PREVALENCE OF COCHLEAR DEAD REGIONS IN DIFFERENT CLINICAL POPULATIONS

by

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Abstract

Prevalence of cochlear dead regions was investigated in sixty-two adults with sensorineural hearing loss. The aims of this study were to 1) assess the prevalence of cochlear dead regions in the population of people with sensorineural hearing loss; 2) assess the prevalence of cochlear dead regions in three sub-populations of people with sensorineural hearing loss: Group 1 was subjects with noise-induced hearing loss (n=15), Group 2 was subjects with otologic diseases associated with sensorineural hearing loss (n=8), and Group 3 was subjects who self-refer to a hearing aid clinic (n=39); 3) relate the presence or absence of cochlear dead regions to absolute threshold, slope of the audiogram, and pure tone average. The threshold-equalizing noise (TEN) test (HL) was used to assess the presence or absence of dead regions. The results suggest: 1) Prevalence of cochlear dead regions was 14.5% among subjects. Prevalence by ear was 10.7%. 2) Classifying by subject, the prevalence in the noise-induced hearing loss group was 13%. Prevalence in the otologic-disease group was 0%. Prevalence in the self-refer group was 18%. These results need to be interpreted with caution due to the small sample size and differences in group sizes. 3) Absolute thresholds at 4 kHz tended to be higher in the subjects with dead regions. Presence or absence of dead regions was not related to slope of the audiogram or pure tone average.

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List of Abbreviations

IHC – inner hair cells

OHC – outer hair cells

PTCs - psychophysical tuning curves

DR – dead region

AN – auditory neuropathy

APD – auditory processing disorder

ABR – auditory brainstem response

OAE – otoacoustic emissions

WIDHH – Western Institute for the Deaf and Hard of Hearing

WSBC – WorkSafeBC

UBC – University of British Columbia

VGH – Vancouver General Hospital

IHS – Island Hearing

SHC – Sound Hearing Clinic

GSI 61 - Grason Stadler Instrument 61

TEN – threshold-equalizing noise

ERB – equivalent rectangular bandwidth

DSL – desired sensation level

AI – articulation index

RGDT – Random Gap Detection Test

MEMR – Middle ear muscle reflex

PTA – pure tone average

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Dedication

This body of work is dedicated to my father, who was the first academic in my life

Chapter 1 – Introduction and Literature Review

1.1 General Introduction

The cochlea is the organ of hearing located within the inner ear. It is responsible for transduction of acoustic energy into an electrical potential that is sent via afferent neurons to the auditory centres of the brain. It also serves as a fine-tuner and amplifier within the hearing system. A cochlear dead region is a special type of sensorineural hearing impairment involving loss or malfunction of the inner hair cells within the Organ of Corti in the cochlea. Until fairly recently, it was difficult to clinically pinpoint the cochlear dead region as the site of lesion in the case of sensorineural hearing loss because clinical tests for cochlear dead regions were not available. The main source of information about a patient's hearing loss has historically been the audiogram, which is a record of minimum response levels to pure tone stimuli. Clinical decisions such as choice of amplification, candidacy for cochlear implants, and candidacy for financial compensation have traditionally been based on pure tone thresholds. However, recent research has suggested that information gained from the audiogram alone is not always sufficient. Variability in treatment outcomes for patients with similar audiograms suggests that more information is necessary over and above the audiogram in order to determine the exact nature of the pathology and to pinpoint the site of lesion. This additional information could potentially help to optimize treatment and management of hearing loss. Development of a clinically feasible test for cochlear dead regions supports that goal.

Recently, a test has been devised for clinical use that is designed to detect and delimit the boundaries of a cochlear dead region, or a region of the cochlea within which the inner hair cells (IHC), which are the transducers of the cochlea, are malfunctioning. This test is known as the threshold-equalizing noise (TEN) test. Its proponents suggest that it is a quick, simple, and

clinically feasible test. Furthermore, this test will identify and delimit the boundaries of cochlear dead regions which in turn could improve the intervention process. However, before the test can be used efficiently in clinical settings, several questions need to be addressed; specifically, to whom should the test be administered? What is the overall prevalence of cochlear dead regions? Are certain populations more at risk for dead regions than others? Currently no data exist that help a clinician decide which patients are most at risk for cochlear dead regions. It is not known whether or not to expect different prevalence in different groups. Targeting different subpopulations of people with sensorineural hearing loss may be informative if prevalence proves to be significantly different in the different groups.

This study attempts to address those questions by assessing the prevalence of cochlear dead regions in a random sample of adults with sensorineural hearing loss, replicating other studies targeting the same population (e.g. Vinay & Moore, 2007a). Furthermore, in hopes of discovering which populations are most at risk for cochlear dead regions, this study targets different subgroups of the population of people with sensorineural hearing loss (SNHL), including those with noise-induced hearing loss, those with otologic diseases associated with SNHL, and those who self-refer (with or without recommendations from doctors) to a clinic to obtain a hearing aid (HA) or assistive listening device. Establishing prevalence within the overall population of those with SNHL and within the different sub-groups should help clinicians decide in what cases a dead region is more likely to occur and thus make most efficient use of clinic time and resources. In sum, the goals of the study are as follows: 1) Evaluate prevalence of cochlear dead regions within the population of people with sensorineural hearing loss; 2) Evaluate prevalence in three different clinical sub-populations: subjects with noise-induced hearing loss, subjects with otologic diseases associated with SNHL, and subjects who self-refer

to a hearing clinic. 3) Determine if presence or absence of dead regions is related to absolute thresholds at 4 kHz, to the slope of the audiogram, and/or to the pure tone average (PTA).

The following sections provide an overview of cochlear dead regions and describe why their correct diagnosis is important.

1.2 Cochlear Physiology

In order to understand dead regions, it is necessary to describe the physiology of a healthy cochlea. During the hearing process, an incoming sound wave travels through the outer and middle ears and impinges upon the oval window of the cochlea, which in turn disturbs the fluids within the cochlea and sets the basilar membrane in motion. The basilar membrane is the part of the Organ of Corti that houses the mechanism responsible for transducing the mechanical motion of the sound wave into an electrical impulse. Displacement of the basilar membrane causes the hair cells to trigger a neural impulse, or an action potential. The action potential that is generated by the basilar membrane motion is sent via the auditory nerve (Cranial nerve VIII) to the auditory centres of the brain. Once the neural impulse reaches the brain, it can be perceived as a sound.

The basilar membrane runs along the length of the cochlea and is tonotopically organized; that is, hair cells near the base of the cochlea respond to high frequencies and progress in descending order to the apex of the cochlea, where the low frequencies are represented.

On a more microscopic level, within the Organ of Corti in the cochlea there are two types of hair cells with two very different structures and functions: outer hair cells (OHCs) and inner hair cells (IHCs). They are called hair cells because both types have hair like structures known as stereocilia on top that function as virtual trap doors to the cell, regulating the polarity of the

contents of the cell. OHCs use this depolarization to trigger electromotility. They contain a protein in the outer sheath of the cell called prestin that causes OHCs to be capable of movement. Their function within the cochlea is to amplify and fine-tune the motion of the basilar membrane as the travelling sound wave is transmitted from the base to the apex of the cochlea. The electromotility of the OHCs causes them to elongate in sympathy with the incoming sound wave, thereby amplifying the response, and sharpening the peak of the point of maximum displacement, thereby fine-tuning the response (Santos-Sacchi, 2003).

OHCs are an important part of the cochlear amplifier (Dallos, 2008). The purpose of this cochlear amplifier is to increase sensitivity to weak sounds (i.e. improve thresholds), improve the frequency selectivity of the basilar membrane, and introduce a compressive nonlinearity into the system, thereby allowing for the large dynamic range in living ears (Robles & Ruggero, 2001; Ruggero & Rich, 1991). Outer hair cells are richly innervated by efferent nerves, or nerves that convey information distally from the central nervous system to the peripheral sense organs.

In the presence of OHC damage, the cochlear amplifier, non-linear compression, and frequency selectivity are compromised. It then follows that providing non-linear amplification and improving audibility might be helpful. Current hearing aid technology in part attempts to restore nonlinearity and improve audibility. From this information one might deduce that patients with outer hair cell pathology tend to have success with hearing aids, and this turns out to be the case. When the cochlea's amplification and frequency selectivity are impaired, as occurs with OHC damage, hearing aids usually provide benefit to the hearing impaired listener (Mackersie, Crocker & Davis, 2004).

Inner hair cells (IHCs), on the other hand, have a very different structure and function. They are located adjacent to the OHCs and are of different size, shape, structure and function.

They exhibit no electromotility and they do not amplify and fine-tune a travelling wave. Instead, they serve as transducers of the cochlea, in that they convert sound waves into electrical impulses. Rather than being predominantly innervated by the efferent (brain to sensory organ) nervous system as the OHCs are, they are primarily innervated by the afferent (sensory organ to brain) nervous system and their primary purpose is to create a neural impulse out of the travelling wave on the basilar membrane and initiate an action potential in the auditory nerve (Pujol, 2004).

More specifically, disturbance of the fluids in the cochlea results in a motion of the basilar membrane in the form of a traveling wave, which starts at the base of the cochlea and moves toward the apex. The displacement of the basilar membrane creates a shearing action between the basilar membrane and tectorial membrane on top of the IHCs. The shearing action results in the turbulence of the endolymph between the tectorial membrane and basilar membrane which in turn causes the stereocilia on top of the IHCs to tilt. This tilting opens a trap door on the top of the cilia which provides a passageway between outside and inside of the cell. The polarity of the fluids inside and outside of the cell is different: the endolymph on the outside of the cell is positively charged; the fluid inside the cell is negatively charged. Opening the trap door causes positively charged ions to rush inside the cell, which triggers the release of a neurotransmitter, glutamate, which in turn depolarizes the afferent fibers at the cell ending and creates an action potential within the auditory nerve. The place along the basilar membrane at which this chemical reaction occurs is thought to convey some of the frequency information of the signal. There is also frequency information encoded in the timing of the neural response, which at some frequencies is phase-locked to the stimulus (Harrison & Evans, 1979). It can therefore be said that IHCs have a characteristic frequency at which they function most

efficiently and pathology of the inner hair cells will impair perception of that frequency (Moore, 2001).

A cochlear "dead region" is a patch of malfunctioning or nonfunctioning inner hair cells, and/or malfunction of the afferent neurons associated with the inner hair cells. It should be noted that IHC pathology usually occurs with concurrent OHC pathology (Moore, 2001). Teasing apart the site of lesion, as mentioned previously, has been problematic due to inadequate testing procedures and insufficient knowledge of symptomatic differences between the two pathologies. The following section provides an historical perspective that describes research leading up to current knowledge.

1.3 Historical Perspective

1.3.1 Early Research

The vast majority of sensorineural hearing loss is associated with OHC damage (Moore 2001, 2004), so IHC pathology has received less attention in the literature, comparatively speaking. However, it has been known for many years that cochlear hearing loss can be associated with IHC pathology. Troland (1929) described "lacunae" in hearing that caused patients to exhibit similar symptoms to patients with dead regions as they are described today. Early anatomical studies of temporal bones of people with hearing loss have demonstrated hearing loss is associated with damage to the IHCs and/or neurons. Loss or compromise of the stria vascularis was also commonly found, which presumably impairs the function of IHCs (Shuknecht, 1955; 1964; Schuknecht & Wollner, 1953). Schuknecht and Gacek (1993) showed that IHC loss and neuronal loss could vary independently of each other, in that IHCs can be dead without substantial loss of neurons and vice versa. However, functionally, IHC loss was suggested to be equivalent to neural loss because the IHC dysfunction blocked the impulse from

getting further up the auditory pathway. This may be helpful in explaining variability in treatment outcomes for patients without differential diagnosis of IHC versus neuronal pathology. It was also found that a relatively small number of surviving IHCs can still give rise to detection of pure tones. This has implications for a phenomenon known as off-frequency listening, discussed later in this paper.

1.3.2 Early Testing for Dead Regions

Cochlear dead regions have been detected using psychophysical tuning curves (PTCs). PTCs use a signal of fixed intensity and frequency at 10dB above threshold, and a masker (usually narrow band noise) of varying intensities and frequencies in order to see which masker frequency best masks the signal. In a healthy cochlea, the most effective masker is one close to the signal frequency (e.g. a pure tone signal at 4000 Hz is best masked by narrow band noise centered around 4000 Hz). In a subject with a cochlear dead region, who is using off-frequency listening (described in more detail later) to detect a tone, the masker is most effective at frequencies other than the signal frequency (i.e. a pure tone signal at 4000 Hz might be masked most effectively by narrow band noise centered around 1000 Hz). In this case, the tip of the PTC is said to "shift", in that the most effective masker is no longer at the characteristic frequency. For the purposes of the above example, a dead region would be considered present at the IHCs along the basilar membrane with a characteristic frequency of 4000 Hz.

While PTCs are a valid diagnostic tool for cochlear dead regions, they are considered too time-consuming and impractical for clinical use, and are intended more for use in clinical research. Furthermore, while PTCs are considered the "gold standard" for diagnosis of cochlear dead regions (Summers et al., 2003), the technique is not above reproach. The interaction of the stimulus and masker can cause beats and combination tones that may be more detectable than the

original signal itself. In other words, the interaction of the two stimuli may skew the results of the measure. For these reasons, the TEN test was devised (Moore, Huss, Vickers, Glasberg, & Alcantara, 2000), intended for use in the clinical setting. Before the TEN test is discussed, it is necessary to explain off-frequency listening, since this is a defining characteristic in cochlear dead regions and is a crucial factor in the efficacy of the TEN test.

1.4 Off-frequency or Off-place Listening

Off-frequency or off-place listening is a defining characteristic of cochlear dead regions. The damage to the IHCs of the cochlea causes abnormal pitch representation at the level of the basilar membrane. Off-frequency listening is defined as using IHCs and/or afferent neurons other than those at the characteristic frequency of a tone to detect the sound. The tone is often detected with reduced amplitude and clarity (Moore, 2004). To illustrate, a tone at 2000 Hz would cause maximal displacement of the basilar membrane (and subsequent IHC stimulation) at the place at which the IHCs and neurons respond optimally to 2000 Hz. However, if that region of the cochlea is "dead," the basilar membrane may be sufficiently displaced at other regions (the region corresponding to 1000 or 4000 Hz, for example) to generate an action potential in the auditory nerve, thus causing a sensation of sound known as off-frequency listening. It is perhaps better referred to as off-place listening, because the ear is not responding to a different frequency, but is responding to the same frequency with sensory cells (inner hair cells) and corresponding nerve fibers that are in a remote location from the peak of excitation produced by that frequency. Recall also that IHC damage usually co-occurs with OHC damage, and OHC damage affects the frequency selectivity and fine-tuning of the basilar membrane (Pujol, 2004). Since the amplitude of the basilar membrane vibration is significantly diminished at the place of off-frequency listening, due to the shape of the traveling wave excitation pattern, tones that fall

within a dead region are far more susceptible to masking noise than those that do not. It is this characteristic that makes testing for dead regions possible using masking paradigms (the TEN test and PTCs).

1.5 The TEN Test

It is not possible to predict from an audiogram alone whether or not a patient has cochlear dead regions (Moore 2001, Moore 2004, Preminger, Carpenter, & Ziegler, 2005, Aazh & Moore, 2007; Halpin, Thornton, & Hasso, 1994; Moore, Huss, Vickers, Glasberg, & Alcantara, 2000). Theoretically, if during testing the presented stimulus falls within a dead region, the hearing loss at that frequency is infinite and the recorded threshold should be NR (no response), since no afferent neural transduction is taking place from the intended site. However, due to off-frequency or off-place listening, a patient with dead regions can respond at levels as low as 50 dB HL for low frequencies, and 70 dB HL for high frequencies (Moore, 2001). This causes an underestimation of hearing loss in patients with dead regions. Given that most decisions about patient care are made based on the audiogram, but that audiograms can be misleading in the case of cochlear dead regions, it seems that the audiogram alone provides insufficient information and the development of a clinically feasible test for dead regions was necessary.

To address the lack of a clinically feasible test for dead regions, Moore, Huss, Vickers, Glasberg and Alcantara (2000) developed a test using threshold-equalizing noise (TEN). Use of the test determines whether there is evidence of off-frequency listening by using masking noise that is spectrally shaped in order to shift all audiometric thresholds to a specified dB level. If the threshold shifts by more than the expected level, it is taken as evidence that off-frequency listening is being used.

The noise level is specified in terms of the average Equivalent Rectangular Bandwidth (ERB) of the auditory filter at a given frequency. To arrive at the ERB, the developers of the TEN test took measurements of the bandwidth of the auditory filter of young, normal-hearing listeners, and converted the area within the critical bandwidth to a rectangle. Theoretically, this results in threshold-equalizing noise, in that the noise can now be expected to produce a threshold of a given level. The noise prevents the upward and downward spread of excitation on the basilar membrane from producing off-place listening (Moore, 2004; Scollie & Glista, 2007). If the threshold-equalizing noise produces more masking than expected, it is taken as evidence that a dead region exists at the test frequency.

A hearing impaired listener with well-functioning IHCs and/or afferent neurons with thresholds at a lower (better) dB level than the TEN will see thresholds increase (worsen) close to the level of the noise in the TEN test. Thresholds at a higher dB level than the TEN should stay the same, because the introduction of masking noise at a significantly lower level should not shift the threshold by more than 7dB (Moore, 2004) for patients within this population. In the case of a dead region, a signal falling within the dead region is detected by IHCs and afferent neurons with characteristic frequencies different from that of the signal frequency; in other words, off-frequency listening occurs. In this case, because the amplitude of the basilar membrane vibration at the remote place is less than at the peak of the traveling wave, the signal is far more susceptible to masking, and the thresholds will shift by 10dB or more. The criteria for a positive dead region diagnosis using the TEN test are a threshold shift that is both 10 dB or more above the unmasked threshold at the test frequency, and 10 dB or more above the level of the threshold-equalizing noise.

An earlier version of the TEN test was calibrated in dB SPL and tested frequencies between 250 and 10,000 Hz (Moore, Huss, Vickers, Glasberg, & Alcantara 2000). The newer, dB HL version of the test (Moore, Glasberg, & Stone, 2004) used in this study, tests only the typical clinical frequencies between 500 and 4000 Hz and is simpler to use because SPL to HL conversion factors are not needed. The HL version also allows for higher levels of masking noise to be used, which reduces the number of inconclusive results obtained when masking is insufficient to demonstrate evidence of off-frequency listening. Both the SPL and HL versions were intended for use on adults, since the norms were established using adult subjects.

In terms of validity, the TEN test has been compared to the current gold standard, which is the aforementioned psychophysical tuning curve. When procedural complications such as detection of beats and combination tones are controlled for, there is good correspondence between PTCs and the TEN test (Huss & Moore, 2003; Moore, 2004).

1.5.1 Advantages and Disadvantages of the TEN test

The main advantages of the TEN test are that it uses existing clinical equipment and techniques, and is quick and relatively simple to administer. Furthermore, because the TEN test uses threshold-equalizing noise, it avoids the confounds to which PTCs are susceptible; namely, beats and combination tones that may interfere with the test results.

Potential disadvantages of the TEN test, as reported by Moore (2004), are as follows. First, the criteria for a dead region (i.e., a 10 dB shift in threshold and masking level) were developed based on a relatively small sample of adults with moderate to severe sensorineural hearing loss. Therefore, interpretation of the test results for different populations (i.e. profoundly deaf or children) should be treated with caution (Moore, Killen, & Munro 2003). For the

purposes of this study, children were excluded, and profound hearing losses were not encountered.

Second, the test does not take individual variation into account. Individual variation in response efficiency (i.e. how loud the signal has to be before the subject will respond) can cause a slight decrease in sensitivity and specificity of the test. It has been shown that response efficiency decreases with age (Patterson, Nimmo-Smith, Weber, & Milroy, 1982). Efficiency of response is difficult to control and was not specifically addressed during the present study, other than by giving explicit instructions to the subjects to respond even when the tone was very quiet.

Third, there can be alternative explanations for having raised thresholds in noise, which can include auditory neuropathy or auditory processing issues. A comorbid auditory processing disorder (APD) or neuropathy would confound the results of the TEN test. The present study attempted to address this concern by administering screening tests for APD, with the intention of excluding any subjects who tested positive for APD. However, it appears that teasing apart IHC pathology from auditory processing issues is difficult, and perhaps the difficulty in auditory processing can arise from improper encoding of the signal at the level of the cochlea. This validates the common complaint of patients with dead regions of being able to detect a sound, but being unable to make sense of it.

Moore (2004) has recommended a more stringent criterion in such cases as described above, such as requiring a 15-dB shift in threshold when a dead region is unlikely to be present (i.e. in mild to moderate hearing loss). This seems to be working backwards from diagnosis to testing, which is not ideal for clinical practice. Clearly, clinical judgment is still a valuable tool in these nascent stages of dead regions research.

Fourth, for maximum precision, the test requires a 2 dB final step size, which can add a small amount of time to a test that many patients find fatiguing. Clinical audiologists are accustomed to dealing with a 5 dB step size, which reduces the accuracy of diagnosis. Changing step size, however, is easily done on most clinical audiometers, and should be encouraged while performing the TEN test. A 2 dB final step size was used during this study.

Fifth, the TEN test gives only a rough approximation (half-octave increments) of a cochlear dead region. Higher precision would mean longer testing. A false negative is possible if the dead region is very small. For the purposes of this study, it was assumed that half-octave increments were acceptable, since these are the frequencies commonly tested during conventional audiometry. As well, it is not yet established whether dead regions smaller than one-half octave have significant deleterious effects on speech perception.

Sixth, because the TEN test detects when off-frequency listening is taking place, it relies upon good hearing in the responding hair cells. If, for some reason (i.e. structural abnormalities) the responding hair cells are not responding optimally, the accuracy of the test will be negatively impacted.

Last, for severe or profound hearing losses, which perhaps are the most likely to have dead regions, it is often not possible to make the TEN intense enough to produce 10 dB of masking. In such cases, since the test is inconclusive, diagnosis of dead regions falls to the judgment of the clinician, which negates the need for a test.

While these shortcomings of the TEN test are readily acknowledged by its developer, research has shown that the test remains a valid and reliable tool for diagnosis of cochlear dead regions. Moore et al. (2000) validated the TEN test in 19 ears of 14 subjects against a

psychophysical tuning curve as the gold standard. Correspondence between the results obtained using the TEN and the PTCs was "very good."

Summers et al. (2003) attempted to refute this evidence by replicating the aforementioned study. Summers found only 56% correspondence between TEN test and PTC results when using the same diagnostic criteria as the previous study (10 dB threshold shift). When a more stringent criterion of 14 dB was implemented, correspondence improved to 89%.

Moore (2004) reviewed the Summers et al. (2003) data and suggested that PTCs as they were performed in the study were not the appropriate method for diagnosis of cochlear dead regions because the interference of beats and combination tones might confound the validity of the test. When beats and combination tones are controlled for, validity is similar to that of the TEN test. Moore concluded, however, that a 15 dB threshold shift criterion was more appropriate in certain cases.

Based on the results of Moore et al. (2000), Summers et al. (2003), and Moore (2004), it can be presumed the TEN test is valid, at least when using a 15 dB threshold shift criterion. This study used a 10 dB threshold shift criterion, as recommended by the developers of the test. Also, using a 10-dB threshold shift criterion was consistent with Vinay and Moore (2001), which this study partially replicates.

Other literature has questioned the necessity of the TEN test. Rankovic (2002) presented evidence that the TEN test provided no additional information regarding hearing aid fitting beyond what was readily obtainable using an existing audiological test and the articulation index (AI). The author examined the data from Vickers, Moore and Baer (2001) using the AI to predict consonant recognition scores. It was suggested that the AI was generally accurate in predicting consonant recognition scores, irrespective of the presence or absence of dead regions.

It was questioned whether an additional clinical test for dead regions was necessary, if the differences in performance could be explained by the differences in thresholds. Moore (2002) examined the same data in greater detail, and found that the AI overestimated the predicted speech perception scores in subjects with dead regions. Because the TEN test measured more incremental improvements in speech perception performance, it was argued that the TEN test did provide valuable information over and above the audiogram.

1.5.2 Details of the TEN Test Procedure

A thorough, step-by-step description of the testing protocol can be found in Appendix 1. Briefly, a TEN test CD is routed through a two-channel audiometer to measure unmasked pure tone thresholds at half-octave increments from 500 – 4000 Hz (2 dB final step size). Once unmasked thresholds are established, continuous threshold-equalizing noise (TEN) is presented ipsilaterally to the test ear (tone and noise in the same ear). Thresholds are then re-measured in the presence of TEN. Generally, a TEN level of 70 dB HL is sufficient to demonstrate evidence of off-frequency listening, though a higher level can be used in cases of severe to profound hearing loss and a lower level in cases of mild hearing losses or loudness discomfort (Vinay & Moore, 2007a). If the absolute threshold shifts by more than 10 dB, and the threshold is 10 dB above the noise level, that is considered a positive diagnosis of a dead region at the test frequency. This process can then be repeated on the opposite ear, if indicated.

1.5.3 Potential Confounding Factors

Studies have shown that the TEN test can lead to false positives in the case of auditory neuropathy or other retrocochlear disorders. Vinay and Moore (2007b) tested eight subjects diagnosed with auditory neuropathy with the TEN (HL) test and with psychophysical tuning curves. The majority of subjects met the criteria for dead regions at one or more frequencies

using the TEN test, but the psychophysical tuning curves did not show shifted tips, suggesting no dead region was actually present. The false positive results on the TEN test suggest there may be other explanations for having raised thresholds in noise. It was suggested that the elevated thresholds in noise were caused by poor neural synchrony and processing efficiency.

To examine this issue further, consider the physiology of the auditory system. Inner hair cells (IHCs) convert a physical sound wave into an electrical impulse. They synapse directly onto the auditory nerve (cranial nerve VIII). It is known from auditory temporal processing studies (e.g. Rance, Cone-Wesson, Wunderlich, & Dowell, 2002) that neural synchrony is important for sound perception. It is also known that accurate sound perception depends on neural firing being phase-locked to the stimulus (Zeng, Kong, Michalewski, & Starr, 2005). If the IHCs were not functioning over a certain area of the cochlea (i.e. a cochlear dead region), it follows that there would be significant temporal "jitter" in neural spike initiation in the auditory nerve (Koppl, 1997). Also, patients with auditory neuropathy and cochlear dead regions tend to exhibit similar symptoms: speech audiometry results are worse than expected from the audiogram and very poor in noise. Other possible shared characteristics are poor temporal processing, poor pitch discrimination, and abnormal loudness growth (Zeng, Kong, Michalewski, & Starr, 2005). Because of this, it was necessary for the purposes of this study to rule out auditory neuropathy or other retrocochlear disorders as a potential confounding factor.

Other studies involving cochlear dead regions have dealt with this problem in different ways. Vinay and Moore (2007a), in a dead region prevalence study, screened all subjects using auditory brainstem response (ABR) and otoacoustic emissions (OAE) testing. Auditory neuropathy is characterized by presence of OAE and absence of ABR (Starr, Picton, Sininger, Hood, & Berlin, 1996). However, the subjects in the study all had sensorineural hearing loss,

which can result in absent OAE. Subjects who did not pass the screening tests for ABR were excluded from the study.

Preminger, Carpenter and Ziegler (2005) also investigated dead region prevalence and ruled out a retrocochlear auditory processing disorder (APD) by comparing the scores on the Synthetic Sentence Identification (SSI) test and the NU-6 word list. Subjects were considered APD positive if the difference between the NU-6 word score and the SSI score was greater than 20% (Stach, Spretnjak, & Jerger, 1990), or if the SSI score was "disproportionately poor," i.e., less than the empirically derived lower boundary of SSI scores as a function of pure-tone average (Yellin, Jerger, & Fifer, 1989). The authors did not explicitly provide the rationale for these APD diagnosis criteria, but it is assumed that people whose speech comprehension in noise was worse than expected from their pure tone thresholds were categorized positive for APD. Subjects who tested APD positive were excluded from the study.

For the purposes of the present study, it was decided that two screening tests for APD and ipsilateral middle-ear muscle reflex (MEMR) would determine the possible presence of auditory processing disorders. This will be discussed in greater detail later in this paper.

1.6 Diagnostic Specificity of DR/AN

One of the perplexities in modern audiological research is that the definition of a cochlear dead region and the definition of auditory neuropathy seem to overlap completely. Moore (2004) defined dead regions as cochlear regions where there are no functioning IHCs and/or neurons. Auditory neuropathy is commonly defined (Berlin, Morlet, & Hood, 2003) as pathology of the auditory nerve, inner hair cells, or the synapse between the inner hair cell and auditory nerve. These definitions are seemingly identical. Clearly, more diagnostic specificity is necessary in order to accurately describe the site of lesion in these types of hearing impairment.

Rapin and Gravel (2003) investigated the lack of diagnostic specificity in the term "auditory neuropathy" and recommended the term be reserved for cases in which the locus of pathology is limited to the spiral ganglion cells, their processes, or the auditory nerve, and that the term "neural hearing loss" be used for pathologies that affect all higher levels of the auditory pathway, from the brainstem to the auditory cortex. Adoption of this terminology would reduce the ambiguity between cochlear dead regions and auditory neuropathy as well, in that the term "auditory neuropathy" would no longer encompass pathology of the inner hair cells.

1.7 Implications of Cochlear Dead Regions for Patients

Correct diagnosis of a cochlear dead region is important, not only for the patient, but also for the various health care professionals and others who historically have made decisions regarding treatment, compensation, and candidacy based primarily on the audiogram. As noted above, pure tone audiometry can lead to an underestimation of the significance of hearing loss for a patient with cochlear dead regions. This has implications when making decisions in medico-legal cases involving hearing loss, where typically greater hearing losses result in higher awards. Also, decisions regarding candidacy for cochlear implants are based partly on thresholds from the audiogram, which are inaccurate in the case of inner hair cell pathology. The clinician may decide to delay implantation until thresholds worsen sufficiently to achieve candidacy, which may affect the viability of the neurons associated with the inner hair cells in the dead region. There has also been discussion (see Moore, 2004) regarding partial implantation of cochlear implants in patients with surviving inner hair cells near the apex of the cochlea in order to preserve low-frequency hearing, but this remains conjecture at this point. Clinicians and surgeons who work with cochlear implants have reported that preservation of low-frequency (apical) hearing sensitivity in cochlear implant patients varies independently of

insertion depth and is related to many more variables than survival of inner hair cells (personal communication, S. Pijl, January 2007).

From a treatment or management perspective, though controversy exists, preliminary research seems to suggest that patients with dead regions should be treated differently from their audiogram-matched, non-dead region counterparts. Of paramount importance is effective intervention and aural rehabilitation. Patients with dead regions have demonstrated poor understanding of speech in noise and report less satisfaction with hearing aids than patients with no dead regions (Preminger, Carpenter, & Ziegler 2005). Patients who test positive for dead regions need to be given realistic and limited expectations for what a hearing aid can help them to accomplish. Speech discrimination is not likely to improve with amplification to the dead regions, and tones that fall within a dead region are sometimes perceived abnormally, such as buzzing, clicking, or off-pitch. Making a patient or client aware of the likely difficulties allows them to make a better-informed decision regarding hearing aids and would perhaps result in increased likelihood of retaining and using the aid than if targeted counselling were not given. A correctly diagnosed dead region facilitates accurate and informed aural rehabilitation.

Correct diagnosis of dead regions also has important implications for hearing aid fittings, though the research is nascent and somewhat less conclusive. Most studies seem to indicate that amplification to prescription targets well within a dead region is at best of little or no benefit, or at worst, impairs speech discrimination performance. It has been suggested that amplification within a cochlear dead region may introduce distortion or result in the masking of adjacent frequencies through the spread of excitation along the basilar membrane, which would impair speech perception (Preminger, Carpenter, & Ziegler, 2005). Dead regions also tend to co-occur

with a reduced dynamic range, so setting conservative targets may preserve comfort for the hearing aid user.

Vestergaard (2003) found that subjects with extensive dead regions commencing from a relatively low frequency do not make effective use of high-frequency speech information, whereas subjects without dead regions do. Put another way, increasing audibility of high-frequency sounds did not lead to improved performance in subjects with dead regions, and subjects with dead regions had lower overall scores than their non-dead region counterparts. However, the same study reported large variability with regard to the ability of audibility to predict recognition scores for both dead-region and non-dead region subjects, and even suggested that subjects with dead regions performed better at recognizing speech of marginal audibility.

Huss and Moore (2005) investigated dead regions and pitch perception, and by asking subjects to match their percept with pure tones, found that pitch perception within a dead region is often (but not always) perceived abnormally. Since pitch is one of the cues used in stress patterns in speech and syllable identification, and also in prosody and intonation which contains important speech cues, subjects with dead regions are more likely to have difficulties with speech perception. Oxenham, Bernstein and Penagos (2004) found that correct tonotopic representation is necessary for complex pitch perception, which also supports the above findings. Schuknecht and Gacek (1993) looked at inner hair cell pathology in the cochlea and found that discrimination of speech sounds may be strongly affected when the loss of inner hair cells exceeds 50%.

Vickers, Moore, and Baer (2001) and Baer, Moore, and Kluk (2002) performed two similar studies that compared speech intelligibility in subjects with high-frequency dead regions

to subjects with no dead regions; the former study presented the stimuli in quiet, and the latter presented the stimuli in noise. Both studies found that subjects with dead regions failed to benefit from increased high-frequency information, whereas subjects with no dead regions did better with more high-frequency information. Several studies (e.g. Moore, 2001, 2004, Amos & Humes, 2001; Ching, Dillon, & Byrne, 1998; Hogan & Turner, 1998; Murray & Byrne, 1986) have suggested that amplification within a dead region should be avoided beyond 1.5 – 2 times the frequency at the edge of the dead region. For example, when the edge of a dead region is found at 1000 Hz, amplification should provide audibility up to 2000 Hz, and beyond that should be avoided. When the two studies above followed the above recommendation, performance for subjects with dead regions improved. To summarize, in the above two studies, subjects without dead regions made effective use of high-frequency information, whereas subjects with dead regions did not, and amplification well within a dead region caused decreased or stable scores while scores improved for subjects without dead regions. The results were similar in quiet and in noisy conditions.

Vinay and Moore (2007c) investigated aided speech recognition in quiet for subjects with and without low-frequency dead regions. High-pass filtered nonsense syllables were presented with different cutoff frequencies to determine if the subjects were making effective use of the low frequencies. Subjects with low-frequency dead regions had lower scores overall, and were only able to make use of frequencies amplified to within 0.57 times the edge frequency of the dead region. In other words, amplifying well within the dead region had deleterious effects. Subjects with low-frequency hearing loss but without dead regions scored higher overall and did not show deleterious effects at 0.57 times the edge frequency of the dead region. A similar study was performed in a noisy condition with similar results (Vinay, Baer, & Moore, 2008). These

results have implications when fitting hearing aids to patients with low-frequency dead regions, in that amplification to prescription targets within a dead region may impair speech perception.

It is important to note that dead regions are often associated with higher absolute thresholds, and it is difficult to tease apart the effects of inner hair cell pathology from the effects of greater hearing loss. Mackersie, Crocker and Davis (2004) addressed this issue when they matched their subjects with dead regions to subjects with equal or near-equal thresholds with no dead regions. Speech perception scores were measured with and without high-frequency amplification. Their findings indicate that while providing high-frequency amplification, speech scores were the same for subjects with and without dead regions in quiet and in low levels of noise. In high levels of noise, however, the subjects with dead regions did more poorly than their non-dead region counterparts. The results indicate that listeners with dead regions benefited from high-frequency amplification (within the dead region) in quiet and low levels of noise, but not in high levels of noise. These finding contradict the above studies that suggest amplification should be avoided within a dead region in quiet and in noise. However, all studies showed that speech perception scores were lower overall in noisy conditions in listeners with dead regions, which reflects the difficulties these patients face in communication.

To summarize, correct and differential diagnosis of cochlear dead regions is imperative to help clinicians provide the best possible service to their patients or clients. Determining the specific nature of the cochlear pathology in sensorineural hearing loss has important implications when awarding financial compensation for hearing loss, when determining candidacy for cochlear implants, when making clinical decisions in amplification, and for optimal aural rehabilitation counselling.

1.8 General Literature Involving Cochlear Dead Regions

Gordo and Martinelli (2007) investigated the benefit of high-frequency amplification for speech recognition in subjects with sensorineural hearing loss with and without cochlear dead regions. All subjects (n=30) had bilateral sloping sensorineural hearing loss. The authors used the TEN test to divide the subjects into two groups: group 1 was comprised of subjects who tested negative for dead regions; group 2 was comprised of subjects who tested positive for dead regions at high frequencies (above 1000 Hz). Speech testing was then carried out in sound field under the following three conditions: unaided, aided with gain applied to targets from 100 – 8000 Hz, and aided with no gain above 2560 Hz. Speech testing consisted of sentence recognition in quiet and in noise at comfortable listening levels.

The results showed that group 1 (no dead region) subjects performed best with a wide bandwidth of amplification (in quiet and in noise). Group 1 scores in the condition with reduced gain at high frequencies were similar to the unaided condition; in other words, the subjects with no dead regions were making use of the high frequency information for speech perception. Group 2 (with high-frequency dead regions) scores were lower overall, especially in the noisy condition. Furthermore, reduced high-frequency gain led to the best speech recognition performance in the subjects with dead regions. The subjects also reported increased clarity of sound and an absence of the hissing sound typically associated with the presence of tones that fall within a dead region. This in turn led to increased comfort and improved hearing aid satisfaction.

It should be noted that the differences between groups 1 and 2 in this study are not solely due to presence or absence of dead regions. Subjects with dead regions also had higher (worse) absolute thresholds than those without dead regions; therefore, as mentioned previously, it is

impossible to predict whether the poorer test performance was due to the greater degree of hearing loss or the presence of a dead region.

Not all evidence supports removal of high-frequency information for patients with dead regions. Mackersie, Crocker and Davis (2004) evaluated the performance of subjects with and without cochlear dead regions for speech perception in quiet, low noise, and high noise. The TEN test was used to assess the presence of dead regions. The subjects were threshold-matched. They tested in two conditions: the first was with a wide bandwidth of amplification, set to DSL (Desired Sensation Level) targets. The second condition avoided high-frequency amplification within a dead region. It was found that both listeners with and without cochlear dead regions achieved higher scores with wider bandwidth amplification, in quiet and low noise. In high levels of noise, it was found that performance for listeners with dead regions reached an asymptote or deteriorated slightly when amplification was provided at frequencies higher than one octave above the estimated boundary of the dead regions. From these results, one should deduce that patients with cochlear dead regions may experience speech perception benefit from high-frequency gain in quiet and low levels of noise, but not in high levels of noise. These findings contradict Vickers, Moore and Baer (2001) who found that speech perception performance in quiet plateaued or got worse when amplification was provided more than ½ to 1 octave above the estimated boundary of the dead region. While this difference in findings may be at least in part due to differences in experimental design (for example, the degree of hearing loss tended to be higher in the Vickers et al. study), it urges caution in implementing large-scale changes in clinical practice.

Cairns, Frith, Munro and Moore (2007) investigated the short-term test-retest repeatability of the TEN (HL) test. Subjects were tested for the presence/absence of a cochlear

dead region, then re-tested within five days. The subjects were divided into two groups: Group 1 was comprised of 15 teenagers (mean age 14 years) with severe to profound sensorineural hearing loss; Group 2 was 20 adults (mean age 74 years) with moderate-to-severe sensorineural hearing impairment. The number of ears that changed category (i.e. that changed from dead region positive to dead region negative or vice versa) was two (8%) for the teenagers and three (7.5%) for the adults. Test-retest repeatability was judged to be "good" when the results were classified by ear or by frequency. Importantly, it was found that the majority of ears that changed category on retest just met the dead-region criteria at an isolated frequency. An immediate re-test was recommended in such cases. This has implications for the results of the present study and will be addressed in the Discussion section. The study also highlighted the importance of using a 2-dB final step size, since reliability was much improved using that criterion.

Marriage, Moore, Ogg and Stone (2008) evaluated whether an aided TEN (HL) test could be used to reliably assess the presence or absence of cochlear dead regions. One of the limitations of the TEN test is that in the population of people with severe to profound hearing loss, who are perhaps most likely to have dead regions, it is often not possible to produce sufficient masking noise to properly administer the test. The authors investigated whether testing with the TEN test in sound field with hearing aids would yield valid results. While the incidence of inconclusive results was markedly reduced using the aided TEN test, the authors concluded it was not a valid clinical tool due to the unpredictable responses of the hearing aids to the testing procedure. For some aids, the gain changed rapidly as a function of the frequency, and distortion of the signal confounded the results. The aided TEN test was not recommended for clinical use.

Vinay and Moore (2009) investigated low-frequency pitch and speech perception in subjects with high-frequency dead regions. High-frequency dead regions were described as dead regions with the edge frequency of 1000 Hz and above. Threshold-matched counterparts with and without dead regions over 1000 – 1500 Hz were evaluated using discrimination tasks of low-frequency sine waves, detection of frequency modulation in low frequencies, and identification of consonants in low-pass filtered nonsense syllables. It was found that subjects with high-frequency dead regions showed enhanced thresholds and discrimination close to the edge frequency of the dead region and improved consonant perception in low frequencies, compared to the non-dead region counterparts. The results suggest high-frequency dead regions are associated with improved ability to process information at low frequencies, suggesting cortical plasticity induced by cochlear dead regions.

1.9 Prevalence of Cochlear Dead Regions

There are relatively few studies directly assessing the prevalence of cochlear dead regions. Preminger, Carpenter and Ziegler (2005) investigated the prevalence of cochlear dead regions in the population of adults (n=49) with moderate sensorineural hearing loss (thresholds between 50 – 80 dB HL). Rather than using the criteria recommended by the TEN test (thresholds in noise should shift by 10 dB in order to test positive for a dead region), they required a 15 dB shift before they declared a subject positive for dead regions. The prevalence of dead regions in their study was 29%. They also found that subjects with dead regions had poorer speech perception in noise than subjects without dead regions, and that subjects with dead regions perceived poorer subjective hearing aid performance in listening situations with reverberation and background noise than subjects without dead regions.

Aazh and Moore (2007) used the TEN (HL) test to evaluate the prevalence of dead regions at 4 kHz in older adults (age 63 – 101 years). Thresholds at 4 kHz ranged from 60 – 85 dB HL. Of 98 tested ears, prevalence of dead regions at 4 kHz was 37% (classifying by ear). The slope of the audiogram was not related to presence or absence of dead regions, nor was the pure tone average useful as a predictor of dead regions. The threshold at 4 kHz tended to be higher for the dead region group versus the non-dead region group, but the authors acknowledged that the threshold was not a useful indicator of dead region presence or absence since high thresholds also occurred with non-dead region subjects. The prevalence of dead regions at 4 kHz for thresholds higher (worse) than 70 dB HL exceeded 50%.

Vinay and Moore (2007a) investigated dead region prevalence in the population of adults (n=317) with sensorineural hearing loss, including everything from mild to profound hearing impairment. Classifying by subject, 57.4% (n=177) tested positive for dead regions at least at one frequency. Classifying by ear, 46% tested positive for dead regions at least at one frequency. The results also confirmed it was not possible to reliably determine the presence or absence of a dead region from the audiogram. A very steep slope of the audiogram was suggestive of a high-frequency dead region, but many steeply sloping losses did not exhibit dead regions, so the slope was not a useful diagnostic indicator. They further found that presence or absence of dead regions did not vary significantly with age or gender.

Preminger et al. (2005), Aazh and Moore (2007) and Vinay and Moore (2007a) are the only studies currently published that specifically address dead region prevalence. Other studies involving dead regions have reported prevalence data as a secondary part of their research. Moore, Killen and Munro (2003) administered the TEN test to a group of teenagers (n=23) with severe to profound hearing loss. The majority of ears tested drew inconclusive results, as it was

impossible to generate enough masking noise to properly conduct the TEN test, due to the extent of the hearing loss. For testable ears, the prevalence of dead regions was 77%. Classifying by subject, 70% of subjects tested positive for a dead region at least at one frequency.

Markessis, Kapadia, Munro and Moore (2006) administered the TEN test to adults (n=35) with moderate to profound hearing loss with a slope of 20 dB or more per octave. The primary objective of the study was to evaluate whether high-pass filtered noise could be used in order to increase patient comfort during the TEN test, and thus enable the tester to use higher noise levels. They concluded that high-pass filtered noise could be used. A secondary goal of the study was to assess the prevalence of dead regions in steeply sloping high-frequency moderate to profound sensorineural hearing loss. In this population, 87% of subjects met the criteria for a cochlear dead region at least at one frequency. In the dead region group, absolute thresholds at 4 kHz were between 65 and 90 dB HL, and 52% of 69 tested ears met the criteria for a dead region at 4 kHz.

Moore, Huss, Vickers, Glasberg, and Alcantara (2000) used the TEN (SPL) test and PTCs to assess 20 ears of 14 subjects with moderate to severe sensorineural hearing loss. It should be noted that the TEN (SPL) test is capable of testing a wider range of frequencies than the TEN (HL) test, so the chances of testing positive for a dead region at least at one frequency are higher when using the SPL version. Sixty-eight percent of subjects tested positive for a dead region in at least one ear. Their results suggested that high-frequency dead regions can coincide with absolute thresholds in the mild-to-moderate hearing loss range. Thresholds higher than 70 dB HL at high frequencies were often associated with a dead region, but there were also cases of equally matched thresholds with no dead regions present.

Table 1 (prevalence study table) summarizes the prevalence of cochlear dead regions from several published studies.

1.10 Summary

In summary, it has been known for some time that cochlear dead regions exist and may require a unique intervention strategy. What has changed recently is that the TEN test has become available, providing a clinically usable tool suited for widespread easy application in clinical settings. Sensitivity and specificity of the TEN test has been investigated as a means of diagnosing cochlear dead regions, and thus far it has been found valid and reliable. The goal of this study was to use the TEN test to evaluate the prevalence of cochlear dead regions within the population of people with sensorineural hearing loss, and examine the relationship between presence/absence of dead regions and slope of the audiogram, severity of the thresholds, age, and gender. A secondary goal was to evaluate prevalence in different clinical sub-populations such as those with noise-induced hearing loss, those with otologic disease-related hearing loss, and those who self-refer to a hearing aid clinic. This was done in hopes of providing guidelines regarding when to administer the TEN test.

Chapter II – Methods

2.1 Subjects

2.1.1 Description of Subjects

The subjects ranged in age from 34-95 years old (mean age=62) and came from a variety of ethnic and socioeconomic backgrounds. No children were tested because the TEN test is based on adult normative data. A total of 62 subjects (112 ears) were tested, 40 male and 22 female. All were diagnosed with sensorineural hearing loss as defined in the following section. The purpose of the study was explained to the subjects, and their consent was obtained for participation in the study. Ethics approval to conduct the study was obtained from the regulatory bodies governing the University of British Columbia, as well as from the various testing sites where necessary.

2.1.2. Inclusion/Exclusion Criteria

In the interest of replicating a study by Vinay and Moore (2007), the following inclusion/exclusion criteria were used (identical to their study):

1) Audiometric thresholds were greater than 15 dB HL for at least one frequency in the range of 250 – 8000 Hz.
2) The air-bone gap in audiometric thresholds was less than or equal to 10 dB at all frequencies from 250 – 4000 Hz.
3) Middle ear function was normal as indicated by tympanometry.

2.1.3 Testing Sites

Testing was carried out at six different facilities: WorkSafeBC, a government agency that awards financial compensation for workplace injuries and disease, including noise-induced hearing loss; Vancouver General Hospital, where the audiology clinic primarily sees

in/outpatients with SNHL; two private audiology clinics (Island Hearing Services and Sound Hearing Clinic) which primarily prescribe and dispense hearing aids to a self-referred population; a non-profit agency (Western Institute for the Deaf and Hard of Hearing) to which patients also self-referred and which sees a similar population as the private clinics; and the audiology teaching facility at the University of British Columbia. All clinics are within the city of Vancouver.

Different locations were chosen with the intention of targeting different sub-populations of people with sensorineural hearing loss. Testing subjects at WorkSafeBC was intended to target the population of people with noise-induced hearing loss (Group 1). Testing at Vancouver General Hospital was meant to target the population of people who are primarily suffering from otologic diseases that are associated with SNHL (Group 2) and includes diseases such as Meniere's disease, acoustic neuroma, and sudden idiopathic hearing loss. Testing subjects from the private and non-profit clinics was meant to target the population of people who self-refer (with or without recommendations from medical professionals) to a hearing clinic for the purpose of obtaining a hearing aid (Group 3). Subjects tested at the University of British Columbia were clients of the private hearing clinics and thus were included in Group 3. For Group 3, some subjects had attended the clinic previously, and some were new clients.

Testers were instructed to target the intended population and exclude atypical cases from the sample.

2.2 Procedures and Equipment

2.2.1. Threshold-Equalizing Noise (TEN) Test

The TEN (HL) test (Moore, Glasberg, & Stone 2004) was used to measure the presence or absence of dead regions in the cochlea. The test CD consists of pure tones at octave and

interoctave frequencies between 500 and 4000 Hz on one channel, and threshold-equalizing noise (TEN) on a second channel. TEN is noise that is spectrally designed to shift a subject's masked thresholds to the level specified on the audiometric dial in dB HL. For example, if the dial is set to 70 dB HL, a normally-hearing subject or a subject with hearing loss and no dead region should have a threshold at or near 70 dB HL. If the masked threshold in the TEN is higher than expected (i.e. 10 dB higher than the TEN and 10 dB higher than the unmasked threshold) that result is positive for a dead region at the test frequency. The presence or absence of a dead region at a specific frequency was based on the criteria suggested by Moore, Glasberg and Stone (2004). For a detailed outline of the testing procedure, please see Appendix I. The test was administered according to the instructions included with the CD. The approximate time it takes to administer the test is ten minutes.

All testing locations used a GSI-61 2-channel audiometer calibrated by ANSI standards (1996). The TEN (HL) test CD was routed through the audiometer. Thresholds were measured using TDH supra-aural earphones. Air conduction thresholds were measured from 0.25 kHz to 8 kHz. Masked thresholds in the threshold-equalizing noise were measured from 0.5 kHz to 4 kHz. The TEN was played continuously. The TEN level per ERB (equivalent rectangular bandwidth) was 70 dB HL by default, unless the subject complained of uncomfortable loudness. A lower intensity level (60 dB HL) was used in cases of milder hearing losses, especially if the subject indicated loudness discomfort (consistent with Vinay & Moore, 2007a). A higher level (as high as 90 dB HL) was used for more severe hearing losses in order to provide at least 10 dB of masking. Testers were permitted to use their judgment to choose the TEN level as long as the level generated sufficient masking to determine whether off-frequency listening was taking place. A 2-dB final step size was used to establish thresholds, and a criterion of a 10-dB

threshold shift was used to diagnose a cochlear dead region. Audiometric thresholds were measured using the modified Hughson-Westlake procedure proposed by Carhart and Jerger (1959). If the subject's minimum response level was beyond the limits of the audiometer, the response was recorded as the upper limit of the audiometer at the test frequency.

For tympanometry, most clinics used a Grason-Stadler middle ear analyzer, but other calibrated immittance bridges that perform the same functions were also used.

2.2.2. APD and AN Screening Tests

As mentioned previously, there may be alternate explanations for having raised thresholds in noise due to poor auditory processing efficiency secondary to retrocochlear disorders. For this reason, three screening tests were chosen to test for auditory processing disorder (APD) and auditory neuropathy (AN): dichotic digits, gap detection, and ipsilateral broadband noise middle-ear muscle reflex (MEMR). These tests were chosen because they are quick and simple to administer, are not linguistically loaded, and because they are a part of a recommended test battery for diagnosis of APD and AN (Rapin & Gravel, 2003). These supplementary tests were administered after the TEN test if the subject tested positive for dead regions. Detailed instructions for the APD tests are included in Appendix II.

To administer the dichotic digits test, the presentation level was set at 50 dB above the subject's speech reception threshold or at the most comfortable loudness level. The subjects wore TDH supra-aural headphones. The test CD was routed through the audiometer and calibrated using the CD's calibration tone. The subjects were instructed that they would be hearing different numbers in each ear at the same time and should repeat all of the numbers heard, regardless of order. The subject heard three practice sets, and additional instructions were provided if necessary. The test consists of 40 pairs of double digits, 80 digits in all (40 per ear).

The test is scored in terms of percent correct per ear (each digit is worth 2.5%). The pass criterion was set at 70%. The test recommends a 90% pass criterion, but since most of the people in the study were older adults, and it has been suggested that people over age 75 have higher prevalence of APD (Stach, Spretnjak, & Jerger, 1990), a lower criterion was selected.

The Random Gap Detection Test (RGDT) was also administered to dead region positive subjects. Impaired gap detection is a characteristic of retrocochlear pathology (Zeng & Liu, 2006). Once again, the test CD was routed through the audiometer and the subject wore TDH headphones. After calibrating the audiometer using the CD calibration tone, the signal was presented binaurally at 50 dB HL above the speech reception threshold or the most comfortable loudness level. The stimuli consisted of brief tones at 500, 1000, 2000, and 4000 Hz. Interstimulus intervals ranged from 0, 2, 5, 10, 15, 20, 25, 30, and 40 milliseconds. The subjects were instructed to verbally respond whether they heard one continuous sound or two separate sounds and given practice and instruction until they were able to complete the task. The RGDT threshold was defined as the time interval at which the subject consistently identifies two tones. The gap detection threshold at each frequency was averaged to obtain the composite gap detection threshold across frequencies. Gap detection thresholds no greater than 20 milliseconds were considered normal, or absence of an auditory processing disorder.

Middle ear muscle reflexes (MEMR) have been shown to be abnormal in people with auditory neuropathy (Berlin et al., 2005). For this reason, MEMR was chosen as a screening test to rule out retrocochlear disorders. If the subject had a recent audiogram in the clinic (within one year) and recorded MEMR, MEMR was not retested for the study. For subjects who underwent MEMR testing in the study, broadband noise was presented ipsilaterally at a screening level of 90 dB HL. Broadband noise was chosen as a stimulus because it typically elicits a MEMR at

lower levels than pure tones (Silman & Gelfand, 1981) to reduce loudness discomfort. If no response was present at 90 dB, the tester increased the level in 5-dB steps until 100 dB. If no response was present at 100 dB, a "no response" was recorded.

Chapter III Results

3.1 Overall Prevalence of Dead Regions

Classifying by subject, 9 of the 62 subjects (14.5%) tested positive for cochlear dead regions at least at one frequency. Four subjects met the criteria for a dead region in both ears, four tested positive for dead regions in the right ear only, and one subject tested positive for a dead region in the left ear only. Classifying by ear, 12 of the 112 ears (10.7%) were diagnosed as having a dead region at one frequency or more. Of 12 ears, 9 had a dead region at one isolated frequency. Eight of those were at 4 kHz, one was at 1.5 kHz. Two subjects had dead regions at more than one frequency: subject 23 from 1.5 – 4 kHz in the right ear, and 3-4 kHz in the left ear. This subject reported during audiometry that tones within the dead region sounded like noise. Subject 47 met the dead region criteria at 3 and 4 kHz in the left ear only. Table 2 shows details of the dead-region positive subjects.

Of the nine subjects who tested positive for dead regions, seven were male and two were female. Ages in the dead region positive group ranged from 36-74 years. The mean age of the dead region positive group was 62. The mean age of the dead region negative group was 64.

3.2 Prevalence by Clinical Sub-Group

Two subjects in Group 1 (noise-induced hearing loss, n=15) tested positive for a dead region at one frequency or more (13%). None of the subjects in Group 2 (otologic-diseased, n=8) tested positive for a dead region, though the sample size was very small. Group 3 (self-refer to a hearing clinic) was the largest group (n=39), and seven of those subjects tested positive for a dead region (18%). Statistical interpretation of these results was not done due to the small sample size and differences in numbers of subjects in each group.

3.3 Relationship of Dead Regions to Audiometric Thresholds

Next, the extent to which a dead region at 4 kHz can be predicted based on audiometric threshold was evaluated. This frequency was chosen since most of the subjects had a dead region only at 4 kHz. The statistical question was posed as what percentage of subjects would have been correctly identified as dead-region positive if a dead region is presumed present at 60, 65, 70, 75, 80, or 85 dB HL? Sensitivity refers to the "hit rate", or the number of dead-region positive ears that are correctly identified (true positive) by absolute threshold. Specificity refers to the "false alarm" rate, or the probability of falsely identifying a cochlear dead region based on threshold. With lower thresholds, true dead-region positive subjects are correctly identified, but the false alarm rate is high (specificity is poor). With higher thresholds, false positives increase, but true negatives improves. These results are consistent with previous research (i.e. Aazh & Moore, 2007; Vinay & Moore, 2007a). The results of these calculations are shown in Table 3.

The mean audiometric threshold at 4 kHz was 59.5 dB HL in the dead-region negative group. The mean threshold in the dead-region positive group was 76.7 dB HL. This is consistent with previous research (Aazh & Moore, 2007) which suggested that thresholds tended to be higher at 4 kHz in subjects with dead regions. However, caution must be urged when

trying to determine presence or absence of dead regions by absolute thresholds, especially from the results of this study which had a limited sample size.

Figure 1 shows the mean audiograms of Groups 1, 2, and 3, and of all the Groups combined for the dead-region negative participants. The mean audiogram of the dead-region positive group (all three groups combined) is also provided. It is interesting to note that the dead region positive group has the same audiometric configuration as the noise induced hearing loss group, except the severity is more pronounced in the dead region positive group. The self-refer group, which had the highest incidence of dead regions, had higher (worse) overall thresholds than the other groups. The otologic-diseased group, which had no incidences of dead regions, had a milder degree of hearing loss and a less steep slope. The overall dead-region negative group's mean audiogram compared to the overall dead-region positive group had lower (better) thresholds and a shallower slope.

3.4 Relationship of Dead Regions to the Slope of the Audiogram

Dead regions have been found to be present in a variety of audiometric configurations, including reverse sloping, flat, and steeply sloping hearing losses (Moore, 2001, 2004; Preminger, Carpenter, & Ziegler, 2005). High-frequency dead regions are often associated with steeply sloping hearing losses, though previous research has suggested no statistically significant relationship because steeply sloping audiograms also occur without dead regions (Vinay & Moore, 2007a; Aazh & Moore, 2007). The slope was determined by the difference in audiometric thresholds from 1000 – 2000 Hz, and from 2000 – 4000 Hz, consistent with previous research (e.g. Aazh & Moore, 2007). In the dead-region negative group, the mean difference in absolute threshold between 2 – 4 kHz was 12.5 dB. The mean difference between 1 – 2 kHz was 9.4 dB. In the dead-region positive group, the mean difference between thresholds

from 2 – 4 kHz was 19.2 dB. The mean difference between 1 – 2 kHz was 17.1 dB. These results suggest a steeper slope in the dead-region positive group. Once again, statistical significance was not investigated due to small sample size and unequal numbers in each group.

3.5 Relationship of Dead Regions to Pure Tone Average

In the dead-region negative group, the pure tone average (PTA) from 0.5 – 2 kHz was 37.5 dB HL. The PTA from 0.5 – 3 kHz was 40.2 dB HL. In the dead-region positive group, the PTA from 0.5 – 2 kHz was 41.4 dB HL. The PTA from 0.5 – 3 kHz was 46.0 dB HL. While there is a slight trend towards a higher PTA in the dead-region positive group, the modest differences in these results suggest the PTA is not a useful predictor of dead regions, which is consistent with previous research (Aazh & Moore, 2007).

3.6 Audiometry Thresholds Compared to TEN Test CD Thresholds

One of the primary concerns mentioned by clinicians who administered the TEN test during this study was the extra time it took to administer the TEN test during an appointment. For this reason, it was decided to compare the thresholds obtained by the TEN test CD to the thresholds in a conventional audiogram within the last year. The hypothesis was if the thresholds turned out to be similar, it may not be necessary to do both types of testing in one appointment. Figure 2 shows a comparison of thresholds generated from standard pure-tone audiometry (recent audiogram within one year) and thresholds generated from the TEN test CD. The results suggest that the thresholds are similar. This may have practical implications when considering clinical testing time, in that the CD thresholds may represent thresholds for both the TEN test and the audiogram. It is important to note that the TEN test thresholds are measured as a 2-dB final step size, and conventional audiometry uses a 5-dB final step size. At 500, 1000, 2000, and

4000 Hz, all CD thresholds were within 3 dB of audiogram thresholds. This suggests no clinically significant difference, since a 5-dB step size is used clinically.

3.7 Results of APD Screening Tests

Only two of the nine dead-region positive participants were able to meet the passing criterion for the dichotic digits test. Five of the nine dead-region positive subjects passed the RGDT. Eight of the nine dead-region positive subjects passed the MEMR. The one subject who did not pass the MEMR was unable to perform the test due to loudness tolerance issues. Only one of the nine dead-region positive subjects was able to pass all three screening tests for retrocochlear disorders. All participants passed at least one screening test.

Chapter IV Discussion

Correct diagnosis of cochlear dead regions is important for treatment and management of hearing loss, optimal aural rehabilitation, medico-legal cases, and when assessing candidacy for cochlear implants. The results described here suggest that the presence or absence of a dead region cannot be reliably determined by absolute threshold at 4000 Hz, slope of the audiogram, or pure tone average. Thus, a clinically feasible test for cochlear dead regions is necessary. The TEN test has been proposed as a valid and clinically feasible tool for the diagnosis of dead regions.

4.1 Prevalence of Dead Regions

Overall prevalence of dead regions appeared lower in this study (14.5%) than a similar study (Vinay & Moore, 2007a) with identical inclusion/exclusion criteria (57%). Possible explanations for this might be the difference in sample size, n=62 in this study, n=317 in Vinay and Moore. The mean audiograms of the subjects may also have been different, but

unfortunately this data was not published in the Vinay and Moore study so comparison was not possible.

The presence or absence of dead regions was not related to the audiometric threshold at 4 kHz, the slope of the audiogram, or the pure tone average. This is consistent with previous research (Vinay & Moore, 2007a; Aazh & Moore, 2007). The results are not surprising when considering the aforementioned shortcomings in the pure tone audiogram as a diagnostic tool. In the case of a cochlear dead region, off-frequency listening causes an underestimation of the actual level of hearing loss at the test frequency, which would cause considerable overlap between dead region and non-dead region audiograms.

Of the three sub-populations of subjects with sensorineural hearing loss (noise-induced hearing loss, otologic diseases, and people who self-refer to a hearing aid clinic), dead regions were most prevalent in the self-referred group (7 out of 39, 18%). Two subjects with noise-induced hearing loss had dead regions (2 out of 15, 13%), and none in the otologic disease group (n=8). However, these results need to be interpreted with caution since the sample size was very small and each group had a different sample size. This preliminary research seems to suggest patients who self-refer to a hearing clinic are more at risk for dead regions. While these results need to be interpreted with caution, there may be good reasons why people who self-refer to a hearing aid clinic are more likely to have dead regions. As mentioned previously, people with dead regions tend to have poorer speech perception, more difficulty understanding speech in adverse listening situations such as background noise and reverberation, and tones that fall within a dead region are often perceived as noise. This might make them more likely to notice a problem with hearing and seek help, which would increase the number of dead-region positive subjects at those sites. While further study is needed before making conclusions regarding

prevalence in different sub-populations of those with sensorineural hearing loss, based on the results of this study further research in this area is justified.

4.2 APD/AN Confound

Three screening tests were selected with the intention of ruling out the retrocochlear APD and AN confounds: dichotic digits, the Random Gap Detection test (Keith, 2000), and ipsilateral broadband noise stapedial reflex testing. Because these tests are not linguistically loaded, are quick and easy to administer, and are usually a part of a test battery for APD, it was thought they could be used as screening tests. Subjects who failed the APD screenings were meant to be excluded from the study.

However, this decision turned out to be problematic. Only one of the nine subjects who tested positive for cochlear dead regions was able to pass all three screening tests to rule out retrocochlear disorders such as auditory neuropathy or APD as a confounding factor. This is perhaps suggestive of difficulty in diagnostic specificity with regard to cochlear versus retrocochlear pathology. It is possible that improper encoding of the auditory signal at the level of the cochlea gives rise to retrocochlear dysfunction. Recall from Schuknecht and Gacek (1993) that IHC loss is functionally equivalent to neural pathology, and that IHC loss and neuronal loss can vary independently of each other. It is difficult to tease apart the site of lesion when each step of the auditory pathway is intricately dependent on previous steps. Because the spiral ganglions of the cochlea synapse directly on to the auditory nerve, pathologies related to them both are intricately connected and differential diagnosis is difficult; perhaps even futile (it could be argued). Improper encoding of the auditory signal at the level of the cochlea gives rise to poor neural transmission of the auditory signal, which in turn causes poor speech perception at the cortical level. This is validated by the common complaint reported by people with dead

regions and/or auditory neuropathy of being able to detect sounds but not being able to make sense of them. Poor temporal processing would make the patient less able to process the rapid sounds of speech, and poor pitch perception would mean sounds would be audible but incomprehensible. These are complaints common to both dead region and auditory neuropathy patients. This might also explain why both disorders lead to worse speech perception scores than expected from the audiogram.

Perhaps a better choice of screening test would have been a screening ABR test, which can rule out AN without being affected by cochlear dead regions. In Vinay and Moore (2007a), all the subjects with cochlear dead regions passed an ABR screening test, suggesting this measure is not affected by inner hair cell pathology. ABR is an objective measure, rather than a behavioural test, which may enable it to be a more accurate measure than the APD screening tests attempted in this study.

4.3 Sensitivity and Specificity of TEN Test

During the course of the study, Cairns, Frith, Munro and Moore (2007) published findings that the test-retest reliability of the TEN test was questionable when a dead region was found at a single isolated frequency. A re-test was recommended in such cases. Most of the subjects in this study did test positive for a dead region at a single isolated frequency, and did not exhibit the symptoms common to listeners with dead regions (e.g. reduced subjective hearing aid performance, poorer than expected speech perception, tones sounding like noise within the dead region). In hindsight, it is likely that under re-test the ears might have changed category. Only one subject (#23) showed dead regions at more than one frequency in both ears, and this subject reported the symptoms described above. It is likely that the false alarm rate of dead

regions in the current study was high, even though the prevalence rate was already lower than reported in other studies.

Interestingly, the Cairns et al. (2007) study reported that the number of ears that changed category (i.e. from dead-region positive to dead-region negative or vice versa) on re-test was less than 5% except at 1.5 and 4 kHz. The percentage of ears that changed category on retest at 1.5 kHz was as high as 20%, and at 4 kHz as high as 12.5%. All the subjects in this study who tested positive for a single isolated dead region did so at 1.5 and 4 kHz, so according to Cairns et al. (2007), it is likely that those who barely met the criteria may have tested negative on retest.

4.4 Limitations of the Study

As mentioned above, small sample size and different numbers of subjects in each group was a major limitation in this study. It should also be mentioned that the "random sample" of subjects with sensorineural hearing loss should be interpreted with caution, because testers and recruiters were not blind, and could have influenced the selection process. Every effort was made to achieve a random sample, but it is recognized that a possible source of error is inherent in the study's methods.

As well, future dead region studies should not use APD screening tests in order to rule out a retrocochlear confound; a screening ABR might be a better choice. However, the current study did use an acoustic reflex screening test, which minimizes the likelihood of neural pathology in participants. Also, with the results from Cairns et al. (2007) now available, subjects who tested positive for a dead region at a single isolated frequency, especially if they just meet the criteria for a dead region, should have been re-tested to confirm the results, since some of the

ears in the Cairns et al. study changed category on re-test. This would improve the sensitivity and specificity of the results.

4.5 Clinical Perspective on TEN Test Use

From a clinical perspective, there may be practical drawbacks of the TEN test. During the course of this study, some subjects reported fatigue (due to the loud levels of uninterrupted broadband noise) during or following the test, especially older adults. While the information gained might be valuable, many clinicians, particularly those in private practice, prefer the client to have a mostly positive experience in the clinic. On the other hand, more thorough testing might create more client confidence in the clinician, and while the test may be fatiguing, the information gained is valuable for the reasons described earlier in this paper. Implementing the use of the TEN test also may be challenging for clinics who book limited time with clients. During this study, some clinics reported that under their current appointment schedule the additional time spent testing (approximately ten minutes) meant a sacrifice to the time spent counseling and talking with the patient. It is acknowledged, however, that presence or absence of dead regions is an important consideration for aural rehabilitation, so the information gained makes the counseling more effective. Clinics who wish to implement use of the TEN test should be aware that appointment times may need to be adjusted.

Additionally, some clinicians showed a strong preference for insert earphones over the supra-aural headphones recommended for the TEN test. The advantages of insert earphones include improved comfort, decreased sound leakage, improved interaural attenuation thus enabling quieter levels of masking noise, reduced occlusion effect, improved attenuation of ambient sounds, and preventing collapsing ear canals. For clinicians who prefer to use insert earphones during audiometric testing, switching to supra-aural headphones to perform the TEN

test was inconvenient. However, no current research is available to support the use of the TEN test with insert earphones. Preliminary research (albeit with a very small sample size) suggests the diagnosis of a dead region is not consistent between supra-aural and insert earphones (DiCecco, 2008; Lee, 2008).

4.6 Directions for Future Research

Since dead region research is a relatively nascent field, there is much that remains to be explored. More study is necessary regarding whether or not hearing care professionals should amplify to prescription targets within a dead region, since current research seems to be inconclusive (e.g. Mackersie et al., 2004 contradicts Gordo & Martinelli, 2007), though clinical judgment and patient satisfaction remain the most important considerations. Recent attention to cochlear dead regions causes a fresh perspective on frequency transposition and frequency compression hearing aids. With new and promising research coming out of the University or Western Ontario on frequency compression technology (e.g. Scollie & Glista, 2007), audiologists and other hearing care professionals have more to offer for these patients than counseling realistic expectations from hearing aids. As always, the benefits and/or risks of amplification to high targets should be considered carefully for both dead-region positive and dead-region negative patients. The efficacy of providing high-frequency amplification should be determined on an individual basis (Scollie & Glista, 2007).

It would also be interesting to see anatomical studies on regeneration or preservation of inner hair cells, possibly involving stem cell research. This in turn might be informative in exploring the preservation of low frequency pitch perception in cochlear implants, which may have implications for patients with high frequency dead regions and relatively preserved low-frequency hearing. As well, additional research into differential diagnosis of IHC pathology

versus neural pathology and the variability in treatment outcomes in subjects with different sites of lesion would be enlightening.

As mentioned previously, more research is also necessary regarding the use of the TEN test using insert versus supra-aural earphones. For clinicians who show a strong preference for insert earphones, it would be more convenient to avoid switching transducers between tests, and currently the test is only recommended for use with TDH supra-aural earphones.

In terms of rehabilitation, research into the effects of FM on speech perception for patients with cochlear dead regions would be informative and perhaps enable hearing care professionals to provide more informed treatment options. Given the similarity of symptoms between AN and cochlear dead regions, perhaps auditory training-style therapy would be beneficial for patients with dead regions, since this type of training is recommended for patients with AN. Retraining the brain to make use of an impoverished or altered speech signal would almost certainly be helpful for people with cochlear dead regions.

Study	n	Age Range	TEN Level	Version of TEN test used	Criteria	More info re: population	Prevalence
Preminger Carpenter and Ziegler 2005	49	21-75	70 dB or best threshold + 10 dB	SPL	15 dB threshold shift, 15 dB above TEN (5 dB step size)	Moderate to severe SNHL (Thresholds between 50-80 dB HL)	14/49 = 29%
Vinay and Moore 2007	308 (556 ears)	17-95 (mean = 57)	70 dB	HL	10 dB threshold shift, 10 dB above TEN (2 dB step size)	Anybody with SNHL – at least one threshold over 15 dB HL	177/308 = 57%
Markessis Kapadia Munro and Moore 2006	35	40-89	80 dB	SPL	10 dB threshold shift, 10 dB above TEN (5 dB step size)	Moderate to profound SNHL with slope ≥ 20 dB per octave	87%
Moore Killen and Munro 2003	23 (40 ears)	12-18	?	SPL	10 dB threshold shift, 10 dB above TEN (5 dB step size)	Severe to profound SNHL	31/40 ears = 77% Subjects 70%
Munro Felthouse Moore and Kapadia 2005	23 (34 ears)	13-19	?	SPL	10 dB threshold shift, 10 dB above TEN (5 dB step size)	Severe to profound SNHL	70%
Vickers Moore and Baer 2001	10	48-76	?	SPL	10 dB threshold shift, 10 dB above TEN (5 dB step size)	High-frequency SNHL	7/10 = 70%
Aazh and Moore 2007	63 (98 ears)	63-101	10 dB higher than threshold at 4KHz, not exceeding 95 dB	HL	10 dB threshold shift, 10 dB above TEN (2 dB step size)	Elderly adults with sloping hearing loss and absolute thresholds 60-85 dB HL at 4KHz	36/98 ears = 37%

Table 1. Summary of current literature regarding dead region prevalence. Listing the correct version of the test used is important because the SPL version covers a wider frequency range, thereby increasing the possibility of having a dead region at least at one frequency.

Subject	Ear with DR	Age	Sex	Group	Acoustic Reflex	Dichotic Digits	Gap Detection	Frequency of DR	Threshold at DR dBHL (from TEN test CD)
12	Right	68	M	1	CNT	Pass	Pass	4 kHz	74
13	Both	61	M	1	Pass	Fail L, Pass R	Pass	4 kHz L, 4 kHz R	86 L 72 R
16	Right	74	F	3	Pass	Fail	Pass	4 kHz	68
17	Both	67	M	3	Pass	Fail L, Fail R	Fail	4 kHz L, 4 kHz R	64 L, 80 R
23	Both	64	M	3	Pass	Fail L, Fail R	Pass	3-4 kHz L, 1.5 – 4 kHz R	NR at 108, 106 L, 76, 92, 98, 98 R
32	Both	65	M	3	Pass	Fail L, Pass R	Fail	4 kHz L, 4 kHz R	76 L 82 R
38	Right	36	M	3	Pass	Pass	Pass	4 kHz	66
47	Left	58	F	3	Pass	Inconclusive	Inconclusive	3-4 kHz	54, 52
55	Right	71	M	3	Pass	Fail	Fail	1.5 kHz	66

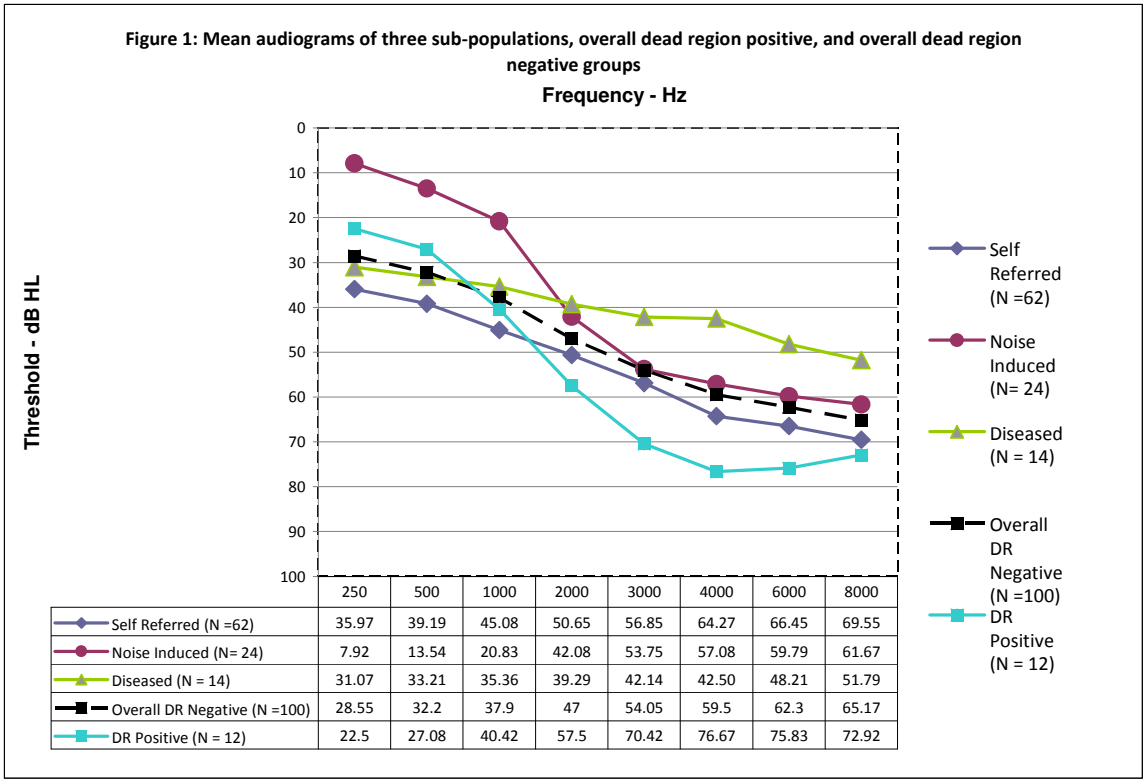
Table 2. Results for dead region positive subjects. Subject 12 could not be tested for acoustic reflexes due to loudness intolerance. Subject 23 reported 4 kHz gap detection very difficult. He also reported that tones didn't sound like tones at 3 and 4 kHz in both ears. Subject 47 was not tested for DD or RGDT because the tester believed she was DR negative. She was included in the study regardless since she passed the acoustic reflex screening test.

Absolute threshold criterion, dB HL	≥60	≥65	≥70	≥75	≥80	≥85
Sensitivity %	92	92	75	58	50	33
Specificity %	14	18	22	34	41	60
Overall % correct	64	46	38	26	21	16

Table 3. Sensitivity and specificity in this study of dead region diagnosis using absolute 4 kHz threshold as criterion. When the criterion encompasses lower thresholds and all thresholds above that number, true dead-region positive subjects are correctly identified, but the false alarm rate is high (specificity is poor). When the threshold criterion increases, false positives increase (the "hit rate" is low), but true negatives improves. The "gold standard" for presence or absence of dead regions was the TEN test. Overall % correct refers to the number of cases that would be correctly identified based on the audiogram.

Absolute threshold criterion, dB HL	≥60	≥65	≥70	≥75	≥80	≥85
Sensitivity %	100	83	63	47	19	8
Specificity %	0	32	62	82	93	98
Overall % correct	50	51	63	69	66	65

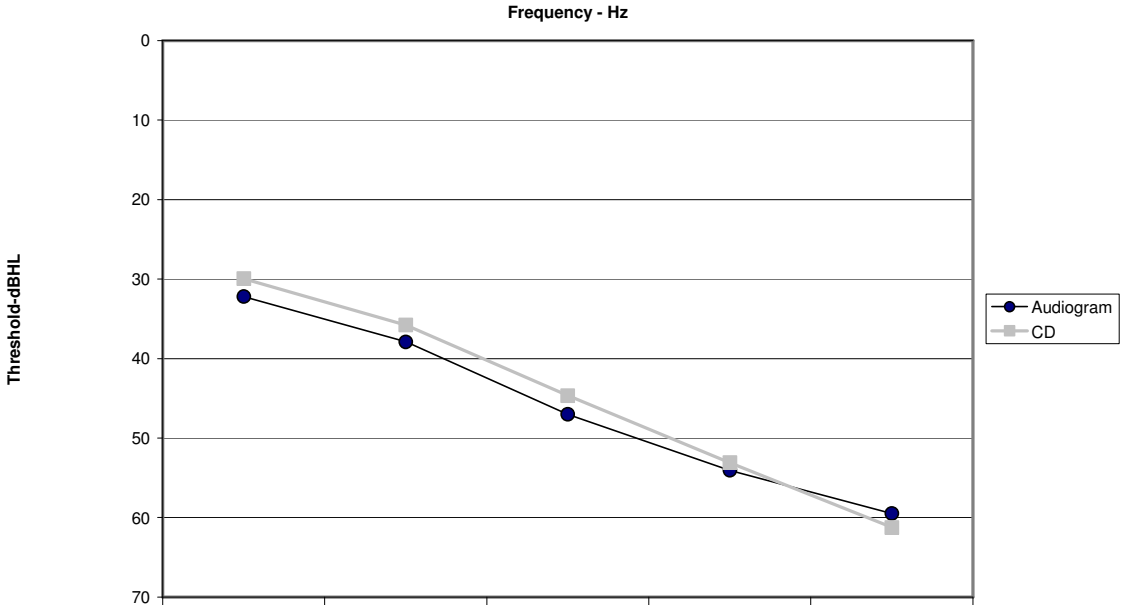
Table 4. From Aazh and Moore, 2007, Sensitivity and specificity of dead region diagnosis by absolute threshold at 4 kHz.



	250	500	1000	2000	3000	4000	6000	8000
Self Referred (N =62)	35.97	39.19	45.08	50.65	56.85	64.27	66.45	69.55
Noise Induced (N= 24)	7.92	13.54	20.83	42.08	53.75	57.08	59.79	61.67
Diseased (N = 14)	31.07	33.21	35.36	39.29	42.14	42.50	48.21	51.79
Overall DR Negative (N =100)	28.55	32.2	37.9	47	54.05	59.5	62.3	65.17
DR Positive (N = 12)	22.5	27.08	40.42	57.5	70.42	76.67	75.83	72.92

Figure 1. Mean audiograms of three subpopulations of subjects with sensorineural hearing loss, overall dead region negative group, and overall dead region positive group (classifying by ear).

Figure 2: TEN test CD thresholds compared to audiometric thresholds within the last year



	500	1000	2000	3000	4000
Audiogram	32.2	37.9	47	54.05	59.5
CD	29.95	35.8	44.67	53.1	61.26

Figure 2: TEN test CD thresholds compared to audiometric thresholds obtained within the previous year.

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Appendices

Appendix I - TEN Test Protocol

1. Put the TEN (**T**hreshold-**E**qualizing **N**oise) test CD in the CD player attached to the audiometer.
2. Choose stimulus on audiometer: put channel 1 of the audiometer on input A (e.g. External A), and put channel 2 on input B (e.g. External B). This puts the tone in channel 1 and the noise in channel 2. The noise and the signal will be presented to the same ear.
3. Choose transducer: **Phones** (ensure patient is wearing TDH 39 headphones).
4. Choose routing: both left or both right, depending on ear tested.
5. Play track 1, set the audiometer so that both line inputs are played continuously (press both interrupt buttons) and adjust both VU meters to read 0 dB. Turn off the two inputs (press the interrupt buttons).
6. Ensure both signals are directed to the desired ear.
7. Find unmasked thresholds at 500, 750, 1000, 1500, 2000, 3000, and 4000 Hz using the CD. The track will play continuously for 10 minutes, so you may use the thumb button of the audiometer to present the stimulus as needed. Use a 10 dB down 5 dB up technique at first, then use a 2 dB step size to find ear the most precise threshold. You may use traditional NBN masking in the contralateral ear if necessary.
8. Choose the desired noise level on the audiometer using the CHANNEL 2 control. The noise level should be the same across all frequencies. Set the noise level at 70 dB_{HL} **unless**:
    - The subject reports discomfort: in this case lower the noise level until the patient is comfortable. This level should be at least 10 dB_{HL} above the lowest (best) threshold in quiet.
    - The subject's hearing thresholds are within the severe to profound range: in this case use a TEN level that is 10 dB_{HL} above the lowest (best) threshold. The maximum possible noise output on the CD is 90 dB_{HL}. If the subject's thresholds in quiet are too high, you will not be able to administer the test.
    - See below for test interpretation.
9. Instruct the patient: "The noise and the tone will be in the same ear. Ignore the noise and respond (push button, raise hand) when you hear the tone hiding within the noise." Re-instruct as necessary.
10. Play the noise continuously in channel 2 (press the interrupt button), and begin the threshold search on Channel 1 at 10 dB above the noise (present stimulus as required using the thumb button in channel one). Use 10 dB down, 5 dB up test technique. Use 2 dB final step size.
11. Using the different tracks on the CD, find the masked threshold at 500, 750, 1000, 1500, 2000, 3000, and 4000 Hz. Record both the TEN level and the masked threshold.
12. If the **masked** threshold is 10 dB (or more) above the threshold in quiet AND is 10 dB (or more) above the threshold-equalizing noise (TEN); then screen for central auditory processing disorder (instructions attached) and broadband noise acoustic reflexes (instructions attached).

Interpreting Results

Five possible scenarios:

1. Masked threshold 10 dB (or more) above absolute threshold AND 10 dB (+) above the threshold-equalizing noise (TEN).

➔ Dead region (DR) present

2. Masked threshold is 10 dB (+) above threshold but NOT 10 dB above the TEN.
   ➔ DR not present
3. Masked threshold is WITHIN 9 dB of absolute threshold but is 10 dB or more above the TEN.
   ➔ Inconclusive
   ➔ Do test again with higher level of TEN
4. Masked threshold is WITHIN 9 dB of absolute threshold and WITHIN 10 dB of TEN.
   ➔ Inconclusive
5. Absolute threshold too high to be measured.
   ➔ Inconclusive but DR likely

IF A DEAD REGION IS FOUND:

1. As mentioned above, please be sure to re-test unmasked threshold using a 2 dB step size.
2. Because there may be other possible explanations for having raised thresholds in noise, it is necessary to run two quick central auditory processing disorder (CAPD) screening tests.
3. Random Gap Detection Test.
4. Dichotic Digit Test.

Appendix II – APD Test Protocols

APD Test Protocols

Instructions for Broadband Acoustic Reflex Testing

1. Set up the immittance bridge for a broadband noise stimulus. This is usually done by pressing the "stimulus" button and toggling through until "BBN" is displayed.

2. Present stimulus at 90 dB HL ipsilaterally (Tympstar and GSI 33 is calibrated in HL). Recall that responses to broadband noise are usually evident at lower levels than for pure tones.

3. If no response is evident, present at 95, then 100 dB. Do not exceed 100 dB presentation level. If no response is present at 100 dB, record "no response".

Dichotic Digit Test (DDT) (TRACK #18)

Administered at 50 dB SL re: SRT or MCL

Instruct your subject that they will be hearing different numbers in each ear at the same time and should repeat all of the numbers heard, regardless of order. Calibrate your CD player using GSI 61 VU-meter nub for the TAPE A/B. The 1st 3 stimulus presentations are for practice. The test consists of double digits, 80 digits in all (40 per ear). The test is scored in terms of percent correct per ear (each digit is worth 2.5%).

Random Gap Detection Test (RGDT) (TRACKS 31-34)

Test Procedure

Step 1: After calibrating the audiometer, present the signal **binaurally** at a comfortable listening level, e.g. 55 dB HL. If the test is administered through earphones connected directly to the CD player, adjust the signal to a level that is comfortably loud for the examiner (assuming the examiner has normal hearing).

Step 2: Administer the practice test.

Instructions to the subject:

Instruct the subject to respond verbally whether s/he heard one or two tones.

Practice/Screening and test administration**:**

The examiner should use the practice test to "teach" the subject how to respond, and to determine that the subject understands the task and is responding appropriately. The examiner can utilize a number of methods to demonstrate the concept of the "gap" including blocks, hummed or whistled notes, or tones through an audiometer. If a subject is having difficulty with the task the examiner can respond with the subject, demonstrating the task.

If a subject has difficulty responding to the practice test, re-instruct and re-administer the practice test. Patients with a temporal processing disorder and some children will be unable to hear the gap, or respond appropriately. If the subject is unable to perform the practice task after three practice sessions, terminate the test.

Step 3: After successful completion of the practice test, proceed to the RGDT administration. It is not necessary to proceed in the order presented on the CD, although the test was normed following that sequence.

Step 4: Do not pause the test within a frequency. If necessary, it is permissible to pause the test between frequencies.

Recording the response

Mark the responses in the following way: In the appropriate block indicated on the score sheet, mark a "1" if the child indicated that he/she heard one sound and mark a "2" if the child indicated that he/she heard two sounds

Calculating the RGDT threshold

The RGDT provides gap detection thresholds measured in milliseconds (msec). The gap detection threshold is defined as the time interval at which the subject consistently identifies two tones.

1. At each frequency identify the shortest interval where the subject consistently identified two rather than one tones. Remember that there is uncertainty at the threshold between one and two tones, and some subjects may have an interval where they vacillate between whether they heard one or two tones.

2. Average the gap detection threshold at each frequency to obtain the composite gap detection threshold across frequencies.
3. Gap detection thresholds can be calculated if the practice/screening test and at least three of four pure tone subtests are completed.
4. Compare the gap detection threshold to the normative values listed in the appendix. Gap detection thresholds less than 20 msec. are normal, indicating that there is no evidence for the existence of a temporal processing disorder.

Appendix III – Consent Form

The University of British Columbia, Western Institute for the Deaf and Hard of Hearing, Vancouver General Hospital, and WorkSafe BC

Consent Form

Project Title: Cochlear Dead Regions – A Prevalence Study in Different Audiological Settings

Principal Investigator:
Dr. Navid Shahnaz
Assistant Professor
School of Audiology & Speech Sciences
University of British Columbia
Phone: 604-822-5953
Email: nshahnaz@audiospeech.ubc.ca

Co-investigators:

Nerissa Davies
M.Sc. Candidate
School of Audiology and Speech Sciences
University of British Columbia
Tel: 778-988-6373

Grace Shyng
M.Sc., Aud (C)
Clinical Assistant Professor
Western Institute for the Deaf and Hard of Hearing
Tel: 604-736-7391

Nirvana Kiarostami
M.Sc., Aud (C)
Audiologist Advisor & Clinical Assistant Professor
WorkSafeBC
Tel: 604-232-7184

Dr. Lorienne M. Jenstad
Assistant Professor
School of Audiology and Speech Sciences
University of British Columbia
Tel. 604- 822- 4716

Amir Soltani
M.Sc., Aud (C)
Clinical Assistant Professor
Downtown-Island Hearing Services
Tel. 604- 688- 5999

Leigh Bush
M.Sc., Aud (C)
Senior Audiologist
Vancouver General Hospital
Tel. 604-875-4111 ext 67962

Mark Hansen
M.Sc., Aud (C)
Owner/Director
Sound Hearing Clinic
Downtown & South Vancouver
Tel. 604-687-1488

Introduction: You are being invited to take part in this study because you have a type of hearing loss we would like to explore (sensorineural hearing loss). There are many different types of hearing loss, and a new test has been developed that might provide your audiologist with more specific information about your hearing loss and what is the best way to help you.

Purpose: The main goal of this study is to use the newly developed TEN (threshold-equalizing noise) test to determine if you have a type of hearing loss called a cochlear dead region. The cochlea is the snail-shaped organ of hearing deep within your inner ear that is responsible for changing sound waves into electrical impulses that get sent up to your brain. A dead region in the cochlea means the inner hair cells in the cochlea are not working properly and electrical impulses are not being properly sent to the brain. The TEN test will tell your audiologist if your inner hair cells are working well or not, and this will help your audiologist decide what is the best way to treat your hearing loss. As well, finding out how common dead regions are in people with your type of hearing loss will help audiologists decide if the TEN test should be given all the time.

Procedure: If you agree to participate in this project, all testing will be done by a certified audiologist or a master's student under supervision of a certified audiologist. The testing uses safe and routine procedures you have probably already experienced in previous audiological testing. You will be asked to listen for tones hiding within a noise, and to indicate when you have heard the tone by pressing a button or raising your hand, whichever is easier for you. The testing will take up to 20-25 minutes and the results will be given to you immediately afterward.

Your participation in these extra tests is entirely voluntary. You may withdraw from this study at any time and without providing any reasons for your decision. Should you decide to withdraw from this study all the data collected before your withdrawal will be discarded permanently from our database. Withdrawal will in no way jeopardize your present or future clinical care.

Inclusion and Exclusion Criteria: You are eligible to participate in this study if you have a hearing loss due to inner ear problem which is called sensorineural hearing loss (SNHL). Potential participants with middle ear problems (infection) will be excluded from this study.

Advantages: This is a test of cochlear function; it is not a treatment. It is hoped that the information obtained will help refine the assessment of hearing loss and improve the process of fitting hearing aids for people with cochlear dead regions. You may experience direct benefit from these tests if a cochlear dead region is found and your audiologist can make better-informed decisions as to how to treat you. If you wear hearing aids, it is possible that your hearing aids can be adjusted to be more comfortable and useful to you. Furthermore, you will be helping all people with hearing impairment by helping audiologists to find out how prevalent cochlear dead regions are and to determine when and to whom the TEN test should be presented.

Disadvantages: All procedures in our testing sessions are well established clinical practices, which pose no risk to you. Apart from the time required to perform the tests, there are no foreseeable disadvantages.

Testing Venue: The testing will take place in one of these locations: Audiology Research Unit in the University of British Columbia, The Western Institute for the Deaf and Hard of Hearing, WorkSafe BC, Vancouver General Hospital, or a private clinic downtown depending on your existing hearing care provider.

Confidentiality: All information that is collected from you will remain confidential. Your identity will be recorded using a code known only to the researchers and only group results, or coded individual results, will be given in any reports about the study. Coded results only (no personal information) will be kept in computer files on a password protected hard drive. Your confidentiality will be respected. No information that discloses your identity will be released or published without your specific consent to the disclosure. Research records and medical records identifying you may be inspected in the presence of the Investigator or their designate by representatives of Health Canada, and the UBC Research Ethics Board for the purpose of monitoring the research. However, no records which identify you by name or initials will be allowed to leave the Investigators' offices.

Consent for Subject to Participate:

I, _____, have read the above study consent form and I consent to participate in this study undertaken by Dr. Navid Shahnaz at the School of Audiology & Speech Sciences at UBC. The researcher assures me that my participation in this experiment is completely voluntary and that I may withdraw from this research at any time without consequences. I understand that I am not waiving any of my legal rights as result of signing this consent form.

If I have any question or desire further information with respect to this study, I may contact Dr. Navid Shahnaz at 604-822-5953. If I have any concerns about my treatment or rights as a research subject, I may contact the Research Subject Information Line at the University of British Columbia Office of Research Services, at 604-822-8598.

I have received a signed and dated copy of this consent form for my records.

Printed name of Participant	**Participant's Signature**	**Date**

Printed name of Witness	**Witness's Signature**	**Date**
Printed name of Investigator	**Investigator's Signature**	**Date**

Appendix IV – Invitational Letter

The University of British Columbia, Western Institute for the Deaf and Hard of Hearing, Vancouver General Hospital, and WorkSafe BC

Invitational Letter

Project Title: Cochlear Dead Regions – A Prevalence Study in Different Audiological Settings

Principal Investigator:
Dr. Navid Shahnaz
Assistant Professor,
School of Audiology & Speech Sciences
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Co-investigators:

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School of Audiology and Speech Sciences
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Tel: 778-988-6373

Grace Shyng
M.Sc., Aud (C)
Clinical Assistant Professor
Western Institute for the Deaf and Hard of Hearing
Tel: 604-736-7391

Nirvana Kiarostami
M.Sc., Aud (C)
Audiologist Advisor & Clinical Assistant Professor
WorkSafeBC
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Dr. Lorienne M. Jenstad
Assistant Professor
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Amir Soltani
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Clinical Assistant Professor
Downtown-Island Hearing Services
Tel. 604- 688- 5999

Leigh Bush
M.Sc., Aud (C)
Senior Audiologist
Vancouver General Hospital
Tel. 604-875-4111 ext 67962

Mark Hansen
M.Sc., Aud (C)
Owner/Director
Sound Hearing Clinic
Downtown & South Vancouver
Tel. 604-687-1488

Dear Potential Participant,

Audiology is a branch of science that is constantly growing. Researchers are always working to find better ways of testing and treating hearing loss. Recently, a new test has been devised that provides an audiologist with more specific information about exactly what is occurring within the ear when we have difficulty hearing. This test is called the Threshold-Equalizing Noise Test, or TEN test. It uses a special type of masking noise that allows an audiologist to tell if a condition called a cochlear dead region is present. By measuring a patient's responses to a tone hiding in the noise, an audiologist can tell where precisely the nature and location of the damage in a person's ear is; that is to say, s/he can tell if a cochlear dead region is present. Knowing this information can be helpful when deciding how to treat a person's hearing loss; it can assist the audiologist in decisions regarding hearing aids, and the audiologist give detailed information to the patient about the nature of his/her pathology and what to expect during treatment.

You are being invited to take part in this study because you have a hearing loss about which we would like to know more. By using the newly developed TEN test, we hope to find out if you have a specific type of hearing loss called a cochlear dead region. The main goal of this study is to find out how prevalent cochlear dead regions are within the population of people with hearing losses similar to yours. Information provided by this study will helps audiologists decide when to administer this test and what people are more likely to have a cochlear dead region. If a cochlear dead region is found in your ear, we will inform your audiologist about the best way to treat your hearing loss. If no dead region is found, we will have gained a lot of information about the prevalence of this disorder in people with your type of hearing loss.

If you agree to take part in this project, you will be invited in to an audiologist's office to undergo a test that will take approximately 20-25 minutes. You will be listening to a noise and asked to push a button or raise your hand when you hear a tone hiding in the noise. The test uses existing clinical techniques and poses no risk to your ear or hearing. The testing will take place in one of these locations: The Western Institute for

the Deaf and Hard of Hearing, WorkSafe BC, Vancouver General Hospital, or a private clinic downtown depending on your hearing care provider.

Thank you for considering participation in this research project. **If you are interested in participating, please contact Dr. Shahnaz at 604-822-9474 or 604-822-5953 for more information at any time.**

_____

Dr. Navid Shahnaz, Principal Investigator

Appendix V – Vancouver General Hospital Ethics Form

1. Research Study Title (and Protocol Number, if applicable):
Cochlear Dead Regions – A Prevalence Study in Different Audiological Settings

2. PI (VCH Site Investigator):	**3. Department: Audiology**	**4. Co-Investigators: Nerissa Davies, Nirvana Kiarostami, Leigh Bush, Mark Hansen, Grace Shyng, Lorienne Jenstad**
Name: Navid Shahnaz Tel: 604-822-5953 Fax: 604-822-6569 Email: nshahnaz@audiospeech.ubc.ca	**Division: Neuro-Otology**	

5. Contact Person:	**6. Internal Mailing Instructions / Address:**
Name: Navid Shahnaz Tel: 604-822-5953 Fax: 604-822-6569 E-mail: nshahnaz@audiospeech.ubc.ca	Leigh Bush Gordon and Leslie Diamond Healthcare Centre 4th Floor, Neuro-Otology 2775 Laurel Street

7. Type of Funding Source: ☐ Industry ☐ Grant ☐ Grant-in-Aid X Unfunded ☐ Other

8. Name of Funding Source(s): n/a

9. Type of Study: ☐ Drug/Natural Health Product Study ☐ Medical Device Study ☐ Chart Review X Other:Hearing test
If a drug/natural health product will be administered to human subjects, obtain a signature of approval on this form from the Pharmacy Department.

10. Vancouver Acute services or resources used in the research study.			**11. Approval signatures required.**			**12. Department cost analysis.**	
Department	**Yes**	**No**	**VGH Site Name of Signatory**	**UBC Hospital Site Name of Signatory**	**Signature**	**Yes**	**No**
Pharmacy	☐	☐				☐	☐
Radiology (MRI, CT, x-ray, ultrasound, etc.)	☐	☐				☐	☐
Clinical Chemistry	☐	☐				☐	☐
Microbiology	☐	☐				☐	☐
Operating Rooms	☐	☐				☐	☐
Anatomical Pathology	☐	☐				☐	☐
Hematopathology	☐	☐				☐	☐
Clinical Unit (1):	☐	☐				☐	☐
Clinical Unit (2):	☐	☐				☐	☐
Clinical Unit (3):	☐	☐				☐	☐
QUIST	☐	☐				☐	☐
Health Records (hard copy)	☐	☐				☐	☐
VCH database: (e.g. PACS, ORMIS, PCIS)	☐	☐				☐	☐
Other database:	☐	☐				☐	☐
Other Resources: (Specify)	☐	☐	Neuro-Otology Leigh Bush			☐	☐

13. **P.I.'s Department Head at Vancouver Acute <u>if different</u> from Department Head who approved the UBC ethics application:**

(print name) (signature) (date)

14. **P.I.'s Division Head:**

(print name) (signature) (date)

NOTES:

15. **P.I.'s Supervisor/Manager:** (See Guidance Notes – Applicable to VCH employees only.) n/a (print name) (signature) (date)	
16. **Principal Investigator:** **Navid Shahnaz** (print name) (signature) (date)	

17. STUDY PERSONNEL: a) The Principal Investigator on this research study (one of the following must apply - select one only): 1. Has a medical appointment at VCH 2. Is an employee of VCH (e.g., nurse, respiratory therapist, manager) 3. Has a VCHRI Affiliated Investigator Appointment 4. Is in the process of applying for a VCH Affiliated Investigator Appointment ***If the Principal Investigator has a VCHRI Affiliated Investigator Appointment, he/she must have a VCH co-investigator named on the research study (on this form and the UBC REB ethics certificate). ***If the Principal Investigator does not fall under one of the above categories, please contact Stephania Manusha at (604) 875-5649 or stephania.manusha@vch.ca b) Will research personnel **not employed by /affiliated with** VCH (e.g. volunteer research assistants, research personnel affiliated with external institutions) participate in the conduct of this study? If YES	☐Yes ☐ No ☐Yes ☐ No ☐Yes ☐ No ☐Yes ☐ No ☐Yes ☐ No
18. PERSONAL HEALTH INFORMATION: a) Will you access identifiable personal information of VCH patients/clients/residents/staff in this research study (e.g., medical records are reviewed and the patient's name is known)? If YES, complete the Security & Confidentiality form (this form may be downloaded from the VCHRI website). Please ensure that the VCH Privacy Office has signed the form before it is submitted to VCHRI.	☐Yes ☐No
19. QUIST, HEALTH RECORDS AND VCH DATABASES: a) Will this research study involve the services of QUIST? (If YES, obtain a signature of approval from QUIST on this form.)	☐Yes ☐No
b) Will you require access to patient medical records located in a Vancouver Acute Health Records Department? (If YES, obtain a signature of approval from the appropriate Health Records Department on this form.)	☐Yes ☐No
c) Will you review patient medical records located in a clinician's office, hospital clinic/ward or hospital department located on the Vancouver Acute Site? If YES, advise where the patient records are located:	☐Yes ☐No
d) Will you require access to a VCH database (e.g. PACS, ORMIS etc.)? If YES, list the database(s) you will require access to: If YES, obtain a signature of approval to use the database for research purposes from the appropriate VCH department.	☐Yes ☐No

e) Will you require access to any <u>internal department/program databases</u> (e.g. orthopedic-trauma database)?	☐Yes ☐No
If YES, which internal database(s)? If YES, do you have approval to retrieve data from the database(s)? (If NOT, obtain a signature of approval from the department/person in charge of the database on this form.)	☐Yes ☐No

20. STUDY PROCEDURES/ASSESSMENTS: For research studies that <u>do not</u> involve the participation of human research subjects or the utilization of VCH Anatomical Pathology diagnostic material (e.g. microscopic slides, tissue blocks or tissue specimens?), this section is not applicable.	☐ **SECTION 20** Not Applicable
a) Will research subject recruitment occur on a hospital ward/clinic? (If YES, a signature of approval from the patient service manager of <u>each</u> hospital ward/clinic must be obtained.) If YES, list the hospital ward(s)/clinics where research subjects will be recruited from:	☐Yes ☐No
b) <u>Where</u> will patient informed consent be obtained? (NOTE: If informed consent will be obtained on a hospital ward/clinic, a signature of approval from the applicable patient service manager must be obtained.)	
c) Will any research study visits/assessments/ take place on a hospital ward or clinic? (If YES, A signature of approval from the patient service manager of <u>each</u> hospital ward or clinic impacted must be obtained.)	☐Yes ☐No
d) If a questionnaire will be administered, where will this occur? e) If a focus group will be held or interview conducted, where will this occur?	☐ N/A ☐ N/A
f) Will research subjects undergo any surgical procedures in the **<u>OPERATING ROOM</u>**? **If YES, a signature of approval from the Operating Room* must be obtained on this form. Prior to signing off on this form, the OR must receive a completed "OR Research Form" and a copy of the study protocol.**	☐Yes ☐No
g) Will tissue specimens be collected from subjects in the **<u>OPERATING ROOM</u>**? If YES, both the Operating Room and Anatomical Pathology must review the study. **<u>STEP 1:</u>** Anatomical Pathology must review the research study protocol, the "Anatomical Pathology Laboratory Utilization Form", The "Specimen for Research Collection – Special Handling Instructions" form and sign the "Request for Approval to Conduct Research at Vancouver Acute" form. **<u>STEP 2:</u>** Once Anatomical Pathology has signed off, the OR must receive and review all documentation outlined above in 20f as well as the "Specimen for Research Collection – Special Handling Instructions" form with Anatomical Pathology's signature of approval. ***REMINDER: Tissue specimens collected in the Operating Room may <u>NOT</u> be picked up from the Operating Room – all tissue specimens must be sent to VCH Pathology. For further information, please see the guidelines posted on the VCHRI website titled***	☐ Yes ☐No

h) Will **VCH ANATOMICAL PATHOLOGY** process tissue specimens collected in the Operating Room or tissue specimens collected in a VCH ward or clinic? If YES, the procedures in 20g (STEP 1 and STEP 2) above must be followed. In addition, the VCH Pathologist involved must be listed as a co-investigator on the research study (on	☐ Yes ☐ No ☐ N/A
i) Does this study involve the utilization of **VCH ANATOMICAL PATHOLOGY** diagnostic material (e.g. microscopic slides, tissue blocks or tissue specimens?) If YES, Anatomical Pathology must review the research study protocol, the "Anatomical Pathology Laboratory Utilization Form", and sign the "Request for Approval to Conduct Research at Vancouver Acute" form.	☐ Yes ☐ No

21. EXTERNAL RESOURCES: a) If VCH will not be performing part of the study (i.e. lab-work, x-rays, CT scans), please advise which procedures will be performed externally and advise who will be performing the procedure and/or analysis:	☐ N/A

22. ADVERTISEMENTS: a) Will any advertisements for recruitment be posted in a hospital ward/clinic? (If YES, a signature of approval from the applicable patient service manager of the hospital ward/clinic must be obtained.)	☐ Yes ☐ No
b) Will any advertisements for recruitment be posted in any general areas of Vancouver Acute (e.g. elevators in JPP)? If YES, once the recruitment advertisement has been approved by the REB, please forward an electronic copy of the recruitment advertisement to Lisa Carver (lisa.carver@vch.ca). Please cc Stephania Manusha stephania.manusha@vch.ca) on the email.	☐ Yes ☐ No

Please submit the following documentation to VCHRI for review:

☐ "Request for Approval to Conduct Research at Vancouver Acute" form with signatures of approval
☐ One copy of the UBC ethics board application

If applicable, please also submit the following documentation:

☐ One copy of the informed consent form(s)/letter of initial contact
☐ One copy of the Health Canada Notice of Compliance or Medical Device License
☐ One copy of the "Security & Confidentiality Review and Agreement for Access to Personal Information for Research Study/Project Purposes"
☐ One copy of the "VCHRI Medical Device Form" (required for studies involving an experimental medical device)
☐ One copy of the "OR Research Form" (required for all studies involving surgical procedures)
☐ One copy of the "Anatomical Pathology Laboratory Utilization Form" (required for studies involving the services of Anatomical Pathology)
☐ One copy of the "Specimen Collection for Research – Special Handling Instructions" form (required for studies involving the collection of tissue in the operating room)
☐ One copy of the Study Protocol - Flowchart of Activities (for industry/grant funded studies, where such a flow chart exists).

The VCHRI research submission should be sent to the following address:

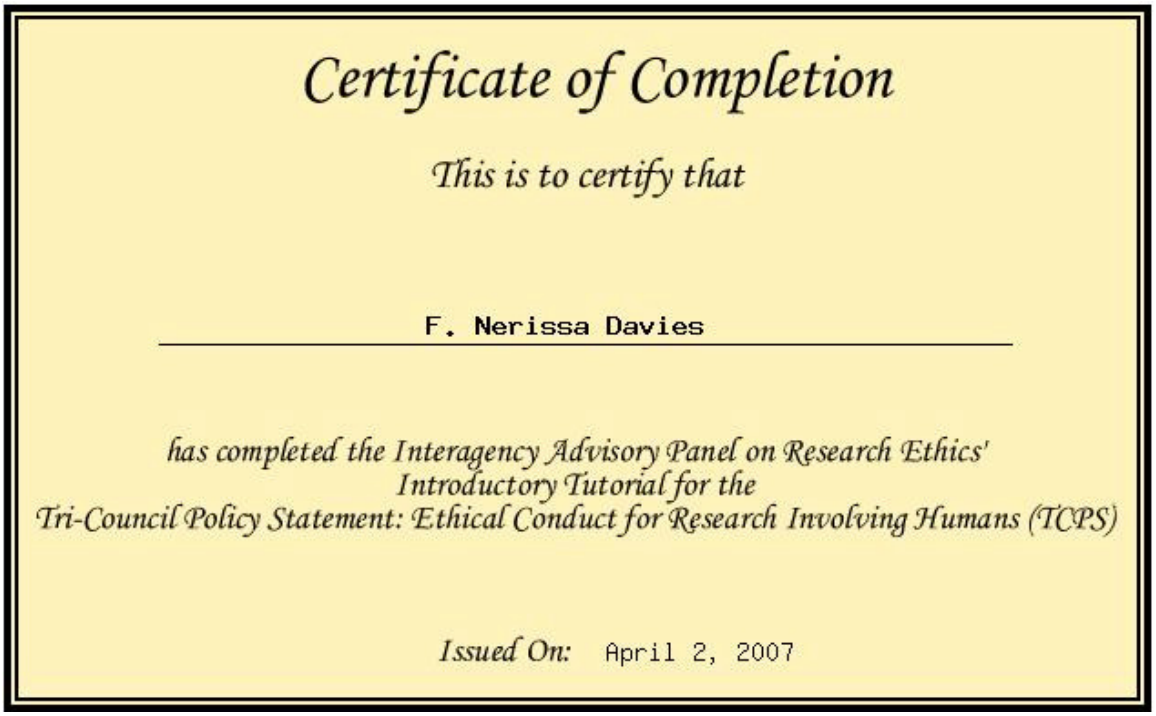
Attention: Wylo Kayle
Willow Chest Centre – Room 163

2647 Willow Street

Vancouver, BC V5Z 3P1

If you have any questions, please contact Wylo Kayle at 604-875-4111 Ext 68368 or wylo.kayle@vch.ca

Appendix VI – UBC Ethics Certificate



Certificate of Completion

This is to certify that

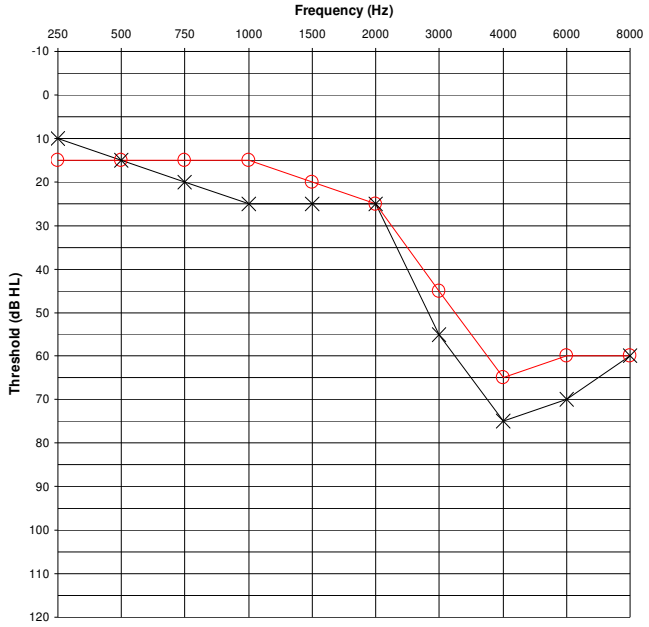
F. Nerissa Davies

has completed the Interagency Advisory Panel on Research Ethics'
Introductory Tutorial for the
Tri-Council Policy Statement: Ethical Conduct for Research Involving Humans (TCPS)

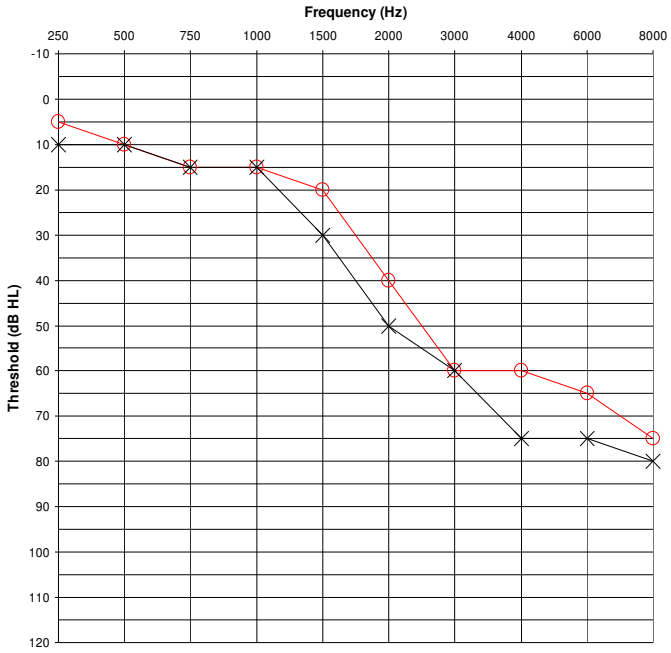
Issued On: April 2, 2007

Appendix VII – Dead Region Positive Audiograms

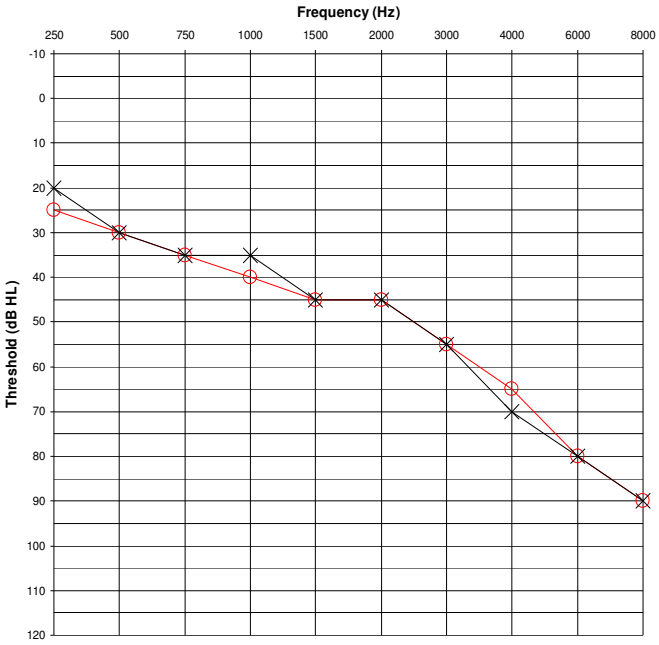
CDR012 – age 68
DR + at 4 kHz both ears
CNT reflex (loudness intolerance)
Passed DD
Passed RGDT



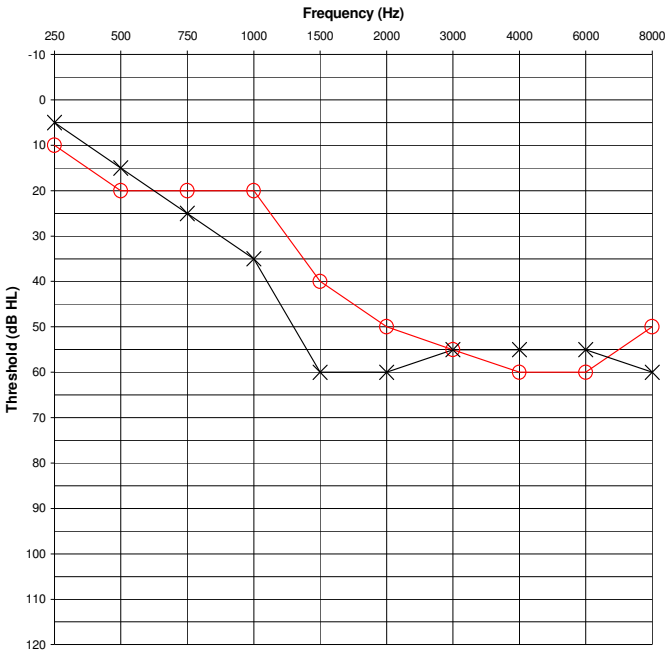
CDR013 – age 61
DR + at 3000 and 4000 Hz in right ear
at 4 kHz in the left
Passed reflex
Failed DD
Passed RGDT



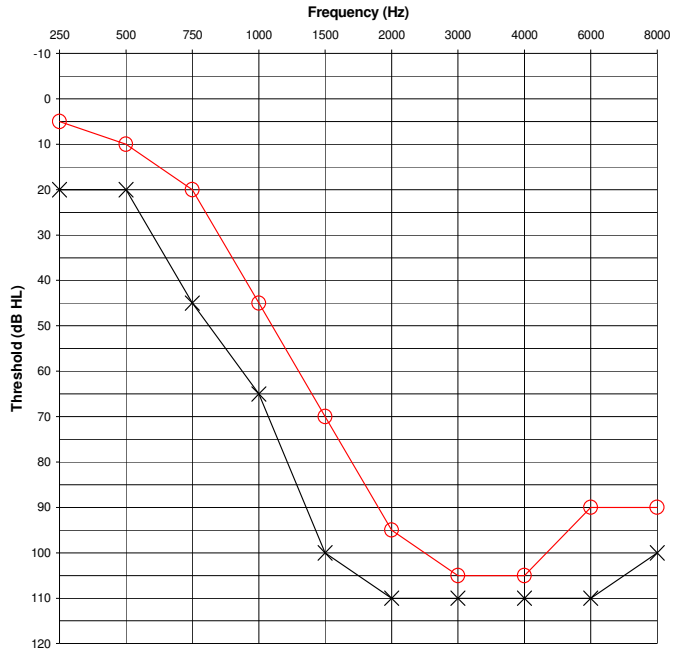
CDR016 - age 74 - FEMALE
DR + at 4 kHz in the right ear
Passed reflex
Failed DD
Passed RGDT



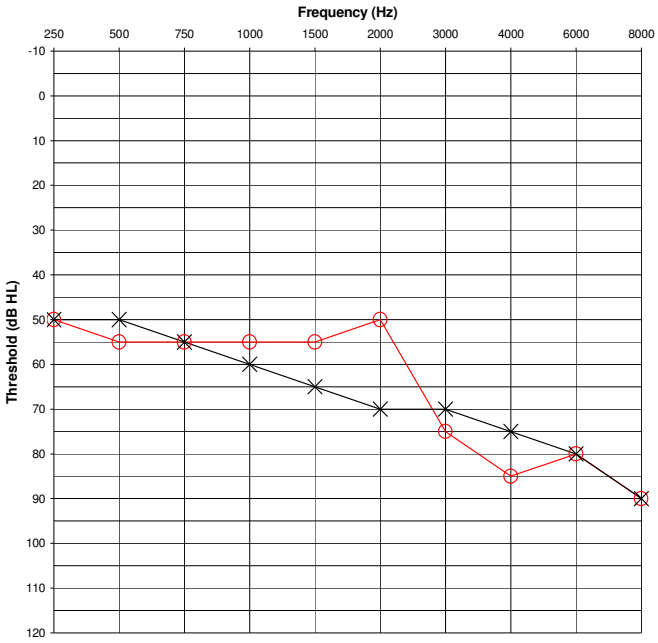
CDR 017 – age 67
DR + at 4 kHz in both ears
Passed reflex
Failed DD
Failed RGDT



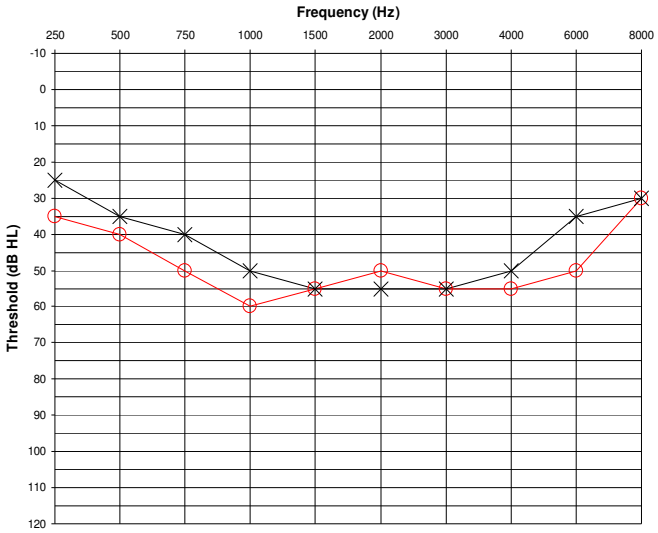
CDR 023 – age 64
Inconclusive in the left ear; beyond limits of equipment – but subject reports tones sound like wind noise or ssshhh at 3000 and 4000 Hz (2 kHz sounds like tone)
Right ear DR positive from 1500 – 4000 Hz. (3 and 4 kHz inconclusive but presumed DR). Tones started sounding like noise at 2 kHz.
Passed reflex
Passed RGDT
Failed DD



CDR 032 – age 55
DR + at 4 kHz in both ears
Failed reflex
Passed DD
Failed RGDT



CDR038 – age 36
DR + at 4 kHz right ear
Passed reflex
Passed DD
Passed RGDT
Age 36, Male



CDR 055 – age 71
DR + at 1500 Hz right ear
Beeps sounded like beeps
Passed reflex
Failed DD
Failed RGDT