ABSTRACT

Title of Document: DEVELOPMENT OF AN EVIDENCE BASED REFERRAL PROTOCOL FOR EARLY DIAGNOSIS OF VESTIBULAR SCHWANNOMAS

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Doctor of Audiology, 2008

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The purpose of this investigation was to identify the presenting symptoms and testing outcomes that were most suggestive of a potential vestibular schwannoma and to propose an audiological referral protocol for MRIs. To that end, a retrospective chart review was conducted to examine radiologic, audiometric, and case history information from patients at Walter Reed Army Medical Center who were referred to the Department of Radiology to rule out retrocochlear pathology. Charts of 628 patients were reviewed from their electronic medical records, although the final patient sample was 328 patients who had complete audiologic data. Analyses were conducted to compare the unaffected and affected ears of the positive MRI group to the better and poorer ears of the negative MRI group. Results were significant between the affected ear of the positive group and the poorer ear of the negative group for pure tone thresholds, speech discrimination scores, and acoustic reflex thresholds. Significant differences between the groups were not generally seen for the comparison of the unaffected ear to the better ear, with the exception of acoustic reflex thresholds. The interaural difference between ears was significant between the two groups for pure tone thresholds and speech discrimination scores; however, the difference was not significant for acoustic reflex thresholds. For all significant differences between the groups, the positive MRI group evidenced poorer audiological results. Additionally, three symptoms/outcomes that led to the patients' referral were significantly different between the two groups: unilateral tinnitus, asymmetrical word recognition, and positive rollover in speech recognition scores. Logistic regression was applied to the audiological tests and symptoms to determine the most predictive set of variables that differentiated between the patients with a positive and negative MRI. The most predictive model yielded a sensitivity of 81.25% and a specificity of 82.59% when applied to the current patient sample. The audiological profile identified may be useful for clinicians in deciding whether their patient should be referred for an MRI to rule out the presence of a vestibular schwannoma.

DEVELOPMENT OF AN EVIDENCE BASED REFERRAL PROTOCOL FOR EARLY DIAGNOSIS OF VESTIBULAR SCHWANNOMAS

By

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Dissertation submitted to the Faculty of the Graduate School of the
University of Maryland, College Park, in partial fulfillment
of the requirements for the degree of
Doctor of Audiology
2008

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Dedication

This dissertation is dedicated to the men and women who honorably serve our country in the United States Military. In addition, this milestone could not have been reached without my family’s inspiration to fulfill my dreams.

Acknowledgements

The author gratefully acknowledges all the insight and contributions of the dissertation committee members: Drs. Sandra Gordon-Salant, Tracy Fitzgerald, Yasmeen Faroqi-Shah, Carmen Brewer, and Robert Dooling. Thank you all for dedicating your time and for always being flexible throughout this project. The author also graciously acknowledges Dr. Sandra Gordon-Salant for her continued mentorship and support over the years and for her unbelievable dedication to the completion of this dissertation. The author would like to recognize the staff at the Walter Reed Army Audiology and Speech Center for their encouragement throughout all of the stages of this investigation. Specifically, the author acknowledges Dr. Therese Walden and the entire staff of the Research Section of the Walter Reed Army Audiology and Speech Center for dedicating their time, expertise, and resources to this investigation. Thank you to Dr. Gregory Hancock for his knowledgeable assistance on the statistics for this study. Finally, the author is thankful for the support and motivation of her family and friends.

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Chapter 1: Introduction

A vestibular schwannoma (VS) (otherwise known as an acoustic neuroma, acoustic neurinoma, or acoustic neurilemoma) is a slow growing, benign tumor that develops on the balance or hearing nerve [inferior or superior portion of the vestibulocochlear nerve (CN VIII)]. The tumor is caused by an overproduction of Schwann cells, usually originating from the vestibular branch of CN VIII; hence the name. Schwann cells wrap around nerve fibers to help support and insulate the nerves, which facilitates conduction. An overproduction of these cells causes the benign tumor to press upon and compress the vestibulocochlear nerve or other surrounding structures. This can cause multiple symptoms that are audiological, vestibular, or otologic in nature. Some commonly reported symptoms are hearing loss, tinnitus (ringing or other subjective noise in the ear), dizziness or vertigo (sensation of spatial rotation or spinning), aural fullness, and otalgia (ear pain). The symptoms are usually unilateral or asymmetric with more severe symptoms present on the side of the lesion. The tumor can also compress the facial (CN VII) or trigeminal (CN V) nerve causing facial paralysis (CN VII) or facial numbness/pain (CN V), or it can press upon the labyrinthine artery, which supplies the blood to the inner ear. The effect on these other structures occurs because they run parallel to the CN VIII in the internal auditory canal (IAC) or areas outside of the canal. The IAC is a bony canal in the petrous portion of the temporal bone that houses CN VIII and CN VII together with the labyrinthine artery. Trigeminal nerve (CN V) involvement usually occurs as the tumor extends from the lateral pons. VSs are benign; however, their severity and risk of morbidity is of concern due to their location and tendency to grow into the cerebellopontine angle (located at the brainstem) and compress the brainstem structures (Cummings et al., 2005).

VSs are thought to account for approximately 8% of tumors arising in the skull with an annual incidence of approximately one in every 100,000 people (National Institute on Deafness and Other Communication Disorders, 2004). Women tend to have a slightly higher incidence than men (3:2 ratio). VSs are usually diagnosed in middle age (30-60 years old); however, VSs have been documented in all age groups including rare cases of sporadic unilateral VS in children (Mazzoni, Dubey, Poletti, & Colombo, 2007). The slow growing tumors are usually sporadic and unilateral, although some patients have bilateral schwannomas. These patients typically have a disease known as Neurofibromatosis II. Neurofibromatosis II (NF2) is a disease that involves nervous system and skin tumor growth as well as ocular abnormalities. None of the patients in this retrospective analysis presented with bilateral VS; therefore, NF2 will not be discussed further.

With recent advances in diagnostic technology and the increasing availability of magnetic resonance imaging (MRI) technology, the incidence of identification of VSs has been rising. Technological advances have been instrumental in identifying smaller tumors that were largely undetectable by past technologies. The new identification of small tumors has also resulted in diagnosis at a younger age (Stangerup, Tos, Caye-Thomasen, Tos, Klokker, & Thomsen, 2004; Tos, Stangerup, Caye-Thomasen, Tos, & Thomsen, 2004).

There are many tests that can potentially indicate the presence of a VS, including audiological, vestibular, evoked potential, and radiologic investigations.

Audiometric testing can include pure-tone audiometry, speech audiometry [especially speech discrimination scores (SDS)], acoustic reflex thresholds, and acoustic reflex adaptation (or acoustic reflex decay). Vestibular testing can include electronystagmography (ENG) or videonystagmography (VNG) evaluations, rotational testing (rotary chair) and more recently, vestibular evoked myogenic potentials (VEMP). Evoked auditory potential evaluations can include auditory brainstem response (ABR) and electrocochleography (ECochG). Finally, radiologic investigations are responsible for identifying or confirming suspected VSs. Radiologic imaging investigations use either computerized tomography (CT scans) or magnetic resonance imaging (MRI).

The most definitive test for diagnosis of a VS is MRI. The final confirmation, however, cannot be made until histological examination of the lesion is performed. The “gold standard” MRI for use in diagnosing potential VSs is a contrast-enhanced MRI of the IACs. The contrast agent used for imaging is a dye made with gadolinium, which is a paramagnetic metal ion. It is used to provide a greater contrast between normal and abnormal tissue because it accumulates in abnormal tissue causing those areas to become enhanced. Gadolinium contrast is generally safe; however, the FDA has issued a warning that it can be dangerous to individuals with renal dysfunction or if there are repeated or high doses of the contrasting agent. For these and other reasons, MRI may be performed with or without the contrasting agent (Cummings et al., 2005). The decision to perform a MRI with or without contrast is usually made by the radiologist, except when it is specified in the referral.

MRI scans can be problematic because they are not available in all locations, there are many patient contraindications to testing, and they are expensive compared to other screening measures. There is essentially no risk to an MRI above normal everyday occurrences; however, additions to the MRI test, such as sedation or use of contrast, introduce some risk. Individuals must be very still during MRI testing. Movement can cause blurred areas and artifacts in the film, which can create difficulties for the radiologist or other medical personnel reading the film. If there is a patient at risk for excessive movement, for example a child, sedation may be needed; however, sedation carries risks not usually associated with non-invasive MRI. Other physical contraindications for MRI scanning include metallic materials or other foreign objects in the body (e.g., pacemakers, metal implants, heart valves, bullet fragments), chemotherapy, or use of insulin pumps. The reason for these contraindications is due to the metallic properties of the items which are inside the patient’s body. The magnetism of the MRI could potentially move or pull at the metal which can blur the MRI image or cause pain, discomfort, or permanent damage to the patient. Patient factors could present other contraindications such as claustrophobia or the physical size of the patient (Edelman & Warach, 1993). Because of these issues, including cost, it is important to reduce the amount of over-referrals for MRI.

The goal of this investigation was to identify the principal symptoms and audiologic characteristics of patients with a confirmed diagnosis of VS via MRI testing. An evaluation of the presenting symptoms and test outcomes between the patients with a VS compared to those who were not diagnosed with a VS, was conducted to identify the most definitive characteristics that differentiate the two groups. The resulting characteristics were used to suggest an effective audiological referral protocol for MRI to rule out VSs in order to improve the specificity and sensitivity of the current referral rates. Specificity is defined as the proportion of patients without a pathology to be correctly identified as negative on a test, whereas the sensitivity of the referral is defined as the proportion of patients with a specific disease that are correctly identified with the pathology (The American Heritage Stedman's Medical Dictionary, 2008*)*. The database in the current study was drawn from patients at Walter Reed Army Medical Center (WRAMC), a large hospital serving the medical care needs of active duty military personnel and their families, as well as retired military and other government personnel. All of the patients in this analysis received their radiologic imaging at WRAMC; however, some of the previous radiologic imaging used (e.g., routine MRI monitoring) was performed at other military facilities. As part of the military health care system, the cost of a medical procedure is not a confounding factor on the MRI referral; therefore, the population investigated in this study was free from the cost-related bias for MRI referral. One factor that challenges the generalizability of the results to the general population is that the study group tended to have a history of hazardous noise exposure because of military service; however, there were many patients in the sample who had no prior history of noise exposure (e.g. spouses, dependents, etc.). Nevertheless, this sample was assumed to include a greater proportion of patients with noise-induced hearing loss compared to the population of civilian patients. Regardless of this limitation, the population at WRAMC presents a unique opportunity to investigate the audiological presentation of VSs because of the comprehensive nature of the evaluation (audiology, otolaryngology, MRI, etc.) and the large number of patients available. The purpose of this investigation was to develop a set of highly predictive symptoms and audiological test results that led to a diagnosis of VS. The resulting referral criteria were intended to reflect the most predictive symptoms and tests with the intent of creating a more sensitive and specific referral protocol than currently appears to be available.

Chapter 2: Literature Review

Presenting Symptoms

General information. Patients usually come to a clinic because they have a set of symptoms or complaints in need of evaluation. The most common presenting symptom of patients with a unilateral VS is hearing loss. Although a majority of patients with a VS present with progressive, asymmetric, or unilateral hearing loss, there is a small percentage of cases in which the hearing is normal or symmetric. A patient with normal pure-tone thresholds can present with a “normal” perception of sound or some distorted quality in the signal that cannot be explained by the pure-tone thresholds on the audiogram. Although the majority of patients exhibit gradual hearing dysfunction, approximately 10% of patients with a VS report one or more instances of sudden onset hearing loss (National Institutes of Health, 1991). Together with hearing loss, other early signs of a VS are unilateral tinnitus and the presence of dizziness or disequilibrium. Later symptoms of VSs are suspected to result from the compressive attributes of the tumor. These later manifestations can include headaches, ataxia, cerebellar signs, and cranial nerve neuropathies. Cranial neuropathies are more prevalent in CN V and CN VII, although others have noted neuropathies of CNs VI, IX, X, and XII. The NIH Consensus Statement (1991) noted that patients suspected of having a VS should be evaluated using a thorough clinical and family history (especially for history of NF2), a physical evaluation with special focus on cranial nerve function, an examination for cataracts, and audiovestibular testing. For audiometric testing, the report suggested air- and bone-conduction testing, speech reception threshold (SRT), speech discrimination scores (SDSs), acoustic reflex thresholds, and acoustic reflex decay. Vestibular testing, according to the consensus, is less useful in the actual diagnosis of a VS, but it may be beneficial for predicting postoperative balance and hearing preservation (National Institutes of Health, 1991).

VSs have stages of growth that may or may not coincide with their presenting symptoms. The first stage is intracanalicular, which is thought to involve symptoms of hearing loss, tinnitus, and vertigo. As the schwannoma grows it becomes cisternal (a cavity or space which serves as a reservoir for some liquid; American Heritage, 2008) which could bring increased hearing loss and more constant disequilibrium rather than vertiginous episodes. The third stage is brainstem compression when facial and corneal hypesthesia (partial loss of sensation; diminished sensibility; American Heritage, 2008) can begin. This stage is also associated with headaches and ataxia (loss of muscular coordination following damage to the central nervous system). Finally, there is hydrocephaly (accumulation of cerebrospinal fluid causing compression and injury to brain tissue; American Heritage, 2008), producing more trigeminal nerve involvement, lower cranial nerve involvement, and co-morbidity factors to occur (Cummings et al., 2005). The tumor is thought to grow the greatest amount in the early years following diagnosis, and then growth tapers off in the following years with occasional shrinking of the lesion (Stangerup, Caye-Thomasen, Tos, & Thomsen, 2006). Although it is assumed that particular symptoms coincide with different stages of tumor growth, there is a significant overlap in the actual presenting symptoms with differing tumor sizes. The high variability in the symptoms is due to different effects of compression and infiltration of the tumor on the cranial nerves and the labyrinthine artery inside and around the IAC.

Symptomatic clinical presentation. Matthies and Samii (1997) described the clinical presentation of 962 patients (1000 total tumors) with known VSs. There were 420 males and 522 females aged 11-86 years old ($M = 46.3$). The average age between genders was not significantly different. The investigators retrospectively analyzed preoperative data, including radiologic findings, case histories, neural examination, and audiometric testing. The best preoperative hearing was noted in younger patients, with increasing age associated with decreasing preoperative hearing thresholds (Matthies & Samii, 1997). The older patients' thresholds could have been affected by presbycusis, which was not accounted for in the analysis. Matthies and Samii found that cochlear nerve involvement was the most frequent presenting symptom (95%). Cochlear nerve involvement referred to the presence of hearing loss and/or tinnitus. Sudden hearing loss was experienced in 16% of the patients at some point in their audiologic history, which led to complete deafness in one fifth of these patients. Tinnitus (included under cochlear nerve involvement) was present in 63% of the patients ($n = 532$). Tinnitus was more prevalent in hearing (51%, $n = 432$) versus deaf ears (12%, $n = 100$), although 46% ($n = 100$) of the deaf ears ($n = 219$) experienced tinnitus. Vestibular symptoms were observed as the second most common symptom, and were found in 61% ($n = 514$) of the patients. This percentage was abnormally high compared to other studies, which report vestibular symptoms in about 10% of VS patients (Moffat, Baguley, von Blumenthal, Irving, & Hardy, 1994; Moffat, Jones, Mahendran, Humphriss, & Baguley, 2004). However, it was similar to studies investigating patients with normal hearing or symmetric hearing loss (Beck, Beatty, Harner, & Ilstrup, 1986; Lustig, Rifkin, Jackler, & Pitts, 1998; Magdziarz, Wiet, Dinces, & Adamiec, 2000). Of the 61% of patients with vestibular symptoms, 31% (*n* = 265) reported only one vestibular symptom, while 30% (*n* = 249) reported a combination of vestibular symptoms (e.g., vertigo, dizziness, general unsteadiness). Symptoms indicative of trigeminal nerve dysfunction were the third most common in patients (7-9%). The authors postulated that the onset of trigeminal nerve symptom(s) is typically two years after the onset of cochlear nerve symptom(s) and one year after the onset of vestibular symptom(s). Frequency of cranial nerve involvements, as evidenced by surgical inspection, was notably higher than the frequency of symptoms noticed by the patient. This finding suggests that there was more extensive anatomical damage than expected from the severity of the patients' presenting symptoms. These observations were consistent with a report by Forton, Cremers, and Offeciers (2004) who found that the ingrowth of a VS into the CNVIII had no increased effects on hearing compared to patients without ingrowth. The authors estimated that only one to two thirds of the anatomical cranial nerve disturbances associated with VSs are reported based on the patients' symptoms, which supported the higher incidence of neural damage compared to the incidence of patient symptoms (Matthies and Samii, 1997).

The investigation by Matthies and Samii was well documented and reviewed the clinical presentation of a very large number of VS patients; however, one of the well known traits of VSs is their varied presentation. The investigation strictly reported the history and audiovestibular symptoms of those patients positively diagnosed with a VS. There was no control group analyzed without the presence of a VS. Many of the results presented were descriptive group comparisons. The addition of statistical analysis would have validated their study's conclusions. There was also a large range of ages in the population, which could potentially account for some of the trends and inverse relationships observed between age and the symptom characteristics. As with most retrospective analyses, the data were collected at different times by different medical professionals; therefore, it can be assumed that there are some inconsistencies in the reporting, suggesting a potential limitation in the validity of the results. This problem is inherent in retrospective studies, and often cannot be avoided.

Baguely, Humphries, Axon, and Moffat (2006) retrospectively investigated data from 941 patients with unilateral VSs. There were 487 males and 454 females with an average age of 54.3 years (no range given). The patients were seen between the years 1986 and 2002, and were diagnosed by ABR, CT scan, or MRI. Data from 939 patients indicated that their initial symptom was progressive hearing loss (61%), sudden hearing loss (8%), tinnitus (12%), imbalance (11%), or some other symptom (8%). Seven hundred and seventeen patients (76%) presented with tinnitus (includes patients with tinnitus as an initial symptom and those with tinnitus accompanying another symptom), and 224 patients (24%) presented with no tinnitus. A self report of hearing was available in 935 patients. Progressive hearing loss was subjectively identified in 85.5%, sudden hearing loss in 10%, fluctuating hearing loss in 0.5%, and no hearing loss in 4%. An analysis comparing the amount of subjective hearing loss and the presence of tinnitus was significant ($n = 935$, $p<0.01$). Specifically, the patients in the sample with less subjective hearing loss were less likely to have symptoms of tinnitus (Baguely et al., 2006).

There are some inherent problems with this study. Although the authors included a large number of patients for all of the statistics, there was not a complete data set for each participant. This could introduce some variability and bias in the outcome. Moreover, audiometric results were not reported. There also was no comparison of differences in audiometric findings between tinnitus and non-tinnitus groups. This study included a very large group of patients, and data were collected from them over 16 years. Over the course of 16 years, there could have been significant variation in testing procedures or clinicians performing the tests. The change in imaging techniques over time was clearly described (i.e., ABR and CT scan to MRI imaging alone), but the potential variability in other test procedures was not addressed.

The literature indicates that the most reported or experienced symptom of a VS is hearing loss or tinnitus (Bagueley et al., 2006; Matthies & Samii, 1997). Some authors group tinnitus with hearing loss under a symptom category such as “cochlear symptoms”; however, tinnitus continues to be a principal presenting symptom in many of the cases. In symptomatic patients, there appears to be a greater emphasis on symptoms of the hearing mechanism and less on symptoms of the vestibular/balance mechanism. Although hearing loss and tinnitus continue to be the most common symptoms, other reports of trigeminal nerve involvement (Matthies and Samii, 1997) and other neurological symptoms (National Institutes of Health, 1991) have been noted in patients with VSs.

Asymptomatic or Incidental Findings. VS patients who are asymptomatic are diagnosed incidentally. Incidental findings of VSs can be found during testing or imaging for other reasons/symptoms besides following an audiovestibular presentation. The patient could also present with intermittent or non-bothersome symptoms that are not sufficiently alarming for the patient to pursue an audiologic evaluation.

Lin, Hegarty, Fischbein, and Kackler (2005) attempted to estimate the prevalence of incidental vestibular schwannomas by retrospectively evaluating data from patients who had undergone intracranial MRI testing. All MRIs of the IACs were excluded because the type of imaging suggests the test was ordered to rule out an abnormality similar to a VS. Out of 46,414 intracranial MRIs over a period of 8 years, there were 505 positive findings for a VS. The authors evaluated the charts of these patients and excluded them if they had an audiogram evidencing hearing loss or if there was any indication of subjective hearing loss, vertigo, or tinnitus prior to the imaging. Of the 505 patients with positive findings, eight cases (6 male, 2 female) were identified incidentally following MRI imaging for other symptoms, although one of the patients was referred for MRI scanning for dizziness. Each of the eight cases was detected using MRI with gadolinium enhancement. Of the eight patients, seven had available audiograms, with three of the patients' results revealing an asymmetric hearing loss. The study suggested that the prevalence of incidental VS identification was approximately 2 in every 10,000 adults. The authors noted that the prevalence of incidental VSs differed between studies because of different exclusion criteria, the number of MRIs reviewed, the geographical region, and referral patterns (Lin et al., 2005).

The above investigation was aimed at identifying the prevalence of incidental VS findings. There were no data presented, and therefore, there were no statistics to compare the individuals to each other or to a group of individuals with VSs not diagnosed through incidental findings. The authors also included only entire intracranial MRIs. The brain MRIs were reported by Lin and colleagues to have thicker slices and wider interspace gaps compared to the MRI of the IACs. The investigators noted that this may cause difficulty identifying VSs unless they are large. It is plausible that small VSs remained undetected in this study. In addition to the potential misdiagnosis by the radiologist, the investigators did not review the scans themselves nor have a second physician corroborate the findings. Not all of the MRIs were performed used gadolinium enhancement; however, the eight cases of incidental VS findings were performed using gadolinium enhancement. The absence of gadolinium contrast reduces the likelihood of identifying a VS. It is also unknown whether the initial incidental finding was the only MRI performed or if the patient received a follow-up, more specific MRI (perhaps of the IACs) to confirm the diagnosis. Finally, the lesions identified in all of the patients were not histologically confirmed, and therefore, these lesions cannot be ruled out as another form of schwannoma such as a facial schwannoma.

A similar investigation reported by Jeyakumar, Seth, Brickman, and Dutcher (2007) also investigated the prevalence of incidental VS findings using a combined retrospective/prospective study. The investigation included patients identified either prior to or during the study period, and all of their clinical follow-up was prospectively performed during the study period. The patients were followed from diagnosis until there was surgical or radiotherapy treatment. Data from a final group of 121 patients were collected; positive results from 15 (12.3%) of the patients were considered to be incidental. Findings were considered incidental if the patient was asymptomatic, and the referral for imaging studies was for reasons other than VS (Jeyakumar et al., 2007).

The number of incidental findings observed in Jeykumar et al. (2007) was substantially larger than reported in Lin et al. (2005). There are multiple possibilities to explain the difference in reports. Jeykumar and colleagues identified 15 patients with “incidental” VS findings. Although the authors claimed that the patients with “incidental” findings had no audiovestibular symptoms, the patients reported ear pain, sudden hearing loss, general hearing loss, ear pressure, tinnitus, and unsteady gait. Other symptomology included headaches, facial twitching, and facial numbness. These symptoms are also known to be associated with VSs (National Institutes of Health, 1991). Of the 15 patients who were “incidentally” identified, only five of them did not present with one or more known symptoms associated with a VS. Similar to other retrospective analyses, the authors did not collect the data themselves; therefore, it can be assumed that there may be some differences in the testing and recording of outcome measures over the course of the data collection. The patients also were described in terms of their clinical symptom presentation, although their audiological data were not clearly outlined.

Incidental findings of VS do account for a small percentage of the diagnosed patients with this disorder. The studies investigating the prevalence of incidental findings are variable because of the patients who are included in the studies and the approach taken in reviewing the cases. It can be expected that a larger proportion of patients with a VS would be defined as "incidentally diagnosed," as reported in Jeyakumar et al. (2007), compared to a group of individuals seen for routine MRI testing as described in Lin et al. (2005). Although "incidental findings" are assumed to be VSs that are not causing symptoms, both Lin et al. and Jeyakumar et al., included data from patients with clearly defined auditory and/or vestibular symptoms.

Symptoms in patients with normal or symmetrical hearing. Magdziarz et al. (2000) reviewed data collected from 369 patients with histologically confirmed VSs. They identified 10 individuals (2.7%) with "normal hearing" [defined as a pure tone average (PTA) at .5, 1, and 2 kHz of <20 dB HL, interaural difference no >10 dB HL at each frequency, and a SDS of better than 90%]; the remainder of the patient population was diagnosed with some notable hearing loss (*n* = 359). The average age of the normal hearing individuals at the time of surgery was 39.1 years old (range: 29-49 years) compared to the average age of the hearing-impaired group, which was 50.2 years old (range: 10-86 years). The difference in age between these two groups was not analyzed statistically. The major presenting symptoms in the "normal hearing" group were disequilibrium, vertigo, and tinnitus compared to the hearing-impaired group whose major presenting symptoms were progressive sensorineural hearing loss, tinnitus, and dysequilibrium. After comparison of the "normal hearing" and hearing impaired groups, Magdziarz et al. matched the "normal hearing" individuals to a selected group of hearing-impaired individuals on the basis of age, tumor size, tumor location, and presence of ABR test results. The matched comparison revealed differences in the audiovestibular symptoms experienced by these two groups, however, these differences were not analyzed statistically. They concluded that among VS patients of similar ages who have comparable tumor size, location, and ABR results, those with normal hearing continue to have different presenting symptoms compared to patients who have hearing loss (Magdziarz et al., 2000).

There are multiple problems with this study. For example, hearing loss resulting from a VS typically begins in the high frequencies, although any configuration of hearing loss may exist (Swartz, 2004). Magdziarz and his colleagues used a pure-tone average (PTA) of thresholds measured at .5, 1, and 2 kHz to define normal hearing, potentially underestimating the hearing loss in the higher frequencies. It is also problematic that there are only 10 individuals represented in the "normal hearing" group. Unfortunately, there were not enough participants in this category to permit comparison with the 359 individuals in the hearing-impaired group. This inadequate comparison was exacerbated by the lenient inclusion criteria for the "normal hearing" group described as a PTA of 20 dB HL or less at .5, 1, and 2 kHz. Finally, no statistical analyses were reported.

Lustig et al. (1998) conducted a retrospective case review of audiometric data in patients with VSs who presented with normal or symmetrical SNHL. Hearing status was determined from the pure-tone thresholds at .5, 1, 2, and 4 kHz. Abnormal, or asymmetric, hearing was considered to be ≥15 dB interaural difference at one frequency, ≥10 dB interaural difference at two or more frequencies, interaural SRT of

≥20 dB HL, or ≥20% interaural difference in SDS. These patients with abnormal or asymmetric hearing loss were excluded from the investigation. All of the patients who did not meet the abnormal or asymmetric criteria were included in the study and classified as having normal or symmetric hearing (loss). All diagnoses of VS were made as a result of MRI with gadolinium enhancement images. The authors found that 29 out of 546 patients (5%) had normal or symmetrical hearing (9 male, 20 female). The average age at diagnosis was 42 years old (no range reported). The average interaural differences were reported for SRT (3.2 dB; unknown referent) and speech discrimination (2.6%). Six of the 29 patients (21%) were diagnosed with NF2 and remained in the analysis. The most common reasons leading to evaluation and subsequent diagnosis among these individuals were disequilibrium or vertigo (41%), CN V and VII abnormalities (38%), routine testing because of NF2 (17%), asymmetrical tinnitus (14%), headaches (14%), unilateral subjective hearing difficulty (14%), and incidental finding (14%). These complaints are in agreement with the symptoms noted by Magdziarz et al. (2000). Although a patient may present with normal or symmetrical hearing loss, the authors recommend evaluation for potential VS if other persistent audiovestibular symptoms and complaints warrant testing (Lustig et al., 1998).

There were some limitations to the report by Lustig et al. (1998). It is difficult to include both individuals with audiovestibular symptoms and those without symptoms (incidental and NF2) in the same group for analysis. Additionally, there was no comparison of the groups of patients presenting with and without NF2 diagnoses. The authors also made no attempt to compare the data of normal hearing individuals to those of patients with symmetrical hearing losses. It is unclear throughout the article if the normal and symmetrical individuals are one and the same, or if there are some differences in the audiometric presentation between the patients classified as having normal versus symmetrical hearing loss.

Beck, et al. (1986) also retrospectively analyzed data obtained from patients with VSs who presented with normal hearing. They found 21 of 408 patients (5%) had “normal” pure-tone thresholds, defined as an average of thresholds at .5, 1, and 2 kHz of ≤ 25 dB HL. Of the 21 “normal hearing” individuals, 10 were male and 11 were female, ranging in age from 21 to 60 years old (*M* = 40 years). All of the patients had unilateral tumors with the exception of one patient who presented with bilateral VSs (one ear had “normal hearing"). Five of the 21 patients (5%) had completely normal (≤ 25 dB HL) hearing from .25 through 8 kHz. The patients' most common presenting symptoms were disequilibrium and subjective hearing impairment. Although they defined these patients as having “normal hearing,” hearing loss in the high frequencies was a prominent presenting outcome (62%) and speech recognition scores ranged from 24% to100% in this group. Other major symptoms were disequilibrium (67%), tinnitus (43%), headache (29%), and facial numbness (14%). When analyzed statistically and compared with the large sample of individuals with abnormal hearing or asymmetrical hearing loss associated with VSs (n=387, mean age: 50 years, no age range presented), the authors found that the “normal hearing” individuals were significantly younger than those with hearing loss ($p < 0.01$). Symptom presentation was similar between groups, although disequilibrium was the primary presenting symptom in 33% of the “normal hearing” group and in only 6% of the larger, hearing loss group.

The criteria used for “normal hearing” in this study were extremely liberal. These patients could have had significant hearing loss in the higher frequencies (>2 kHz), despite meeting the criteria for “normal hearing.” As noted above, only five of the 408 patients had normal hearing across the audiometric range. The audiometric data reported in this study, therefore, were somewhat misleading. All of the cases in the Beck et al. study were histologically confirmed, which is a notable strength.

It is difficult to distinguish the symptoms exhibited by patients with normal hearing and those with hearing loss diagnosed with VSs. In the studies presented, there is a liberal definition of normal hearing. The comparison of patients with normal hearing throughout test frequencies compared to individuals with normal hearing through selected test frequencies is complicated. Nevertheless, it is clear that there are differences in symptom presentation between patients with normal or symmetric hearing loss and those with asymmetric hearing impairment. Most normal or symmetric patients with VSs primarily experience disequilibrium, vertigo, tinnitus, facial or trigeminal neuropathy, and headaches (Beck et al., 1986; Lustig et al., 1998; Magdziarz et al., 2000) compared to patients with hearing loss who exhibit more cochlear symptoms (i.e. hearing loss and tinnitus). The “normal hearing” patients also tend to be younger than the hearing-impaired patients diagnosed with a VS (Beck et al., 1986). The reason for the age difference between patients with and without hearing loss could be multifactorial, including length of time with the VS, the amount of damage caused by the VS, and the increasing incidence of presbycusis with age.

Sudden Sensorineural Hearing Loss. The prevalence of sudden sensorineural hearing loss (SSHL) in patients with a diagnosis of VS is higher than the prevalence of VSs among patients with SSHL. There are many factors that can cause a SSHL (tumor, inflammatory infection, reduced blood supply, perilymphatic fistula, etc.), which is assumed to account for the difference in prevalence. For example, Aarnisalo, Suoranta, and Ylikoski (2004) found that four out of 82 cases (5%) of SSHL had a diagnosis of VSs. Similarly, Cadoni, Cianfoni, Agostino, Scipione, Tartaglione, Galli, and Colosimo (2006) reported that one out of 54 patients (2%) with SSHL was diagnosed with a VS.

In a review of VS patients, Sauvaget, Kici, Kania, Herman, and Tran Ba Huy (2005) noted SSHL was present in the patient's history in 28 of 139 cases (20%). Of the 28 patients who presented with SSHL, 82% (n = 23) experienced only one instance of SSHL whereas the other 18% (n = 5) experienced more than one episode prior to their diagnosis. In 54% of the patients with SSHL, the SSHL was an isolated symptom. In the other 46%, there was another accompanying symptom(s), primarily tinnitus, dizziness, and/or vertigo. Sauvaget et al. (2005) noted that the incidence of SSHL occurred significantly more often with small tumors than large tumors, which was in agreement with other reports (Ogawa, Kanzaki, Ogawa, Tsuchihashi & Inoue, 1991; Yanagihara & Asai, 1993). Although sudden hearing loss was found to be associated with smaller tumors, other researchers have found SSHL to be associated with equal proportions of small, medium, and large tumors (Pensak, Glasscock, Josey, Jackson, & Gulya, 1985). Hearing recovery was noted in about 50% of the patients with SSHL. Sauvaget and colleagues noted that their reported incidence of

SSHL (20%) was higher than the majority of other studies. The presence of SSHL in VS patients has been reported in different studies as low as 3% (Matthies & Samii, 1997) and as high as 23% (Fang, Yang, & Jiang, 1997), although most of the literature notes that the prevalence of SSHL is between those extremes (Aslan et al., 1997; Berg, Cohen, Hannerschlag, & Waltzman, 1986; Moffat, Baguley, von Blumenthal, Irving, & Hardy, 1994; Ogawa, et al., 1991; Pensak et al., 1985; and Yanagihara & Asai, 1993). Sauvaget et al. (2005) recommended that all patients presenting with SSHL should be evaluated for potential VSs. The authors postulated that the onset of SSHL, in cases of the VS, is likely caused by one of the following precipitators: mechanical compression of the auditory branch of CN VIII, acute vascular compromise to the inner ear (compression or restriction of the labyrinthine artery), a biochemical change in the inner ear fluids, or endolymphatic hydrops, although they noted the last cause is less likely.

Moffat et al. (1994) retrospectively examined preoperative findings (symptoms and test results) of 284 patients aged 20-79 years old (*M* = 55) with histologically confirmed VSs. Thirty four (12%) of the 284 patients experienced sudden deafness, whereas the rest of the population experienced no hearing loss (4.2%), fluctuating hearing loss (.7%), or progressive hearing loss (83.1%). The top presenting symptoms in the entire population were progressive SNHL (60.2%), sudden SNHL (10.2%), imbalance (10.2%), and tinnitus (8.1%). The most common configuration of hearing loss was sloping followed by flat, dead ears, “cup-shaped”, corner, and rising, with a higher proportion of dead ears found in the sudden onset group compared to the rest of the patient population. Moffat et al. did not find any significant differences between those who presented with sudden deafness and the rest of the population for tumor size, caloric irrigation result, imbalance, facial numbness, or shape of the audiogram. Few statistics were provided to support their conclusions. The authors concluded that the main etiology responsible for sudden onset hearing loss in cases of VS is compression of the internal labyrinthine artery (Moffat et al., 1994). There was also no analysis of the demographic attributes of the two groups (e.g., age).

Sudden hearing loss could be caused by many different factors. Previous literature is inconsistent regarding the specific factors that contribute to SSHL in patients with VSs, as well as the relationship between tumor size and the presence of SSHL (Moffat et al., 1994; Sauvaget et al., 2005). Recovery from SSHL has also been found in VS cases (Berg et al., 1986; Nageris & Bahar, 2001). Overall, the literature suggests that MRI should be performed in all cases of SSHL.

Potential Effect of Noise Exposure

Noise-induced hearing loss is usually evidenced on the audiogram as poor thresholds between 3 and 6 kHz with a tendency to have a “notched audiogram” configuration (Cummings, 2005). Noise exposure is also often linked to tinnitus. Patients with high frequency asymmetrical hearing losses or asymmetrical tinnitus are often referred for MRI of their IACs to rule out the presence of retrocochlear pathologies. Hazardous noise exposure usually affects the ears similarly, although noise has been known to cause increased hearing loss on one side or the other depending on the location of the sound source (e.g., gunfire) (Cummings et al., 2005).

Baker, Stevens-King, Bhat, and Leong (2003) retrospectively analyzed data collected from patients with a positive history of excessive hazardous noise exposure concomitant with military service. The patients were referred for MRI due to their asymmetrical high frequency hearing loss without consideration of their past noise exposure. Out of 152 total scans, 2.6% (4 individuals) were diagnosed with a VS. The investigators compared the prevalence of VSs in the noise exposed group to a non-military group (assumed non-noise exposed) of 152 scans which resulted in a 1.3% hit rate (2 individuals). The group without noise exposure was comprised of civilian patients who were referred for MRIs to rule out VSs within the same period as the military group with reported noise exposure. Statistics were only reported for the noise exposed military group. Left-sided hearing loss (76%, $n = 116$) was significantly more prevalent than right-sided hearing loss (24%, $n = 36$) ($p < 0.001$), with 33.6% ($n = 51$) experiencing hearing loss and tinnitus in the same ear. Baker et al. (2003) postulated that the more prevalent left-sided hearing loss was associated with a high prevalence of right handedness, and the result of the firearm angle producing a greater noise exposure on the left side. The authors concluded that VSs were equally identified in individuals with known noise-induced hearing loss when compared with the general population without previous significant noise exposure, although they noted that statistical significance was not determined because groups were not age or sex matched. Noise exposure cannot be assumed to explain the asymmetry of hearing loss between ears regardless of the configuration of the audiogram (Baker et al., 2003).

It appears that that there is no difference in the prevalence of VS between those patients with noise exposure versus those without previous noise exposure. However, Baker et al. (2003) underscore the difficulty in identifying patients for MRI referral based on ear asymmetry, because patients with a history of noise exposure frequently experience such ear asymmetry and tinnitus. Unfortunately, this study did not present supporting evidence for sensitive audiologic measures to predict tumor presence in a noise exposed population.

Occupational noise exposure has also been evaluated to rule out the risk of VS following hazardous noise exposure. Edwards, Schwartzbaum, Nise, Forssen, Ahlbom, Lonn, and Feychting (2007) retrospectively investigated data obtained from 783 VS patients identified from the Swedish Cancer Registry and 101,756 control participants who were randomly selected from the Swedish Population Registry. The age range of all the participants was 21 to 84 years old. Each participant's occupation (identified in the census), and its relation to noise exposure (measured over different time periods), was identified using a job matrix classification scheme. The control participants were never diagnosed with VS, intracranial tumors, or other types of cancer. Control participants were matched based upon their age and sex to patients presenting with VSs. The authors used unconditional logistic regression models that were adjusted for age, sex, and socioeconomic status in order to create an estimate of the participant's risk for VS. There were 599 cases and 73,432 controls in the final analysis. There was no evidence of increased risk for VS, regardless of the amount of noise exposure, the length of the exposure, the duration of the exposure, or the latency period (Edwards et al., 2007). Although the idea of objectively measuring the noise and creating the job matrix was positive, there was no description of any of the procedures used in collecting the noise measurements nor how they created their job matrix. Moreover, no statistics were presented. A positive aspect of this study was their large participant groups.

Noise-induced hearing loss does not seem to have an effect on the prevalence of VS (Baker et al., 2003), nor does it increase the risk of VS growth (Edwards et al., 2007). Noise exposure is a common problem in our society in general, and among a military population, in particular. The noise exposure could cause some of the symptoms such as asymmetrical hearing loss or tinnitus; however, it is more likely that the hearing loss occurs similarly on both sides (Cummings et al., 2005). It remains important to test patients with these notable asymmetries and other otologic and neurologic difficulties regardless of their past history of noise exposure (Baker et al., 2003). Some reports of military populations with noise-exposure have suggested referral for MRI if there is an asymmetry of ≥15 dB at two adjacent frequencies or a ≥15 dB average over .5, 1, 2, 3, 4, 6, and 8 kHz (Caldera & Pearson, 2000).

Audiological Presentation

VSs can cause many different effects on a patient's hearing. Hearing, if characterized simply by pure-tone thresholds, could present in a multitude of degrees and/or configurations. Pure-tone thresholds could range anywhere from within normal limits to profound sensorineural hearing loss with any configuration of the hearing loss in the afflicted ear. Although hearing loss can be variable, it is typical for patients with a VS to present with a unilateral (afflicted side), high frequency sensorineural hearing loss with disproportionately poor speech recognition in reference to the pure-tone thresholds. The hearing loss could occur gradually, suddenly, or fluctuate. Additionally, the patient could have a distorted quality of sound that is not measured by pure-tone testing or monosyllabic words (National Institutes of Health, 1991; Swartz, 2004).

Pure-tone audiometry. A patient's hearing status is characterized by their pure-tone audiogram. The audiogram consists of air-and bone-conduction thresholds assessed in each ear. The results indicate the type of hearing loss (conductive, sensorineural, or mixed), the configuration (e.g., rising, sloping, cookie-bite, etc.), and the degree of hearing loss (e.g., mild, moderate, severe, etc.). Abnormalities in the audiogram (i.e., the presence of hearing loss) are found in the majority of patients with VSs (Baguely et al., 2006; Forton et al., 2004; Matthies & Samii, 1997; Sauvaget et al., 2005).

In a review of 120 cases of VS, Portmann, Dauman, Duriez, Portmann, and Dhillon (1989) characterized their audiological presentation. Pure-tone testing revealed 94% (n = 113) of the patients to have some hearing loss. In 88 of the cases, there was a unilateral hearing loss noted compared to a bilateral hearing loss in 25 patients. In 12 of the patients, the hearing loss was reported as having a sudden onset. The other 6% of patients presented with normal hearing (≤ 15 dB; no referent). The configuration of hearing loss identified was primarily sloping (48%) or flat (47%), with rising or "cookie-bite" configurations noted in the remaining patients. Thresholds could not be obtained in 14% of the patients because their hearing loss exceeded the intensity limits of the audiometer (Portmann et al., 1989). Hearing loss is a common problem with VSs; however, because Portmann and colleagues did not define the demographics of their population (i.e., age or gender), it is difficult to attribute the hearing loss to other etiologies except the VS. This investigation was descriptive, with no statistical analysis to quantify or validate their results.

Results from Portmann et al. (1998) were consistent with other results reported by Neary, Newton, Laoide-Kemp, Ramsden, Hiller, and Kan (1996) who described the audiological findings in 93 patients with a diagnosed VS. The majority of the patients presented with a hearing loss in the affected ear ($n = 78$), with the remainder of patients presenting with normal hearing ($n = 1$), no response in the affected ear to the limits of the audiometer ($\mathrm{n} = 11$), or no available test results ($n = 3$). They also found that a sloping configuration was most common among patients with a VS, and was observed in 68% of their sample. Other configurations noted were flat, rising, peaked, and normal.

Caye-Thomasen, Dethloff, Hansen, Stangerup, and Tomsen (2007) prospectively examined data from a group of 156 patients ages 15-77 years ($Mdn = 57$). The patients presented with unilateral, strictly intracanalicular VSs. The goal of the study was to document the course of hearing changes in this subset of patients. At the time of diagnosis, the mean PTA (.5, 1, 2, and 4 kHz) ($M = 51$ dB HL) of the affected ear was significantly poorer than the average PTA ($M = 20$ dB HL) of the contralateral ear ($p < 0.0001$). The afflicted ear had significantly higher (i.e., poorer) PTAs. However, over the course of follow-up ($M = 4.6$ years), both ears evidenced an increase in PTA. The increase in PTA in the unaffected ear is assumed to be a result of presbycusis. An investigation into the risk of increased hearing loss over time compared those patients with perfect SDSs at diagnosis with those without perfect

SDSs. The group without perfect speech discrimination (*n* = 130) had a significantly higher risk ($p < 0.01$) of losing 10 dB of hearing in their PTA, although they did not have a higher risk of losing their speech discrimination. There was no analysis of age between these two groups. Overall conclusions were that the risk, rate, and degree of hearing loss in the afflicted ears were not significantly related to age, gender, or most tumor characteristics with the exception of absolute volumetric tumor growth rate (Caye-Thomasen et al., 2007).

The investigation by Caye-Thomasen and colleagues began with significantly more potential participants (*N* = 325) than were actually analyzed (*N* = 152) because of either availability of test data or diagnosis imaging technique, which could potentially bias the data. The authors note this potential bias, although they maintain that there is no selection bias occurring because all of their patients were part of the "watch and monitor" group. Selection bias can still factor in because the reasons for the "watch and monitor" group were not given. The patients ranged in age from 15-77 years old, which is a large age range. The authors noted that there was no effect of age on any of the variables; however, the time that lapsed over the course of follow-up could have introduced some internal validity problems.

Graamans, Van Dijk, and Janssen (2003) investigated hearing deterioration in patients with non-growing VSs assessed using MRI imaging over time. They prospectively analyzed the data collected from 49 individuals (25 females, 24 males) ranging in age from 21-82 years old (*M* = 58) who were diagnosed with VSs. They excluded any individuals with cystic tumors or neurofibromas. The patients were not surgically treated because of advanced age, poor health, refusal of treatment, and/or the presence of the tumor in the better hearing ear. The authors compared the patient's audiometric thresholds of .125 to 8 kHz and the slope of the audiogram. Results indicated decreased hearing in 44 of their 49 participants over time (range of time for follow-up: 1-14 years; *M* = 7 years) characterized as an increase in the pure-tone average (.5, 1, and 2 kHz); the remaining 5 participants experienced essentially no change in their hearing. There was a significant correlation between the hearing loss decrement and follow-up duration in both the afflicted ear and the contralateral ear. When the authors subtracted the thresholds from the contralateral ear from the thresholds of the afflicted ear with the VS (assuming any changes were due to presbycusis or causes other than the tumor), the correlation remained significant, suggesting the tumor had caused the significant hearing loss over the course of follow-up. All correlations were calculated using the corrected hearing levels. An analysis of the data indicated a significant difference between the increase in hearing threshold and follow-up time at all frequencies except 8 kHz. The hearing loss was most evident at 1 and 2 kHz, although correlations were modest (1 kHz: r=0.39; 2 kHz: r=0.34). The authors noted that a decline in hearing thresholds in the presence of stable tumors is an indication that tumor growth is not necessarily related to hearing function (Graamans et al., 2003).

The main problem with this investigation is the variability between the evaluations of the study participants. The purpose of the evaluation was to analyze non-growing VSs over time; however, the range of follow-up time was one to 14 years with a mean of seven years. Although there could be stability in the tumor over the course of this time, the difference between the thresholds one year later versus 14 years later could cause differences which are presumably due to aging.

Speech discrimination. A standard speech test that is administered in the clinic examines the maximum word recognition score at a relatively high sound level (PB_{max}). Most patients with normal hearing score approximately 100% on this speech test, and patients with a cochlear lesion score are expected to score between a 0 and 100% depending on the signal audibility and population of functioning hair cells. People with retrocochlear lesions often score poorer than expected on this measure (Hannley & Jerger, 1981). A common speech test for retrocochlear pathology includes the presentation of monosyllabic words at different intensities to test for "rollover." A performance-intensity, phonetically-balanced (PI-PB) function is a representation of the average percent correct scores plotted as a function of intensity (Katz, 2002). PI-PB rollover is observed at the point where an increase in intensity causes a decrease in the percent correct score. Rollover is quantified by the rollover index ($(PB_{max}-PB_{min})/PB_{max}$) (Hall & Mueller, 1997), where PB_{max} is the maximum score achieved and the PB_{min} is the minimum score achieved at a higher intensity level. The significance of the rollover could depend on the test used, the speaker, presentation level, etc. For example, if a patient has an SDS of 88% at 65 dB HL and a SDS of 42% at 90 dB HL, they would be identified as having positive rollover. Although this speech test may identify some patients with retrocochlear pathologies (Hannley & Jerger, 1981), the sensitivity and specificity rates of this test are not known because it is dependent on the rollover index used. Therefore, general speech discrimination will be discussed.

One useful metric for determining if an individual is achieving the expected speech recognition score for their hearing sensitivity is the Articulation Index (AI) originally described by French and Steinberg (1947). The AI predicts an individual's SDS based on the person's hearing thresholds, the spectral characteristics in the speech signal, and any noise in the system. The AI takes into account the importance of different frequencies to speech intelligibility for a particular speech recognition test, and provides weights that reflect this frequency importance function (Pavlovic, 1984). In the simplest of terms, the AI provides an index for speech discrimination prediction that accounts for audibility of the signal using different frequency bands which are important for speech perception. The AI has been used over the years to assist researchers and clinicians in determining the effects of hearing loss, aging, noise, and amplification on speech understanding performance. Although this method provides accurate predictions in patients with normal to moderate hearing loss, it tends to overestimate performance in people with severe-to-profound hearing loss (Pavlovic, 1984). It also tends to overpredict performance by older patients compared to younger patients (Hargus & Gordon-Salant, 1995). Another critique of the AI is that it does not take into account the level distortion factor. The level distortion factor suggests that at a certain intensity level (dB SPL), the auditory system is penalized for further increases in the intensity of the signal (ANSI S3.5-1997). Although studies of patients with VS have examined speech recognition performance, none have applied the AI to determine if these patients perform more poorly than expected based on the signal audibility.

Patients diagnosed with a VS appear to have disproportionately low SDSs compared to patients without VSs. Caye-Thomasen et al. (2007), in a study previously described, found the initial SDS ($M = 60\%$) of the affected ear in patients with a VS was significantly poorer than the SDS ($M = 96\%$) of the contralateral ear ($p < 0.0001$). Over the course of follow-up, the afflicted ear had significantly higher (i.e., poorer) PTAs and lower SDSs, while the contralateral ear only experienced an increase in PTA. Caye-Thomasen et al. found that 17% (26 participants) of their population had perfect SDSs at diagnosis. All of the patients who presented with perfect speech scores at diagnosis had SDSs greater than 70% at their most recent follow-up (mean follow-up time: 4 years). The final mean SDS for the "perfect speech score" group was 95% (range: 80-100). As previously mentioned, the group without perfect speech discrimination ($n = 130$) had a significantly higher risk ($p < 0.01$) of losing 10 dB of hearing in their PTA, although they did not have a higher risk of losing their speech discrimination (Caye-Thomasen et al., 2007). These results are consistent with the findings reported for SDS by Graamans et al. (2003). Most of the speech scores did not correlate significantly with the follow-up duration with the exception of a low correlation coefficient ($r= -0.167$) between maximum discrimination and follow-up duration.

Although SDSs have been useful in identifying patients with a VS when there is hearing loss present (Caye-Thomasen et al., 2007; Graamans et al., 2003; Magdziarz et al., 2000), SDSs failed to identify a retrocochlear pathology among "normal hearing" patients diagnosed with a VS (Beck, et al.,1986; Magdziarz et al., 2000). Analogous results were reported by Jeykumar et al. (2007), who noted a significant difference between symptomatic (hearing loss present) and asymptomatic (no hearing loss present) groups. They found that the average interaural difference in SDSs was greater in the symptomatic group ($p < 0.001$) than in the asymptomatic group.

Acoustic reflex thresholds and acoustic reflex adaptation (decay). Stapedius reflex testing involves the presentation of pure-tone (.5, 1, 2, or 4 kHz) or broad band stimuli to the ear, while simultaneously recording a change in immittance in either the ipsilateral (same side as the stimuli) or contralateral (opposite side of the stimuli) ear. Individuals with normal auditory systems having thresholds up to approximately 75 dB HL typically have measureable acoustic reflex thresholds. Acoustic reflex thresholds are typically observed at levels 65 to 125 dB HL in individuals with normal or cochlear hearing loss (Gelfand, Schwander, & Silman, 1990). Elevated acoustic reflex thresholds are elicited at levels that are higher than the upper limit of the normal range. Elevation of acoustic reflex thresholds has been linked to retrocochlear pathology, specifically with the stimuli presented in the affected ear. Metz (1952) initially described the absence of the acoustic reflex threshold in two VS patients. More recent investigations have reported substantial variation in the acoustic reflex thresholds in patients diagnosed with VS, depending on the criteria used (Hirsch & Anderson, 1980; Jerger & Jerger, 1983). It is also known that acoustic reflexes can be absent in individuals with significant cochlear hearing loss (more than 75 dB HL) (Gelfand et al., 1990; Silman & Gelfand, 1981), or in individuals with other disorders affecting the acoustic reflex arc (i.e. conductive pathology, CN VIII lesion, etc.).

Gelfand et al. (1990) collected acoustic reflex data on a sample of participants with either normal hearing or cochlear hearing loss. The study included 2,748 ears (*N* = 1,374 participants; 1,321 males and 53 females). They tested contralateral acoustic reflexes up to a maximum intensity of 125 dB HL. Participants had measureable hearing thresholds (≤110 dB HL) at .5, 1, and 2 kHz and normal middle ear function. They were classified as not having a retrocochlear lesion on the basis of negative results of acoustic reflex adaptation test, normal radiologic scans, stable hearing sensitivity, no neurological symptoms, and negative case histories. Gelfand and colleagues examined the acoustic reflex threshold as a function of pure-tone hearing threshold and found that acoustic reflexes were present with thresholds <45 dB HL. For thresholds of 70 dB HL, the probability of an absent acoustic reflex was approximately 10% which continued to increase with increasing severity of the hearing loss. They computed the 90th percentile for acoustic reflexes as a function of signal frequency and pure-tone threshold, and found that 12.2% of these ears (*n* = 334 ears) presented with elevated acoustic reflex thresholds outside of the 90th percentile for only one frequency, 3.6% (*n* = 99 ears) had elevated thresholds at two frequencies, and 2% (*n* = 56 ears) had elevated reflexes at all test frequencies. Therefore, 17.8% of the ears tested had elevated reflexes above the 90th percentile (Gelfand et al., 1990). Although this result is for patients with normal hearing or a cochlear hearing loss, the report acknowledges that elevation of acoustic reflexes also occurs in the absence of a VS.

Assessment of acoustic reflex adaptation involves presentation of pure tones at .5 or 1 kHz at a level 10 dB higher than the elicited acoustic reflex threshold.

Although adaptation can be measured either in the contralateral or ipsilateral ears, most investigations report the use of contralateral stimuli because results are less affected by artifact. The test for adaptation monitors the magnitude of the acoustic reflex response over a ten second period of time. Individuals with normal auditory systems or cochlear lesions do not exhibit a change in the magnitude of the acoustic reflex response over the 10 second period. Adaptation is considered positive if there is a reduction of ≥50% of the initial response magnitude of the reflex. Positive acoustic reflex adaptation has been associated with retrocochlear disorders (Jerger, Harford, Clemis, & Alford, 1974).

Acoustic reflex thresholds have been thought to predict retrocochlear pathologies for many years; however, there are many different criteria that can be used to differentiate the acoustic reflexes between patients. Prasher and Cohen (1993) investigated the effectiveness of multiple acoustic reflex criteria in detecting retrocochlear pathology in patients with identified CPA tumors. They applied multiple criteria values to data obtained from patients with cochlear and retrocochlear lesions. The best criteria were an interaural difference >15 dB at more than one frequency (Chiverals, 1977) and an interaural difference of >10 dB at two or more adjacent frequencies (Prasher & Cohen, 1993). Both Chiverals (1977) and Prasher and Cohen (1993) reported high false positive detection rates using raw acoustic reflex threshold values (re: clinical norms) in differentiating patients with and without retrocochlear lesions.

Dauman, Aran, and Portmann (1987) investigated the acoustic reflex threshold and acoustic reflex adaptation in 61 cases (31 males, 30 females) of diagnosed CPA or IAC tumors. Only patients with normal tympanograms and absent air-bone gaps during pure-tone testing (both suggesting normal middle ear function) were included in the analysis. Dauman and colleagues analyzed contralateral acoustic reflex thresholds at .5, 1, 2, and 4 kHz and acoustic reflex adaptation measured contralaterally at .5 and 1 kHz. Results indicated an abnormality in the acoustic reflex in 89% of the cases. Five of the participants had bilateral abnormalities noted in the acoustic reflexes, and two of these five participants were diagnosed with bilateral tumors. In 11% of the sample, there were no abnormalities noted in either the acoustic reflex thresholds (within 10 dB of the other ear) or acoustic reflex adaptation. In 45% of the patients, there were no acoustic reflexes elicited at the limits of the equipment. The patients were separated into two groups: one group with entirely absent acoustic reflexes and the other with a reflex elicited at one or more frequencies. They found that the amount of hearing loss was greater in the group with absent reflexes compared to those with at least one present reflex. Patients with measureable acoustic reflexes exhibited both negative (34%) and positive (66%) adaptation results. For the group with a negative adaptation outcome, 14% had other reflex abnormalities (elevation, absence of reflex at other frequencies, etc), while the other 20% had normal acoustic reflexes. In comparison, patients with positive reflex adaptation had abnormalities in their reflex thresholds (60%), with only a small percentage of the patients exhibiting normal acoustic reflexes (6%). Dauman et al. concluded that acoustic reflexes and acoustic reflex adaptation are good indicators of retrocochlear pathology; however, the presence of normal acoustic reflexes does not exclude the presence of a tumor. This report did not report exclusively cases of VS; however, the majority of cases were VSs.

Similar to findings with SDS, acoustic reflexes and acoustic reflex adaptation appear to be sensitive to retrocochlear pathology when the patient has a hearing loss. Mixed results have been found regarding the presence of abnormal acoustic reflex thresholds and acoustic reflex decay in patients with “normal hearing.” Magdziarz et al. (2000) found that ipsilateral and contralateral acoustic reflexes largely failed in the detection of VS in patients with “normal hearing;” however, these measures were useful in diagnosing patients with some degree of hearing loss. Beck et al. (1986) reported that 54% of their “normal hearing” patients had abnormal acoustic reflexes, and recommended the use of acoustic reflex thresholds and adaptation in the battery of tests for diagnosing a VS. Finally, Sheehy and Inzer (1976) found abnormal acoustic reflex thresholds or positive reflex adaptation in 80% of their population of patients with a VS, who would not have been diagnosed by pure tones alone.

Referral Patterns

MRI referrals have been extremely beneficial to the diagnosis of VSs. They have effectively increased the reported annual incidence of diagnosed VSs, which is largely due to the increase in detection of small, intrameatal tumors (Stangerup et al., 2004). Unsuspected (asymptomatic) VSs have also been diagnosed more frequently. A study by Anderson, Loevner, Bigelow, and Mirza (2000) found an average of 7 unsuspected VSs that were diagnosed per 10,000 MRIs.

Moffat, Jones, Mahendran, Humphriss, and Baguley (2004) reviewed data from patients who had undergone removal of a VS over a recent 10-year-period, and compared them to patients who had undergone removal between the years of 1983 to 1993, to investigate the differences in referral patterns over the two time intervals. The principal presenting symptoms between the two groups were extremely similar. The top four symptoms were progressive hearing loss, tinnitus, imbalance, and sudden hearing loss. This is in agreement with the NIH consensus statement of early manifestations of the tumor (National Institutes of Health, 1991) as well as multiple other reports (Baguely et al., 2006; Cheng, Smith, & Tan, 2003; Matthies & Samii, 1997; Moffat et al., 1994; Portmann et al., 1989; Sauvaget et al., 2005). Moffat et al. (2004) also found that otolaryngologists were the primary referral source for VS diagnosis for both groups. Their estimate of the incidence of VS was between .5 and 2 patients per 100,000/year (Moffat et al., 2004).

There have been other established protocols over the years concerning MRI referral to rule out the presence of a VS or other retrocochlear pathology. Most of the existing protocols for referral are based on some degree of asymmetrical hearing loss and a past history of one or more symptoms. Obholzer, Rea, and Harcourt (2004) evaluated MRI scanning for detection of VSs. A total of 392 scans were reviewed. The data from patients identified with a VS (*n* = 36) and from patients who made up the last 100 negative MRIs were reviewed, with the final analysis including 36 positive MRIs and 92 negative MRIs. Of the patients diagnosed with a VS, 32 out of 36 presented with asymmetrical hearing loss as their primary symptom. Nineteen of the 32 patients with asymmetrical hearing loss also reported asymmetrical tinnitus. The remaining patients complained of tinnitus (*n* = 2) or dizziness (*n* = 1) as their primary symptoms, although all three of these patients had asymmetrical hearing loss noted on their audiogram. The final patient had trigeminal parasthesia (*n* = 1) with a symmetrical audiogram. Unilateral or asymmetrical tinnitus was noted in 45% of the positive MRI group (diagnosed with VS) and in 47 percent of the negative MRI group, which did not yield a significant difference between groups. Obholzer and colleagues calculated sensitivity and specificity rates for the asymmetry in the patients' pure tone thresholds. They evaluated the asymmetry at each pure tone frequency (.25, .5, 1, 2, 4, 8 kHz), for combinations of frequencies (any frequency, any two frequencies, two adjacent frequencies, any three frequencies, three adjacent frequencies, average of .25-8 kHz), and for six previously established protocols. The sensitivity and specificity rates for each of the previously stated variables were calculated for asymmetries of 15 dB, 20 dB, and a third protocol using a 15 dB asymmetry for unilateral hearing loss and a 20 dB asymmetry for asymmetrical hearing loss. Results suggested the most sensitive individual frequency was 2 kHz using a 15 dB asymmetry (91% sensitivity and 60% specificity), and the most sensitive criterion overall was an asymmetry of 15 dB at any frequency (100% sensitivity and 29% specificity). Although these criteria provided high sensitivity rates, the goal was to have the best combination of sensitivity and specificity in predicting the outcome of the MRI. The best combination of sensitivity and specificity was for an asymmetrical hearing loss of ≥15 dB at two adjacent frequencies if there was a unilateral hearing loss, and for a 20 dB asymmetry at two adjacent frequencies if there was a bilateral hearing loss (97% sensitivity and 49% specificity). They found that this profile of symptoms would have reduced the number of scans, from 392 to 218 scans (Obholzer et al., 2004).

In this investigation, there was no comparison of patients whose data were analyzed vs. those whose data were not analyzed. The reason why all of the scans were not analyzed was not clearly stated in the report. There were also no data on the patients' audiograms, only the sensitivity and specificity rates of the different frequencies and criteria were reported. The patients with negative MRIs whose data were not analyzed in the study could have presented with alternate symptoms or different audiometric characteristics compared to the 92 patients included in the analysis.

Another protocol was described in a report by Sheppard, Milford, and Anslow (1996). They reviewed the scans of 892 patients, with 38 VSs diagnosed. The patients were referred from two different facilities and data were reported on 18 of the 38 patients diagnosed with a VS. These patients presented with an asymmetry of 15 to 92 dB between ears, which was calculated from the subtracted average of both ears (.25, .5, 1, 2, 4, and 8 kHz). There were no other data reported. The final suggested protocol was a 15 dB average asymmetry between ears, or if there was normal hearing, the presence of unilateral tinnitus. This is in agreement with the report by Valente, Neely, Peterein, and Goebel (1995), which showed that unilateral tinnitus was the primary presenting symptom in their normal hearing patients with diagnosed VSs. Sheppard et al. also suggested an upper age limit of 70 years old for screening. The authors concluded that the risks, time, and cost do not warrant the screening of older patients.

Although Sheppard et al. (1996) recommended a protocol for MRI referral, they did not provide data analyses to derive this protocol. With the exception of the minimal asymmetry data on 18 of the patients diagnosed with a VS, there were no other data presented.

Magnetic Resonance Imaging

As described throughout the literature review, the “gold standard” MRI for use in diagnosing potential VSs is a contrast-enhanced MRI of the IACs. The final confirmation, however, cannot be made until histological examination of the lesion is performed. An MRI is a radiologic scan that uses magnetism and radio waves to produce visual images of the body. MRI utilizes hydrogen atoms (found in water), and for this reason it is more useful in imaging soft tissues and organs compared to other scans such as x-rays or computerized tomography (CT scan). It is especially good for identifying tumors, infection, and inflammation (Cacace, Tasciyan, & Cousins, 2000). The contrast agent used for MRI is a dye made with gadolinium, which is a paramagnetic metal ion. The contrasting agent looks like water and is non-radioactive. It is used to provide a greater contrast between normal and abnormal tissue because it accumulates in abnormal tissue causing those areas to become enhanced. Gadolinium contrast is generally safe; however, the FDA has issued a warning that it can be dangerous to individuals with renal dysfunction or if there are repeated or high doses of the contrasting agent. For this reason and others, MRI can be performed with or without the presence of the contrasting agent (Cummings et al., 2005).

Conventional spin MRIs are typically used for both contrast and non-contrast enhanced MRIs of the IAC. For conventional spin MRIs, there may be a T1 (longitudinal relaxation time) weighted or T2 (transverse relaxation time) weighted

MRI performed. MRIs that are T1 weighted have shorter repetition and echo times, giving the image superior anatomy imaging, high signal to noise ratio, and a shorter imaging time compared to T2 images. Gadolinium enhancement is used with T1 weighted images. MRIs which are T2 weighted are used to highlight pathologic lesions. Typically, the two types of conventional spin MRIs are used in conjunction with each other for diagnosis. Another, more recent form of MRI, is known as a T2 weighted fast spin echo (FSE) MRI. The T2 weighted FSE MRIs use pulse sequencing, giving multiple phase encoding steps instead of just one, allowing for an ultra high resolution image of the body. The FSE MRI allows for significantly faster scanning and eliminates the need for gadolinium contrast use (Wilkinson & Paley, 2008). MRI referrals have been extremely beneficial to the diagnosis of VSs. They have effectively increased the reported annual incidence of diagnosed VSs, which is largely due to the increase in detection of small, intrameatal tumors (Stangerup, Tos, Caye-Thomasen, Tos, Klokker, & Thomsen, 2004).

Allen, Harnsberger, Shelton, King, Bell, Miller, Parkin, Apfelbaum, and Parker (1996) investigated the sensitivity and specificity of the T2 weighted FSE versus gadolinium-enhanced T1 weighted conventional spin echo MRI for VS diagnosis. They found no difference in the specificity or sensitivity of the two scanning methods noting two false negative results (out of 100) for the T2 weighted FSE and two false positive results, one each for the FSE and the conventional spin MRI. They concluded that T2 weighted FSE MRIs were an inexpensive option for detecting VSs. This conclusion was also reached by Verret, Adelson, and Defatta (2006) who compared the two types of MRIs in patients with asymmetrical hearing loss and by Daniels, Shelton, and Harnsberger (1998) who found that the T2 weighted FSE was an effective screening measure for VSs in sudden hearing loss patients.

Imaging results are subject to the interpretation of the technician or physician reading the scans. There is some degree of human error expected in reading MRIs. Briggs, Flynn, Worthington, Rennie, and McKinstry (2008) evaluated the need for a second opinion in reading CT scans and MRIs. They reviewed second opinion reports that occurred over a 12 month period (365 cases). Major discrepancies were characterized as changes that affected the medical care of the patients, whereas a minor discrepancy did not change the medical management of the patient. Rates of discrepancy were 13% major and 21% minor, with two thirds of the second opinions in agreement with the initial reading. Peterson, Gatterman, Carter, Humphreys, and Weibel (2007) investigated interexaminer reliability in identifying degenerative changes in the spine on MRI. Their agreement percentages ranged from 71-92% depending on the part of the spine evaluated. Although this is an unrelated pathology, it provides additional evidence that there is some amount of skill, experience, and human error involved in reading imaging studies.

Summary

VSs have a history of variable presentation. In the past, there have been mixed results regarding which test procedures (pure-tone audiometry, acoustic reflexes, etc.) yield the most sensitive MRI referral protocol for detection of VSs. There also have been differences in recommended referral protocols for MRI of the IAC. The primary presenting symptom continues to be hearing loss. The hearing loss could be unilateral, asymmetric, or fluctuating, and may produce distorted sound perception;

regardless, the hearing loss remains the most common presenting symptom (Beck et al., 1986; Lustig et al., 1998; Matthies & Samii, 1997; Moffat et al., 1994; National Institutes of Health, 1991). In addition to hearing loss, other symptoms occur frequently in the presenting population. Tinnitus is extremely common and tends to be more prevalent in hearing versus non-hearing ("dead") ears (Matthies & Samii, 1997). Disequilibrium, although not a primary presenting symptom in patients with hearing loss, tends to be the primary presenting symptom in patients with normal or symmetric hearing (Beck et al., 1986, Lustig et al., 1998, Magdziarz et al., 2000). The outcome measures also have evidenced different results depending on the population being examined. Pure-tone thresholds continue to be the gold standard audiometric test to examine any asymmetry between the ears. Other test measures, such as acoustic reflex thresholds, acoustic reflex adaptation, ABR, and a vestibular test battery (e.g., ENG/VNG, VEMP, etc.) have shown abnormalities in various proportions of patients with and without a VS (Beck et al., 1986, Lustig et al., 1998, Magdziarz et al., 2000; Matthies & Samii, 1997). Because MRIs now identify smaller VSs than in the past, an evaluation of the effectiveness of audiologic test procedures and reliance on patient-reported symptoms for recommending patients for MRI testing in suspected cases of VS is needed. The purpose of this investigation was to devise a set of criteria that would maximally distinguish a patient with a potential VS from a patient who would likely not have a VS in order to create an evidence-based audiological referral protocol for MRI testing.

Chapter 3: Experimental Questions and Hypotheses

The primary goal of this study was to determine an effective method for identifying suspected cases of VSs while minimizing over-referral for MRI and inconvenience to the patient. The specific goals were to: examine the sensitivity and specificity of tests used for screening to rule out retrocochlear lesions, identify predictive symptoms (using a selective set) for retrocochlear lesions that result in a referral for a MRI, and identify the audiometric tests and outcomes of the tests which greatly predict the early identification of retrocochlear lesions. The specific experimental questions are as follows:

1. Is there a significant difference in the audiological presentation of patients identified with a VS and patients without a VS, based on the following standard test measures:
    a. Pure-tone thresholds
    b. Speech discrimination score
    c. Acoustic reflex thresholds
    d. Asymmetry in these measures
2. Is there a significant difference between the groups of patients identified with a VS and those patients without a VS in reference to presenting audiovestibular or neurological symptoms (e.g. asymmetric hearing loss, asymmetric tinnitus, vertigo, headaches, etc.) on the MRI referral?

3. Is there a set of audiological results and/or patient-reported symptoms that maximally distinguishes the patients with and without a VS among those patients referred for MRI?
4. Is there a difference between the group of patients diagnosed with a VS and those patients without a VS in the demographics or history?
    a. Is there a difference in age between groups?
    b. Is there a difference between the gender distribution between groups?
    c. Is there a difference between groups for their history of hearing loss (e.g. newly documented, stable/established hearing, progressive hearing loss, etc.)?

The hypothesis for this investigation is that there is not a single audiometric test outcome or a single presenting symptom that best differentiates patients with and without a VS, but rather there will a group or set of audiometric measures and symptoms that predict the outcome of the patient's MRI. It is expected from previous literature that asymmetrical hearing loss, SDSs, and acoustic reflex thresholds will have some impact on characterizing the patients with and without a diagnosed VS; however, it is hypothesized that a combination of such tests will provide more sensitive and specific referral criteria for patients suspected to have a VS.

Chapter 4: Method

Participants

This study was a retrospective analysis of data obtained from all patients (military healthcare beneficiaries) who received a MRI scan of their IACs in the Department of Radiology at Walter Reed Army Medical Center from November 2005 through October 2007. A list of patients who were referred during that time for a MRI of their IACs was provided. Prior to medical care in the military health care system, patients sign a release form. This form gives consent for access to patient medical records for purposes of research and to compile data in order to provide more evidenced-based medical treatment and efficient care (Appendix A).

Patients who were under the age of 18 years old were not included in the study because VSs are very rare in this population, and their MRIs were likely performed for other referral reasons. Therefore, all individuals, male and female, who were referred for MRI to rule out retrocochlear pathology over the age of 18 years old, were included. There were no exclusions based upon ethnic background or overall health status.

Patients who were scanned (via MRI) to rule out a VS, specifically, or to rule out retrocochlear pathology, were considered for the study. Referrals for MRI for other reasons were excluded from the investigation. If a patient was listed more than once, indicating multiple MRIs, their follow-up MRIs were excluded from the data collection.

The MRIs were reviewed by a radiologist who identified any potential pathology on the scans. Patient MRIs were either with contrast, without contrast, or both. The majority of the non-contrast MRIs were T2 weighted FSE images. All of the VSs were identified using contrast enhancement. The radiologist also noted whether a follow-up study was necessary for increased clarity of the image. It is unknown in the majority of the cases in this investigation whether there was a "second" reading or not. It is assumed that the radiologist who reviewed the scan wrote the report, and the physician who ordered the scan then reviewed the scan and the report for accuracy; however, this is typically not noted in the patient's electronic medical record. The diagnosis of VS was made following identification on the MRI, although there was no histological confirmation in many cases. Of all of the MRIs reviewed, patients were diagnosed with a VS, another retrocochlear pathology, or identified as having no retrocochlear lesions. The main focus of this investigation was to develop a referral protocol for VS; therefore, only those with VSs will be analyzed as part of the "positive" diagnosis.

Initial data were collected on 628 patients who received an MRI between November 2005 and October 2007. Audiological data were incomplete on 300 patients, including missing pure-tone thresholds, speech recognition scores, and/or ipsilateral or contralateral acoustic reflex thresholds. Patients were excluded from the final analysis if they did not have complete data in both ears for pure-tone thresholds, speech recognition scores, and contralateral acoustic reflexes. The final group of patients included 19 positive diagnoses and 309 patients with negative diagnoses for VS. The positive group consisted of 10 males and 9 females aged 31-73 years old (*M*=53.37, *SD*=12.82). There were 221 males and 88 females in the negative group ranging in age from 20-85 (*M*=48.28, *SD*=13.32). Figure 1 represents the breakdown

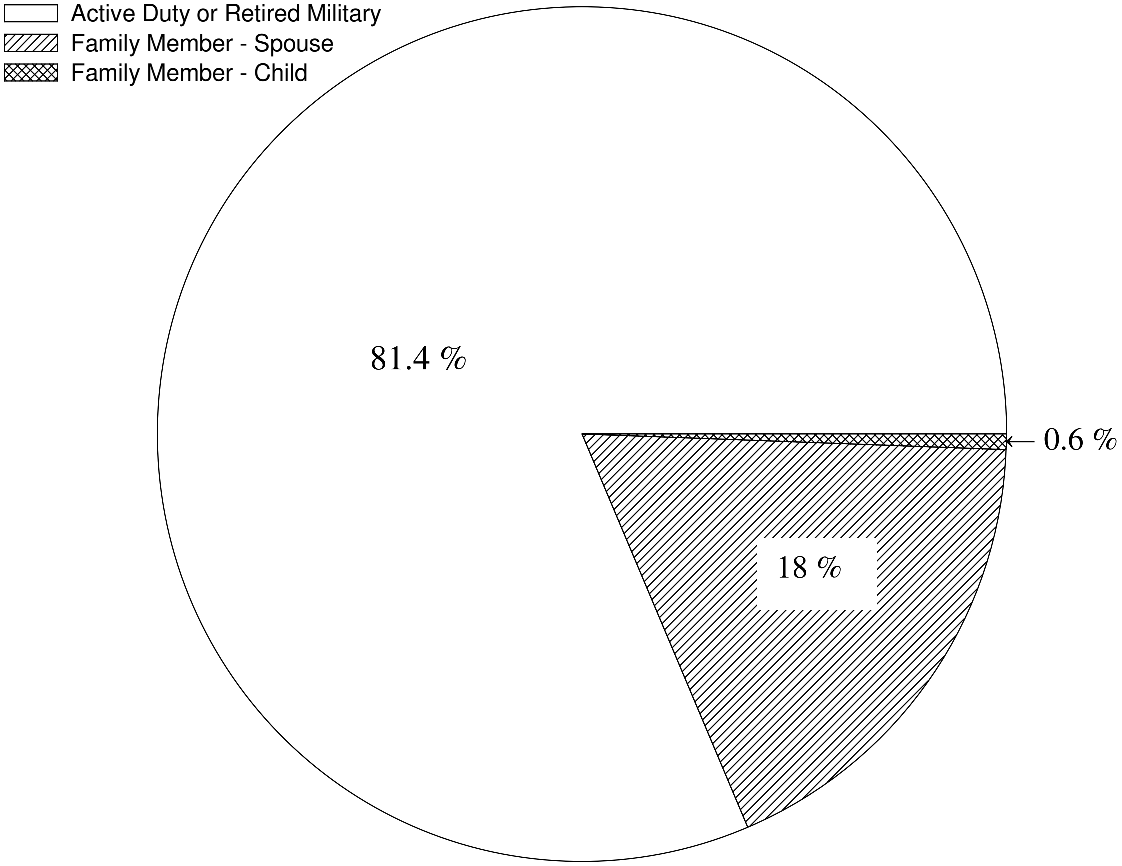


Figure 1: Depiction of type of patient (n = 328)

of patients (*N* = 328) by type, including active duty or retired military personnel (*n* = 267), spouses (*n* = 59), and children (*n* = 2).

Because data were collected from a military hospital, it can be assumed that many of the patients have been exposed to hazardous noise. The presence or effect of noise-induced hearing loss on these patients could not be parsed out because the necessary information could not be obtained reliably through retrospective analysis; however, if the patient's history of previous noise exposure was mentioned in their report it was recorded. Reported hazardous noise exposure is shown in Figure 2. There were individuals with reported history of hazardous noise exposure (*n* = 170), history of blast exposure (*n* = 19), no history of noise exposure (*n* = 48), and individuals with no report of past noise or blast exposure (*n* = 91). It is assumed that these data are an approximation considering they are based on patient report alone. There is likely more noise and blast exposure than actually reported.

Each patient's history of hearing loss was also identified. Patients were classified as having a newly identified hearing loss, a stable or established hearing loss, a progressive hearing loss, or no hearing loss. It is likely that many of the patients reported in the "newly identified" group have lived with hearing loss for longer than reported; however, for the purposes of this investigation, they were still noted as "new."

Testing

No prospective testing was performed. Data were reviewed retrospectively. Data collection included demographic information (age and sex) about the patient, their history of hearing loss, the kind of MRI (with contrast, without contrast, or

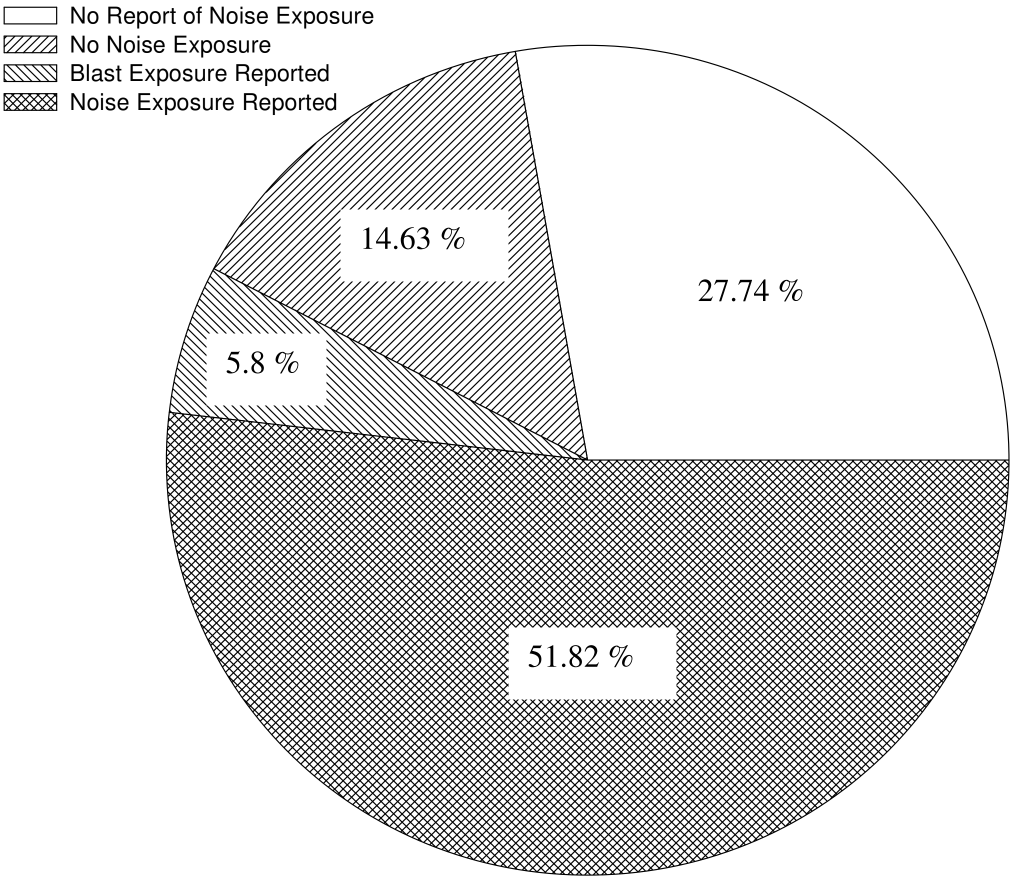


Figure 2. Patients (*n* = 328) by history of hazardous noise.

both), and if they had any other related scans performed. Also reviewed were symptoms that led to the referral, particularly the presence of hearing loss, self-reported tinnitus, vestibular symptoms, neurological symptoms, headaches, aural fullness, history of Meniere's Disease, and sudden symptom onset. Initial data collection on the patients' primary presenting symptoms was based on previous literature; however, as the charts were

The patients' audiological data were analyzed. Audiometric data included: pure-tone thresholds, SDSs, results of tympanometry, acoustic reflex thresholds, and evidence of acoustic reflex decay. For patients with a positive diagnosis, all analyses refer to the "affected" or "unaffected" ear, whereas for the patients with negative diagnoses, all analyses refer to the "better" or "poorer" ear. Pure-tone thresholds (collected previously) were analyzed at .25, .5, 1, 2, 3, 4, 6, and 8 kHz in both ears. Bone-conduction thresholds were recorded; however, they were only used to assess the presence of any air-bone gaps (>10 dB HL). Any patient with air-bone gaps was excluded from the study. If a patient has a conductive hearing loss, this does not preclude them from having a VS. However, the hearing loss is not thought to be directly related or caused by the presence of a VS, and therefore, the patients with conductive hearing loss were not included in the study. For speech testing, if there was a single presentation level, the SDS was reported regardless of the intensity of the signal; however, if there was more than one presentation level (e.g., testing for normal and loud intensities), the score obtained at the highest intensity level was analyzed. Tympanometry data were collected, but no statistical testing was performed. Tympanometry data were accessed only to provide validity to other immittance measures supporting normal tympanic membrane mobility. In conjunction with the absence of air-bone gaps, unremarkable tympanometry suggested normal middle ear function. If a tympanogram was considered abnormal (i.e., flat or negative pressure), the patient was excluded from the analysis. Acoustic reflex thresholds were collected .5, 1, and 2 kHz both ipsilaterally and contralaterally; however, because most of the patients did not have ipsilateral acoustic reflex data, only contralateral acoustic reflex thresholds were analyzed. The acoustic reflex threshold (dB HL) was noted at each frequency, and if there was no acoustic reflex present at the limits of the equipment, a nominal value of 115 dB HL was assigned. Acoustic reflex decay at 1 kHz was identified as positive or negative. These data were noted for each group; however, the results were not analyzed statistically because the data were sparse.

Additionally, the presence of any positive outcome, such as a vestibular weakness (from caloric testing) or positive rollover in speech testing that was noted on the referral, was analyzed because they were results leading to the referral. The analysis only compared the presence or absence of the outcome in each group; however, the specific test results (i.e., amount of vestibular weakness or rollover SDS) were not analyzed statistically because of their sparse availability in the sample.

Procedures

Medical record information was accessed through an electronic medical record system. All medical records for the military are kept through electronic chart management, although paper records were accessed if necessary because the electronic medical record has only been in existence for a couple of years. Patients were identified by a list provided by the Radiology Department at WRAMC. The patient list included the name and social security number of each person receiving an MRI of the IAC, together with the date of the imaging. The patient was found in the electronic medical record by searching for their record using their first name, last name, social security number, or some combination of the three identifiers. Once the patient's chart was accessed, only records pertaining to the referral for MRI of the IAC were accessed. This included information from the radiology report, notes from audiology, otolaryngology, neurology, primary care, or other potential referral sources. The data for each patient were entered into a database (Microsoft Excel Spreadsheet) excluding all personal identifying information.

Data Analysis

Numerous techniques were used to analyze this large data set and answer the questions posed. A first step was to identify the better and poorer ear of each participant. To that end, pure tones were identified in the right and left ear. An average of pure-tone thresholds across all test frequencies was calculated for each ear; the ear with the lower average was determined to be the "better" ear, and the other ear termed the "poorer" ear. If the mean pure-tone thresholds were equal, an arbitrary ear was chosen for the better ear. The ear was randomly chosen within the Microsoft Excel database. This procedure was needed for seven patients in the negative MRI group. The right ear was chosen as the better ear for six of the seven patients. For each patient with a diagnosed VS, data are reported for the "unaffected" ear, or the ear without the VS, and the "affected" ear, or the ear with the VS. The unaffected ear was identified as the better ear. The difference between ears was calculated for each frequency and the PTAs (1, 2 , and 4 kHz). The difference between ears was defined as:

$$\text{Difference Between Ears} = \text{Poorer Ear Threshold} - \text{Better Ear Threshold} \qquad (1)$$

In most cases, the poorer ear threshold was greater than the better ear threshold, so there was a positive difference between ears. However, there were many occasions when the better ear threshold was higher than the poorer ear threshold at a specific frequency causing the difference to be negative. Analyses of pure-tone thresholds and PTAs were performed using non-parametric two independent sample tests, or the Mann-Whitney U test. A separate Mann- Whitney U test was conducted at each frequency in each of the better ear, poorer ear, and difference between ears conditions.

A determination of pure-tone asymmetry between ears was made with four different rules at each frequency or adjacent frequencies: asymmetrical at a single frequency, two-adjacent frequencies, three-adjacent frequencies, or an asymmetrical high frequency average (at 4, 6, and 8 kHz). For each of the rules, the asymmetry was noted as either present or absent at a certain criterion (> 0, 10, 15, 20, 25, 30, 35, 40, 45, 50, or over 55 dB HL). Separate chi-square statistics (MRI result x Presence of asymmetry) were used to find the criteria that were significantly different between the groups. For each criterion, a d' calculation was also performed using the equation:

$$d' = Z(\text{False Alarm Rate}) - Z(\text{Hit Rate}) \text{ (Turner \& Nielsen, 1984)} \qquad (2)$$

In this investigation, the patients encompassed a large age range (20-85 years old) with varying degrees of hearing loss. One issue concerned whether or not the hearing loss reflected changes associated with aging or changes associated with the presence of the VS. For this reason, age and gender corrections using published normative data (Morrell et al., 1996) were applied to pure-tone thresholds at .5, 1, 2, and 4 kHz to analyze the extent of hearing loss that was not attributed to age. The normative data represented the age and gender specific medians for cross sectional change in hearing level. The correction was applied by subtracting the median value from the absolute threshold at each designated frequency. For example, if the threshold for a 30 year old male was 10 dB HL at 1000 Hz and the correction factor was (-2.6), than his age- and gender-corrected threshold would be 12.6 dB HL. The age and gender corrected pure-tone thresholds were found for the better and poorer ears. The difference between ears for corrected thresholds was also calculated using Equation 1. Separate Mann-Whitney U tests were run on each of the four frequencies for the better ear, the poorer ear, and the difference thresholds.

The speech discrimination score was recorded for the better and poorer ears. The difference between ears was calculated using the following formula:

$$\text{Difference Between Ears} = \text{Better Ear Percent Correct} - \text{Poorer Ear Percent Correct} \tag{3}$$

The raw SDS data were analyzed using separate Mann-Whitney U tests for the better ear, the poorer ear, and the difference between ears.

Because speech testing was performed at a range of intensity levels, the patients' SDS in each ear was compared to their AI predicted score. To calculate each patient's AI predicted score, their threshold values at .25, .5, 1, 1.5, 2, 3, 4, and 6 kHz were needed. Because there were no data available for 1.5 kHz, the threshold value at this frequency was interpolated from the thresholds at 1 and 2 kHz. The following is an example of how the predicted AI score was obtained using the octave-band method. The data needed are provided in Table 1. AI information was obtained using a formula reported by Pavlovic (1987), which provided the band importance for each frequency and the average vocal effort at a normal conversational level (50 dB HL). The speech peaks were then adjusted for the intensity level used to obtain that participant's SDS (80 dB HL) (see Table 1). To calculate the AI, the pure-tone threshold is then subtracted from each adjusted speech peak at the corresponding frequency. However, if this value was greater than 30, then 30 is used as the outcome; if the value was less than 0, then a value of 0 is used (see Table 2). Each frequency's outcome was then multiplied by its band importance. The sum of these results divided by 30 was the AI score (see Table 3). For the example patient, the AI score is 0.63855. An AI value is between zero and one. A calculator was formatted in Microsoft Excel to compute the AI for each ear of each patient using the formula reported by Pavlovic (1987). The AI was transformed into a percent correct score using the transfer function for monosyllabic words (ANSI S3.6, 1969). The observed SDS was then subtracted from the AI predicted SDS to find the difference in scores. A positive difference indicated poorer performance on the speech discrimination task than was predicted by the AI. The difference in scores for the better and poorer ears were analyzed using separate Mann-Whitney U tests.

Table 1

Band importance function and speech peaks for NU-6 words

Frequency (kHz)	Band Importance*	Speech Peaks* (50 dB HL)	Adjusted Sp. Peaks (80 dB HL)
.25	.0617	51.2	81.2
.5	.1671	56.5	86.5
1	.1943	50.3	80.3
1.5	.1321	48.4	78.4
2	.1328	47.3	77.3
3	.1285	48.4	78.4
4	.1039	48.1	78.1
6	.0796	33	63

*Data from Pavlovic (1987)

Table 2

Example of Calculation of AI (octave-band method): Speech Peak-Threshold = x (If<0, then 0; If >30, then 30, otherwise-x)

Frequency (kHz)	Speech Peaks (dB HL)	Threshold (dB HL)	Result
.25	81.2	15	30
.5	86.5	15	30
1	80.3	55	25.3
1.5	78.4	60	18.4
2	77.3	65	12.3
3	78.4	65	13.4
4	78.1	65	13.1
6	63	60	3

Table 3

*Example of Calculation of AI (octave-band method): Band Importance*Result*

Frequency (kHz)	Band Importance	Result (Step 2)	Result #2
.25	.0167	30	1.851
.5	.1671	30	5.013
1	.1943	25.3	4.91579
1.5	.1321	18.4	2.43064
2	.1328	12.3	1.63344
3	.1285	13.4	1.7219
4	.1039	13.1	1.36109
6	.0796	3	.2388

$\Sigma = 19.16566$

AI = 19.16566/30

The acoustic reflex thresholds for each patient at each frequency were reported as the lowest threshold (in dB HL) where an acoustic reflex could be elicited. The raw scores, including absent reflexes represented as 115 dB HL, were analyzed using separate Mann-Whitney U tests for each frequency (.5, 1, and 2 kHz) for the better and poorer ear depending on the ear in which the stimulus was presented. The absolute interaural difference between the acoustic reflex thresholds was also calculated (Prasher & Cohen, 1993). Prasher and Cohen predicted that the most sensitive acoustic reflex criteria separating cochlear and retrocochlear losses was an interaural difference >10 dB at two adjacent frequencies. The acoustic reflex thresholds were also categorized as normal, elevated, or absent (no response at the limit of the equipment) using normative data reported by Gelfand et al. (1990). However, in a clinical setting, both elevated or absent acoustic reflexes are considered abnormal; therefore, a third classification of reflexes categorized the reflexes as either normal or abnormal. For the categorical classifications, chi square statistics were performed with post hoc testing performed for the three-variable classification using separate chi square statistics and sequential Holm's Bonferroni corrections.

Another approach to data analysis evaluated the primary presenting symptoms and/or outcomes in both the positive and negative MRI groups that led to the MRI referral. Initially, the symptoms that led to the MRI referral were categorized based upon symptoms that were identified by previous reports. However, following partial data collection, there were many symptoms/outcomes reported on the referral that were not included in the initial categorization. Subsequently, all of the patient's charts were reviewed and altered as needed including the new categories. For each of the symptoms/outcomes, the patients were classified as having the symptom/outcome prompting the MRI referral or not having the symptom/outcome. Separate chi square statistics were performed for each symptom/outcome.

The final approach to data analysis was a logistic regression analysis to determine if there is a set of audiological results or patient-reported symptoms that maximally distinguishes between the patients with and without a VS. Variables representing each audiological test and particular symptoms were chosen. The audiological results were chosen following previous reports suggesting that asymmetrical hearing loss, poor SDS, and acoustic reflexes are somewhat predictive in identifying VS. These variables included the difference in pure-tone thresholds between the better and poorer ears, the criteria for asymmetrical hearing loss (>15 dB HL) for each rule (single frequency, two-adjacent frequencies, three-adjacent frequencies, and high frequency average), difference between the better and poorer ear SDSs, raw contralateral acoustic reflex data in both ears, and unilateral tinnitus. Both a forward and backward logistic regression were performed. Both types of logistic regression models were used to identify the model that provided the most distinguishing variables between the two groups.

This investigation was approved by the Institutional Review Boards for Human Subjects Research of both WRAMC and the University of Maryland-College Park.

Chapter 5: Results

For all Mann-Whitney U test statistics, the z-score is presented in place of the U-statistic because the size of the sample is large ($n = 328$) (WINKS Software). For each of the chi-square analyses, the chi square statistic (x^2) is presented.

Effect of Group on Patient Demographics

The age difference between the two groups was analyzed using a Mann-Whitney U test, and the gender difference between the two groups was analyzed using a chi square analysis. There were no age ($z = -1.556$, $p>.05$) or gender ($x^2 = 3.066$, $df = 1$, $p>.05$) differences between the two groups.

Patients' history of hearing loss was analyzed using a chi square analysis. The results are shown in Table 4. Significant differences between the positive and negative MRI groups for reported history of hearing loss were only noted for newly identified and progressive hearing loss patients. The negative MRI group had a significantly greater proportion of newly identified hearing loss patients compared to the positive MRI group, and the positive MRI group had significantly more progressive hearing loss patients than the negative group.

Effect of Group on Audiological Presentation

Pure-Tone Audiogram. Pure-tone thresholds for the right ear are presented in Figure 3a. Results of the Mann-Whitney U test (Table 5) were significant across all frequencies between groups, with the positive MRI group having poorer thresholds than the negative MRI group. Left ear thresholds (see Figure 3b) were not significantly different between groups with the exception of 1 and 2 kHz, where the positive MRI group had poorer thresholds. Although right ear thresholds were

Table 4

Chi square analysis results for the proportion of patients in the two MRI groups reporting different hearing histories.

Hearing Loss History	Proportion of Patients (positive MRI)	Proportion of Patients (negative MRI)
*Newly Identified	.421	.644
Stable	.053	.091
*Progressive	.421	.142
None (no hearing loss)	.105	.123

*p<.005

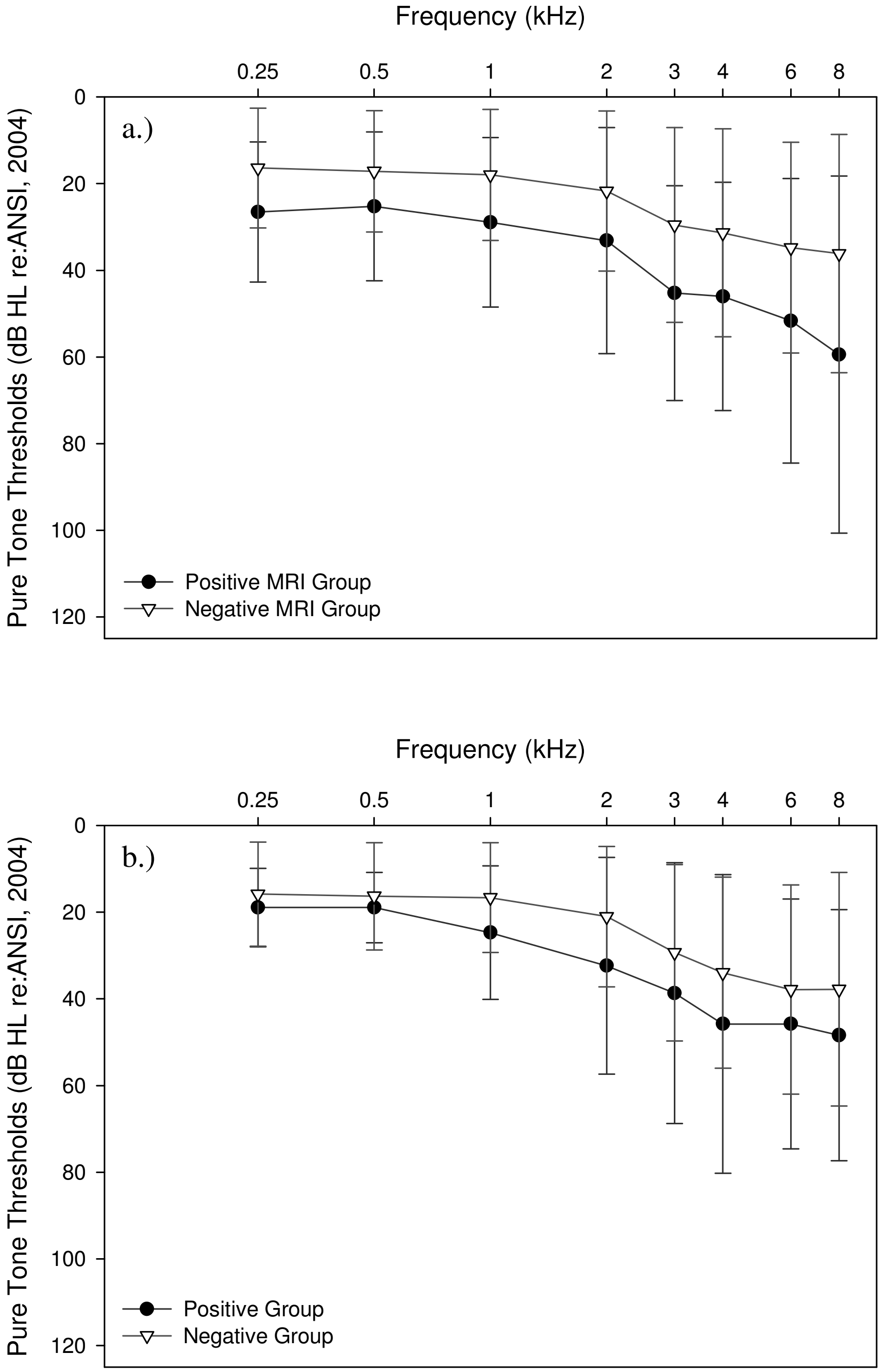


Figure 3. Average results for the right ear (panel a) and left ear (panel b) for positive (*n* = 19) and negative (*n* = 309) groups. Error bars indicate 1 standard deviation from the mean.

Table 5

Mann-Whitney U results for pure-tone thresholds in the right and left ears. Z scores reflect differences between the two groups.

Ear	Frequency (Hz)	*Z* score	*p*-value
Right	250	-3.359	.001***
Right	500	-2.175	.030*
Right	1000	-2.754	.006**
Right	2000	-2.104	.035*
Right	3000	-2.917	.004***
Right	4000	-2.546	.011*
Right	6000	-2.243	.025*
Right	8000	-2.454	.014*
Left	250	-1.921	.055
Left	500	-1.901	.057
Left	1000	-2.525	.012*
Left	2000	-2.088	.037*
Left	3000	-1.081	.280
Left	4000	-1.212	.225
Left	6000	-1.101	.271
Left	8000	-1.612	.107

* $p<.05$ ** $p<.01$ *** $p<.005$

significantly different between the two groups, it is expected that this result is an effect that does not relate to the presence or absence of a VS. Therefore, the remainder of the results will reference the better, or unaffected ear for positive MRI patients, and poorer, or affected ear for the positive MRI group. Figure 4a and Table 6 indicate the audiometric thresholds for the better ear in both groups. Group comparisons, using separate Mann-Whitney U tests at each frequency, were not significant with the exception of .25 kHz where the positive MRI group had higher (i.e., poorer) thresholds than the negative group. The poorer ear thresholds, shown in Figure 4b, were significantly different between groups across all test frequencies (see Table 6) with the positive group having poorer thresholds.

The difference in patient thresholds between ears was calculated as noted in Equation 1. A Mann-Whitney U test was performed for each of the frequencies. The threshold difference between ears (see Figure 5) was significantly different between groups at .5, 1, 2, 3, 4, and 8 kHz (see Table 7), with the positive MRI group exhibiting larger difference thresholds.

The PTA (average at 1, 2, and 4 kHz) in the better and poorer ears for each group and the difference in PTA are depicted in Figure 6. The better ear PTA was not significantly different between groups ($z = -1.663$, $p = 0.96$); however, the poorer ear PTA was significantly different ($z = -3.368$, $p = .001$) between the groups. The interaural difference in PTA was also significantly different between groups ($z = -2.976$, $p = .003$) with the larger interaural PTA difference observed in the positive MRI group.

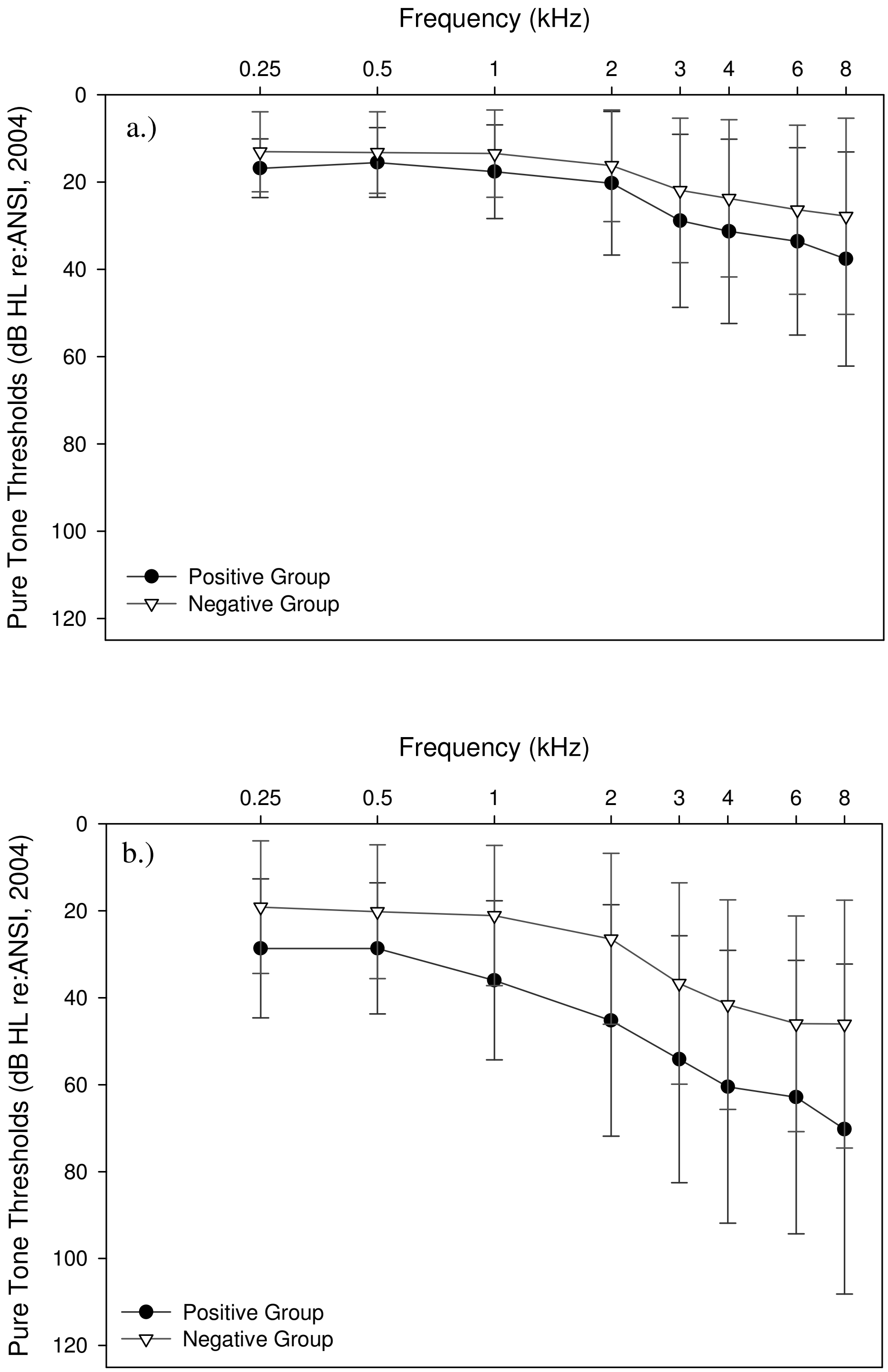


Figure 4. Average results for the better ear (panel a) and poorer ear (panel b) for the positive (*n* = 19) and negative (*n* = 309) groups. Error bars indicate 1 standard deviation from the mean.

Table 6

Mann-Whitney U results comparing pure-tone thresholds in the two groups separately for the better and poorer ears. Z scores represent the differences between the two groups.

Ear	Frequency (Hz)	*Z* score	*p*-value
Better	250	-2.581	.010*
Better	500	-1.453	.146
Better	1000	-1.777	.076
Better	2000	-1.040	.298
Better	3000	-1.676	.094
Better	4000	-1.748	.080
Better	6000	-1.516	.129
Better	8000	-1.805	.071
Poorer	250	-2.956	.003***
Poorer	500	-2.818	.005**
Poorer	1000	-3.736	.0005***
Poorer	2000	-3.312	.001***
Poorer	3000	-2.676	.007**
Poorer	4000	-2.546	.011*
Poorer	6000	-2.301	.021*
Poorer	8000	-2.577	.010*

* p<.05 ** p<.01 *** p<.005

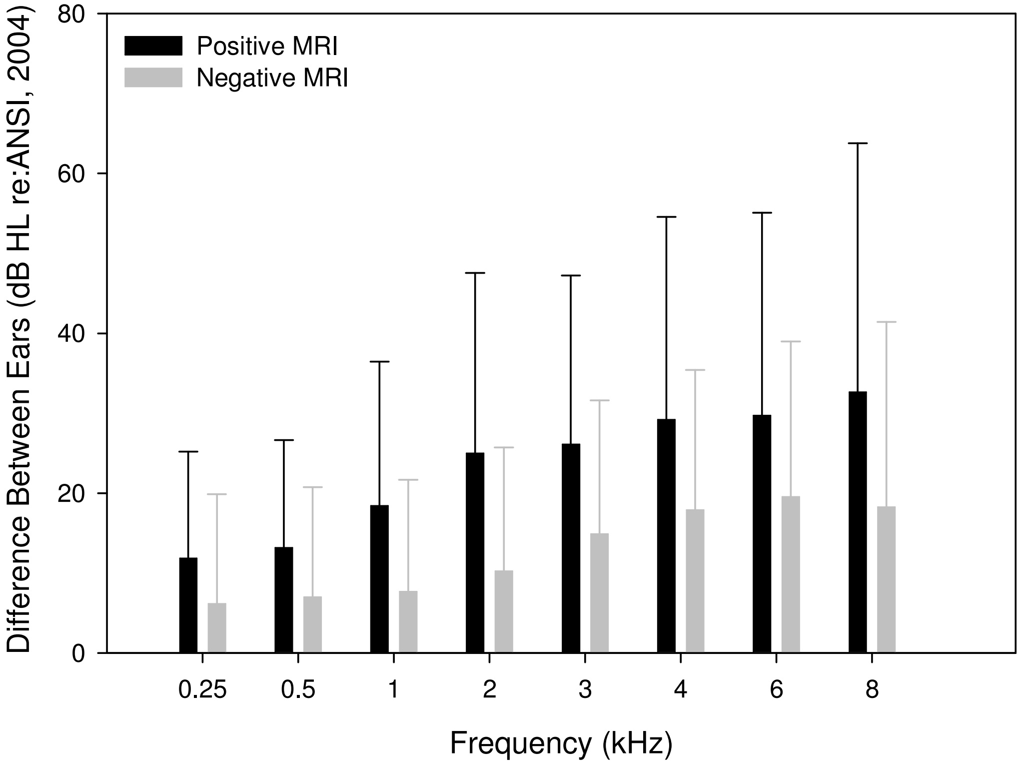


Figure 5. Average difference in pure-tone thresholds between ear results for positive (*n* = 19) and negative (*n* = 309) groups. Error bars indicate 1 standard deviation from the mean.

Table 7

Mann-Whitney U results comparing the two groups' pure tone threshold differences between ears. Z scores reflect differences between the two groups.

Frequency (Hz)	*Z* score	*p*-value
250	-1.750	.080
500	-3.228	.001***
1000	-2.929	.003***
2000	-3.201	.001***
3000	-2.321	.020*
4000	-2.071	.038*
6000	-1.641	.101
8000	-2.257	.024*

* p<.05 ** p<.01 *** p<.005

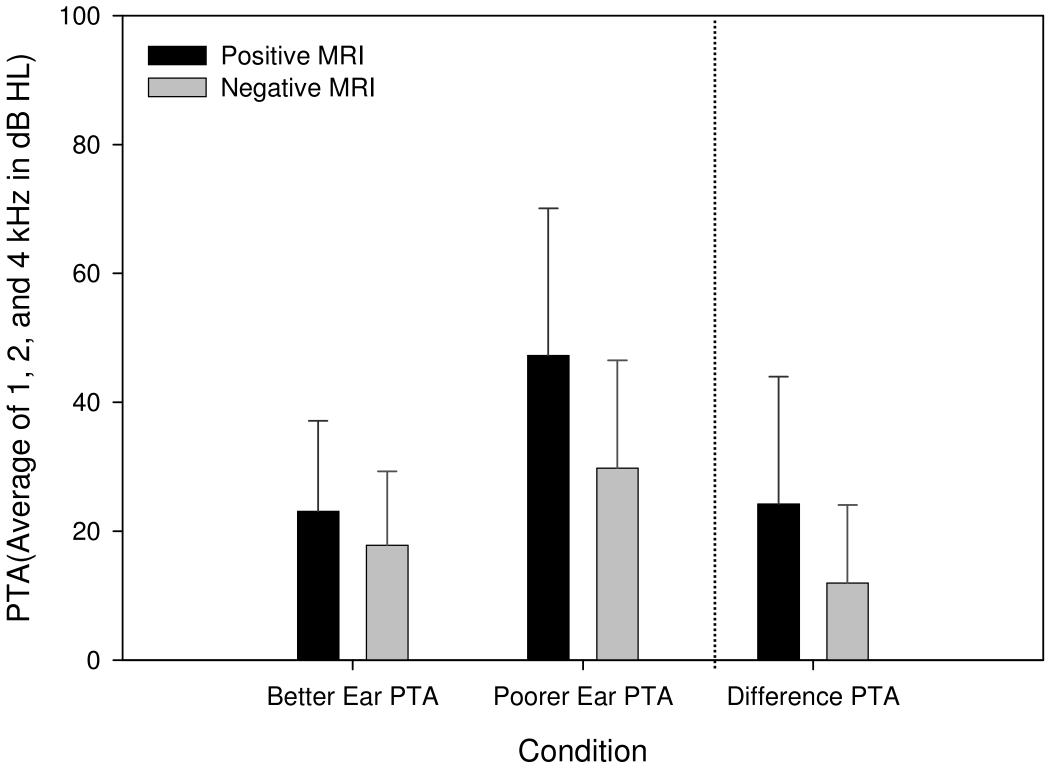


Figure 6. Average better ear PTA (1, 2, and 4 kHz), poorer ear PTA, and difference between PTA results for positive (*n* = 19) and negative (*n* = 309) groups. Error bars indicate 1 standard deviation from the mean.

Degree of asymmetry was examined for four rules (single frequency, two adjacent frequencies, three adjacent frequencies, and high frequency average). The ROC curve results are shown in Figure 7. Each of the four rules is plotted as a separate curve, with each criterion of asymmetry (0, >10 through >55 dB HL, in 5 dB steps) plotted as a separate data point. For each rule and criterion value, d' was calculated using Equation 2. The d' values are shown in Table 8. The highest d', or best predicted criterion, was d' = 1.26 using the HFA rule with a 55 dB HL asymmetry (indicated by a single asterisk on Figure 7). The rules with the largest d' values were the HFA and three adjacent frequency rules. In comparison, the single frequency rule had the lowest d' values overall.

The proportion of patients in each group presenting with different degrees of asymmetry for each rule were evaluated using chi square analyses. This analysis was separate from the d' values calculated. Specifically, the chi square analyses identified at which criteria the groups were significantly different across each of the asymmetrical rules. The results of the chi square analysis for each of the criteria for each of the four pure-tone calculation rules are shown in Table 9. The results show that there were at least three significant criteria for each rule, and these were generally observed for greater degrees of asymmetry. Significant differences between groups were noted when the asymmetry criterion exceeded 45 dB HL for the single frequency rule, 35 dB HL for the two-adjacent frequency rule, and 30 dB HL for the HFA rule. The three adjacent frequency rule revealed a different pattern with scattered significant differences noted at criteria greater than 10, 25, 30, 35, 40, and 45 dB HL.

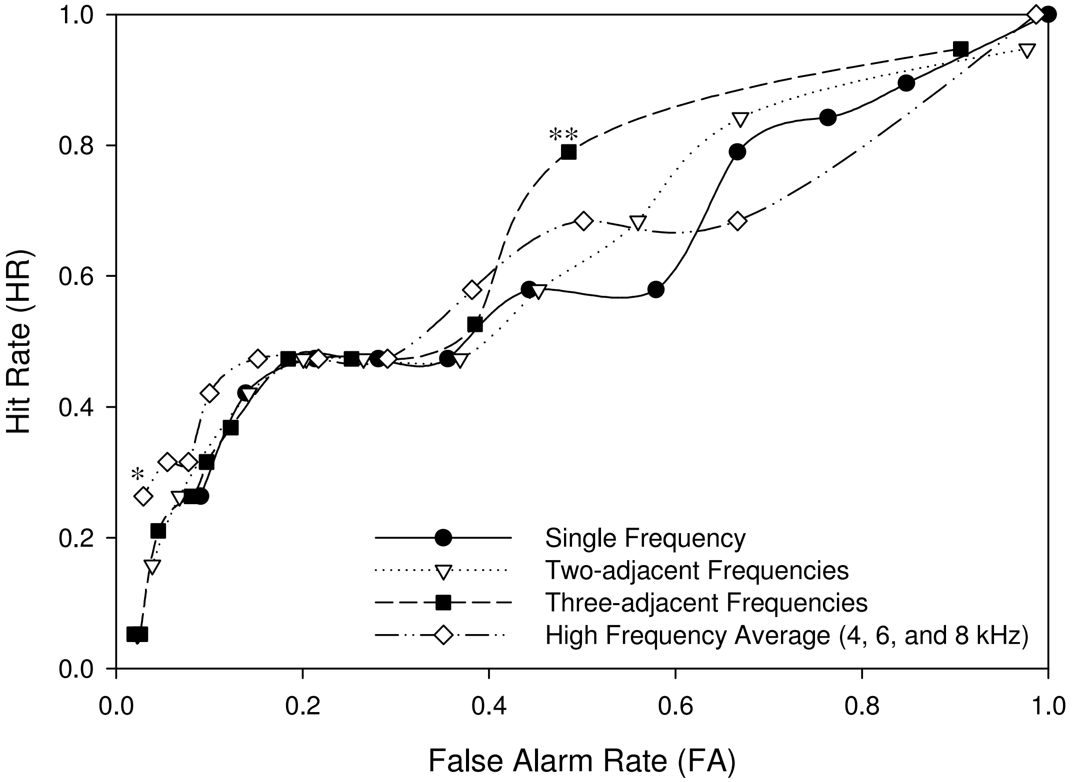


Figure 7. Receiver operator curves (ROC) displaying the hit rate (for *n* = 19) versus false alarm rate (for *n* = 309) for each of four rules (single frequency, two adjacent frequencies, three adjacent frequencies, and high frequency average). Each data point, within a rule, indicates the hit rate and false alarm rate for a particular criterion of asymmetry (i.e., greater than: 0, 10, 15, 20, 25, 30, 35, 40, 45, 50, 55 dB), with data points on the left indicating maximal asymmetry and data points on the right indicating minimal asymmetry. The criterion with a single asterisk represents the best d' criterion. The criterion with a double asterisk represents the criterion which was the best compromise between the hit and false alarm rates for this data set.

Table 8

D' values calculated for each criterion presented separately for four pure tone calculation rules.

Rule 1: Asymmetrical at a Single Frequency

Criterion	HR	FA	d'
0	1.000	1.000	*CNC*$^+$
10	.8947	.8479	.22
15	.8421	.7638	.28
20	.7895	.6667	.37
25	.5789	.5793	0
30	.5789	.4434	.34
35	.4737	.3560	.30
40	.4737	.2812	.51
45	.4737	.2136	.73
50	.4211	.1392	.88
55	.2632	.0906	.70

Rule 2: Asymmetrical at Two-Adjacent Frequencies

Criterion	HR	FA	d'
0	.9474	.9773	-.38
10	.8421	.6699	.56
15	.6842	.5599	.33

Table 8 (cont.)

D' values calculated for each criterion presented separately for four pure tone calculation rules.

Criterion	HR	FA	d'
20	.5789	.4531	.32
25	.4737	.3689	.27
30	.4737	.2654	.56
35	.4737	.2006	.77
40	.4737	.2006	.77
45	.4211	.1424	.87
50	.2632	.0680	.86
55	.1579	.0388	.76

Rule 3: Asymmetrical at Three-Adjacent Frequencies

Criterion	HR	FA	d'
0	.9474	.9061	.30
10	.7895	.4854	.84
15	.5263	.3851	.36
20	.4737	.2524	.60
25	.4737	.1845	.83
30	.3684	.1230	.82

Table 8 (cont.)

D' values calculated for each criterion presented separately for four pure tone calculation rules.

Criterion	HR	FA	d'
35	.3158	.0971	.82
40	.2632	.0809	.77
45	.2105	.0453	.89
50	.0526	.0259	.33
55	.0526	.0194	.45

Rule 4: Asymmetrical High Frequency Average (4, 6, and 8 kHz)

Criterion	HR	FA	d'
0	1.000	.9871	*CNC*
10	.6842	.6667	.05
15	.6842	.5016	.48
20	.5789	.3819	.50
25	.4737	.2913	.48
30	.4737	.2168	.72
35	.4737	.1521	.96
40	.4211	.1003	1.08
45	.3158	.0777	.94

Table 8 (cont.)

D' values calculated for each criterion presented separately for four pure tone calculation rules.

Criterion	HR	FA	d'
50	.3158	.0550	1.12
55	.2632	.0291	1.26

* $p<.05$ ** $p<.01$ *** $p<.005$

$^{+}$ CNC = could not calculate

Table 9

Results of chi square analysis calculated for each criterion presented separately for four pure tone calculation rules.

Rule 1: Asymmetrical at a Single Frequency

Criterion	Proportion of patients (positive MRI)	Proportion of patients (negative MRI)	x^2	LSD *p*-value
0	1.000	1.000	CNC⁺	*CNC⁺*
10	.8947	.8479	.309	.750
15	.8421	.7638	.617	.580
20	.7895	.6667	1.228	.322
25	.5789	.5793	0.000	1.000
30	.5789	.4434	1.329	.342
35	.4737	.3560	1.073	.331
40	.4737	.2812	3.192	.115
45	.4737	.2136	6.865	.020*
50	.4211	.1392	10.832	.004***
55	.2632	.0906	5.889	.031*

Rule 2: Asymmetrical at Two-Adjacent Frequencies

Criterion	Proportion of patients (positive MRI)	Proportion of patients (negative MRI)	x^2	LSD *p*-value
0	.9474	.9773	.676	.383
10	.8421	.6699	2.439	.136

Table 9 (cont.)

Results of chi square analysis calculated for each criterion presented separately for four pure tone calculation rules.

Criterion	Proportion of patients (positive MRI)	Proportion of patients (negative MRI)	x^2	LSD *p*-value
15	.6842	.5599	1.127	.346
20	.5789	.4531	1.142	.346
25	.4737	.3689	.838	.465
30	.4737	.2654	3.875	.064
35	.4737	.2006	7.605	.018*
40	.4737	.2006	7.868	.009**
45	.4211	.1424	10.419	.004***
50	.2632	.0680	9.344	.011*
55	.1579	.0388	5.814	.048*

Rule 3: Asymmetrical at Three-Adjacent Frequencies

Criterion	Proportion of patients (positive MRI)	Proportion of patients (negative MRI)	x^2	LSD *p*-value
0	.9474	.9061	.366	1.000
10	.7895	.4854	6.619	.016*
15	.5263	.3851	1.496	.235
20	.4737	.2524	4.496	.056
25	.4737	.1845	9.315	.005**

Table 9 (cont.)

Results of chi square analysis calculated for each criterion presented separately for four pure tone calculation rules.

Criterion	Proportion of patients (positive MRI)	Proportion of patients (negative MRI)	x^2	LSD *p*-value
30	.3684	.1230	9.109	.008**
35	.3158	.0971	8.762	.011*
40	.2632	.0809	7.155	.021*
45	.2105	.0453	9.420	.015*
50	.0526	.0259	.480	.420
55	.0526	.0194	.945	.344

Rule 4: Asymmetrical High Frequency Average (4, 6, and 8 kHz)

Criterion	Proportion of patients (positive MRI)	Proportion of patients (negative MRI)	x^2	LSD *p*-value
0	1.000	.9871	.249	1.000
10	.6842	.6667	.025	1.000
15	.6842	.5016	2.388	.157
20	.5789	.3819	2.913	.096
25	.4737	.2913	2.827	.121
30	.4737	.2168	6.634	.021*
35	.4737	.1521	13.074	.002***
40	.4211	.1003	17.575	.001***

Table 9 (cont.)

Results of chi square analysis calculated for each criterion presented separately for four pure tone calculation rules.

Criterion	Proportion of patients (positive MRI)	Proportion of patients (negative MRI)	x^2	LSD *p*-value
45	.3158	.0777	12.213	.004***
50	.3158	.0550	18.667	.001***
55	.2632	.0291	23.993	.001***

[+] CNC = could not calculate

Another analysis attempted to clarify the extent of hearing loss observed in patients with VSs that is not attributed to aging, by correcting individual pure tone thresholds based on published normative data for males and females of different ages (Morrell et al., 1996). Thresholds in the better and poorer ears at .5, 1, 2, and 4 kHz were corrected and results are shown in Figure 8. The better ear thresholds shown in Figure 8 (panel a) do not appear to be different, although the poorer ear thresholds (panel b) show large differences between groups at 1 kHz and above. Mann-Whitney U analyses were conducted to determine if group differences in the age- and gender-corrected thresholds were significant. The results are shown in Table 10. The better ear (see Figure 8a) pure tone thresholds were not significantly different between the two groups at any of the frequencies, although the poorer ear (see Figure 8b) pure tone results were significantly different between the two groups across all frequencies, with higher thresholds noted in the positive MRI group. The difference between the ears (see Figure 9) was also significantly different between the two groups at .5, 1, and 2 kHz, with patients with VS having higher interaural differences in pure tone thresholds.

Speech Discrimination Scores. Mean SDSs for the better ear and poorer ear, as well as the mean difference between scores, are shown in Figure 10. A Mann-Whitney U test was performed for each of the comparisons. The SDS in the better ear was not significantly different between groups (z = -.437, *p* = .662). However, the poorer ear SDSs were significantly different between groups (z = -3.422, *p* = .001), with the patients diagnosed with a VS having significantly lower SDSs than patients

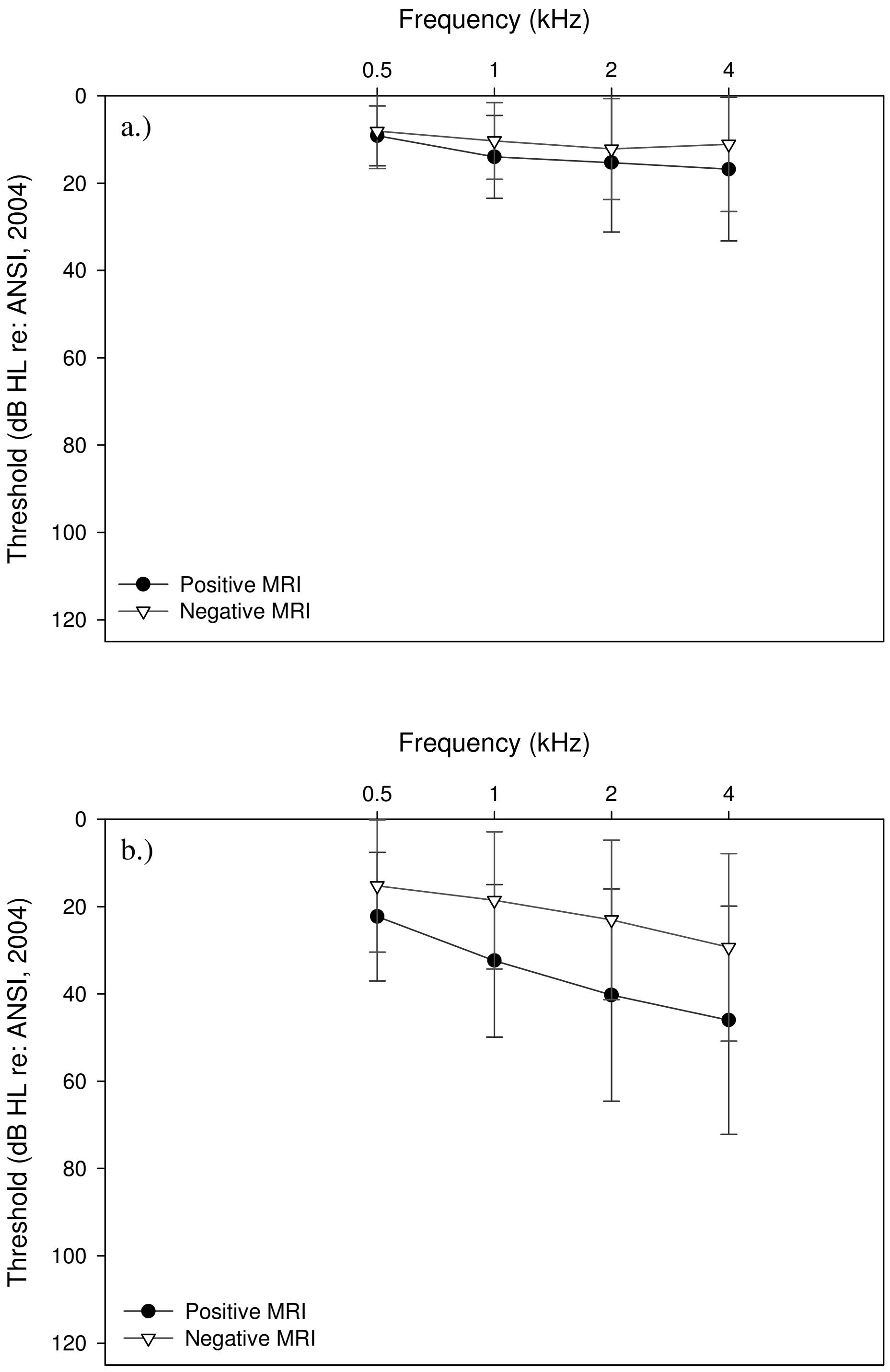


Figure 8. Age and gender corrected thresholds in the better ear (panel a) and the poorer ear (panel b) for the positive VS group (n = 19) and the negative VS group (n = 309). Error bars represent 1 standard deviation from the mean

Table 10

Mann-Whitney U test results for between-group comparisons of pure tone thresholds that were corrected for age and gender

Better and Poorer Ear Thresholds			
Ear	Frequency (Hz)	*Z* score	*p*-value
Better	500	-1.020	.308
	1000	-1.713	.087
	2000	-.750	.453
	4000	-1.790	.073
Poorer	500	-2.826	.005**
	1000	-3.750	.0005***
	2000	-3.430	.001***
	4000	-2.895	.004***

Difference Between Ears		
Frequency (Hz)	*Z* score	*p*-value
500	-2.421	.015*
1000	-2.924	.003***
2000	-3.133	.002***
4000	-1.896	.058

* $p<.05$ ** $p<.01$ *** $p<.005$

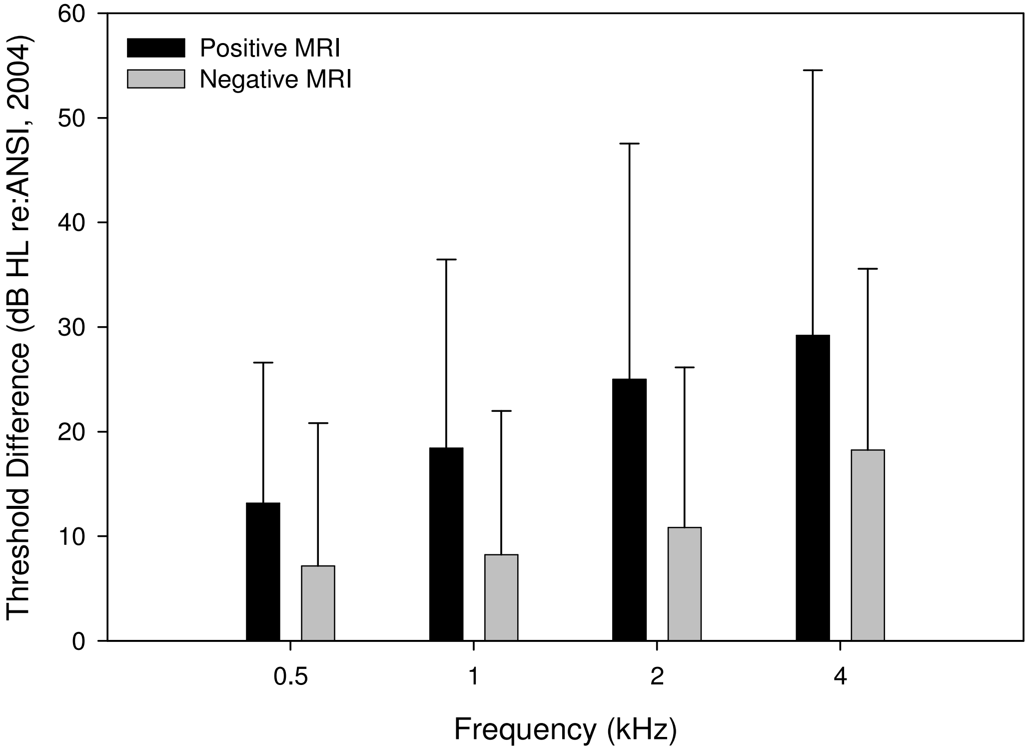


Figure 9: Age and gender corrected thresholds for the difference between ears for the positive VS group (*n* = 19) and the negative VS group (*n* = 309). Error bars represent 1 standard deviation from the mean.

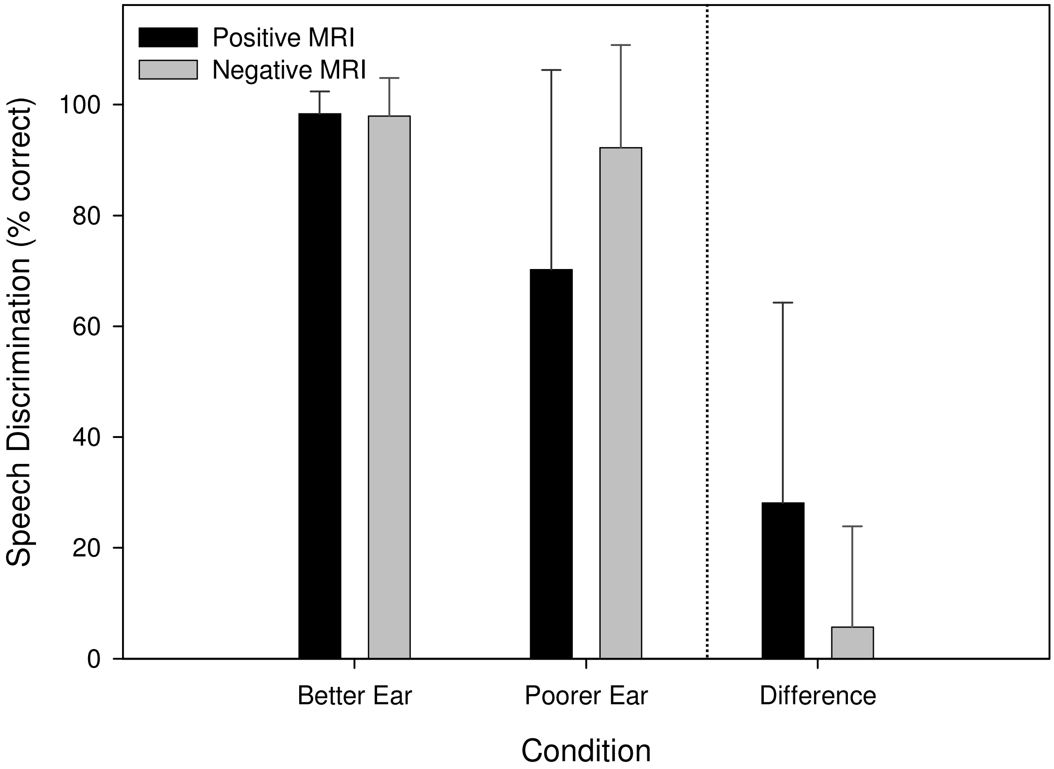


Figure 10. Mean SDSs in the better ear and the poorer ear for patients with a positive MRI (*n* = 19) and a negative MRI (*n* = 309). The difference between the ears is also shown. Error bars represent 1 standard deviation from the mean.

without a VS. The interaural difference scores were also significantly different between groups (z = -3.625, *p* = .0005), with the larger difference between scores noted in the group with a positive MRI. Figure 11 presents box plots, based on the same data for the better and poorer ears of both groups. Each box represents the 25th (bottom of the box) to the 75th percentile (top of the box) of speech scores for each group and ear condition. The whiskers, or error bars, represent the 10th (bottom whisker) to the 90th (top whisker) percentile of speech scores. There was no representation for the 90th percentile because there was a ceiling effect when the scores were grouped in each ear for both groups. The black dots show the outliers that were not included of the 10th to the 90th percentile of scores. For the negative MRI group, there was one outlier (for the poorer ear) which was identified as a score from a patient with another retrocochlear disorder. The median score is represented by the solid line, and the mean is the dotted line.

Each patient's predicted score using the AI was calculated following the example presented previously (see Tables 1 though 3). The patient's observed percent correct score was then subtracted from their predicted score. Results are shown in Figure 12. The difference between the predicted and the observed scores in the better ear was not significantly different between groups (z = -1.591, *p* = .112); however, this difference was significant in the poorer ear (z = -2.832, *p* = .005) with the patients with a VS having a greater difference between their predicted AI score and their observed SDS. A positive difference between the predicted and the observed AI scores indicated poorer performance than expected using the AI. The difference

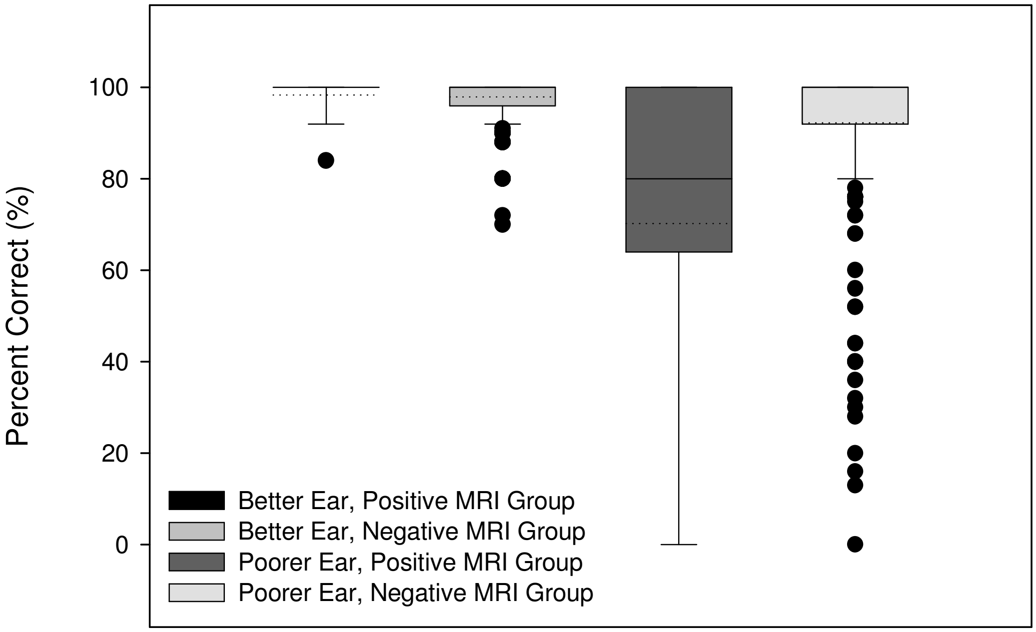


Figure11. Mean SDSs in the better ear and the poorer ear for patients with a positive MRI (*n* = 19) and a negative MRI (*n* = 309). The box represents the values for the 25th (bottom of the box) to the 75th (top) percentile of speech scores. The error bars indicate the 10th (lower bar) to the 90th percentile (not represented due to ceiling effect). The black dots represent the outliers that were not included in the 10th to 90th percentile of scores. There were many more outliers identified for the negative MRI group because the majority (10th to 90th percentile) of patients had much higher SDSs than those patients represented as outliers. For the negative MRI group, there was one outlier (for the poorer ear) which was identified as a score from a patient with another retrocochlear disorder.

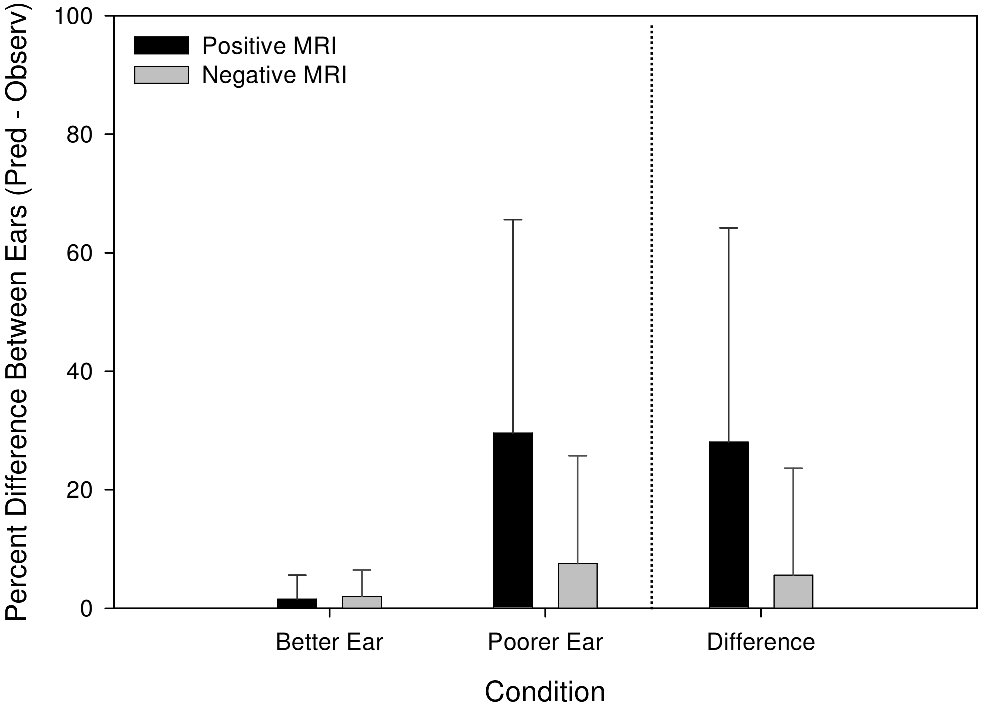


Figure 12. For each person in the positive group (*n* = 19) and the negative group (*n* = 309), an AI predicted score was calculated. Their observed SDS was subtracted from their predicted AI score. The results are shown above for the better and poorer ears, and the difference between these two results. The error bars represent 1 standard deviation from the mean.

between the predicted and observed scores for each ear was used to find the difference between the ears. The better ear difference was subtracted from the poorer ear difference. Results of the Mann-Whitney U test indicated a significant difference between the two groups ($z = -3.245$, $p = .001$). The positive MRI group exhibited a significantly larger difference between the two scores compared to the negative MRI group.

Acoustic Reflex Thresholds. Reflex thresholds at .5, 1, and 2 kHz were recorded in the stimulus ear with a contralateral presentation. The mean acoustic reflex thresholds for the better and the poorer ear are shown in Figures 13a (better ear) and b (poorer ear). Complete data were not available for all participants. A Mann-Whitney U test comparing the positive and negative MRI groups was performed for each frequency for the better and poorer ears. Results of the analysis are shown in Table 11. Statistically significant differences were noted with the stimulus presented to the better ear at 1 and 2 kHz and to the poorer ear at .5, 1, and 2 kHz. For all of the analyses that were significant, the positive MRI group had significantly higher thresholds than the negative MRI group. Based on the findings reported by Prasher and Cohen (1993), the absolute interaural differences in acoustic reflex thresholds were calculated (see Figure 14). An analysis of these threshold differences failed to reveal any group effects at any frequency: .5 kHz ($z = -.537$, $p > .05$), 1 kHz ($z = -.630$, $p > .05$), and 2 kHz ($z = -.056$, $p > .05$). Prasher and Cohen's specific criteria stated a >10 dB difference at two-adjacent frequencies. A chi square analysis for their criterion using data from the current patient population was not significant ($x^2 = .811$, $p > .05$).

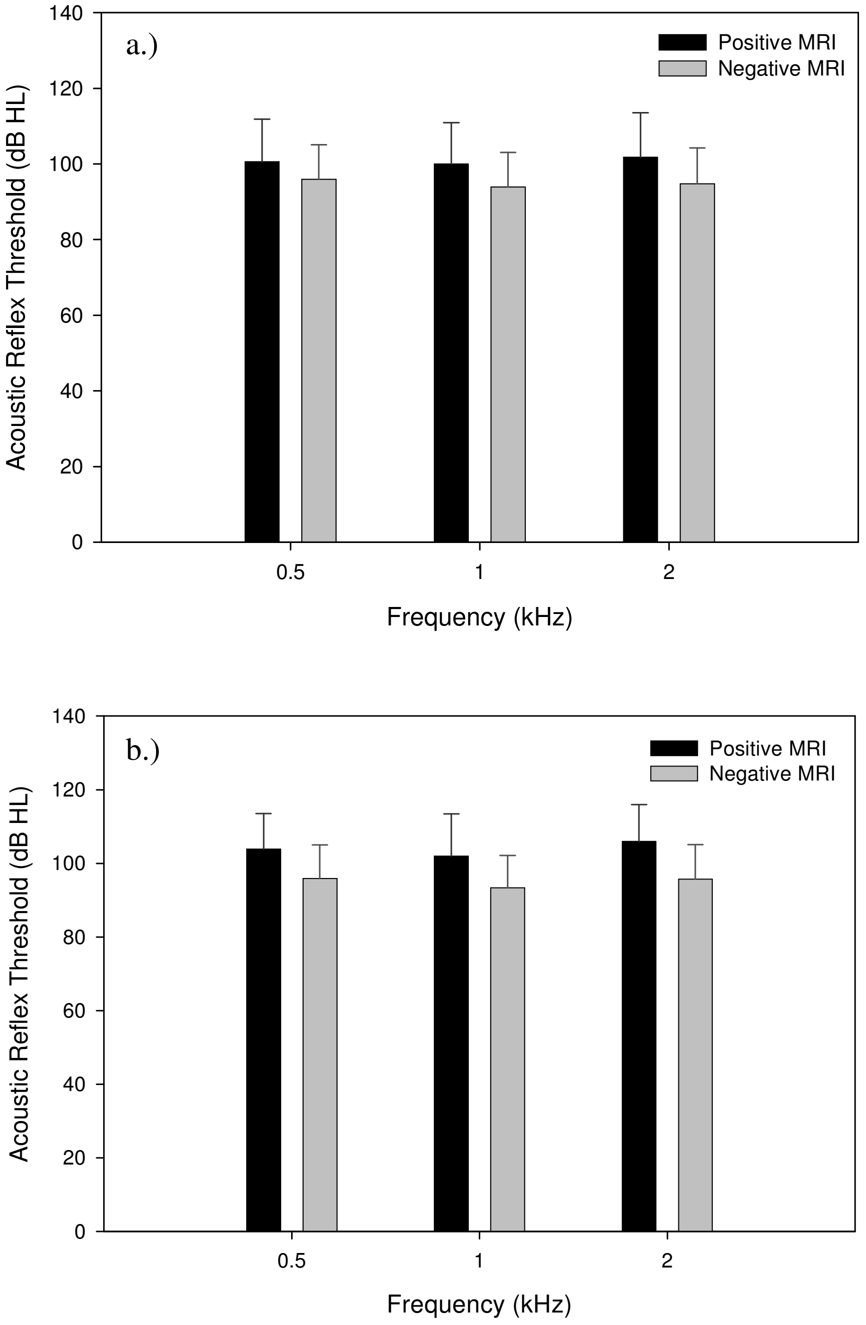


Figure 13. Average acoustic reflex thresholds (dB HL) for the better ear (panel a) and poorer ear (panel b) at .5, 1, and 2 kHz for the positive VS patients (*n* = 19) and the negative VS patients (*n* = 309). Data were not complete for every condition (see Table 11). Error bars represent 1 standard deviation from the mean.

Table 11

Mann-Whitney U test results of group differences in acoustic reflex thresholds for the better and poorer ears. The number of participants with data in each condition is listed for each group (n).

Stimulus Ear/ Frequency (Hz)	*n* (positive MRI)	*n* (negative MRI)	*Z* score	*p*-value
Better				
500	19	297	-1.928	.054
1000	19	301	-2.773	.006**
2000	17	278	-2.537	.011*
Poorer				
500	18	300	-3.171	.002***
1000	18	306	-2.999	.003***
2000	16	281	-3.633	.0005***

* *p*<.05 ** *p*<.01 *** *p*<.005

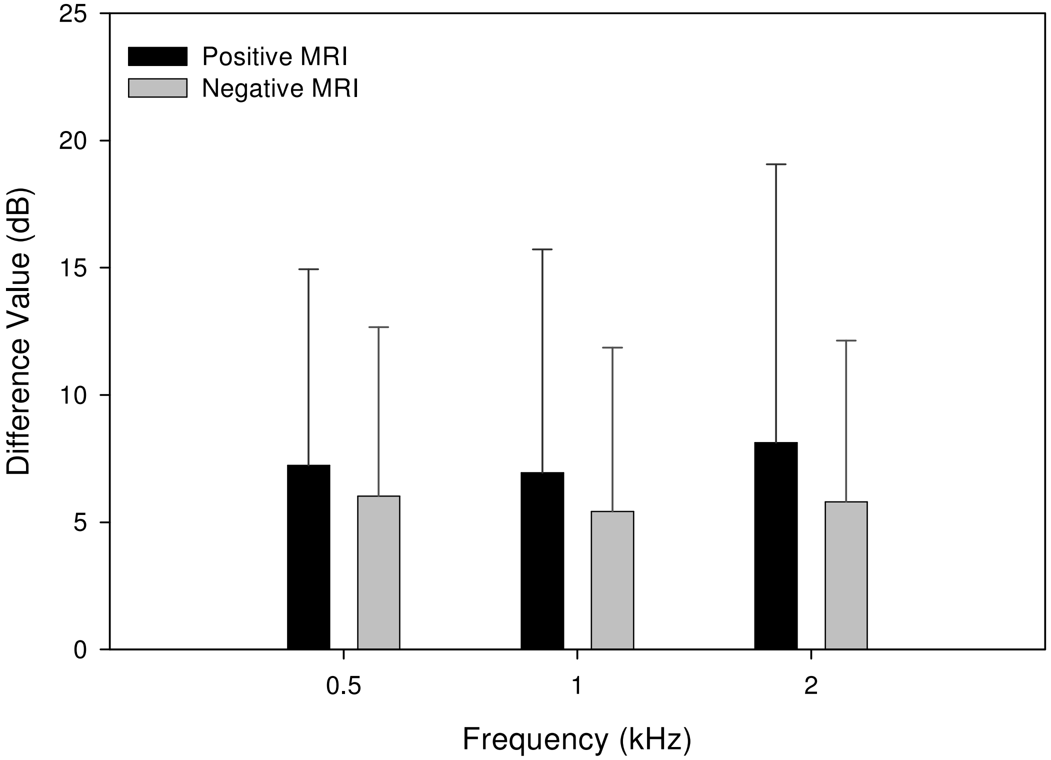


Figure 14. Absolute differences in acoustic reflex thresholds between the ears in the contralateral condition at .5, 1, and 2 kHz for the positive MRI group (*n* = 19) and negative MRI group (*n* = 309). Data were not complete for every condition (see results). Error bars represent 1 standard deviation from the mean.

Acoustic reflex thresholds were also categorized as normal, elevated, or absent using the normative values reported by Gelfand et al. (1990). Results are presented in Figure 15a (better ear) and b (poorer ear). The results for each ear are separated into panels for each group, and show the proportion of patients who had normal, elevated, or absent acoustic reflex thresholds. An omnibus chi square test was performed separately for each of the three frequencies in the better and poorer ears to determine whether the groups differed on the proportion of patients with normal, elevated, or absent acoustic reflexes. Results for each of the chi square analyses were statistically significant (see Table 12). Post hoc comparisons using 2x2 chi square comparisons are presented in Table 13. Results were ordered based on their *p*-value and ordered from lowest to highest before a Holm's Sequential Bonferonni Correction was applied. Significant findings were only those with a p-level less than the adjusted alpha for each comparison. Post hoc comparisons for .5 kHz in the better ear revealed no statistically significant comparisons between the group with a VS and the group without a VS. Statistically significant differences were found between the groups in the better ear at 1 kHz for comparisons of normal vs. elevated reflexes and normal versus absent reflexes. The negative MRI group exhibited significantly more reflexes classified as "normal" than the positive MRI patients. A statistically significant difference was also noted in the better ear at 2 kHz with the positive MRI group having fewer normal reflexes and more absent acoustic reflexes compared to the negative MRI group. Similar statistical results were found when the stimulus was presented to the poorer ear at .5 kHz and 2 kHz. At each of these frequencies, a greater proportion of patients with a positive MRI had absent reflexes than patients

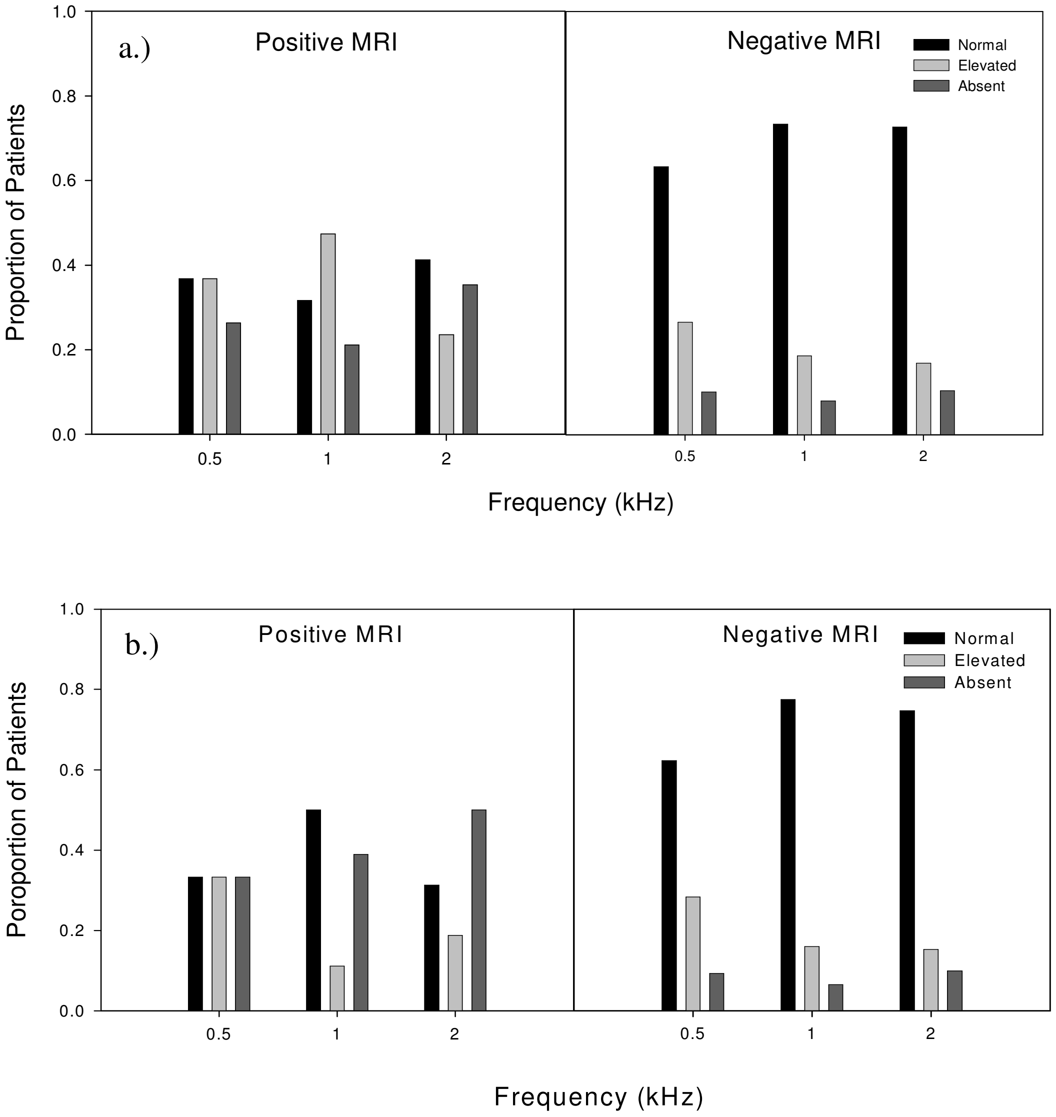


Figure 15. Proportion of patients in each group who had normal, elevated, and absent acoustic reflex thresholds in the better ear (panel a) and poorer ears (panel b) at .5, 1, and 2 kHz for the positive VS patients (n = 19) and the negative VS patients (n = 309). Data were not available on all participants (see Table 12).

Table 12

Chi square results of group differences in acoustic reflexes threshold categories (normal, elevated, or absent). The number of participants with data is represented for each group (n).

Comparison Frequency (Hz)	*n* (positive MRI)	*n* (negative MRI)	x^2	*p*-value
Better				
500	19	297	6.953	.031*
1000	19	301	15.184	.001***
2000	17	278	10.995	.004***
Poorer				
500	18	300	11.650	.003***
1000	18	306	23.300	.0005***
2000	16	281	24.088	.0005***

* p<.05 ** p<.01 *** p<.005

Table 13

Post hoc chi square results reordered for Holm's Bonferroni Correction.

	Comparison Frequency (Hz)	x^2	LSD *p*-value(adjusted alpha)
Better	500		
	Normal vs Absent	6.865	.022(0167)
	Normal vs. Elevated	2.610	.136(.025)
	Elevated vs. Absent	1.052	.325(.05)
Better	1000		
	Normal vs. Elevated	13.014	.001(.0167)****
	Normal vs. Absent	8.967	.016(.025)****
	Elevated vs. Absent	.003	1.000(.05)
Better	2000		
	Normal vs. Absent	11.308	.005(.0167)
	Normal vs. Elevated	2.043	.234(.025)
	Elevated vs. Absent	1.747	.304(.05)
Poorer	500		
	Normal vs. Absent	12.203	.003(.0167)****
	Elevated vs. Absent	3.485	.086(.025)
	Normal vs. Elevated	1.856	.209(.05)
Poorer	1000		

Table 13 (cont.)

Post hoc chi square results reordered for Holm's Bonferroni Correction.

Comparison Frequency (Hz)	x^2	LSD *p*-value(adjusted alpha)
Normal vs. Absent	21.865	. 0005(.0167)****
Elevated vs. Absent	8.347	.007(.025)****
Normal vs. Elevated	.008	1.000(.05)
Poorer 2000		
Normal vs. Absent	24.857	.0005(.0167)****
Elevated vs. Absent	4.286	.052(.025)
Normal vs. Elevated	2.246	.150(.05)

****p<alpha

with a negative MRI. The negative MRI group also had a greater proportion of patients with normal acoustic reflexes compared to the positive MRI group. In the poorer ear at 1 kHz, however, there was a significant difference between the groups for the normal vs. absent comparison and for the elevated vs. absent comparison with the positive MRI group having a greater proportion of absent acoustic reflexes compared to the negative MRI group.

A third analysis of the acoustic reflex thresholds compared the proportion of patients with normal acoustic reflex thresholds vs. abnormal acoustic reflex thresholds. The two previous categories of “elevated” acoustic reflex thresholds and “absent” acoustic reflex thresholds were combined to form a category labeled “abnormal” acoustic reflex thresholds. Figure 16a and b show the proportion of patients in the two groups who have acoustic reflex thresholds classified as normal and abnormal for the better and poorer ear, respectively. Results of the chi square analysis are shown in Table 14. Statistically significant results were found for each stimulus ear at each frequency. A smaller proportion of positive MRI patients had normal acoustic reflexes than the negative group and a larger proportion of positive MRI patients had abnormal reflexes than the negative MRI group.

Acoustic Reflex Adaptation. Acoustic reflex adaptation (decay) results were not analyzed statistically. A large proportion of the patients in the study sample did not have results for this test. Anecdotally, with the contralateral stimulus presented to the better ear, there were two individuals with positive adaptation and 93 individuals with negative adaptation in the negative MRI group. In the positive MRI group, there were no individuals with a positive adaptation

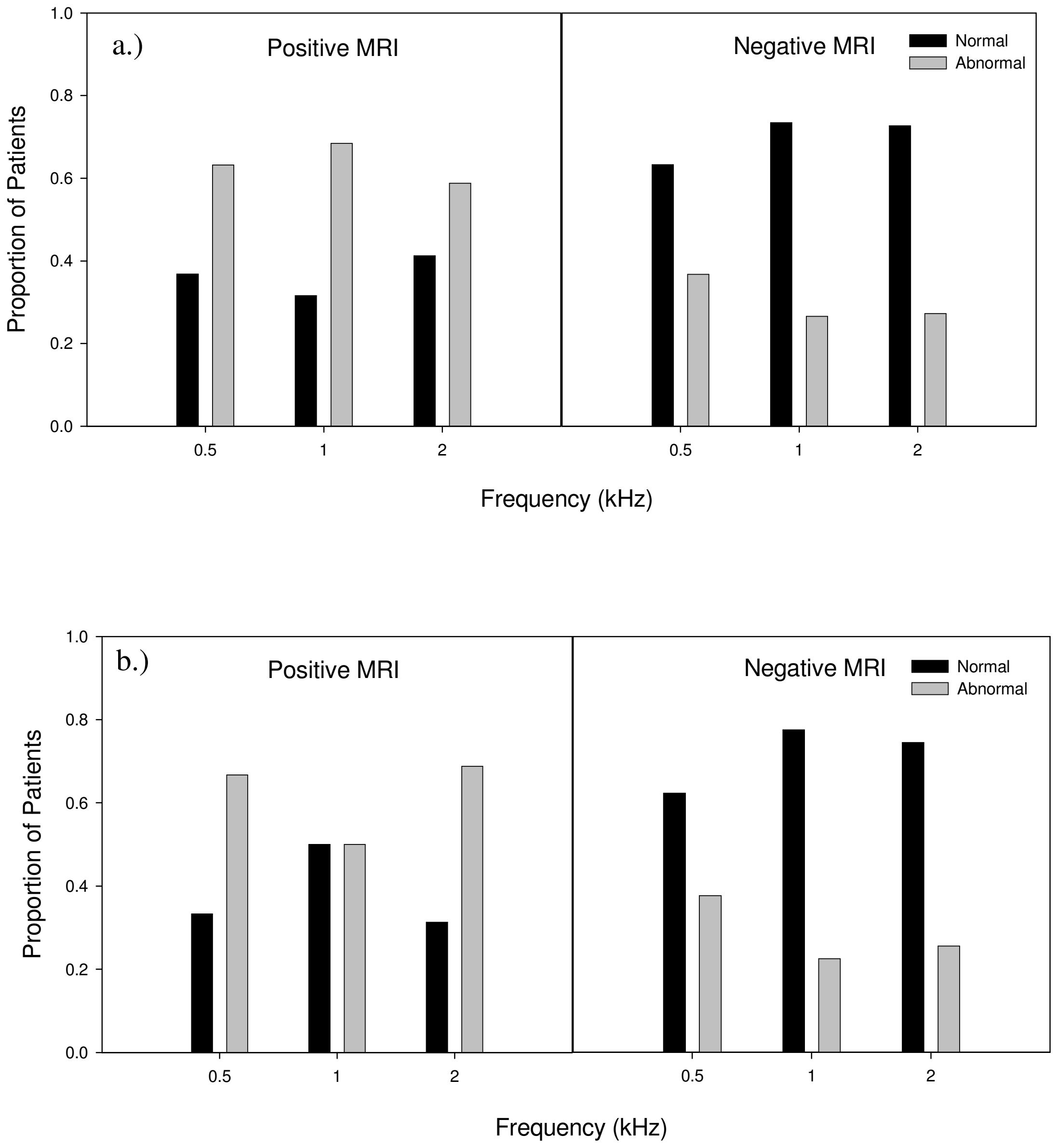


Figure 16. Proportion of patients in the VS (n = 19) and the non-VS (n = 309) groups who presented with normal versus abnormal acoustic reflex thresholds. Thresholds are shown for the better ear (panel a) and poorer ear (panel b) at .5, 1, and 2 kHz. Data were not available on all participants (see Table 14).

Table 14

Chi square results of group differences in acoustic reflex categories (normal or abnormal). The number of patients with available data is shown for each group (n).

Stimulus Ear Frequency (Hz)	*n* (positive MRI)	*n* (negative MRI)	x^2	LSD *p*-value
Better				
500	19	297	5.290	.028*
1000	19	301	15.178	.0005***
2000	17	278	7.689	.011*
Poorer				
500	18	300	5.986	.023*
1000	18	306	7.008	.019*
2000	16	281	14.073	.001***

* $p<.05$ ** $p<.01$ *** $p<.005$

result and nine individuals with negative adaptation results (for stimuli presented to the better ear). With the stimulus presented to the poorer ear, there was one individual in each group with a positive adaptation outcome, compared to negative results observed in 97 individuals in the negative MRI group and eight individuals in the positive MRI group.

Presenting Symptoms/Outcomes

The second experimental question asks whether there was a difference between the groups in terms of their presenting symptoms or outcomes that led to the MRI referral. The presenting symptoms/outcomes of all of the patients are reported in Table 15. This table also shows the number of participants in each group reporting these symptoms and the results of the chi square statistical analysis comparing the frequency of each reported symptom in the positive and negative MRI groups. The only symptoms/outcomes that were statistically significant between the groups were asymmetrical word recognition, presence of positive rollover, and unilateral tinnitus.

Logistic Regression Analysis

The third experimental question addresses whether there was a set of audiological outcomes and presenting symptoms that maximally distinguishes the patients with and without a positive MRI. To that end, a logistic regression analysis was performed. Variables for the model were chosen to represent each clinical test (pure tone audiometry, speech discrimination, and acoustic reflexes) and the presenting symptoms that were significantly different between the two groups. The variables chosen for the audiologic test outcomes were selected to represent the most clinically relevant variables. For instance, raw acoustic reflex thresholds were entered

Table 15

Results of the chi square analysis for the patients' primary presenting symptoms. The number of patients in each group who presented with the symptoms is also represented (n)

Symptom	Positive MRI (*n*)	Negative MRI (*n*)	*df*	*LSD p*-value
Hearing Loss				
Asymmetrical	12	152	1	.345
Unilateral	5	98	1	.800
Sudden	1	10	1	.487
Progressive	8	44	1	.004***
Fluctuating	1	7	1	.383
Subjective	0	7	1	1.000
Asymmetrical SDS	6	5	1	.0005***
Positive Rollover	2	3	1	.029*
Tinnitus				
Asymmetrical	2	32	1	1.000
Unilateral	12	107	1	.024*
Bilateral/Unspecified	0	41	1	.146
Vestibular				
Vertigo	6	71	1	.406
Imbalance	2	8	1	.108
V. Weakness	3	15	1	.077

Table 15 (cont.)

Primary presenting symptoms

Symptom	*n* Positive MRI	*n* Negative MRI	*df*	*LSD p*-value
Neurologic				
Otalgia	1	6	1	.344
Bells Palsy	0	5	1	1.000
Trigeminal Neuralgia	1	4	1	.259
Extremity Weakness	0	3	1	1.000
Headache	1	11	1	.517
Aural Fullness	2	37	1	1.000
History of Meniere's Dx	0	8	1	1.000
Sudden Onset of Symptoms	3	22	1	1.000
Unknown	0	1	1	1.000
Other	1	18	1	1.000

* $p<.05$ ** $p<.01$ *** $p<.005$

instead of categorically classified acoustic reflexes because it is more likely that the raw acoustic reflex values would be used clinically. The variables entered into the regression model were: the differences at each frequency in pure-tone thresholds (.25 – 8 kHz) between the better and poorer ear (continuous variable), the criteria for asymmetrical hearing loss (>15 dB HL) for each rule (single frequency, two-adjacent frequencies, three-adjacent frequencies, and high frequency average) (binary variable), the difference between the better and poorer ear SDSs (continuous variable), the raw contralateral acoustic reflex thresholds in both ears (continuous variable), and the presence or absence of unilateral tinnitus (binary variable). The total number of variables entered was 43. Continuous variables were entered as raw values, whereas binary variables were entered as a one (patient has the symptom or asymmetry) or zero (patient does not have the symptom or asymmetry). A forward and a backward stepwise regression were performed because the outcome of the two methods was expected to produce different models. Both the forward and backward models used the Wald method, which applies the z statistic with a chi square distribution. Agresti (1996) found that the Wald test was not appropriate for small sample sizes, but this investigation has a large sample size. Demidenko (2007) advocated the use of the Wald test because the z-score statistic is routinely used for significance testing of regression coefficients.

The forward stepwise regression results can be seen in Table 16 (included predictor variables) and 17 (excluded variables). There were 286 cases included in the model and 42 excluded cases (three positive MRI and 39 negative MRI cases). After three steps, the model indicated the predictor variables to be unilateral tinnitus, the

Table 16

Results of the forward logistical regression for included predictor variables.

Variable	B coefficient	S.E. (standard error)	Wald	Significance
Unilateral tinnitus^{++}	1.296	.603	4.616	.032
Interaural Difference in SDS^{+++}	.018	.010	2.939	.086
Mean ART^{+} poorer ear at 1 kHz^{+++}	.090	.029	9.519	.002
Constant	-12.496	2.998	17.377	.0005

$^{+}$ART = Acoustic reflex threshold

$^{++}$ Binary variable = entered in equation as a 1 or 0 value

$^{+++}$ Continuous variable = entered in equation as the raw calculated value

Table 17

Results from the forward logistic regression for all excluded variables.

Variable	Score++	Significance
Difference between ears		
250 Hz	.841	.359
500 Hz	1.278	.258
1000 Hz	.002	.968
2000 Hz	1.313	.252
3000 Hz	.138	.710
4000 Hz	1.050	.305
6000 Hz	.434	.510
8000 Hz	.345	.557
Mean ART+ Better Ear		
500 Hz	.456	.499
1000 Hz	2.052	.152
2000 Hz	.862	.353
Mean ART+ Poorer Ear		
500 Hz	.507	.477
2000 Hz	1.378	.241
Two Adjacent Frequency Asymmetry		

Table 17 (cont.)

Results from the forward logistic regression for all excluded variables.

Variable	Score^{++}	Significance
15 dB	.211	.646
20 dB	.279	.598
25 dB	1.320	.251
30 dB	.043	.836
35 dB	.495	.842
40 dB	.495	.842
45 dB	.394	.530
50 dB	.512	.474
55 dB	.364	.547
Three Adjacent Frequency Asymmetry		
15 dB	.105	.745
20 dB	.0005	.997
25 dB	.614	.433
30 dB	.063	.801
35 dB	.103	.749
40 dB	.148	.701
45 dB	.447	.504

Table 17 (cont.)

Results from the forward logistic regression for all excluded variables.

Variable	Score[++]	Significance
50 dB	.720	.396
55 dB	.005	.943
High Frequency Average Asymmetry		
15 dB	.467	.494
20 dB	.220	.639
25 dB	.001	.980
30 dB	.801	.371
35 dB	1.925	.165
40 dB	1.707	.191
45 dB	.412	.521
50 dB	.895	.344
55 dB	.709	.400

[+] ART = Acoustic Reflex Threshold

[++] Score = The score test is used to decide whether the variable would be significant if included in the model difference between the SDSs between ears, and the mean acoustic reflex threshold in the poorer ear at 1 kHz. The resulting regression equation with a cutoff value of (.060) was:

$$\hat{g} = 1.296(\text{unilateral tinnitus}) + .018(\text{difference in SDS}) + .090(\text{acoustic reflex threshold in the poorer ear at 1 kHz}) - 12.496. \tag{4}$$

The cutoff value was set at (.060) because that was the percentage of the current sample of patients who were diagnosed with a VS.

The model was applied to the data of the positive and negative MRI groups to determine its accuracy in classification. The model correctly identified 11 out of 16 VS patients that were counted in the model. Using this model, there would have been five patients diagnosed with VS who were not identified. The regression equation made a false positive prediction in 61 out of the 270 patients included in the model resulting in a sensitivity rate of 68.75% (11/16 – correctly identified as having a suspected VS) and a specificity rate of 77.4% (209/270 – correctly identified as not having a VS).

A backwards regression model was also attempted using the same variables and the same cutoff value as in the forward regression method (see Tables 18 and 19). The same number of excluded cases was noted using this method. All of the possible predictor variables were inserted and after 38 steps, predictor variables were identified as: unilateral tinnitus, the difference between thresholds at 2 kHz, the raw acoustic reflex threshold at 2 kHz in the poorer ear, the asymmetry values for the rules >25 and >55 dB HL at two-adjacent frequencies, >50 dB HL at three-adjacent

Table 18

Results of the backward logistical regression for included predictor variables.

Variable	B coefficient	S.E. (standard error)	Wald	Significance
Unilateral tinnitus^{+++}	2.078	.723	8.247	.004
Difference between Ears				
2000 Hz^{++++}	.061	.023	7.170	.007
Mean ART^{+} poorer ear at 2 kHz^{++++}	.120	.033	12.763	.0005
2 Adjacent Frequency Asymmetry				
25 dB^{+++}	-3.860	1.475	6.844	.009
55 dB^{+++}	4.239	1.750	5.869	.015
3 Adjacent Frequency Asymmetry				
50 dB^{+++}	-7.489	2.539	8.699	.003
HFA^{++} Asymmetry				
35 dB^{+++}	3.285	1.309	6.297	.012
Constant	-16.522	3.659	20.485	.0005

$^{+}$ART = Acoustic reflex threshold

$^{++}$ HFA = High frequency average

$^{+++}$ Binary variable = entered in equation as a 1 or 0 value

$^{++++}$ Continuous variable = entered in equation as the raw calculated value

Table 19

Results from the backward logistic regression for all excluded variables.

Variable	Score^{++}	Significance
Difference in pure tone thresholds between ears		
250 Hz	.284	.594
500 Hz	.001	.980
1000 Hz	.239	.625
3000 Hz	.044	.813
4000 Hz	1.525	.217
6000 Hz	.056	.813
8000 Hz	.044	.834
Difference in SDS	.430	.512
Mean ART^{+} Better Ear		
500 Hz	.096	.747
1000 Hz	1.581	.209
2000 Hz	.006	.936
Mean ART^{+} Poorer Ear		
500 Hz	.127	.721
1000 Hz	.261	.610
2 Adjacent Frequency Asymmetry		

Table 19 (cont.)

Results from the forward logistic regression for all excluded variables.

Variable	Score++	Significance
15 dB	.016	.898
20 dB	.548	.459
30 dB	.221	.639
35 dB	.462	.497
40 dB	.462	.497
45 dB	.0005	.989
50 dB	.334	.563
3 Adjacent Frequency asymmetry		
15 dB	.072	.789
20 dB	.068	.794
25 dB	.856	.355
30 dB	.303	.582
35 dB	.489	.485
40 dB	.054	.817
45 dB	.410	.522
55 dB	.492	.483

Table 19 (cont.)

Results from the backward logistic regression for all excluded variables.

Variable	Score[++]	Significance
High Frequency Average Asymmetry		
15 dB	2.216	.137
20 dB	2.195	.138
25 dB	.214	.643
30 dB	.017	.897
40 dB	.095	.757
45 dB	.015	.903
50 dB	.133	.715
55 dB	.016	.900

[+] ART = Acoustic Reflex Threshold

[++] Score = The score test is used to decide whether the variable would be significant if included in the model frequencies, and >35 dB HL for the high frequency average. The regression equation was:

$$\hat{g} = 2.078(\text{unilateral tinnitus}) + .061(\text{difference in threshold at 2 kHz}) + .120(\text{acoustic reflex threshold in the poorer ear at 2 kHz}) + (-3.860)(\text{asymmetry} >25 \text{ dB HL at two-adjacent frequencies}) + 4.239(\text{asymmetry} >55 \text{ dB HL at two-adjacent frequencies}) + (-7.489)(\text{asymmetry} >50 \text{ dB HL at three-adjacent frequencies}) + 3.285(\text{asymmetry} >35 \text{ for high frequency average}) - 16.552 \tag{5}$$

Again, the model was applied to the existing data set. The backwards regression model identified 13 out of 16 VS patients and predicted a false positive outcome in 47 out of the 270 negative MRI patients resulting in a sensitivity rate of 81.25% (13/16 – correctly identified as having a suspected VS) and a specificity rate of 82.59% (223/270 – correctly identified as not having a VS).

Sub-Analyses

Positive MRI group vs. negative group without retrocochlear disorders. Although patients in the negative MRI group were those not diagnosed with a VS, some of them were diagnosed with other types of retrocochlear lesions including: vascular loops, meningiomas, cysts, and Chiari malformations (n = 19). These individuals were removed from the negative group for a new analysis, and this new negative group had 290 patients. Re-analyses with this limited data set were performed for pure tone thresholds in the better and poorer ears, the difference in pure tone thresholds between ears, the raw SDSs, and the raw acoustic reflex thresholds. The results (shown in Appendix B) for each of these measures in all of the different conditions revealed exactly the same significant differences as in the main analyses of this investigation. There was no difference in the results when the negative group included other retrocochlear disorders compared to when these patients were removed from the analysis.

Positive MRI group vs. group with other retrocochlear disorders. The 19 patients who were removed for the previous sub-analysis formed a new group called "other" retrocochlear disorders. The positive MRI patients (*n* = 19), who were diagnosed with a VS, were compared to the group with other retrocochlear disorders (*n* = 19). Analyses were performed for pure tone thresholds in the better and poorer ears, the difference in pure tone thresholds between ears, the raw SDSs, and the raw acoustic reflex thresholds. Results can be found in Appendix C. This comparison revealed some differences between the two groups. The pure tone threshold results for the better ear revealed significant differences between the two groups at .25, 3, 4, and 6 kHz, with the patients in the positive MRI group having poorer thresholds than the group with other retrocochlear disorders. The poorer ear results were significantly different between groups across test frequencies with the exception of .5 kHz. The patients with diagnosed VSs had poorer pure tone thresholds across test frequencies. This suggests that, although these other retrocochlear disorders could be causing similar symptoms and outcomes, the patients with the VSs continued to have poorer thresholds. The interaural difference in pure tone thresholds was only significant between the groups at 3 and 8 kHz. Speech discrimination abilities between the groups remained significant in the poorer ear and in the difference between the better and poorer ear score, similar to the main analysis. Finally, the acoustic reflex thresholds were significantly different between groups in both the better and the poorer ears at 1 and 2 kHz. In summary, the most evident differences between these groups are the pure tone thresholds in the poorer ear, SDSs, and the acoustic reflex thresholds in both ears. These patterns are similar, but not identical to the overall comparison of the positive and negative MRI groups. These speculations should be interpreted with caution considering the large difference in the two group sample sizes in the main investigation compared to the equal group numbers in this sub-analysis.

Chapter 6: Discussion

The overall purpose of this study was to identify the principal symptoms and audiologic characteristics of patients with a confirmed diagnosis of VS (via MRI testing). To attain this goal, an evaluation was conducted to assess the differences in symptom presentation and audiologic test results between all patients who were referred for an MRI of their IACs at WRAMC within a 25 month time period (November 2005 through October 2007). The audiometric tests investigated were pure tone thresholds, speech discrimination, and acoustic reflex thresholds. In conjunction with the presenting symptoms, the outcome of this study aimed to produce an evidence-based referral protocol for MRI to rule out the presence of VS.

Data collection for this investigation was entirely retrospective. Patient information was obtained from the Radiology Department at WRAMC. Data were recorded on all 628 patients provided; however, this analysis included patients with at least audiometric data including pure tone thresholds, speech discrimination results in both ears, and attempted contralateral acoustic reflex thresholds. The final number of patients whose data were analyzed was 328, 19 of whom had a positive MRI indicative of a VS.

Effect of Group on Audiological Presentation

Pure-Tone Audiogram. The first experimental question addresses the differences between patients with a positive MRI and a negative MRI in terms of their pure-tone audiograms. Pure tone thresholds were analyzed multiple ways. The first comparison was between the groups for thresholds in their right ear and their left ear. It was hypothesized that this comparison would not be a beneficial comparison between groups because of the random presentation of hearing losses in both ears. Analyses of the pure tone thresholds revealed significantly different thresholds between groups across all test frequencies in the right ear and significantly different thresholds between groups at 1 and 2 kHz in the left ear. All differences suggested the group with the positive MRIs had poorer, or worse, thresholds than the group with negative MRIs. Patients in the positive MRI group had generally higher thresholds in the right ear compared to the left ear (average of pure tone thresholds across all test frequencies). The average of all pure tone thresholds was 39.10 dB in the right ear and 34.21 dB in the left ear. Thirteen of the 19 patients (68.4%) in the positive MRI group presented with an affected right ear. In contrast, the patients in the negative MRI group had fairly equivalent averaged pure tone thresholds across all test frequencies for the right and left ears. The mean pure tone threshold was 25.59 dB in the right ear and 25.97 dB in the left ear. One hundred and thirty nine out of 309 patients (44.98%) in the negative MRI group presented with a poorer right ear. Because hearing loss occurred in both ears for both groups but at different frequencies of presentation, this method of evaluating the pure tone thresholds was not expected to provide the answer to the hypothesized question. There were no previous reports comparing pure tone thresholds for the right and left ear of patients with a VS and a control group. This appears to be a novel finding and likely reflects the poorer hearing sensitivity, overall, of patients with a positive MRI compared to the patients with a negative MRI, especially in the affected ear. There were also more positive MRI patients with an affected right ear ($n = 13$) compared to an affected left ear ($n = 6$).

The second analysis of the pure tone thresholds involved comparing the better ear and the poorer ear for the negative MRI group and the unaffected and affected ear for the positive MRI group. The ears were classified following the calculation of the average of pure tone thresholds across test frequencies. The ear with the lower mean threshold was identified as the better ear for the negative MRI group; however, the ear without the VS was noted as the unaffected ear for the positive MRI group. It was expected that a VS would cause increased hearing loss (Baguely et al., 2006; Caye-Thomasen et al., 2007; Forton et al., 2004; Graamans et al., 2003; Matthies & Samii, 1997; Neary et al., 1996; Portmann et al., 1989; and Sauvaget et al., 2005); therefore, the better ear of the negative MRI group was compared to the unaffected ear of the positive MRI group. An analysis comparing the better ear to the unaffected ear revealed no significant differences between groups across test frequencies with the exception of .25 kHz. The comparison of the poorer ear to the affected ear indicated significantly different thresholds between groups across all test frequencies. All significantly different results showed that the positive MRI group had significantly poorer thresholds than the negative MRI group in the affected/poorer ear.

In the majority of the cases, patients with a VS exhibit hearing loss at least in the affected ear (Baguely et al., 2006; Caye-Thomasen et al., 2007; Forton et al., 2004; Graamans et al., 2003; Matthies and Samii, 1997; Portman et al., 1989; Sauvaget et al., 2005). There have been no previous reports that compared patients with and without a diagnosed VS on the basis of their audiogram (better vs. poorer ear). There have only been reports of patients with a diagnosed VS analyzing the difference between their affected and unaffected ears, with the affected ear showing significantly poorer thresholds across test frequencies than the unaffected ear (Caye-Thomasen et al., 2007; Graamans et al., 2003; Portmann et al., 1989).

Obholzer et al. (2004) calculated the sensitivity and specificity rates for different asymmetry criteria across test frequencies. Although there were no data presented on the patients' audiograms, the thresholds in the mid to high frequencies (2-8 kHz) had higher sensitivity rates than those in the lower frequencies (.25- 1 kHz). This could be expected because VSs typically affect the higher frequencies first, which is assumed to be the result of the tumor's compression on the outer surface of CN VIII. However, this observation contrasts with the current results, because the greatest threshold differences between groups were in the low to mid frequencies (.25-3 kHz). There are a few possible reasons for this contrast. First, it is possible that the patients in the current study may have had more hearing loss than the patients reported in Obholzer et al. (2004). Another possibility is that the patients' hearing thresholds in the current investigation were affected by hazardous noise exposure, which affects the mid to high frequencies the most. There are no previous reports available to compare the better and poorer ears of patients with and without VSs; however, the literature does suggest the affected ear is poorer than the unaffected ear and the mid to high frequencies are more affected than the lower frequencies.

The difference between ears (interaural asymmetry) was also assessed by subtracting the better ear threshold from the poorer ear threshold across test frequencies. A positive result suggested that the poorer ear threshold was higher than the better ear threshold. In the majority of cases, this was true; however, for some frequencies in selected patients, the better ear threshold was higher than the threshold in the poorer ear. The analyses revealed significant differences between the groups at the frequencies .5, 1, 2, 3, 4, and 8 kHz. The positive MRI group had significantly larger differences at those frequencies compared to the negative MRI group. The largest z scores, or most significant differences, were seen for .5, 1, and 2 kHz.

The most significant differences found for the interaural asymmetry are consistent with the findings reported by Graamans et al. (2003). Graamans and colleagues used a similar technique to find the difference between ears for patients with diagnosed VSs (subtracted the unaffected ear from the affected ear thresholds), and they found the most significant hearing loss occurred at 1 and 2 kHz over time. There have been no other reports documenting the frequency specific differences between the ears comparing patients with and without a diagnosed VS. The asymmetry between ears, whether the patient has a unilateral or bilateral hearing loss, has been documented as one of the most common occurrences in patients with a VS (National Institutes of Health, 1991).

Many investigations have used a PTA to assess a patient's hearing. In this study, a PTA of 1, 2, and 4 kHz was used. The average of these three frequencies is considered a high frequency PTA, and is best used to reflect the impact of noise exposure or pathology on hearing (Baker et al., 2003; Caye-Thomasen et al., 2007; Neary et al., 1998; Portmann et al., 1989). To that end, the PTA at 1, 2, and 4 kHz was used to evaluate the hearing in the better ear (unaffected in the positive group), poorer ear (affected in the positive group), and the difference between ears. The PTA comparison between better and unaffected ears was not significantly different;

however, the PTA analysis between the poorer and the affected ears was significantly different between groups, with the positive MRI group having a larger PTA in the affected ear than the negative MRI group. There have been no reports using PTA comparing the better and poorer ears for patients with and without a VS.

The PTA difference between ears (interaural asymmetry) was also analyzed. The result revealed a significant difference between the groups, with patients diagnosed with a VS having a larger difference between PTAs compared to the negative MRI group. Caye-Thomasen et al. (2007) used a PTA of .5, 1, 2, and 4 kHz to compare the ears within each patient who had a diagnosed VS (affected and unaffected). They found that the affected ear PTA was significantly higher than the PTA of the patient’s unaffected ear, which is consistent with the current investigation. There have been no previous reports that analyzed the PTA interaural difference between patients with and without a diagnosed VS, but the current study reveals that the PTA may be a useful calculation when attempting to differentiate between patients with and without a VS.

Many referral criteria for a MRI of the IACs have used the degree of asymmetry between the ears, established at one or more frequencies. The degree of asymmetry between ears was evaluated in the current investigation by using four different asymmetry rules: single frequency, two adjacent frequencies, three adjacent frequencies, and a high frequency average (HFA) using 4, 6, and 8 kHz. Significant differences between the two groups tended to occur with an increase in the asymmetry criteria, suggesting that the groups with positive and negative MRIs differed the most at higher asymmetry criteria (e.g., >55 dB).

For each criterion within each rule, a d' value was calculated. The d' value represented the hit rate, or the proportion of correct identifications, compared to the false alarm rate, which is the proportion of patients who presented with the asymmetry but did not have a VS. The rules with the highest d' values overall were the HFA and the three adjacent frequencies rule. According to the d' values, the best criterion would be >55 dB HL asymmetry using the high frequency average, which had a hit rate of 26.32% and a false alarm rate of 2.91%. Although these rates resulted in the highest d' value, the hit rate was very low, and it would only identify five of the 19 patients with a positive MRI. The optimal criterion would maximize the number of hits and minimize the number of false alarms. The criterion closest to the ideal was >10 dB HL asymmetry at three adjacent frequencies. The hit rate for this criterion was 78.95% with a false alarm rate of 48.54%. Using this criterion, 15 out of the 19 patients with a VS would have been identified. This criterion had many more false alarms than the best d' criterion; however, it is more important to identify more patients with a VS, while managing the number of false alarms.

Previous reports have suggested different asymmetry criteria for referral. Obholzer et al. (2004) recommended using a > 15 dB asymmetry at two adjacent frequencies for unilateral hearing loss and >20 dB asymmetry at two adjacent frequencies for bilateral hearing loss. Using the criteria proposed by Obholzer et al. (2004), there would have been 13 patients in the positive MRI group (hit rate: 68.42%) and 173 patients in the negative MRI group (false alarm rate: 55.99%) identified. That criterion would have resulted in fewer hits and a greater number of false alarms than the optimal criterion found in the current study. Sheppard et al.

(1996) suggested a 15 dB average asymmetry between ears or the presence of unilateral tinnitus if there is normal hearing. Using that criterion, there would have been 10 patients identified in the positive group (hit rate: 52.63%) and 100 patients in the negative MRI group (false alarm rate: 32.36%). Out of the patients identified using the suggested protocol by Sheppard et al. (1996), 1 patient in the positive MRI group and 20 patients in the negative MRI group were identified because they reported unilateral tinnitus and had normal hearing thresholds. The proposed protocol by Sheppard et al. (1996) identified fewer patients with a positive MRI than the optimal criterion of >10 dB at three adjacent frequencies, although the false alarm rate was better controlled.

If the asymmetries are compared visually by looking at the ROC curve seen in Figure 7, another perspective on the different rules can be seen. The rules, which are represented by different symbol/lines, appear to be very similar in the lower left portion of the graph and diverge as both the hit and false alarm rates decrease below 30-35 dB HL. No criterion for any rule resulted in 100 % identification of the VS patients and 0% identification of the patients with a negative MRI. The criterion that appears to be the best according to the figure would be > 10 dB asymmetry at three adjacent frequencies (noted by the double asterisk in Figure 7).

In addition to raw pure tone thresholds, age and gender-corrected thresholds were analyzed because of the large age range of individuals included in the study. Morrell et al. (1996) identified the median pure tone thresholds for both genders across age ranges for the frequencies .5, 1, 2, and 4 kHz. Corrected thresholds for the current sample were calculated for the better and poorer ears. The analysis revealed no significant differences between the groups for the corrected thresholds in the better ear indicating that after the thresholds were adjusted for the participant’s age and gender, there was no difference between groups at any of the frequencies. In the better ear, neither of the groups exhibited very much hearing loss (up to a mild loss at 4 kHz) that was not accounted for by age and gender. The poorer ear thresholds revealed significant differences between groups at all frequencies, with the positive MRI group having significantly larger threshold values after the correction. This suggests that after the adjustment, the patient’s affected ear with the VS continued to have more hearing loss than the negative MRI group, although the patients in the negative MRI group had worse thresholds than predicted by age and gender in their poorer ear.

Progressive hearing loss in cases of VS has been documented by many other studies (Caye-Thomasen et al., 2007; Graamans et al., 2003; Moffat et al., 1994). The effect of age or gender was not discussed in any of the studies reviewed, which is likely because age and gender corrections are not routinely performed in clinics. With a patient sample, such as the one for this study, the age and gender corrected thresholds permits a better comparison of pure tone thresholds between patients who may have hearing loss attributed, in part, to the aging process. The group diagnosed with VSs continues to demonstrate poorer thresholds than the negative MRI group, underscoring the finding that hearing thresholds are significantly affected in cases of VS.

The age and gender corrected thresholds were also used to calculate the interaural difference between the ears. The difference between ears, after threshold correction, was significantly different between the groups for the frequencies .5, 1, 2, and 4 kHz. This is similar to the results found by Graamans et al. (2003). They found that after they corrected the thresholds by subtracting the affected ear thresholds from the unaffected ears thresholds (therefore controlling for age-related hearing loss within each patient) the most evident hearing loss was at 1 and 2 kHz. It is possible that the thresholds at 1 and 2 kHz are particularly important following a correction (either using normative data or the contralateral ear) because the frequencies affected most by age are the highest frequencies (>2 kHz). The thresholds at 1 and 2 kHz may be more sensitive to identifying patients with VS than the high frequencies alone. There were no other reports using the interaural difference following age and gender corrections for hearing loss.

Speech discrimination score. The first experimental question also addressed the differences between the positive and the negative MRI groups in their SDS. Each of the patients included in this investigation was required to have at least one SDS for each ear to allow a comparison between ears. The SDSs were measured at many different intensity levels. For patients with multiple SDSs assessed at various intensities, the score obtained with the highest intensity level was recorded. The results of the analyses between the two groups did not reveal a significant difference in the better ear scores. In the current study, the average SDSs for the better ear were 98.32% and 97.92% for the positive and negative MRI groups, respectively. These averages were in good agreement with the unaffected ear SDS of 96% reported by Caye-Thomasen et al. (2007). The current study analysis did reveal a difference in the poorer ear scores, with the positive MRI group having lower SDSs (average: 70.21%)

compared to the negative MRI group (average: 92.24%). The average SDS of the affected ear in the current study was higher than in the previous report by Caye-Thomasen et al. (2007), which reported an average SDS of 60%. There could be many reasons for this difference, including differences between the audiograms of the patients in the two studies, differences in the intensity of the signal presentation for the test, and the length of time the patient was afflicted with the pathology. There were no available reports comparing the better and poorer ear SDSs between patients with and without a diagnosed VS.

The interaural difference between SDSs was significant between the groups, with the positive MRI group having a larger interaural difference than the negative MRI group. The average interaural difference in SDS was 28.11% and 5.7% for the positive and negative groups, respectively. Caye-Thomasen et al. (2007) found that the SDS in the affected ears was significantly poorer than that in the contralateral ears, in patients with a diagnosed VS.

The nature of the group differences in SDS in the current study is revealed through examination of the box plot (Figure 11). The boxes show that the 25th to 75th percentile scores were larger for the poorer ears of both groups compared to the better ears. The largest box was observed for the poorer ear of the positive MRI group, indicating that this group's affected ear had the greatest variability in scores. Finally, there were many more outliers for the negative MRI group for both ears compared to the positive MRI group. This could be caused by the large number of patients in the negative MRI group (*n* = 309). However, another observation is that the scores associated with the outliers in the negative group in the poorer ear are as low as the bottom 10th percentile score for the positive MRI group's poorer ear. Only one of these outlier scores was identified from a patient with a different retrocochlear pathology. This shows that the negative MRI group had some patients (without any retrocochlear disorder) with very poor SDSs, although the majority of the negative MRI group had better SDS scores.

The comparison of AI scores to observed scores permitted an assessment of the distortion imposed by the hearing loss, for a particular listener and speech level. The results showed that the better ear was not significantly different between the two groups, as expected. The magnitude of the difference was very similar between the two groups (positive MRI group: 1.5 % difference; negative MRI group: 1.97% difference). The poorer ear analysis, in contrast, revealed a significant difference between the two groups for the difference between the predicted and observed SDSs. The magnitude of the difference scores was very different, with the positive group averaging a difference score of 29.59%, while the negative MRI group only averaged a difference score of 7.58%. Thus, the positive MRI group had much larger differences between the AI predicted score and their observed score than the negative MRI group, indicating that their SDS was significantly worse than predicted from their audiogram. This finding is in agreement with the report by Hannley and Jerger (1981), which noted that patients with a retrocochlear lesion often scored poorer than expected on speech discrimination tasks. However, there was no other literature which compared the AI predicted and the observed SDS in patients with and without a VS.

The interaural difference between the predicted and observed scores was also analyzed. There was a significant difference between the two groups for the interaural difference between the predicted and observed scores. Minimal between-group differences were seen for the predicted vs. observed calculation in the better ear, but large between-group differences in the predicted vs. observed calculation were found in the poorer/affected ear. This result reflects that poor speech discrimination performance in the poorer ear is likely associated with distortion in that ear, and not because of reduced signal audibility (which could have occurred because of greater hearing loss in that ear if a constant presentation level was used for both ears). There have been no previous reports that compared the interaural difference between the predicted and the observed SDS for patients with and without a diagnosed VS.

While some investigators have reported that the SDS is particularly poor in patients with a VS (Caye-Thomasen et al., 2007; Graamans et al., 2003; Hannley & Jerger, 1981; Magdziarz et al., 2000), others have found that the SDS is not a good predictor for VS in patients with normal hearing or patients who are asymptomatic (Beck et al., 1986; Jeykumar et al., 2007; Magdziarz et al., 2000). One of the patients in the current sample with a positive MRI presented with normal hearing at all test frequencies and perfect SDS scores, which agrees with the previous reports' findings for patients with normal hearing. All of the other positive MRI patients had hearing loss, and for those patients, a poorer than predicted SDS appears to be indicative of effects of the VS in their affected ear.

Acoustic reflex threshold. The first experimental question also asks about the difference between acoustic reflex thresholds and acoustic reflex adaptation between the positive and negative MRI groups. Acoustic reflex thresholds were analyzed in three different ways. The first method of analysis used the raw acoustic reflex thresholds in the better and the poorer ears at each frequency. The analysis of the acoustic reflex thresholds in the better ear revealed significant differences between the groups at 1 and 2 kHz. These results were not expected because previous literature reports differences with the stimulus in the affected ear only (Dauman et al., 1987; Hirsch & Anderson, 1980; Jerger & Jerger, 1983). In this investigation, the positive MRI group exhibited higher acoustic reflex thresholds in their unaffected ear compared to the better ear of the negative MRI group. The higher acoustic reflex thresholds cannot be explained by the VS itself compressing the CN VIII, because the stimulus is presented to the better or unaffected ear whose CN VIII is intact. There may be other factors, perhaps caused by the VS, that potentially could disrupt the conduction of the signal along the descending part of the acoustic reflex arc [i.e., tumor compressing the CN VII (facial) in the IAC]. The analysis of the poorer ear raw acoustic reflex thresholds revealed significant differences between the groups at all frequencies, with the positive MRI group having higher acoustic reflex thresholds than the negative group. This result was expected because a lesion compressing CN VIII fibers likely affects the excitatory response of neurons tuned to specific frequencies that may correspond to the stimulating tone. As a result, a higher level stimulus may be required to stimulate adjacent neurons that are tuned to frequencies close to the stimulating frequency.

Other researchers have also reported abnormally high acoustic reflexes in the affected ears of patients diagnosed with VSs. This was first reported by Metz (1952) who found an absence of the acoustic reflex threshold in two patients with a VS. Abnormal acoustic reflexes thresholds are found in patients with VS (Hirsh & Anderson, 1980; Jerger & Jerger, 1983), although abnormal acoustic reflex patterns are also observed in patients with other retrocochlear disorders or significant cochlear hearing loss (Gelfand et al., 1990; Silman & Gelfand, 1981). There have been no previous reports of patients having elevated/absent acoustic reflexes with the stimulus presented to their unaffected ear, specifically for VSs. There have been studies investigating patients with brainstem lesions who often exhibit bilateral elevated/absent acoustic reflex thresholds, and present ipsilateral acoustic reflex thresholds (Jerger & Jerger, 1974; Jerger & Jerger, 1975). There have been no reports comparing the raw acoustic reflex thresholds of patients with and without a diagnosed VS.

The interaural difference between the raw acoustic reflex thresholds in both ears was analyzed, and failed to show any significant differences between the groups at any frequency. Prasher and Cohen (1993) suggested that an interaural difference of >10 dB at two adjacent frequencies was indicative of a VS. Data from the current patient population showed no significant differences between the groups for interaural acoustic reflex differences >10 dB at two adjacent frequencies.

This contrasting finding could be related to very different sample sizes of the groups in the current study, or it could have been affected by the amount of hearing loss in both groups. In the study by Prasher and Cohen (1993), they applied their criterion to the acoustic reflex data of 63 patients with confirmed CPA tumors, whereas the current study included only 19 patients with VSs. It also was not specified whether the tumors were VSs, or not (Prasher & Cohen, 1993). Both the current investigation and the study by Prasher and Cohen (1993) compared the retrocochlear hearing loss to a cochlear hearing loss group. A second reason for the contrasting findings could have been the extent of hearing loss in the cochlear hearing loss group (negative MRI group for this study) between the two studies. In the study by Prasher and Cohen (1993), they analyzed patients with confirmed CPA tumor having at least one pure tone threshold greater than 55 dB HL at .5, 1, 2, or 4 kHz. This group was compared to a cochlear hearing loss group used in their previous study with similar thresholds. Exact audiograms were not provided in the report. In the current investigation, the negative MRI group included individuals with cochlear hearing loss (n = 290) and patients with other retrocochlear disorders (n = 19). The patients' pure tone thresholds ranged from normal to profound across test frequencies. This indicates that there were some patients in the current study with better hearing and some patients with poorer hearing compared to the patients represented in the study by Prasher and Cohen (1993). In summary, these results suggest that the interaural difference of >10 dB in acoustic reflex thresholds at 2 adjacent frequencies is not the most appropriate criterion for distinguishing between patients with a positive and a negative MRI in this patient sample.

The second method of analysis was to characterize the raw acoustic reflex thresholds as normal, elevated, or absent using the normative data reported by Gelfand et al. (1990). The results of the analysis revealed no significant differences between the groups at .5 kHz in the better ear; however, statistically significant results were noted between the two groups for normal vs. elevated and normal vs.

absent acoustic reflexes at 1 kHz and for normal vs. absent reflexes at 2 kHz in the better ear. The differences showed that the positive MRI group had fewer normal reflexes than elevated or absent reflexes compared to the negative MRI group. This result is consistent with the previous finding for the raw acoustic reflex thresholds in the better ear, although it provides no further insight into the reason for the larger number of patients with abnormal reflexes with the stimulus presented to the better ear. It is possible that the VS in the poorer ear was pressing on the CN VII in that ear and causing a disruption in the descending part of the acoustic reflex arc. This theory would be more plausible if the effect was seen at all three frequencies; however, it remains a possible reason for abnormal reflexes with the stimulus presented to the better ear. A second possibility is that the acoustic reflexes were recorded for the wrong ear. This possibility cannot be ruled out because all data collection for this investigation was retrospective and relies on the accuracy of other clinicians. With the stimulus presented to the poorer ear, the patients in the positive MRI group had a significantly larger proportion of individuals with absent acoustic reflexes than the negative MRI group, which is consistent with expectations. However, the two groups did not differ on the proportion of cases with elevated reflexes. Because there were significant differences between the groups with the stimulus presented to the poorer ear, the possibility of the clinician recording the wrong ear is not considered a large detriment to this investigation.

Similar to the raw acoustic reflex thresholds, the categorized acoustic reflex thresholds were expected to be significantly different between the two groups in the poorer ear (affected ear) but not in the better ear (Hirsh & Anderson, 1980; Jerger &

Jerger, 1983; Metz, 1952). There have not been any investigations that have classified the acoustic reflex thresholds into the three categories (normal, elevated, and absent) and compared patients with and without a diagnosed VS.

Perhaps a more clinical view of acoustic reflexes would be to classify them as normal or abnormal, which is the third method of analysis. The results of this analysis revealed statistically significant differences between the two groups in both ear conditions for all test frequencies. This suggests that the positive MRI group had significantly more abnormal reflexes and the negative MRI group had significantly more normal reflexes for all frequencies in both conditions. Although this method could be considered the most clinically relevant because of the classification of the acoustic reflexes, it is difficult to presume that clinics reference normative data in judging whether acoustic reflexes are normal or abnormal. There have been no previous investigations that have used this classification method in comparing the acoustic reflexes between patients with and without a diagnosed VS.

In this investigation, 18 of 19 patients in the positive MRI group presented with some hearing loss of varying degree, and all 18 patients were classified as having abnormal reflexes at one or more frequencies for each condition. The patient with normal hearing presented with normal acoustic reflexes in all conditions (Gelfand et al., 1990). Three of the 18 patients with abnormal reflexes had an opposite pattern than expected, with more abnormal acoustic reflexes observed with the stimulus presented to the better ear than to the poorer ear. Two of the three patients had one abnormal acoustic reflex threshold (2 kHz condition for both patients), whereas the other patient had normal acoustic reflex thresholds across test frequencies with the stimulus presented to the affected ear. For these patients, the reasons for this contrast could have been clinician error in recording, pathological interference for the descending acoustic reflex pathway, or some other unexplained clinical reason. It is unlikely that the descending pathway was affected in these patients because the ascending pathway was not affected. Magdziarz et al. (2000) noted that ipsilateral or contralateral acoustic reflexes were not beneficial in identifying VSs in patients with normal hearing, but they were more sensitive in patients with hearing loss. The results of the current study are in agreement with the results reported by Magdziarz et al. (2000). In contrast, Beck et al. (1986) reported that over 50% of their patients with normal hearing with VSs had abnormal acoustic reflex thresholds. This was not seen in the current patient sample, but there was only a single patient with normal hearing. Acoustic reflexes have shown fair results in detecting the presence of a VS depending on the criteria used (Chiverals, 1977; Dauman et al., 1987; Prasher & Cohen, 1993), but there are individuals with no diagnosed retrocochlear pathology with abnormal reflexes (Gelfand et al., 1990). The presence of abnormal acoustic reflexes without any diagnosed retrocochlear pathology could also account for some of the variability in the acoustic reflex thresholds with the stimulus presented to the better ear.

Acoustic reflex adaptation. There were not enough patients with acoustic reflex adaptation data to analyze the differences between the two groups. It is presumed that many of the patients in this sample did not have acoustic reflex adaptation data because they had absent or elevated acoustic reflex thresholds; however, there were multiple patients without acoustic reflex adaptation results who had normal acoustic reflex thresholds. In the better ear, there were two individuals with positive adaptation in the negative MRI group and zero participants with positive acoustic reflex adaptation from the positive MRI group. It is possible that there was a clinician error in recording or in the test procedure itself. Neither of these two patients was identified as having another retrocochlear disorder on their MRI; however, there could have been an underlying pathology that was overlooked. With the stimulus in the poorer ear, there was one patient in each group with positive acoustic reflex adaptation. These results are somewhat inconsistent with the results found by Dauman et al. (1987). They found that 66% patients with a diagnosed retrocochlear lesion had positive acoustic reflex adaptation. Of these, 6% had normal acoustic reflex thresholds. The percentage of patients in this study who had positive acoustic reflex adaptation could not be defined because of the scarcity of the data, but the predicted percentage is much lower than reported by Dauman et al. (1987). It appears that in the current patient sample, the acoustic reflex adaptation was not useful in distinguishing between the positive and negative MRI groups.

Presenting Symptoms

Effect of Group. The second experimental question concerned whether there would be a difference between groups in their presenting symptoms noted on the MRI referral. In the current patient population, the evaluation of the presenting symptoms is complicated by the fact that all of the patients were referred for MRI of their IACs to rule out retrocochlear pathology. This implies that many of the patients presented with similar symptoms, independent of their audiological results. There were no patients who were classified as "incidental findings," although there were two patients diagnosed with a VS (via MRI) who had normal or essentially normal hearing. An examination of the patients' presenting symptoms reveals that the most common symptoms were (percentages reflect the percentage of patients in the positive MRI group with the symptom): cochlear [with hearing loss as the primary (89.5%) and tinnitus (73.7%) as the second most common symptom], then vestibular (42%), followed by sudden onset of symptoms (15.8%), aural fullness (10.5%), neurological symptoms (10.5%), and headaches (5.3%). The same symptoms were the most common in the negative MRI group. These symptoms are similar to those reported in previous studies. Matthies and Samii (1997) found that the most common presenting symptoms were cochlear symptoms (e.g., hearing loss and tinnitus), vestibular symptoms (e.g., vertigo), and trigeminal neuralgia. Baguely et al. (2006) reported similar symptoms, but the percentages were slightly lower than those found in the current investigation. Baguely et al. (2006) reported that cochlear symptoms were the most prevalent, followed by tinnitus, imbalance, or some other symptom. In the current study, there were also 19 patients whose presenting symptoms fell into the "other" category. The other category included CN VI neuropathy and possible middle ear dehiscence.

The only symptoms/outcomes that resulted in statistically significant differences between groups were unilateral tinnitus, asymmetrical word recognition, and positive rollover. The unilateral tinnitus finding was in contrast to the results reported by Obholzer et al. (2004), which found no significant difference between the two groups for unilateral or asymmetric tinnitus. There are several potential reasons for this inconsistency. First, Obholzer et al. (2004) used a larger sample of positive

MRIs and a smaller sample of negative MRIs than the current investigation. Second, asymmetrical tinnitus and unilateral tinnitus were treated as separate symptoms in the current study compared to a single symptom. Combining these two groups in the previous study may have obscured significant findings. Finally, tinnitus is a self-reported symptom that cannot be identified or measured. Therefore, it is possible that there were some errors (or bias) in collecting the data from patients.

Sudden Hearing Loss. The presence of sudden hearing loss has been noted in the literature, with most reports recommending MRI following a report of sudden loss in hearing (Moffat et al., 1994; Sauvaget et al., 2005). In this investigation, there were 11 patients who experienced a sudden hearing loss, as noted on their MRI referral or in their medical record. There may have been a greater number of patients who experienced sudden hearing loss and either did not report it or it wasn't noted in their medical record. Of the 11 people with reported SSHL, one was in the positive MRI group and the other 10 were in the negative MRI group. This result is consistent with the literature, which indicates that there are more individuals presenting with SSHL than individuals with a VS presenting with SSHL (Aarnisalo et al., 2004; Cadoni et al., 2006). In the current study, one out of 19 patients who were positively diagnosed with a VS (approximately 5%) had SSHL, which is in agreement with previous estimations (Aarnisalo et al., 2004).

Presenting Symptoms in the Group Diagnosed with VS. Either asymmetrical or unilateral hearing loss was noted in 17 of the 19 patients in the positive MRI group, or 89%. Tinnitus was reported in 12 of these patients, and vestibular problems were observed in seven of them. Other symptoms were observed sporadically among this sample. The frequency of symptoms associated with patents with hearing loss was similar to previous reports (Baguely et al., 2006; Matthies & Samii, 1997).

Two of the patients in the positive MRI group did not have hearing loss. One of the patients had hearing sensitivity that was borderline normal (20-25 dB HL at some frequencies), while the other patient had normal hearing sensitivity across all test frequencies. The patient with borderline normal hearing exhibited positive rollover, unilateral tinnitus and trigeminal neuralgia. The other patient with normal hearing experienced unilateral tinnitus and vertigo. The symptom presentation in these two patients is in agreement with past reports on patients with normal hearing (Beck et al., 1986; Lustig et al., 1998; Magdziarz et al., 2000). In particular, the unilateral tinnitus in these patients with normal hearing was in agreement with the findings reported by Valente et al. (1995) for MRI referral in patients presenting with normal hearing and unilateral tinnitus.

Logistic Regression

The logistic regression analysis was conducted to identify the set of audiological outcomes and patient symptoms that would be most useful in correctly identifying patients with and without VSs. Forward and backward analyses were conducted with 43 variables entered into each analysis. The forward logistic regression revealed three predictor variables: unilateral tinnitus, the difference between ears for SDS, and the raw acoustic reflex threshold in the poorer ear at 1 kHz. The sensitivity of this model was 68.75%, and the specificity was 77.4%. However, the backwards model revealed seven predictor variables: unilateral tinnitus, the difference in pure tone threshold between the two ears at 2 kHz, the raw acoustic reflex threshold in the poorer ear at 2 kHz, the two-adjacent frequency asymmetry at both >25 and >55 dB HL, the three-adjacent frequency asymmetry at >50 dB HL, and the high frequency asymmetry at >35 dB HL. The sensitivity for this model was 81.25%, and the specificity was 82.59%. The backwards model appears to be quite promising; however, there is a limitation in estimating the sensitivity and specificity this way. Because the sensitivity and specificity rates were calculated using the same data that predicted the regression equations, it is possible that the findings overestimate the actual sensitivity and specificity rates.

Both forward and backward regression models were tested in order to determine which model better differentiated between the patients with positive and negative MRIs. The only similarity in the predictor variables between the two models was unilateral tinnitus. Clinically, it is expected that the forward regression model would be easier to use because fewer predictor variables were identified, and the predictor variables are all clinical outcomes or presenting symptoms. In the backwards regression model, there were many more variables, and four of the predictor variables require the application of the asymmetry rules and criteria. Although it may be clinically more difficult to apply, the backwards model resulted in a greater sensitivity and specificity rate compared to the forward regression model.

Clinical Implications

There are many clinical implications resulting from this investigation. First, it is clear that the affected ear has increased pure tone thresholds compared to the poorer ear of those individuals without a diagnosed VS. The difference between ears is a useful calculation in deciding how much interaural asymmetry exists between the ears. In particular, using the asymmetrical rules and criteria could be especially useful. It is clear that the single frequency asymmetry was not useful in differentiating between the positive and negative MRI groups; however, the other three rules showed statistically significant differences between the groups especially with increasing criterion asymmetry.

In the previous literature, there was little to no control of age or gender on evaluation of pure tone thresholds. In this investigation, the use of age and gender corrected thresholds permitted analysis of the patients' pure tone thresholds that were not confounded by age-related changes in hearing. This is especially important because most of the patients were >45 years of age and males, and this group is known to have significant age-related hearing loss (Morrell et al., 1996). The poorer (or affected) ears of both groups evidenced poorer thresholds than expected based on age and gender, with the affected ears of the positive MRI group showing more hearing loss than the negative MRI group. This confirms that the patients with VSs have significant hearing loss in the affected ear, that exceeds hearing loss associated with aging.

The PTA does not provide any useful diagnostic differences between the two groups beyond identifying patients with and without hearing loss. However, using a PTA to identify normal hearing, as was done in reports by Beck et al. (1986) and Magdziarz et al. (2000), is a common practice, and may overestimate the number of patients with a VS having normal hearing thresholds. The use of a PTA in these cases did not include the high frequencies. High frequencies are usually affected first because of the compression of the VS on the CN VIII. Patients with a high frequency asymmetrical hearing loss could be missed using this calculation.

Speech discrimination appears to be a useful tool in differentiating between the positive and negative MRI groups, especially using the affected ear or the interaural difference between the two scores. The use of the AI predicted score compared to the observed score would be extremely beneficial particularly because the AI accounts for possible limitations in audibility associated with the hearing loss. The magnitude of difference between the two groups on this measure was large, for the poorer ear and interaural difference between ears. The use of a simplified AI calculation for clinical purposes may prove particularly valuable for identifying cases of VS.

Acoustic reflex thresholds, especially with the stimulus presented to the poorer ear, are also useful in distinguishing between the patients with a positive and negative MRI. Similar findings were observed with the comparison of the raw acoustic reflex thresholds and the two categorization schemes. Thus, the use of the raw acoustic reflex thresholds may be the simplest in the clinical setting.

The inclusion of the self-reported symptoms is essential in the intake evaluation of a patient with a possible VS. The most common symptoms in this investigation were in agreement with past studies (hearing loss, tinnitus, vestibular, and neurologic symptoms). It appears that unilateral tinnitus is an especially important symptom for the identification of patients with a VS because it was identified as a predictor variable in both the forward and backward logistic regression models.

The most important finding of this study is that there is no single outcome or symptom that is the most predictive of patients with a potential VS. It is the combination of audiological test outcomes and calculations in conjunction with the presenting symptoms, that provides the best differentiation between the patients with a positive and negative MRIs.

Limitations of the Study

There are many limitations in this study. The first limitation was the retrospective nature of the study. With retrospective data collection, the study outcome is based on the results obtained by other clinicians. There could have been differences in the methods used while testing, differences or errors in the recording of data, or differences in the interpretation of test results or patient reported symptoms. The second limitation was the exclusion of patients because of missing data, especially because there were two patients with diagnosed VSs who were excluded. With the small number of patients identified with positive MRIs, the loss of two patients with positive findings could have changed some potential results. The third limitation was the large difference in size between the two groups. The difference is expected because of the prevalence of VSs, but the small number of patients in the positive MRI group and the large number in the negative MRI group could have affected the results. A fourth limitation was the prevalence of hazardous noise exposure within the current patient population. The high prevalence of hazardous noise exposure, and its effects on hearing, could have influenced the results between the positive and negative MRI group. The final limitation of the study is that there was not a new patient sample to test the logistic regression models. The predictive value of the regression models on a new patient sample is unknown. It is also possible that with a new sample, the forward regression model may be more predictive than the backward regression.

Follow-up Studies

Future studies should be performed to validate the current results. There have been studies conducted that have suggested protocols for MRI referral, but they concentrated on pure tone thresholds and presenting symptoms. There have not been any studies that investigated all of the clinical audiology tests in conjunction with the presenting symptoms. The studies should also validate the use of age and gender corrections in the diagnosis of VSs. Most of the previous literature ignores the effect of age on pure tone thresholds. The usefulness of the AI predicted score compared to the observed score should also be validated. Neither age nor gender corrections or the AI are routinely used clinically, however, they have proven to be useful in differentiating between patients with and without a diagnosed VS. It would be useful to validate the current findings on a patient population with and without hazardous noise exposure. The current analysis was performed on a patient population that was largely exposed to hazardous noise. The results may or may not be applicable to a non-hazardous noise exposed population. Finally, a study that validated the current findings on a sample of males vs. females with VSs would be useful to determine whether the current results can be generalized to both males and females.

Summary and Conclusions

A total of 628 charts were reviewed of patients who received an MRI of the IACs from November 2005 to October 2007. A final sample of 19 positive MRIs and

309 negative MRIs was selected for analysis based on the completeness of their records. Audiological outcomes including pure tone thresholds, speech discrimination, and acoustic reflex thresholds, as well as the patients' self-reported symptoms, had an impact on whether the patient was referred for an MRI of their IACs to rule out the presence of a VS. The principal findings were:

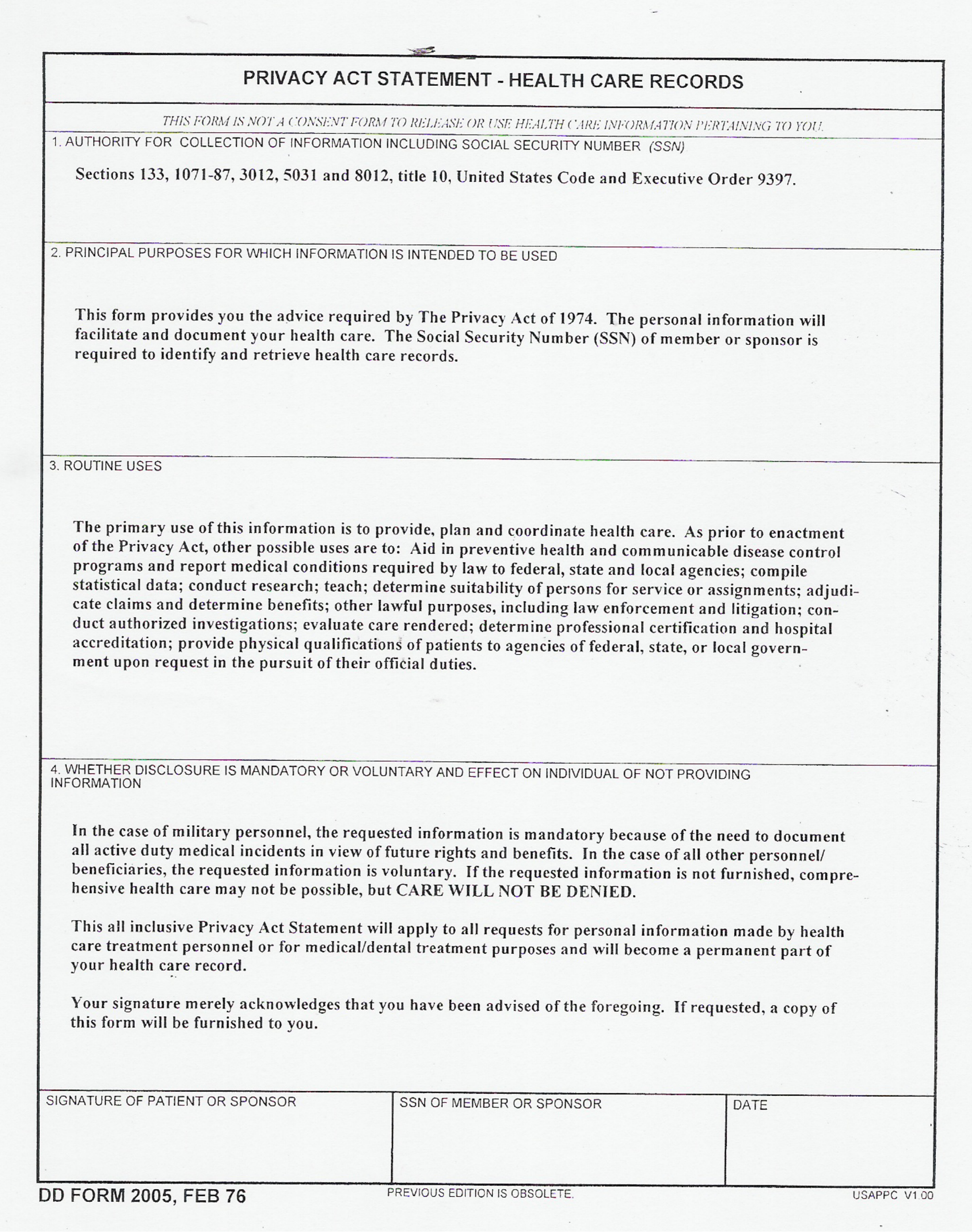
1. Patients with positive MRIs had significantly worse pure tone thresholds in their affected ears compared to the poorer ears of the negative MRI group, which suggests that the presence of the VS caused more hearing loss than was observed on average in the negative MRI patients. This effect remained following correction for age-related hearing loss. This effect was not significant in the unaffected vs. better ear comparison.
2. Speech discrimination scores were not significantly different between groups for the better ear, but they were significantly different for the poorer ear analysis. The results were the same when the patients' observed scores were compared to the AI predicted scores. The positive MRI group had poorer speech discrimination abilities on average compared to the negative MRI group, and the positive MRI group had poorer than predicted speech discrimination based on the audibility of the signal.
3. Raw acoustic reflex thresholds were significantly poorer in both the better ear (at 1 and 2 kHz) and the poorer ear (at .5, 1, and 2 kHz) in the positive MRI group compared to the negative MRI group. Similar results were observed for categories of normal and abnormal acoustic reflex thresholds.

4. The most common symptoms in both groups were hearing loss, tinnitus, vertigo, otalgia, CN dysfunction, a sudden onset of symptoms, aural fullness, and headaches. The only significant differences between the two groups were noted for unilateral tinnitus, asymmetrical word recognition, and positive rollover.
5. The most predictive model for differentiating between the positive MRI group and the negative MRI group was found using a backward logistic regression, which resulted in a sensitivity of 81.25% and a specificity of 82.59% when applied to the current sample of patients.

Taken together, it is obvious that there are more important differences between patients with and without a diagnosed VS than simply pure tone thresholds. When assessing the need for patient referral for an MRI, it is essential that their audiological characteristics and their presenting symptoms be taken into account prior to the decision. As expected, it is not the individual test outcome or the presence of a single symptom that is the most predictive of a VS, but a combination of outcomes and symptoms that provides the best prediction of the presence of a VS. The current study shows that the most important audiological data and symptoms to include in a protocol are unilateral tinnitus, the difference in pure tone threshold between the two ears at 2 kHz, the raw acoustic reflex threshold in the poorer ear at 2 kHz, and the presence of an asymmetry of >25 and >55 dB HL at two-adjacent frequencies, >50 dB HL at three-adjacent frequencies, >35 dB HL for the high frequency average.

List of Appendices

Appendix A



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Sections 133, 1071-87, 3012, 5031 and 8012, title 10, United States Code and Executive Order 9397.

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This form provides you the advice required by The Privacy Act of 1974. The personal information will facilitate and document your health care. The Social Security Number (SSN) of member or sponsor is required to identify and retrieve health care records.

3. ROUTINE USES

The primary use of this information is to provide, plan and coordinate health care. As prior to enactment of the Privacy Act, other possible uses are to: Aid in preventive health and communicable disease control programs and report medical conditions required by law to federal, state and local agencies; compile statistical data; conduct research; teach; determine suitability of persons for service or assignments; adjudicate claims and determine benefits; other lawful purposes, including law enforcement and litigation; conduct authorized investigations; evaluate care rendered; determine professional certification and hospital accreditation; provide physical qualifications of patients to agencies of federal, state, or local government upon request in the pursuit of their official duties.

4. WHETHER DISCLOSURE IS MANDATORY OR VOLUNTARY AND EFFECT ON INDIVIDUAL OF NOT PROVIDING INFORMATION

In the case of military personnel, the requested information is mandatory because of the need to document all active duty medical incidents in view of future rights and benefits. In the case of all other personnel/beneficiaries, the requested information is voluntary. If the requested information is not furnished, comprehensive health care may not be possible, but CARE WILL NOT BE DENIED.

This all inclusive Privacy Act Statement will apply to all requests for personal information made by health care treatment personnel or for medical/dental treatment purposes and will become a permanent part of your health care record.

Your signature merely acknowledges that you have been advised of the foregoing. If requested, a copy of this form will be furnished to you.

SIGNATURE OF PATIENT OR SPONSOR	SSN OF MEMBER OR SPONSOR	DATE

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Appendix B

Table 20

Sub-analysis of positive and negative MRI group without other retrocochlear pathologies

Better and Poorer Ear Thresholds

Ear	Frequency (Hz)	*Z* score	*p*-value
Better	250	-2.553	.011*
Better	500	-1.395	.163
Better	1000	-1.718	.086
Better	2000	-1.042	.297
Better	3000	-1.582	.114
Better	4000	-1.616	.106
Better	6000	-1.413	.158
Better	8000	-1.770	.077
Poorer	250	-2.910	.004***
Poorer	500	-2.830	.005**
Poorer	1000	-3.759	.0005***
Poorer	2000	-3.340	.001***
Poorer	3000	-2.581	.010*
Poorer	4000	-2.473	.013*
Poorer	6000	-2.227	.026*
Poorer	8000	-2.508	.012*

Table 20 (cont.)

Sub-analysis of positive and negative MRI group without other retrocochlear pathologies

Difference Between Better and Poorer Ears

Frequency (Hz)	*Z* score	*p*-value
250	-1.749	.080
500	-3.258	.001***
1000	-2.964	.003***
2000	-3.226	.001***
3000	-2.259	.024*
4000	-2.041	.041*
6000	-1.591	.112
8000	-2.201	.028*

Speech Discrimination Scores

Condition		*Z* score	*p*-value
Better Ear			
	Raw	-.400	.689
	AI predicted-observed	-1.578	.115
Poorer Ear			
	Raw	-3.343	.001***

Table 20 (cont.)

Results for sub-analysis of positive MRI group and negative MRI group without other retrocochlear pathologies

Speech Discrimination Scores

Condition		*Z* score	*p*-value
	AI predicted-observed	-2.786	005**
Difference Between Ears			
	Raw	-3.538	.0005***

Acoustic Reflex Thresholds (Raw Data)

Stimulus Ear	Frequency (Hz)	*Z* score	*p*-value
Better	500	-1.871	.061
Better	1000	-2.717	.007**
Better	2000	-2.505	.012*
Poorer	500	-3.200	.001***
Poorer	1000	-3.006	.003***
Poorer	2000	-3.629	.0005***

-* *p*<.05 ** *p*<.01 *** *p*<.005

Appendix C

Table 21

Results for sub-analysis of positive MRI group and group with other retrocochlear pathologies

Better and Poorer Ear Thresholds

Ear	Frequency (Hz)	*Z* score	*p*-value
Better	250	-2.107	.035*
Better	500	-1.652	.099
Better	1000	-1.898	.058
Better	2000	-.698	.485
Better	3000	-2.206	.027*
Better	4000	-2.680	.007**
Better	6000	-2.231	.026*
Better	8000	-1.644	.100
Poorer	250	-2.560	.010**
Poorer	500	-1.837	.066
Poorer	1000	-2.351	.019*
Poorer	2000	-1.994	.046*
Poorer	3000	-2.898	.004***
Poorer	4000	-2.592	.010*
Poorer	6000	-2.423	.015*
Poorer	8000	-2.211	.027*

Table 21 (cont.)

Results for sub-analysis of positive MRI group and group with other retrocochlear pathologies

Difference Between Better and Poorer Ears

Frequency (Hz)	*Z* score	*p*-value
250	-1.220	.223
500	-1.899	.058
1000	-1.593	.111
2000	-1.947	.052
3000	-2.281	.023*
4000	-1.782	.075
6000	-1.690	.091
8000	-2.192	.028*

Speech Discrimination Scores

Condition	*Z* score	*p*-value
Better Ear		
Raw	-.717	.473
AI predicted-observed	-1.244	.214
Poorer Ear		
Raw	-2.987	.003***

Table 21 (cont.)

Results for sub-analysis of positive MRI group and group with other retrocochlear pathologies

Speech Discrimination Scores

Condition		*Z* score	*p*-value
	AI predicted-observed	-2.461	.014**
Difference Between Ears			
	Raw	-3.248	.001***

Acoustic Reflex Thresholds (Raw Data)

Stimulus Ear	Frequency (Hz)	*Z* score	*p*-value
Better	500	-1.944	.052
Better	1000	-2.519	.012*
Better	2000	-2.117	.034*
Poorer	500	-1.893	.058
Poorer	1000	-2.051	.040*
Poorer	2000	-2.559	.011*

* $p<.05$ ** $p<.01$ *** $p<.005$

References

Aarnisalo, A.A., Suoranta, H., and Ylikoski, J. (2004). Magnetic resonance imaging findings in the auditory pathway of patients with sudden deafness. *Otology & Neurotology, 25*, 245-249.

Adams, A. & Dixon, A.K. (Eds.). (2008). *Grainger & Allison's diagnostic radiology: a textbook of medical imaging*. (5th ed.). Philadelpiha: PA: Elsevier Churchill Livingstone.

Agresti, A. (1996). An *Introduction to Categorical Data Analysis*. John Wiley and Sons, Inc:New York.

Allen, R.W., Harnsberger, H.R., Shelton, C., King, B., Bell, D.A., Miller, R., Parkin, J.L., Apfelbaurn, R.I., and Parker, D. (1996). Low-cost high-resolution fast spin-echo MR of acoustic schwannoma: an alternative to enhanced conventional spin-echo MR? *American Journal of Neuroradiology, 17*, 1205-1210.

The American Heritage® Stedman's Medical Dictionary. Retrieved April 25, 2008, from Dictionary.com website: http://dictionary.reference.com/browse/sensitivity

Anderson, T.D., Loevner, L.A., Bigelow, D.C., & Mirza, N. (2000). Prevalence of unsuspected acoustic neuroma found by magnetic resonance imaging. *Otolaryngology Head and Neck Surgery, 122*(5), 643-646.

Aslan, A., De Donato, G., Balyan, F.R., Falcioni, M., Russo, A., Taibah, A. et al. (1997). Clinical observations on coexistence of sudden hearing loss and VS. *Otolaryngology Head and Neck Surgery, 117*, 580-582.

Baguely, D.M., Humphriss, R.L., Axon, P.R., & Moffat, D.A. (2006). The clinical characteristics of tinnitus in patients with VS. *Skull Base: An Interdisciplinary Approach, 16*(2), 49-57.

Baker, R., Stevens-King, A., Bhat, N., & Leong, P. (2003) Should patients with asymmetrical noise-induced hearing loss be screened for VSs? *Clinical Otolaryngology, 28*, 346-351.

Beck, H.J., Beatty, C.W., Harner, S.G., & Ilstrup, D.M. (1986). Acoustic neuromas with normal pure tone hearing levels. *Otolaryngology Head and Neck Surgery, 94*(1) 96-103.

Berg, H.M., Cohen, N.L., Hammerschlag, P.E., & Waltzman, S.B. (1986). Acoustic neuroma presenting as sudden hearing loss with recovery. *Otolaryngology-Head and Neck Surgery, 94*, 15-22.

Breslow, N.E. & Chatterjee, N. (1999). Design and analysis of two-phase studies with binary outcome applied to Wilms tumour prognosis. *Applied Statistics, 48*(4), 457-468.

Briggs, G.M., Flynn, P.A., Worthington, M., Rennie, I., & McKinstry, K.S. (2008). The role of the specialist neuroradiology second opinion reporting: is there added value? *Clinical Radiology, 63*(7), 791-795.

Cacace, A.T., Tasciyan, T., & Cousins, J.P. (2000). Principles of functional magnetic resonance imaging: application to auditory neuroscience. *Journal of the American Academy of Audiology, 11*, 239-272.

Cadoni, G., Cianfoni, A., Agostino, S., Scipione, S. Tartaglione, T., Galli, J., & Colosimo, C. (2006). Magnetic resonance imaging findings in sudden sensorineural hearing loss. *The Journal of Otolaryngology, 35*(5), 310-316.

Caldera, S.R. & Pearson, C.R. (2000). Risk management of asymmetrical hearing impairment in an armed forces population. *Journal of Laryngology and Otology, 114*(5), 345-349.

Caye-Thomasen, P., Dethloff, T., Hansen, S., Stangerup, S-E. & Thomsen, J. (2007). Hearing in patients with intracanicular VSs. *Audiology and Neurotology, 12*, 1-12.

Chandrasekhar, S., Brackman, D. & Devgan, K. (1995). Utility of auditory brainstem response audiometry in diagnosis of acoustic neuromas. *American Journal of Otology, 16,* 63-67.

Cheng, G., Smith, R., & Tan, A.K.W. (2003). Cost comparison of auditory brainstem response versus magnetic resonance imaging screening of acoustic neuroma. *The Journal of Otolaryngology, 32*(6), 394-399.

Chiverals, K. (1977). A further examination of the use of the statpedius reflex in the diagnosis of acoustic neuroma. *Audiology, 16*(4), 331-337.

Cummings, C.W., Flint, P.W., Haughey, B.H., Robbins, K.T., Thomas, J.R., Harker, L.A., et al. (2005). Otolaryngology Head and Neck Surgery. (4th ed). (C.W. Cummings, Ed.) (Chapter 155). Philadelphia, PA: Mosby, Inc.

Daniels, R.L., Shelton, C., & Harnsberger, H.R. (1998). Ultra high resolution nonenhanced fast spin echo magnetic resonance imaging: cost-effective screening for acoustic neuroma in patients with sudden sensorineural hearing loss. *Otolaryngolgoy Head and Neck Surgery*, *119*(4), 364-369.

Dauman, R., Aran, J.M., & Portmann, M. (1987). Stapedius reflex and cerebellopontine angle tumors. *Clinical Otolaryngology, 12*, 119-123.

Demidenko, E. (2007). Sample size determination for logistic regression revisited. *Statistics in Medicine, 26* (18), 3385-3397.

Don, M., Kwong, B., Tanaka, C., Brackman, D., & Nelson, R. (2005). The stacked ABR: a sensitive and specific screening tool for detecting small acoustic tumors. *Audiology & Neurotology, 10*, 274-290.

Edelman, R.R. & Warach, S. (1993). Magnetic resonance imaging. *New England Journal of Medicine, 328*(10), 708-716.

Edwards, C.G., Schwartzbaum, J.A., Nise, G., Forssen, U.M., Ahlborn, A., Lonn, S., & Feychting, M. (2007). Occupational noise exposure and risk of acoustic neuroma. *American Journal of Epidemiology, 166*, 1252-1258.

Fang, Y., Yang, W., & Jiang, S. (1997). Sudden hearing loss in acoustic neuroma. *Zhonghua Er Bi Yan Hou Ke Za Ahi, 32*, 277-279.

Forton, G.E., Cremers, C.W.R.J., & Offeciers, F.E. (2004). Acoustic neuroma ingrowth in the cochlear nerve: does it influence the clinical presentation? *Annals of Otology, Rhinology, and Laryngology, 113*, 582-586.

French, N.R. & Steinberg, J.C. (1947). Factors governing the intelligibility of speech sounds. *Journal of the Acoustical Society of America, 19,* 90-119.

Gelfand, S.A., Schwander, T., & Silman, S. (1990). Acoustic reflex thresholds in normal and cochlear-impaired ears: effects of no-response rates on 90th percentiles in a large sample. *Journal of Speech and Hearing Disorders, 55*, 198-205.

Godey, B., Morandi, X., Beust, L., Brassier, G., & Bourdiniere, J. (1998). Sensitivity of auditory brainstem response in acoustic neuroma screening. *Acta Otolaryngologica, 118*, 501-504.

Gordon, M. & Cohen, N. (1995). Efficacy of auditory brainstem response as a screening test for small acoustic neuromas. *American Journal of Otology, 16*, 136-139.

Graamans, K., Van Duk, J.E., Janssen, L.W. (2003). Hearing deterioration in patients with a non-growing VS. *Acta Otolaryngologica, 123*, 51-54.

Gravetter, F.J. & Wallnau, L.B. (2007). *Statistics for the Behavioral Sciences*. (7th ed.). Belmont, CA: Thomas Wadsworth.

Hall III, J.W. & Mueller III, H.G. (1997). *Audiologists' Desk Reference: Diagnostic Audiology Principles, Procedures, and Protocols* (2nd ed.). Singular Publishing Group, Inc.: San Diego, CA.

Hargus, S.E. & Gordon-Salant, S. (1995). Accuracy of speech intelligibility index predictions for noise masked young listeners with normal hearing and for elderly listeners with hearing impairment. *Journal of Speech and Hearing Research, 38*(1), 234-243.

Hannley, M. & Jerger, J. (1981). PB rollover and the acoustic reflex. *Audiology, 20*(3), 251-258.

Hirsch, A. & Anderson, H. (1980). Elevated stapedius reflex threshold and pathologic reflex decay. *Acta Otolaryngologica, Suppl 368.*

Jerger, J. Harford, E., Clemis, J., & Alford, B. (1974). The acoustic reflex in eighth nerve disorders. *Archives of Otolaryngology, 99*, 409.

Jerger, J. & Jerger, S. (1974). Auditory findings in brainstem disorders *Archives of Otolaryngology, 99*, 342-350.

Jerger, S. & Jerger J. (1975). Extra- and intra-axial brain stem auditory disorders. *Audiology, 14,* 93-117.

Jerger, S. & Jerger, J. (1983). Evaluation of diagnostic audiometric tests. *Audiology, 22*, 144-161.

Jeyakumar, A., Seth, R., Brickman, T.M., Dutcher, P. (2007). The prevalence and clinical course of patients with "incidental" acoustic neuromas. *Acta Oto-Laryngologica, 127*, 1051-1057.

Katz, J. (Ed.), Burkard, R.F., & Medwetsky, L. (Assoc. Eds.). (2002).*Handbook of Clinical Audiology*. New York: Lippincott Williams & Wilkins.

Kernohan, M.D., Blackmore, K.J., Johnson, I.J.M., & Zammit-Maempel, I. (2006). Magnetic resonance imaging: is a signle scan ever enough for the diagnosis of acoustic neuroma? *The Journal of Laryngology & Otology, 120*, 1061-1063.

Klockhoff, I. & Lindblom, U. (1967). Meniere's disease and hydrochlorothiazide (dichlotride)-a critical analysis of symptoms and therapeutic effects. *Acta Otolaryngologica, 63*, 347-365.

Lin, D., Hegarty, J.L., Fischbein, N.J., & Jackler, R.K. (2005). The prevalence of "incidental" acoustic neuroma. *Archives of Otolaryngology Head and Neck Surgery, 131*, 241-244.

Lustig, L.R., Rifkin, S., Jackler, R.K., & Pitts, L.H. (1998). Acoustic neuromas presenting with normal or symmetrical hearing: factors associated with diagnosis and outcome. *The American Journal of Otology, 19*, 212-218.

Magdziarz, D.D., Wiet, R.J., Dinces, E.A., & Adamiec, L.C. (2000). Normal audiologic presentations in patients with acoustic neuroma: an evaluation using strict audiologic parameters. *Otolaryngology Head and Neck Sugery, 122*(2), 157-162.

Matthies, C. & Samii, M. (1997). Management of 1000 VSs (acoustic neuromas): clinical presentation. *Neurosurgery, 40*(1), 1-10.

Mazzoni, A., Dubey, S.P., Poletti, A.M., & Colombo, G. (2007). Sporadic acoustic neuroma in pediatric patients. *International Journal of Pediatric Otorhinolaryngology, 71*, 1569-1572.

Metz, O. (1952). Studies on the contraction of the tympanic muscles as indicated by changes in the impedance of the ear. *Archives of Otolaryngology, 55*, 536-543.

Moffat, D.A., Baguley, D.M., von Blumenthal, H., Irving, R.M., & Hardy, D.G. (1994). Sudden deafness in VS. *The Journal of Laryngology and Otology, 108*, 116-119.

Moffat, D.A., Jones, S.E.M., Mahendran, S., Humphriss, R., & Baguley, D.M. (2004). Referral patterns in vestibular scwannomas-10 years on. *Clinical Otolaryngology, 29*, 515-517.

Montaguti, M., Bergonzoni, C., Zanetti, M.A., & Ceroni, A.R. (2007). Comparative evaluation of ABR abnormalities in patients with and without neurinoma of VIII cranial nerve. *Acta Otorhinolaryngologica Italica, 27*, 68-72.

Morrell, C.H., Gordon-Salant, S., Pearson, J.D., Brant, L.J., & Fozard, J.L. (1996). Age- and gender-specific reference ranges for hearing level and longitudinal changes in hearing level. *Journal of the Acoustical Society of America, 100*(4), 1949-1967.

Nageris, B.J. & Popovtzer, A. (2003). Acoustic neroma in patients with completely resolved sudden hearing loss. *Annals of Otology, Rhinology, and Laryngology, 112*, 395-397.

National Institute on Deafness and Other Communication Disorders (NIDCD) (2004). Vestibular schwannoma (acoustic neuroma) and neurofibromatosis. Retrieved March 28, 2008, from http://www.nidcd.nih.gov/health/hearing/acoustic_neuroma.asp.

National Institutes of Health (NIH) Consensus Statement (1991). Acoustic neuroma. *Dec 11-13; 9*(4), 1-24.

Neary, W.J., Newton, V.E., Laoide-Kemp, M.A., Ramsden, R.T., Hillier, V.F., & Kan, S.W. (1996). A clinical, genetic, and audiological study of patients and families with unilateral vestibular schwannomas. II. Audiological findings in 93 patients with unilateral vestibular schwannomas. *The Journal of Laryngology and Otology, 110*, 1120-1128.

Obholzer, R.J., & Harcourt, J.P. (2004). Magnetic resonance imaging screening for VS: analysis of published protocols. *The Journal of Laryngology & Otology, 118*, 329-332.

Ogawa, K., Kanzaki, J., Ogawa, S., Tsuchihashi, N., & Inoue Y. (1991). Acoustic neuromas presenting as sudden hearing loss. *Acta Otolaryngologica Supplement, 487*, 138-143.

Online Mendelian Inheritance in Man, OMIM (TM). McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD), {2/13/2008}. MIM Number: {101000}: {8/13/2007}: . World Wide Web URL: http://www.ncbi.nlm.nih.gov/omim/

Pavlovis, C.V. (1984). Use of the articulation index for assessing residual auditory function in listeners with sensorinerual hearing impairment. *Journal of the Acoustical Society of America, 75*(4), 1253-1258.

Pavlovic, C.V. (1987). Derivation of primary parameters and procedures for use in speech intelligibility predictions. *Journal of the Acoustical Society of America, 82*, 413-422.

Pensak, M.L., Glasscock, M.E., 3rd, Josey, A.F., Jackson, C.G., & Gulya. A.J. (1985). Sudden hearing loss and cerebellopontine angle tumors. *Laryngoscope, 95*, 1188-1193.

Peterson, C.K., Gatterman, B., Carter, J.C., Humphreys, B.K., & Weibel, A. (2007). Inter- and intra-examiner reliability in identifying and classifying degenerative marrow (modic) changes on lumbar spine magnetic resonance scans. *Journal of Manipulative and Physiological Therapeutics, 30*(2), 85-90.

Portmann, M., Dauman, R., Duriez, R., Portmann, F., and Dhillon, D. (1989). Modern diagnostic strategy for acoustic neuromas. *Archives of Otirhinolaryngology, 246*(5), 286-291.

Prasher, D. & Cohen, M. (1993). Effectiveness of acoustic reflex threshold criteria in the diagnosis of retrocochlear pathology. *Scandinavian Audiology, 22*, 11-18.

Rupa, V., Job, A., George, M., & Rajshiekhar, V. (2003). Cost-effective initial screening for VS: auditory brainstem response or magnetic resonance imaging? *Otolaryngology Head and Neck Surgery, 128*, 823-828.

Samii, M., Matthies, C., & Tatagiba, M. (1991). Intracanalicular acoustic neurinomas. *Neurosurgery, 29*(2), 189-199.

Sauvaget, E., Kici, S., Kania, R., Herman, P., & Ba Huy, P.T. (2005). Sudden sensorineural hearing loss as a revealing symptom of VS. *Acta Oto-Laryngologica*, *125*, 592-595.

Sheehy, J.L. & Inzer, B.E. (1976). Acoustic reflex test in neuro-otologic diagnosis: A review of 24 cases of acoustic tumors. *Archives of Otolaryngology, 102*, 647-653.

Sheppard, I.J., Milford, C.A.M. & Anslow, P. (1996). MRI in the detection of acoustic neuromas-a suggested protocol for screening. *Clinical Otolaryngology, 21*, 301-304.

Silman, S. & Gelfand, S.A. (1981). The relationship between the magnitude of hearing loss and acoustic reflex threshold levels. *Journal of Speech and Hearing Disorders, 46*, 312-316.

Stangerup, S.E., Tos, M., Caye-Thomasen, P., Tos, T., Klokker, M., & Thomsen, J. (2004). Increasing annual incidence of vestibular schwannoma and age at diagnosis. *The Journal of Laryngology & Otolgy, 118*, 622-627.

Stangerup, S.E., Caye-Thomasen, P., Tos, M., & Thomsen, J. (2006). The natural history of vestibular schwannomas. *Otology & Neurology, 27*, 547-552.

Swartz, J.D. (2004). Lesions of the cerebellopontine angle and internal auditory canal: diagnosis and differential diagnosis. *Seminars in Ultrasound, CT, and MRI, 25*(4), 332-352.

Tierney, P.A., Chitnavis, B.P., Sherriff, M., Strong, A.J., & Gleeson, M.J. (1998). The relationship between pure-tone thresholds and the radiological dimensions of acoustic neuromas. *Skull Base Surgery, 8*(3), 149-151.

Tos, M., Stangerup, S.E., Caye-Thomasen, P., Tos, T., and Thomsen, J. (2004). What is the real incidence of VS? *Archives of Otolaryngology Head and Neck Surgery, 130,* 216-220.

Turner, R.G. & Nielsen, D.W. (1984). Application of clinical decision analysis to audiological tests. *Ear and Hearing, 5*(3), 125-133.

Valente, M., Neely, J., Peterein, J., & Goebel, J. (1995). Four cases of acoustic neuromas with normal hearing. *Journal of the American Academy of Audiology, 6*(3), 203-210.

Verret, D.J., Adelson, R.T., & Defatta, R.J. (2006). Asymmetric sensorineural hearing loss evaluation with T2 FSE-MRI in a public hospital. *Acta Oto-Laryngologica, 126*, 705-707.

Welling, D.B., Glasscock, M.E., Woods, C.I., & Jackson, C.G. (1990). Acoustic neuroma: a cost-effective approach. *Otolaryngology Head and Neck Surgery, 103*, 364-370.

Wilkinson, I.D. & Paley, M.N.J. (2008). Magnetic resonance imaging: Basic principles. In A. Adam & A.K. Dixon (Eds.), Adam: Grainger and Allison's Diagnostic Radiology, 5th ed. (Chapter 5). Orlando, FL: Churchill Livingstone.

WINKS Software. Mann Whitney Test. http://www.texasoft.com/winkmann.html. Accessed July 5, 2008.

Yanagihara, N. & Asai, M. (1993). Sudden hearing loss induced by acoustic neuroma: significance of small tumors. *Laryngoscope, 103*, 308-311.