towfighi, J., Lord, S., Lipton, A., Harvey, H. A., & Brown, B. (1983). Cis-platinum ototoxicity: Clinical experience and temporal bone histopathology. *The Laryngoscope, 93*(12), 1554-1559. doi:10.1288/00005537-198312000-00007

Sturgeon, J. (2004). Clinical uses of cisplatin. In P. S. Roland & J. A. Rutka (Eds.), *Ototoxicity* (pp. 50-59). New York: BC Decker Inc.

Swanepoel, D. W., Mngemane, S., Molemong, S., Mkwanazi, H., & Tutshini, S. (2010). Hearing assessment-reliability, accuracy, and efficiency of automated audiometry. *Telemedicine and e-Health, 16*(5), 557-563. doi:10.1089/tmj.2009.0143

Varni, J. W. (2019). *Pediatric Quality of Life Inventory 4.0*. Retrieved from http://www.pedsql.org/about_pedsql.html

Ventry, I. M., & Weinstein, B. E. (1982). The hearing handicap inventory for the elderly: A new tool. *Ear and Hearing*, *3*(3), 128-134.

Vermorken, J. B., Kapteijn, T. S., Hart, A. A. M., & Pinedo, H. M. (1983). Ototoxicity of cis-diamminedichloroplatinum (II): Influence of dose, schedule and mode of administration. *European Journal of Cancer and Clinical Oncology, 19*(1), 53-58. doi:10.1016/0277-5379(83)90398-x

Vermorken, J. B., Mangioni, C., & Van Oosterom, A. T. (1983). Vincristine, bleomycin, mitomycin C and cisplatin (VBMP) in squamous cell carcinoma of the uterine cervix (SCCUC). *International Journal of Gynecological Cancer, 10*(5), 358-365.

Wake, M., Takeno, S., Ibrahim, D., Harrison, R., & Mount, R. (1993). Carboplatin ototoxicity: an animal model. *The Journal of Laryngology & Otology*, *107*(07), 585-589. doi:10.1017/s0022215100123771

Ware, J. E., Kosinski, M., Keller, S. D. (1994). *SF-36 Physical and Mental Health Summary Scales*. Boston: The Health Institute, New England Medical Center.

Wilcoxon, F. (1945). Individual comparisons by ranking methods. *Biometrics Bulletin*, *1*(6), 80-83.

Williams, W. (2010). *The calculation of maximum permissible ambient noise level for audiometric testing to a given threshold level with a specified uncertainty*. Retrieved from https://dspace.nal.gov.au/xmlui/handle/123456789/479

Windmill, I. M., & Freeman, B. A. (2013). Demand for audiology services: 30-yr projections and impact on academic programs. *Journal of American Academy of Audiology, 24*(5), 407-416. doi:10.3766/jaaa.24.5.7

APPENDIX A

INSTITUTIONAL REVIEW BOARD APPROVAL

UNIVERSITY OF
NORTHERN COLORADO

Institutional Review Board

DATE:	June 26, 2017
TO:	Ashley Stumpf, B.S
FROM:	University of Northern Colorado (UNCO) IRB
PROJECT TITLE:	[1070484-2] Pilot Study: Performance of wireless automated hearing tests system adapted for ototoxicity monitoring in an outpatient cancer treatment center
SUBMISSION TYPE:	Amendment/Modification
ACTION:	APPROVED
APPROVAL DATE:	June 26, 2017
EXPIRATION DATE:	June 26, 2018
REVIEW TYPE:	Expedited Review

Thank you for your submission of Amendment/Modification materials for this project. The University of Northern Colorado (UNCO) IRB has APPROVED your submission. All research must be conducted in accordance with this approved submission.

This submission has received Expedited Review based on applicable federal regulations.

Please remember that informed consent is a process beginning with a description of the project and insurance of participant understanding. Informed consent must continue throughout the project via a dialogue between the researcher and research participant. Federal regulations require that each participant receives a copy of the consent document.

Please note that any revision to previously approved materials must be approved by this committee prior to initiation. Please use the appropriate revision forms for this procedure.

All UNANTICIPATED PROBLEMS involving risks to subjects or others and SERIOUS and UNEXPECTED adverse events must be reported promptly to this office.

All NON-COMPLIANCE issues or COMPLAINTS regarding this project must be reported promptly to this office.

Based on the risks, this project requires continuing review by this committee on an annual basis. Please use the appropriate forms for this procedure. Your documentation for continuing review must be received with sufficient time for review and continued approval before the expiration date of June 26, 2018.

Please note that all research records must be retained for a minimum of three years after the completion of the project.

If you have any questions, please contact Sherry May at 970-351-1910 or Sherry.May@unco.edu. Please include your project title and reference number in all correspondence with this committee.

Hello Ashley,

I am the second and final reviewer of your IRB application. First, let me commend you on the thoroughness and clarity of your application. I am approving your application, however, please update the phone number and name of office provided in each of the Consents to 970-351-1910 and the Office of Research. Good luck with this important research.

Sincerely,

Nancy White, PhD, IRB Co-Chair

This letter has been electronically signed in accordance with all applicable regulations, and a copy is retained within University of Northern Colorado (UNCO) IRB's records.

APPENDIX B

WIRELESS HEADSET SYSTEM SURVEY FOR OPERATORS

CREARE WIRELESS HEADSET SYSTEM SURVEY FOR OPERATORS

College of Natural and Health Sciences

School of Human Sciences

Operator Subject #_____

Listener Subject #_____

Trial Number #_____

Headset Prototype_____

Wireless Headset Fit and Comfort SURVEYS:

Thank you for helping with our research project. Below are a few brief questions to help us learn more about the new equipment we are developing for hearing testing.

SECTION A: FOR LISTENERS

The survey consists of a series of questions asking you to either rate statements from strongly disagree to strongly agree or fill in the blank. Your answers should reflect your feelings and opinions. Therefore, there are no right or wrong answers, so please answer honestly. The survey should take approximately 5-10 minutes to complete. (Note: this survey will be sized and adapted for proper display on the Tablet device).

SECTION A: FOR MOBILE SCREENER OPERATOR		
1.	Is this the first time you have performed a hearing test?	YES NO
2.	If YES, have you previously received training on how to give a hearing test?	YES NO
3.	What is your professional background?	

Please circle the appropriate response (SD, D, N, A, SA) for each statement that best describes your feelings and/or opinions. Please answer all questions and do not leave any blank.

SD = Strongly Disagree D = Disagree SWD= Somewhat Disagree N = Neither Agree or Disagree SWA= Somewhat Agree A = Agree SA = Strongly Agree

1.	The wireless hearing test devices' instructions are clear and easy to follow.	SD	D	SWD	N	SWA	A	SA
2.	The wireless hearing test device is an accurate way to measure hearing.	SD	D	SWD	N	SWA	A	SA
3.	The wireless hearing test device is complicated to use.	SD	D	SWD	N	SWA	A	SA
4.	The wireless hearing test device allows you to identify which ear is being tested.	SD	D	SWD	N	SWA	A	SA
5.	The headset was easy to place on the listener.	SD	D	SWD	N	SWA	A	SA
6.	The wireless technology stayed connected during use.	SD	D	SWD	N	SWA	A	SA
7.	The headset stayed in the proper position during the hearing test.	SD	D	SWD	N	SWA	A	SA
8.	The wireless hearing test software (app) was intuitive.	SD	D	SWD	N	SWA	A	SA
9.	The hearing test results were not available to review.	SD	D	SWD	N	SWA	A	SA
10.	The wireless hearing test system allows me to monitor progress toward test completion.	SD	D	SWD	N	SWA	A	SA
11.	The wireless headset fits the listener.	SD	D	SWD	N	SWA	A	SA
12.	The headset visually appeared to seal the ear adequately	SD	D	SWD	N	SWA	A	SA

13.	It takes practice to be able to use the wireless hearing test system.	SD	D	SWD	N	SWA	A	SA
14.	General background noise in the room did not interfere with the hearing test.	SD	D	SWD	N	SWA	A	SA
15.	I would use this wireless hearing test system if available to me.	SD	D	SWD	N	SWA	A	SA
16.	Are there additional comments or feedback you can offer related to the use and functionality of this wireless test device?							

APPENDIX C

WIRELESS HEADSET SYSTEM SURVEY FOR LISTENERS

CREARE WIRELESS HEADSET SYSTEM SURVEY FOR LISTENERS

College of Natural and Health Sciences

School of Human Sciences

Operator Subject #_____

Listener Subject #_____

Trial Number #_____

Headset Prototype_____

Wireless Headset Fit and Comfort SURVEYS:

Thank you for helping with our research project. Below are a few brief questions to help us learn more about the new equipment we are developing for hearing testing.

SECTION A: FOR LISTENERS

The survey consists of a series of questions asking you to either rate statements from strongly disagree to strongly agree or fill in the blank. Your answers should reflect your feelings and opinions. Therefore, there are no right or wrong answers, so please answer honestly. The survey should take approximately 5-10 minutes to complete. (Note: this survey will be sized and adapted for proper display on the Tablet device).

Section A: FOR MOBILE SCREENER LISTENER

Please circle the appropriate response (SD, D, N, A, SA) for each statement that best describes your feelings and/or opinions. Please answer all questions and do not leave any blank.

SD = Strongly Disagree D = Disagree SWD= Somewhat Disagree N = Neither Agree or Disagree SWA= Somewhat Agree A = Agree SA = Strongly Agree

1.	It was easy for the person to put the headset on me.	SD	D	SWD	N	SWA	A	SA
2.	The headset fit well and sealed my ears from outside noise.	SD	D	SWD	N	SWA	A	SA
3.	There was no discomfort during the placement of the headset on my ears.	SD	D	SWD	N	SWA	A	SA
4.	The headset felt stable on my head and did not change position (move) while taking the hearing test.	SD	D	SWD	N	SWA	A	SA
5.	The headset was not a problem to wear.	SD	D	SWD	N	SWA	A	SA
6.	It was easy to press the button on the computer tablet when I heard a sound.	SD	D	SWD	N	SWA	A	SA
7.	The tablet computer made the hearing test better.	SD	D	SWD	N	SWA	A	SA
8.	Providing a hearing test while receiving chemotherapy was beneficial to me.	SD	D	SWD	N	SWA	A	SA
9.	Traveling to get multiple hearing tests during chemotherapy would be problematic for me.	SD	D	SWD	N	SWA	A	SA
10.	Scheduling to get multiple hearing tests during chemotherapy would be problematic for me.	SD	D	SWD	N	SWA	A	SA
11.	I knew about risk of hearing loss from chemo treatment.	SD	D	SWD	N	SWA	A	SA
12.	It is important to me to have my hearing monitored during chemotherapy treatment.	SD	D	SWD	N	SWA	A	SA

13.	Are there additional comments or feedback you can offer related to the use and functionality of this wireless test device?

APPENDIX D

RECIPROCAL AGREEMENT

It was a pleasure meeting you!

Garza, Mandy <Mandy.Garza@bannerhealth.com>

Mon 10/10/2016 1:46 PM

To:Meinke, Deanna <Deanna.Meinke@unco.edu>; Stumpf, Ashley <atki6998@bears.unco.edu>;

2 attachments (116 KB)

Protocol Template for Banner IRB iRIS 10Oct2016.docx; Adult Consent and HIPAA Auth TEMPLATE iRIS 10Oct2016.docx;

Dear Dr. Meinke and Ashley,

First, I would like to thank you for taking the time to meet with the research team at NCMC last Tuesday. We truly appreciate the collaboration, and we are looking forward to working together on this project.

Please see the attached template documents including a Protocol Template and Consent and HIPAA Template.

Please let me know if I can be of any additional assistance. Again, we look forward to working together!
M.

Mandy Garza, RN, BSN, OCN, CCRC
RN Clinical Research Specialist Supervisor
Oncology Services - Northern Colorado

North Colorado Medical Center
Oncology Research – Cancer Institute
1801 16th Street
Greeley, CO 80631

Office: 970-810-6380
Fax: 970-810-6135

Banner Health

We exist to make a difference in people's lives through excellent patient care