WIDEBAND REFLECTANCE IN NORMAL SCHOOL-AGED CHILDREN AND IN CHILDREN WITH OTITIS MEDIA

by

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Abstract

In addition to the high prevalence of otitis media with effusion (OME), researchers are motivated to develop methods for early and accurate OME diagnosis because of the financial strain on the health care system associated with its diagnosis and management, and the medical and developmental consequences that may manifest if OME is left untreated. Standard (226 Hz) and high frequency (1000 Hz) tympanometry have traditionally been used clinically to assess middle ear status in children. A relatively new advanced middle ear analysis technique is Wideband reflectance (WBR). WBR has the potential to provide more information regarding the status of the middle ear than the methods currently being used clinically. This technique provides frequency-specific information about sound conduction through the peripheral auditory system. As a result of its recent introduction as an analysis method there is limited normative data available for this measurement system for pediatric populations and for those with middle ear pathology. Development of normative pediatric WBR data may render this technique a highly useful diagnostic tool for assessing the mechano-acoustical properties of middle ear function and for differentiating between healthy and pathological middle ears.

WBR patterns from 55 subjects (102 ears) with normal middle ear status and 39 subjects (57 ears) with varying degrees of middle ear pathology were measured. The mean and the 5th and 95th percentile ranges were graphically presented. Repeated measures analysis of variance was performed with frequency as the within subjects factor and age (child versus adult), middle ear condition (normal, mild negative pressure, severe negative pressure or effusion), race (Caucasian versus Chinese) and/or gender as the between subjects factors. Frequency-specific significant WBR pattern differences existed for reactance-based

and impedance-based measures, between pediatric and adult groups, Caucasian children and Chinese children, and all four middle ear conditions. Wideband reflectance must be further explored within a pediatric population before results can be generalized, but this measurement technique shows promise of providing a better understanding of the mechanico-acoustic properties of the middle ear and the changes to the system's functioning with middle ear pathology.

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Chapter I Introduction and Literature Review

1.1 General introduction

Middle ear infection (otitis media) is the second most prevalent childhood disease after the common cold. According to Hendley (2002) there are five million cases of otitis media in the United States per year, and there is an annual cost of four billion dollars (U.S.) associated with its diagnosis and management (Stool, 1994). In addition, otitis media is the primary reason for antibiotic prescription in children (Hendley, 2002) and it is estimated that 91% of children have at least one episode of otitis media during their first two years of life (Casselbrant, Mandel, Kurs-Lasky, Rockette & Bluestone, 1995). The prevalence of recurrent middle ear infection has grown since the 1980s, which may be attributed to the increased use of child care facilities combined with the greater incidence of allergies among children (Lanphear, Byrd, Auinger & Hall, 1997). An increased rate of otitis media (OM) is also positively correlated with passive tobacco smoke exposure (Etzel, Pattishall, Haley, Fletcher & Henderson, 1992) and negatively associated with prolonged breast-feeding (Owen, et al., 1993). Permanent damage to the peripheral auditory system, whether it is high frequency sensorineural hearing loss or damage to the middle ear structures, may result if OM is left untreated (Roark & Berman, 1997). Chronic middle ear pathology may also disrupt normal speech, language and cognitive development (Casby, 2001; Feldman & Gelman, 1986; Mody, Schwartz, Gravel & Ruben, 1999; Nittrouer, 1996; Shriberg, Frial-Patti, Flipsen & Brown, 2000).

Otitis media is a general term for several different clinical conditions, which include acute otitis media (a rapid onset of middle ear infection and inflammation), and otitis media with effusion (OME), where fluid is present behind the eardrum without signs of an active

infection (Sagraves, Maish & Kameshka, 1992). OME is thought to represent between 25% and 35% of the total cases of otitis media (Stool, 1994). Mora et al. (2002) predict that 80% of children experience at least 1 episode of OME. While there is no statistically significant difference in the incidence or prevalence of OME between genders, the highest occurrence is in children less than 6 years of age (Thrasher & Allen, 2005). OME can be relatively asymptomatic, where decreased hearing acuity is the only sign of pathology. Although OME typically occurs in conjunction with bouts of acute otitis media, it is also possible for OME to occur in children who have no history of ear pathology.

In addition to the high prevalence of OME, researchers are motivated to develop methods for early and accurate OME diagnosis because of the financial strain on the health care system associated with its diagnosis and management, and the medical and developmental consequences that may manifest if OME is left untreated. A relatively new advanced middle ear analysis technique is Wideband reflectance (WBR). WBR has the potential to provide more information regarding the status of the middle ear than the methods currently being used clinically. As a result of its recent introduction as an analysis method there is limited normative data available for this measurement system, particularly for pediatric and special populations, and for those with specific middle ear pathologies. The purpose of this research project is to use WBR to explore the mechano-acoustic properties of the middle ear system within a pediatric population consisting of children with healthy middle ear status and varying degrees of middle ear pathology, in an attempt to begin forming a database that can be used towards rendering WBR a highly useful diagnostic tool for pediatric audiologists.

1.2 Etiology of otitis media with effusion

The Eustachian tube is the passageway connecting the middle ear cavity and the nasopharyngeal cavity and plays a vital role in maintaining healthy middle ear status. Bluestone (2004) reviews the three roles of the Eustachian tube: to maintain atmospheric pressure within the middle ear cavity (which allows for maximal sound transmission through the middle ear system), to protect the middle ear from pathogens, and to drain fluids from the middle ear to the nasopharynx via a mucocilliary transport system. Eustachian tube malfunction can lead to middle ear pathology. If the Eustachian tube becomes blocked, then its roles cannot be fulfilled. A blockage of the Eustachian tube can occur for several reasons. Commonly the tube gets obstructed due to swelling along its mucus membrane lining (Bluestone & Klein, 1995, p. 21). Upon blockage of the Eustachian tube, pressure in the middle ear cannot be equalized. Negative pressure develops within the closed cavity as the cells lining the walls of the middle ear consume oxygen. As the pressure of the middle ear space falls below that of atmospheric pressure, the middle ear becomes less efficient at conducting sound along the conductive auditory pathway to the inner ear. If the blockage persists, middle ear pressure will further decrease and will eventually draw serous fluid from the mucosa lining. The fluid drawn into the middle ear cavity thickens as cell contents combine with serous fluid; this occurs as middle ear pressure becomes more negative. (Bluestone & Klein, 1995, p. 29).

There are several developmental and anatomical differences between child and adult Eustachian tubes that contribute to the greater risk of otitis media in children. The length of the Eustachian tube increases with age. Ishijima, Sando, Balaban, Suzuki and Takasaki (2000) found that the average length of the Eustachian tube in infants 3 months of age is 21.2

mm, and is 37 mm in adults. Similarly, the ratio between the length of the cartilaginous and junctional portion to the length of the bony portion of the Eustachian tube is 8:1 in infants and is 4:1 in adults. In addition to differences in length and structural make-up, the Eustachian tube changes in orientation as a child develops; this is presumably reflective of the growth of the face (Ishijima et al., 2000). Bluestone (2004) reviews the developmental and anatomical differences between child and adult Eustachian tubes. The shorter length and horizontal orientation of the tube increases the ability of secretions from the nasal and pharyngeal cavities to enter the middle ear space, which leads to infection of the cavity.

Yamaguchi, Sando, Hashida, Takahashi and Matsune (1990) used light microscopy to investigate the histology of the mid-cartilaginous portion of the Eustachian tube and found that cartilage cells are significantly denser in children under the age of 7 years compared to adults. Matsune, Sando and Takahashi (1993) found that the density of elastin in Eustachian tube cartilage increases with increasing age. The structural composition of the immature Eustachian tube, (such as the cartilaginous portion having a greater number of cells and a lower density of elastin), in addition to a smaller tubal lumen can cause a functional obstruction of the tube (Bluestone, 2004). Matsune, Sando & Takahashi (1992) also investigated the distribution of the goblet cells and submucosal glands in children up to age 7 with and without histories of otitis media. It was concluded that in the Eustachian tubes of children with otitis media both the goblet cella and submucosal glands were present in significantly higher numbers. The authors suggest that with these cells and glands in higher density, airflow within the Eustachian tube is more readily restricted, which leads to a less efficient mechanism of middle ear cavity drainage. This indicates that the physiological composition of the Eustachian tube can place certain children at greater risk of chronic OME.

The anatomical development of the structures surrounding the Eustachian tube was investigated by Kitajiri, Sando and Takahara (1987). They found that both the Eustachian tube and its surrounding structures continue to develop until an individual reaches 19 years of age. Their study revealed that the area of the tubal lumen increased fivefold from birth to adulthood and that the pharyngeal portion of the tube underwent the most significant development. In addition, there was an increased number of cartilage glands and a larger amount of muscle mass associated with adult Eustachian tubes. The area of the two Eustachian tube muscles was significantly larger in an adult compared to an infant: the adult tensor and levator veli palatini muscles were 5.1 and 11.1 times larger respectively than the size of those in the infants (Kitajiri et al., 1987). Bluestone (2004) explains how the opening mechanism of the Eustachian tube is underdeveloped in infants and young children. Instead of the tube aperture dilating during behaviours such as swallowing and yawning, the immature Eustachian tube will constrict. This constriction is due to the physiological immaturity of the Eustachian tube muscle, the tensor veli palatini, and the angle at which it is anchored to the Eustachian tube cartilage. A mechanical obstruction, which can apply pressure to the Eustachian tube and force its constriction, may also occur due to enlarged adenoids or tonsils that have not yet been surgically removed. Bluestone highlights that this postnatal Eustachian tube development is normal, and that it is not necessary to address the state of the Eustachian tube in treating OME. It is important to be aware of the factors contributing to the increased risk of developing the disease at a young age.

If the function or development of the Eustachian tube is pathological, corrective measures may be required. A study by Swartz and Bluestone (2003) investigated older children and adults with chronic OME and found that Eustachian tube opening mechanisms

were abnormal. For example, swallowing constricted the Eustachian tube instead of causing its dilation. The subjects' Eustachian tubes were functioning similarly to the immature Eustachian tubes of younger children. Swartz and Bluestone proposed that older children and adults with dysfunctional Eustachian tubes do not outgrow their high susceptibility to OME.

The Eustachian tube and its accessory structures play a vital role in the maintenance of middle ear status and do not reach adult-like maturity until 19 years of age. Over the course of this development, infants and young children are increasingly susceptible to OME that can be especially pronounced in those with craniofacial abnormalities. Certain children may be more prone to Eustachian tube constriction due its physiological make-up; this increases the risk of OME beyond that which can be attributed to their young age alone.

1.3 Clinical issues surrounding otitis media with effusion

The primary reason for treating OME in children is to avoid potential developmental sequelae associated with the disease (Roberts et al., 2004). This has motivated numerous studies investigating whether persistent middle ear effusion negatively impacts hearing acuity, speech and language development, or academic performance. Most research to date has focused on the presence of OME as the independent variable, and not the hearing loss that can result from the fluid present. As hearing acuity may still fall within the normal range when middle ear effusion is present, studies failing to find a correlation between chronic OME and speech and language development may be underestimating the adverse effects of a chronic fluctuating conductive hearing impairment. Roberts et al. (2004) argue that there is little converging evidence as to whether OME negatively impacts speech and language development. There have been numerous studies, and most differ in the populations tested,

methodology and outcomes. No single study is able to investigate all aspects of speech and language. Moreover the absence of consistent testing procedures makes it difficult to compare the results between studies.

1.3.1 Speech and language development

Children who suffer from chronic OME are at risk of developing a conductive hearing loss. The primary concern for these children is that elevated hearing thresholds will restrict their access to language, which may lead to either receptive or expressive reduced linguistic competence, and to impaired speech production. Roberts et al. (2004) indicate that there are two different views regarding the effects of OME on later language development. One view contends that development occurs within a critical period predicting that a fluctuating conductive hearing loss during the critical years has significant and permanent effects on the development of language and central auditory processing (Feldman & Gelman, 1986). The second view follows a connectionist model where mental processes are considered to be the product of an interaction between inputs from lower-level units and that learning modifies the weighting of the various input sources (Roberts et al., 2004). The connectionist model argues that while limited auditory input may result in temporary language and auditory deficits that children are still able to learn a significant amount of language, due to its redundant nature, by using the information that is available to them (such as residual hearing and vision). It is further believed that following the reinstatement of normal hearing thresholds that any pre-existing processing difficulties will spontaneously resolve due to the plasticity of the nervous system. Seidenberg and MacDonald (1999) argue that language learning is a process where a child accumulates information from infancy and, based on experience, a child is able to formulate a repertoire of probabilistic constraints and

linguistic rules. These constraints and rules are presumed to be readily modified as new experiences occur.

A meta-analysis conducted by the Agency for Healthcare Research and Quality (2002) evaluated the long-term effects of chronic OME on receptive language, expressive language and cognitive verbal intelligence in children older than 3 years of age. They found no significant effect of early OME on any of the language measures. The authors acknowledged that the studies in their analysis varied in terms of the OME risk factors considered, the measurement methods and units used, and the ages at which language was assessed. They also recognized that the results of the studies were not able to be generalized to special populations, such as children with craniofacial defects, genetic abnormalities or other developmental disorders. Roberts et al. (2004) noted that this meta-analysis failed to assess all aspects of language. For example, there was no evaluation of syntax or vocabulary. A meta-analysis conducted by Casby (2001) investigated the relationship between having a history of OME and the development of receptive and expressive language. Casby found that with middle ear effusion present at a young age children performed below their age-matched peers on both the receptive and expressive language measures.

Roberts et al. (2004) highlight the need for researchers to measure auditory thresholds rather than simply the duration for which effusion is present. Children with middle ear effusion may not have a hearing loss and those who do vary in the extent to which their thresholds are elevated. A mild conductive impairment may prevent a child from detecting unstressed and non-salient phonemes, such as /s/, and subsequently a difference may not be detected between the words *boat* and *boats*. In the event that /s/ is not audible, or in the presence of a chronic fluctuating hearing loss where it is not consistently audible, a child may

form abnormal linguistic rules for pluralization. Hearing acuity dictates the amount of auditory information available to higher auditory, speech and language centers, which plays a role in their development. Nittrouer (1996) found that children with a history of chronic OME have immature strategies for weighting features of the speech signal, which is related to an underdeveloped sensitivity to its phonemic structure. The author proposed that this decreased phonemic awareness may be a result of limited or fluctuating auditory input.

Mody, Schwartz, Gravel and Ruben (1999) investigated speech perception and verbal memory in children with and without histories of chronic OME. The pattern of errors produced by the two groups (OME-positive and OME-negative) was similar; however, the OME-positive group performed the tasks with a significantly larger number of errors. The children with histories of recurrent OME had impaired word recognition when the phonemes were minimally different, yet they did not differ from the OME-negative group when multiple cues were available. This suggests that the OME-positive group had more difficultly differentiating between the minimally different word pairs because they were required to perceive fine auditory discriminations, which may not be possible in the presence of even slightly elevated hearing thresholds. A study by Shriberg, Frial-Patti, Flipsen and Brown (2000) investigated the phoneme recognition abilities of children with recurrent OME and found that children's hearing level at 12-18 months of age was able to predict their phoneme recognition abilities at 3 years of age. Specifically, a hearing impairment at a young age was positively correlated with impaired phoneme recognition two years later. The deletion and substitution of phonemes, and the decreased ability to recognize diphthongs were the most common errors.

Shriberg and Smith (1983) and Paden, Matthies and Novak (1989) found that children with a history of middle ear pathology produced a significantly higher frequency of speech errors than their age-matched peers with normal middle ear status. Despite this evidence, a recent study by Campbell et al. (2003) investigated the risk factors associated with speech delay of unknown etiology and found that chronic OME was not significantly related to impaired speech production. Roberts et al. (2004) argue that evidence for a relationship between chronic OME and speech delay is inconclusive, and that the correlation does not appear to be strong. The authors suggest a more significant relationship exists between auditory thresholds and impaired speech and language development.

1.3.2 Auditory thresholds and central auditory processing

Several studies have investigated the association between OME and hearing acuity. Conventional testing of the peripheral auditory system uses pure tone audiometry to determine hearing thresholds for a range of speech frequencies (500, 1000, 2000 and 4000 Hz) via air and bone conducted stimuli. The results from three cross-sectional studies of children with persistent OME revealed that approximately half of the children had pure tone thresholds of 20 dB_{HL}, which is within normal limits for this age-group (Hunter, Margolis & Giebink, 1994; Fria, Cantekin & Eichler, 1985; Kokko 1974). Hearing thresholds exceeding 35 dB_{HL} were noted for roughly 20% of the children, where 10% of these children had thresholds ranging between 40 and 50 dB_{HL} (Fria, Cantekin & Eichler, 1985; Kokko 1974). A large-scale study by Sabo, Paradise, Kurs-Lasky and Smith (2003) tested a sample of 1055 children with the presence of bilateral or unilateral middle ear effusion and those without a history of middle ear pathology. The children ranged from 6 months to 5.9 years of age. Hearing acuity was poorest in children with bilateral middle ear effusion, intermediate in

children with unilateral effusion, and was best in children without middle ear effusion. The authors concluded that in the presence of bilateral middle ear effusion, a child's hearing thresholds are typically 10-15 dB_{HL} higher than are those of their age-matched peers with healthy middle ear status. Studies evaluating the amount of hearing loss associated with persistent OME indicate that the loss is generally mild, but can range up to a moderate level. Children typically will not have hearing thresholds greater than 50 dB_{HL}, providing that the cochlea and retrocochlear pathways are normally functioning (Fria, Cantekin & Eichler, 1985; Kokko 1974). In children with any degree of permanent hearing loss, the overlaying fluctuating loss associated with OME can cause a significant impairment. It is also important to bear in mind that while audiological thresholds of 20 dB_{HL} are considered to be the border of the normal hearing acuity range for the pediatric population, having hearing thresholds at this level will result in restricted access to the speech signal and does not discount the possibility of slight negative consequences for speech and language development.

In addition to the attenuation of sound, Hartley and Moore (2003) found that middle ear effusion alters the temporal characteristics of auditory input. The authors studied the effects of varying degrees of effusion viscosity. Typically, the amount of hearing loss increases with effusion viscosity. Hartley and Moore concluded that low and medium viscosity effusion delays sound transmission through the middle ear to a greater extent for low frequency input (1-6 kHz) compared to high frequency input (8-16 kHz), and that high viscosity effusion impedes sound transmission to a smaller extent but roughly evenly across the frequency range. The results of the study suggest that children with chronic middle ear fluid may experience a temporally distorted auditory signal in addition to one that is attenuated. This implies that as OME fluctuates so does the intensity level and temporal

spectrum of the auditory signal and the amount of information contained within the auditory message. It therefore becomes more difficult for children with OME to form linguistic rules and constraints with the auditory input that they receive.

The hearing loss associated with OME is typically conductive in nature, but there is evidence of an additional sensorineural component. Hunter et al. (1996) assessed the hearing acuity of children following tympanosotomy surgery. Children with histories of OME exhibited poorer high frequency hearing thresholds than did children without histories of middle ear disease. The impaired high frequency hearing was evident following the resolution of middle ear effusion. The authors found a strong positive correlation between the degree of permanent high frequency hearing loss and the length of time for which middle ear effusion is present and number of intubations. Margolis, Saly and Hunter (2000) also found that children with a history of chronic middle ear effusion were likely to have permanent hearing loss in the extended high frequency range. The authors concluded that neither middle ear impedance nor reflectance could account for this high frequency hearing loss because the middle ear transfer function wanes over this frequency range; it was attributed to pathology in the basal-most region of the cochlea.

The effects of a peripheral hearing impairment can manifest the length of the auditory pathway, through to the cortical centers of auditory perception. Central auditory processing is the way in which we process the stimuli that are detected by the lower levels of the auditory system. Central processing allows for the perception of degraded acoustic signals and the understanding of an auditory stimulus in the presence of competing stimuli. For example, such as the ability to comprehend filtered speech and speech in the presence of background noise (ASHA Task Force on Central Auditory Processing Consensus

Development, 1996). Central processes also include the temporal aspects of audition (temporal resolution, temporal masking, temporal integration and temporal ordering) and sound localization and lateralization.

Adequate input from the peripheral auditory system is required for normal functioning of the central pathways. In the presence of a conductive hearing loss, such as that resulting from middle ear effusion, there is distortion in and a reduction in the intensity of the acoustic stimuli reaching the central auditory system. Impaired central auditory processing can result from a fluctuating acoustic signal. There is debate to whether a bilateral or unilateral fluctuating conductive hearing impairment will cause a greater decrement in central auditory processing. Studies by King, Parsons and Moore (2000) and Hogan and Moore (2003) have shown that, due to the plasticity of the central auditory system, neural pathways reorganize with altered auditory input. Animal models of OME are frequently used to study the effect of a temporary or fluctuating conductive hearing loss. These models are made by rearing animals with one or two ears plugged, to simulate a unilateral or bilateral conductive hearing loss. The auditory system localizes sound using monaural and binaural cues and the individual's head transfer function (the modification of the acoustic signal that occurs as a result of the shape and size of an individual's head and pinnae and torso). In the presence of monaural occlusion, compensatory action by the nervous system includes modification of its auditory spatial organization to rely predominantly on information transmitted from the unoccluded ear (King et al., 2000). The authors also found that normal sound localization abilities can be recovered following the removal of a prolonged unilateral occlusion.

Moore et al. (1999) reared ferrets as animal models of OME. They studied the effect of ear plugging on binaural unmasking (the increased ability to perceive a signal in noise that occurs when stimuli are presented binaurally), and found binaural unmasking to be impaired by a unilateral conductive hearing loss. There was an improvement in binaural hearing following restoration of normal peripheral hearing, but normal functioning was not attained until several months later (Moore et al., 1999). Hogan and Moore (2003) found impaired binaural hearing when effusion was present for at least half of the time during the first five years of a child's life. Hall, Grose and Pillsbury (1995) found that long-term effects of OME persist beyond the restoration of normal hearing thresholds. For example, the recovery of normal binaural unmasking levels took up to two years following tympanostomy surgery. A longitudinal study by Hogan, Meyer and Moore (1996) found that the impaired central auditory processing in individuals with a childhood history of recurrent OME can continue until adolescence. The implications of the abovementioned studies may be extended to a child's needs and performance in a classroom setting. With recurrent OME and associated fluctuating conductive hearing loss central auditory processing may be impaired. Central processing deficits may persist upon resolution of the effusion and the reinstatement of normal hearing thresholds. Central auditory processing difficulties include impaired understanding of speech in an adverse acoustic environment (such as a reverberant room or in the presence of background noise), and a reduced ability to localize auditory stimuli. Long-term considerations, such as providing supplementary visual information and encouraging preferential seating in the classroom, may be beneficial for OME-prone children, even if peripheral hearing appears normal.

Children with chronic OME were investigated prior to and following the placement of pressure equalization tubes (Pillsbury, Grose & Hall, 1991). Masking level differences (measures of signal detection in background noise) measured prior to surgery were abnormally low in cases where a hearing loss was present. Despite the reinstatement of normal hearing thresholds masking level differences remained abnormally small following the tympanosotomy surgeries. Pillsbury et al. found an increased incidence of reduced masking level differences post-surgery if the pre-surgery hearing loss had been asymmetrical. A study by Hall and Grose (1993) found that some children with a history of chronic OME and decreased masking level differences had prolonged wave III and V auditory brainstem response latencies, as well as prolonged I-III and I-V interpeak intervals. They concluded that the reduction in masking level differences seen in children with chronic OME may be a result of abnormal auditory processing at the level of the brainstem. Johnston and Green (2002) presented verbal stimuli in the presence of background noise and found that the word recognition ability of OME children was impaired in the noisy conditions compared to the age-matched control group.

Hall, Grose, Dev, Drake and Pillsbury (1998) investigated children with histories of OME and their central auditory processing abilities for both simple and complex tasks, prior to and following myringotomy and tympanostomy surgery. The children were tested on their ability to detect a signal in background noise. The noise was composed of either a single modulation pattern or several modulation patterns, which was presumably a more complex task. Prior to tube placement, the children had impaired performance on both the simple and complex tasks, compared to the age-matched control group. Six months following the surgery there was no significant difference in the performance on the simple task between the

OME children and the normal children. The children with histories of OME, however, had significantly poorer performance on the complex task when tested one year following surgery, compared to those with no history of OME. The authors concluded that a positive correlation exists between the complexity of an auditory task and the amount of time required to recover normal functioning following the resolution of long-standing middle ear effusion.

Otitis media with effusion can be associated with a mild to moderate, unilateral or bilateral, conductive hearing impairment. The abovementioned studies reveal that hearing loss of this nature can impair the functioning of the central auditory system, and that its effects can persist beyond the reinstatement of normal hearing thresholds. This has been attributed to the neural reorganization that occurs due to the presence of chronic effusion. Several studies have found the reduced central auditory processing to be temporary. The same studies concluded the time course of recovery was influenced by factors such as bilateral versus unilateral effusion and simple versus complex auditory processing tasks. Another concern for children with chronic OME, resulting in chronically fluctuating hearing acuity, is that elevated auditory thresholds will restrict their access to language. This may lead to either receptive or expressive reduced linguistic competence and impaired speech production. Restoring normal peripheral hearing and accelerating the medical management process are key motivators in developing a method to accurately diagnose middle ear pathology. A reliable diagnostic method will limit the adverse effects of elevated hearing thresholds on the child's speech and language development and academic performance.

1.4 The middle ear system

An audiologist is likely to be the first medical professional to suspect the presence of middle ear effusion because he or she will conduct a series of tests to assist with the

diagnosis of OME. Tympanometry, a fundamental component of an audiologist's test battery, is used routinely to assess middle ear status in both adult and pediatric populations. This type of measurement was first proposed by von Bekesy (1932), who noted that acoustic impedance was influenced by the air pressure in the external auditory meatus. Tympanometry measures changes of acoustic immitance as ear canal pressure is swept through a range of values. Acoustic immitance is a term that encompasses both acoustic impedance and acoustic admittance referring to the flow of energy through the middle ear system. Acoustic impedance is the middle ear opposing the flow of energy through the system while acoustic admittance refers to the ease with which energy is able to flow through the middle ear system. In order to understand the ways in which middle ear effusion alters acoustic admittance and the rationale behind tympanometric measurements, the acoustical transmission properties of the middle ear system must be explained.

Three variables contribute to middle ear admittance: mass, stiffness and friction. Susceptance refers to the mass and stiffness elements of the system with total susceptance referring to the sum of the mass susceptance and the compliance (inverse of stiffness) susceptance. Mass susceptance is the admittance offered by the mass constituents of the middle ear system, and compliance susceptance is the admittance offered by the stiffness components of the middle ear system. The susceptance components are frequency dependent; admittance varies as a function of the input frequency. If the middle ear system is being described in terms of impedance, then the mass and stiffness components of the system are discussed in terms of reactance. Mass reactance and stiffness reactance are the components that act to impede the flow of energy through the middle ear system. Friction is a force that opposes motion; specifically, it causes the dissipation of energy between objects

in motion. Friction, also termed resistance, is always present in the middle ear system and is independent of input frequency.

Allen, Jeng and Levitt (2005) explain the acoustic transmission properties of the middle ear system in terms of impedance (reactance and resistance). The impedance of the eardrum is reflective of middle ear impedance (i.e. the mechanical load imposed upon the eardrum by the middle ear system). For input frequencies below 1000 Hz, the middle ear impedance is dominated by stiffness reactance, largely due to the stiffness of the annular ligament surrounding the tympanic membrane (Lynch, Nedzelnitsky & Peake, 1982). The majority of the low frequency sound energy reaching the eardrum is reflected in the retrograde direction. An even smaller proportion of sound energy is transmitted through the middle ear system for frequencies below 800 Hz (Puria & Allen, 1998). Eardrum impedance is stiffness-based for low frequency input with the relative contribution of resistance decreasing with frequency. For frequencies of 100 Hz, the effect of reactance contributing to eardrum impedance can be up to ten times greater than the effect of resistance; whereas when the frequency approaches 1000 Hz, the stiffness reactance and resistance components are roughly equivalent (Allen et al., 2005).

Above 6000 Hz, eardrum impedance is dominated by mass-based reactance, largely due to the mass of the ossicles. Most of the high frequency sound energy reaching the tympanic membrane is reflected in the retrograde direction (Allen, Jeng & Levitt, 2005). For the mid-frequency range (i.e. 1000 – 5000 Hz), the stiffness reactance and the mass reactance of the middle ear system react in a complex fashion, with the end result being only a small net reactance value following the summation of the various stiffness-based and mass-based components (Allen et al., 2005). This indicates that the input frequencies are approaching

the characteristic frequency of the middle ear system, which is its resonant frequency. Resonant frequency of the middle ear is the frequency at which sound energy flows most readily through the system; it is the system's natural frequency. Resonance is achieved when the mass and stiffness elements are equal and resistance is the only variable contributing to middle ear impedance. Low net reactance through the mid-frequency range means that the primary force contributing to the middle ear impedance is resistance, and a significant proportion of the sound energy reaching the tympanic membrane is transmitted through the middle ear system to the oval window of the cochlea. This is not the case for the frequencies lower than 1000 Hz or greater than 5000 Hz, where the reactance components are large compared to the resistance. High levels of impedance occur for sounds falling outside this mid-frequency range and as a result acoustic energy is not transmitted through the middle ear system with high efficiency.

Allen, Jeng and Levitt (2005) explain that the sound energy reflected at the level of the eardrum serves as a useful predictor of middle ear status, particularly when the frequency-specificity of the reflected energy is considered. The authors reveal that several middle ear pathologies can be identified based on the magnitude and latency of reflected energy across the frequency range.

1.5 Tympanometry

Tympanometry has traditionally been conducted in clinics using a 226 Hz probe tone to generate a measure of middle ear admittance as a function of ear canal pressure. Several measures can be obtained from the tympanogram, such as static admittance, tympanometric peak pressure, tympanic width, equivalent ear canal volume and tympanometric configuration. Studies have shown however, that these parameters do not reliably assess

middle ear status. For example, static admittance has been shown to change with increasing probe tone frequency independent of middle ear status. Higher probe tone frequencies provide more accurate discriminations between normal and pathological ears, compared to the 226 Hz tympanometry, for both low impedance pathologies (Van Camp, Creten, van de Heyning, Decraemer, & Van peperstraete, 1983) and high impedance pathologies (Shahnaz & Polka, 1997). Elner, Ingelstedt and Ivarsson (1971) found that the use of tympanometry to indirectly measure middle ear pressure generally overestimates the actual value, sometimes by as much as 100%. The frequency-sweep direction can also bias the estimate of middle ear pressure. Elevated tympanometric peak pressure may be a valid indicator of acute otitis media (Margolis & Nealson, 1993); however, Nozza, Bluestone, Kardatzke and Bachman (1994) concluded that decreased tympanometric pressure does not reliably detect middle ear disease. Using 226 Hz tympanometry to obtain an equivalent ear canal volume measure was shown to overestimate actual ear canal volume by an average of 25% in adult subjects (Shanks & Lilly, 1981), which was attributed to the compliance of the ear canal walls. Equivalent ear canal volume can be overestimated to an even larger extent in children and infants (by approximately 400%) due to their highly compliant ear canal walls (Keefe et al., 2000).

Early investigation into the effect of probe tone frequency on tympanometric shape was conducted by Colletti (1976; 1977). Colletti (1976) investigated multifrequency tympanograms in patients with a variety of pathophysiological middle ear conditions using probe tone frequencies ranging from 200 to 2000 Hz. Results revealed that different tympanometric patterns emerged with different middle ear pathologies when multifrequency probe tones were used. Colletti concluded that multifrequency tympanometry provided a

more sensitive measure of sound transmission through the middle ear system than did traditional low frequency tympanometric methods. Other studies have reported that patients with confirmed middle ear pathologies generate normal 226Hz tympanograms, but that abnormal patterns emerge when tested at higher probe tone frequencies (Hunter & Margolis, 1992).

Resonant frequency of the middle ear system can be measured using multifrequency tympanometry. Colletti (1977) found that middle ear pathologies affect the dynamics of middle ear sound transmission. Mass-loading pathologies (such as middle ear effusion) can decrease the resonant frequency of the middle ear system; whereas, an increase in middle ear stiffness (such as stapes fixation evident in otosclerosis patients) can increase its resonant frequency.

In addition to estimating middle ear resonant frequency, multifrequency tympanometry can provide valuable clinical information from analyzing the tympanometric patterns produced over a range of probe tone frequencies. By taking the resistance and reactance elements of the system into account, Vanhuyse, Creten and Van Camp (1975) developed a model to predict tympanometric morphological patterns as a function of middle ear status. The model predicts that as the susceptance of the middle ear increases from a negative value (a mass-dominated system) to a positive value (a stiffness-dominated system), there is a corresponding change in the pattern of the susceptance and conductance tympanograms.

While the diagnostic capability of multifrequency tympanometry is significantly improved over traditional low-frequency tympanometric measures, particularly in younger patients, there continue to exist several limitations of this testing method. One major

limitation of multifrequency tympanometry is that probe tones are restricted to low and mid frequencies, because when probe tones above 2000 Hz are used standing waves are generated in the ear canal. This restricts the range over which middle ear testing can occur. Further more, due to the highly compliant nature of the ear canal in young patients, tympanometric measures, which change the pressure of the canal, are not able to obtain reliable measures of middle ear status. With middle ear pathologies highly prevalent among the population of patients from infancy to school-aged children, a reliable method of assessing middle ear status is required.

1.6 Wideband Reflectance

Wideband reflectance (WBR), originally proposed by Teele and Teele (1984), is a recently developed measure of middle ear sound transmission that evolved from acoustic reflectometry. Preliminary studies have shown that reflectance measures may address the shortcomings of tympanometric testing. Human audition occurs when sound energy travels through the external auditory meatus to the tympanic membrane. It is either transmitted through the middle ear system to the inner ear, absorbed by the soft tissues of the ear canal wall, or is reflected by a structure along the transmission pathway. Sound propagation through the auditory system depends on the integrity of its structures. Similar to tympanometry, WBR measures the energy flow through the auditory system as a function of frequency, but unlike tympanometry, static WBR testing occurs at a constant pressure, typically an ambient level. A probe tone inserted into the ear canal emits an acoustic stimulus that consists of frequencies 250 Hz to 10 000 Hz (up to 8000 Hz with the Mimosa system). Based on the energy emitted from the probe, the computer provides a frequency-

specific measure of energy reflectance in the ear canal. The WBR software depicts the middle ear variables as a function of frequency on a logarithmic scale.

Measures of acoustic power flow (power reflectance, power absorption and transmittance) and normalized impedance (acoustic resistance, acoustic reactance and impedance magnitude) can be generated by WBR testing (Allen, Jeng & Levitt, 2005). The acoustic power wave that reaches the eardrum is partially transferred through the middle ear, while a proportion of this energy is reflected back in a retrograde direction into the ear canal. Allen et al. (2005) define power reflectance as "the percentage of incident power that is reflected back into the ear canal". This value ranges from 0 %, which indicates that all of the energy has been absorbed by the middle ear system, to 100 %, where all of the energy is reflected by the system. Power reflectance varies as a function of frequency, as does the acoustic impedance of the tympanic membrane. The acoustic power of the retrograde reflected wave can be defined in terms of both magnitude and latency, and when considered as a function of frequency, can discriminate between normal and pathological middle ears, as well as help to reveal the nature of a middle ear disorder (Allen et al., 2005). This pressure wave consists of both amplitude and phase components, which both vary in the frequency domain. The magnitude can be determined by the amplitude of the wave, and the latency by its phase. The acoustic pressure wave can also be defined in terms of its real and imaginary components. Power reflectance, also termed Energy reflectance (ER), is only one of several possible middle ear measures that can be made using WBR techniques.

Another measure of acoustic power is transmittance, which is depicted in decibel units. Measures of normalized impedance (acoustic resistance, acoustic reactance and impedance magnitude) can also be generated. Reflectance and impedance are complex

quantities, meaning they consist of magnitude and phase values. Impedance can be subdivided into two constituents: the real component which represents resistance and the imaginary component which represents reactance (Allen et al., 2005). The three impedance variables are mathematically altered by the WBR system. Impedance, reflectance and resistance are normalized using the characteristic impedance of an average adult ear canal, in an attempt to compensate for the effect of the ear canal on the measure of the middle ear. The characteristic impedance (Z_c) can be calculated using the equation defined in Formula (1), where ρ is defined as the density of air, c as the speed of sound, and S as the area of the ear canal. The middle ear variables of impedance (net impedance, reactance and resistance) are measured by the WBR system, and then divided by the characteristic impedance to obtain normalized values.

$$Z_c = \frac{\rho c}{S} \qquad (1)$$

Normalized values are used to decrease the variability of the measures, both between-subject and between-test variation (Allen et al., 2005). These normalized values are dimensionless, as they represent ratios of numbers with identical units. It is of clinical relevance to determine which of the middle ear variables reveals the most information regarding middle ear status.

Middle ear pathologies can impede sound conduction through the middle ear system. Impaired conduction is a function of the pathology's effect on the reactance components of the system. For example, middle ear effusion increases mass reactance of the middle ear

system. This decreases power absorption and increases energy reflectance of the middle ear at high frequencies (Feeney, Grant & Marryott, 2003). Increased stiffness reactance occurs in conjunction with ossicular discontinuity and otosclerosis (Voss, Rosowski, Merchant & Peake, 2001b). In this case, power absorption in the middle ear is high, but the system fails to adequately transmit sound energy to the cochlea. The effect of middle ear pathologies on WBR measures has not been extensively studied. Investigations to date however, indicate WBR is a potentially useful diagnostic tool for discriminating between normal and impaired conductive mechanisms. The utility of WBR will ultimately depend on the normative data compiled and the extent to which reflectance measures differ between populations.

Several studies have investigated WBR patterns from individuals with otitis media. A case study by Hunter and Margolis (1997) revealed abnormal WBR patterns in the presence of confirmed middle ear effusion. Low frequency tympanometry indicated normal middle ear admittance, but energy reflectance measures were elevated above those obtained from individuals with normal middle ear status. Margolis, Saly and Keefe (1999) investigated WBR in an individual with recurrent otitis media. They found that the negative middle ear pressure (associated with otitis media) generated WBR patterns consistent with those measured in individuals with normal middle ear status in conditions where ear canal was pressurized. Abnormal patterns result when WBR is performed under ambient canal pressure and middle ear pressure is negative. Margolis et al. indicate WBR can distinguish individuals with normal middle ear status from those with middle ear effusion; conventional low frequency tympanometry did not make this distinction.

A preliminary study by Jeng, Levitt, Lee and Gravel (1999) used WBR to assess middle ear status in children aged 2.5 to 5 years, with histories of chronic OME. Reflectance

results were compared between those with normal middle ear status and those with middle ear effusion. The authors found that power absorption (PA) ratios of the OME group were reduced across the frequency range compared to the control subjects. Absorption ratios were nearly zero for probe frequencies below 1000 Hz. The greatest discrepancy between the OME and normal PA results were seen from probe tone frequencies 1000 to 2500 Hz. This frequency range carries important speech information and its inadequate transmission through to the inner ear may reduce the perception of critical linguistic cues. Jeng et al. also noted that the resistance and reactance curves differed between the OME and the control subjects. At frequencies below 2000 Hz, the reactance of the OME subjects was reduced compared to the controls, meaning there was increased negative reactance at low frequencies due to the increased stiffness in the presence of middle ear effusion. Between 1000 and 6000 Hz the resistance measured from the OME group was reduced overall compared to the control group and the graph of resistance had a smaller spread compared to that of those with normal middle ear status. The results of this preliminary study show that WBR measures are able to detect a difference between normal ears and those with effusion present, and that the differences are frequency-dependent. The authors propose that WBR testing may prove to be a useful screening tool in young patients, where tympanometric testing is of limited validity. A shortcoming of this study is the small sample size that was tested, where only fifteen control subjects and three OME subjects participated. More testing is required before reliable normative data can be generated.

Systematic shifts are evident in the WBR patterns generated from normal middle ears from those with pathologies such as otitis media, otosclerosis, ossicular discontinuity and tympanic membrane perforation, when an ambient-pressure measurement technique is used

(Feeney, Grant & Marryott, 2003). Pressurized WBR measurements, however, are able to provide information that is not available when WBR patterns are recorded at an ambient pressure level (Margolis, Saly & Keefe, 1999; Margolis, Paul, Saly, Schachern & Keefe 2001). When two animal subjects had Eustachian tube dysfunction induced, significant differences were noted between WBR patterns at varying ear canal pressure levels (Margolis et al., 2001). The authors concluded that obtaining WBR patterns at any single ear canal pressure level does not provide optimally complete information regarding the middle ear status, and that multiple pressure levels are required in order to more thoroughly quantify the effects of a middle ear pathology. A study by Keefe and Simmons (2003) compared the test performance of ambient-pressure versus pressurized acoustic transfer function measures on the ability to identify conductive hearing loss in older children and adults. Using a fixed specificity of 0.90, the sensitivities measured for 226 Hz tympanometry, ambient-pressure WBR and pressurized WBR were 0.28, 0.72 and 0.94, respectively. The authors concluded that WBR conducted at an ambient ear canal pressure level is able to provide sufficient information for screening purposes but that pressurized measures were more useful as a diagnostic tool. One of the limitations of this study, as indicated by the authors, is that in order to determine the tympanometric peak pressure, a tympanogram was first generated using a 226 Hz probe tone. In the case where a flat tympanogram was generated and a peak pressure was not assigned by the machine, a pressure value of 0 daPa was adopted. Keefe and Simmons indicated that a test protocol for pressure sweep parameters must first be established prior to using this type of test technique clinically.

Conductive hearing loss associated with OME was predicted by measures of energy reflectance (Piskorski, Keefe, Simmons & Gorga, 1999). At a fixed sensitivity of 90%,

specificity was achieved as high as 94%. The authors found energy reflectance measures for frequencies 2000 to 4000 Hz were the best indicators of middle ear pathology. WBR has the unique ability to reliably assess middle ear sound transmission at high frequencies, which is important for the accurate detection of middle ear effusion. Adequate propagation of 2000 to 4000 Hz through the middle ear system is essential for the perception of these frequencies, which is necessary for normal speech and language development. Keefe and Levi (1996) conducted WBR measures on three infants with otitis media. WBR data indicate that a multifrequency assessment of middle ear function is more sensitive than a single frequency measure. This is analogous to behavioural audiometry, where measurement of a single hearing threshold cannot be generalized to represent hearing sensitivity across a range of stimuli. A multi-frequency assessment is required to provide an accurate overall measure of hearing acuity.

A case study by Hunter and Margolis (1997) followed a 9-year-old girl (JB) with recurrent otitis media. She received tympanosotomy surgery at the age of 4 years, had an osteoma removed at 5 years of age, and had since had several recurring episodes of otitis media. JB's audiogram revealed a 10 dB_{HL} air-bone gap in the right ear, although the air conduction hearing thresholds were within normal limits (better than or equal to 20 dB_{HL}). Video otomicroscopy was able to identify a fluid line and air bubbles in the middle ear cavity. Standard single frequency 226Hz tympanometry revealed normal static admittance and tympanometric width, and a tympanometric peak pressure of -260 daPa. The effusion did not fill the entire middle ear cavity. The residual middle ear space was adequate to generate a tympanogram peak.

In this study, multifrequency tympanometry was more sensitive than standard tympanometry to the presence of middle ear effusion. For probe tone frequencies 226 to 500 Hz, the tympanometric patterns produced were flattened, with irregular peaks and valleys that did not follow the Vanhuyse model. At 560 Hz, the susceptance tympanogram had a central notch. This notch appeared to signify the resonant frequency of the middle ear system. However, the notch did not deepen and progress into subsequent Vanhuyse forms with increasing probe tone frequency. The susceptance tympanogram became flat as the probe tone frequency increased beyond 800 Hz, indicating that the admittance of the middle ear was reduced. Extrema on the susceptance and conductance tympanograms emerged at probe tone frequencies above 1400 Hz, but still did not follow the Vanhuyse model.

WBR was measured at three different pressure values (+300, 0, -300 daPa) and was compared to the WBR pattern obtained from individuals with normal middle ear status. JB's WBR results at -300 daPa best approximates those from normal subject at ambient pressure; however, these two patterns do not entirely overlap. The 1200 and 4000 Hz regions are associated with low reflectance in normal subjects, but JB's WBR results (when middle ear pressure is compensated) revealed significantly higher reflectance in these two regions. When JB's WBR was measured at ambient pressure, results revealed abnormally high energy reflectance (close to 1.0) through a frequency range where the normal subjects have reflectance ratios of roughly 0.5. The WBR results at +300 and 0 daPa also revealed a sharp decrease in reflectance between 4000 and 8000 Hz. This pattern was not evident in the results from the normal subject or when a pressure value of -300 daPa was used. The authors concluded WBR may be able to indicate abnormal middle ear status, but adequate norms are required before this can be confirmed.

This case study of an individual with recurrent OME demonstrates that low frequency 226 Hz tympanometry lacked the sensitivity to detect the middle ear effusion. Multifrequency tympanometry resulted in abnormal patterns at all probe tone frequencies above 226 Hz, suggestive of middle ear pathology. Wideband reflectance measures at ambient pressure deviated significantly from the pattern observed in individuals with normal middle ear function. Multifrequency tympanometry and WBR can be sensitive measures to this type of middle ear pathology, although the utility of WBR prevails due to the larger range of test frequencies that can be used to generate a broader measurement of the middle ear system. The utility of WBR as a clinical tool depends on the development of adequate normative data.

There are several strengths of WBR. This measurement technique is fast and non-invasive. Middle ear transmission properties can also be tested over a wide range of frequencies (up to 10 000 Hz), which leads to an optimally complete assessment of the middle ear through the range of speech frequencies. Wideband reflectance measurements are able to confirm normal middle ear acoustic transmission in infants and older children (Keefe et al., 2003). This technique provides frequency-specific information about sound conduction through the peripheral auditory system, and can predict conductive hearing loss among an OME-prone pediatric population with greater efficacy than 226 Hz tympanometry (Piskorski, Keefe, Simmons & Gorga, 1999). Contrary to tympanometry, the generation of standing waves within the ear canal is not of concern when acoustic power flow is measured and the depth of probe tip insertion is not critical (Jeng, Levitt, Lee & Gravel, 1999). Additionally, because pressure is maintained at an ambient level, highly compliant infant ear canals will not confound test results (Keefe et al., 2000). And finally, more than a single

resonant frequency of the middle ear system can be measured. Current limitations of WBR are due to its recent development. This measurement system is not yet being used clinically and there is limited normative data, particularly for pediatric and special populations and for those with various middle ear pathologies. The limitations can be overcome by further research with and better understanding of the equipment and the results that are generated.

The WBR studies to date involve primarily adult subjects and discuss middle ear function in terms of power reflectance or power absorption only. A recent study by Shahnaz and Bork (2006) determined normative adult WBR values for power absorption, admittance, susceptance and conductance of the middle ear. Data of this sort do not currently exist for a pediatric population. It is known that the outer and middle ears do not reach adult-like maturity until adolescence and that the relative reactance contributions of the mass-based and stiffness-based components of the middle ear system change with increasing age, but the differences in middle ear sound transmission properties between child and adult populations are unclear. If middle ear cavity volume varies with body mass index and middle ear transmission properties vary as a function of body size, as was proposed by Shahnaz and Bork (2006), then it would follow that middle ear acoustic transfer functions would differ between adult and pediatric populations. Increased middle ear volume decreases the stiffness of the middle ear system and leads to a degradation in the acoustic transfer of high frequency sounds (Relkin, 1988). Shahnaz and Bork attempted to control for the effect of body size by comparing the energy reflectance patterns between Caucasian female and Chinese male subjects, which are known to be more comparable in body size than either male-female pairs within the same race. This comparison was able to account for some of the reflectance differences between the Caucasian and Chinese subjects. If a smaller middle ear cavity space

exists in children compared to adults, and therefore the pediatric middle ear system achieves resonance at a higher frequency, then children's middle ears may be more efficient at transferring high frequency sounds through to the inner ear. A smaller degree of high frequency power reflectance may be evident among this population.

Middle ear transmission properties have been proposed to vary with gender and/or race. Margolis and Heller (1987), Roup, Wiley, Safady and Stoppenbach (1998), Shahnaz and Davies (2006), and Wan and Wong (2002) have found that middle ear tympanometric measures differed either in terms of race, gender or both. It is for this reason Shahnaz and Davies (2006) suggested that gender-specific and race-specific (Caucasian and Chinese) normative data be used for low frequency and multifrequency tympanometry. Shahnaz and Bork (2006) found both gender and racial differences between Caucasian and Chinese young adults with normal middle ear function. The authors proposed that body size may have contributed to some of this variation between the subject groups, particularly if increased body size is correlated with increased middle ear cavity size, increased middle ear ossicle mass, and increased area of the tympanic membrane and stapes footplate (Shahnaz & Bork, 2006).

If middle ear structures or transmission properties vary as a function of ear, gender and/or race, then WBR test performance may be compromised by normative data that is not optimally homogenous. It is essential to explore the effects of potentially confounding variables when establishing normative data. It is for this reason that the pediatric normative WBR data collected in this study will be analyzed for the effects of ear, gender and race.

1.7 Goals of the thesis

The high prevalence of OME, the financial strain associated with its management, and the potential developmental and medical complications that arise if it is left untreated have all motivated researchers to develop methods for its early and accurate diagnosis. The goal of this research project is to explore the mechanico-acoustical properties of the middle ear within a pediatric population consisting of children with healthy middle ear status and middle ear pathology, using WBR to determine whether variables such as ear, gender and race affect the WBR patterns measured.

The middle ear characteristics of children with OME differ from those with healthy middle ear status. Middle ear effusion increases the mass of the system. The mass-based reactance of the middle ear system dominates eardrum impedance at high frequencies, and increased mass can lead to elevated high frequency energy reflectance, resulting in poor acoustic transfer of high frequency sounds to the inner ear (Allen, Jeng & Levitt, 2005). Development of normative pediatric WBR data may render this technique a highly useful diagnostic tool for assessing the mechano-acoustical properties of middle ear function and for differentiating between healthy and pathological middle ears among this population.

1.7.1 Specific research questions addressed by the thesis

There are three specific questions addressed by the current study:

1. What WBR patterns are generated by a pediatric population with healthy middle ear status, for middle ear energy reflectance, normalized impedance, normalized reactance and normalized resistance and do these WBR patterns differ as a function of ear, gender and race?

2. Do the energy reflectance WBR values obtained from a pediatric population differ from the adult normative data found by Shahnaz and Bork (2006), and do ER differences exist between Caucasian and Chinese male and female children?

3. How does the normative pediatric data compare to the WBR patterns of children with middle ear pathology, specifically, middle ear effusion and negative middle ear pressure?

Chapter II Methods

2.1 Subjects

2.1.1 Description of control group subjects

The control group subjects consisted of fifty-five participants (102 ears). Twenty-eight of the control subjects were female (52 ears) and twenty-seven were male (50 ears). Twenty-seven of the subjects were Caucasian (51 ears), twenty were Chinese (37 ears), four were Middle Eastern (6 ears), and four (8 ears) were of mixed ethnic origin. The control subjects ranged in age from 5 years, 1 month to 6 years, 11 months, with the mean age being 6.15 years. Age and ethnicity were reported by the parents.

2.1.2 Description of diseased group subjects

Subjects with middle ear pathology were categorized into three groups according to its severity: those with a mild degree of negative middle ear pressure, those with a severe degree of negative middle ear pressure, and those with middle ear effusion. The negative pressure ranges of the two diseased groups were arbitrarily chosen. There were seventeen subjects (24 ears) with mild negative middle ear pressure (-100 to -199 daPa), and their mean age was 6.42 years. Subjects were included regardless of ethnic origin. Nine of these subjects were Caucasian (11 ears), four were Chinese (7 ears), two were Middle Eastern (3 ears), one was Mexican (2 ears) and one (1 ear) was of mixed ethnic origin. There were twelve subjects (18 ears) with severe negative middle ear pressure (-200 daPa or more negative), and of these subjects nine (14 ears) were Caucasian, two (3 ears) were Chinese, and one (1 ear) was Middle Eastern. The mean age of this group was 6.57 years. There were ten subjects (15 ears) with middle ear effusion, and their mean age was 7.24 years. Of this

group, nine (14 ears) were Caucasian and one (1 ear) was of mixed ethnic origin. Age and ethnicity were reported by the parents.

2.1.3 Inclusion and exclusion criteria for control group subjects

1. Meet the ASHA (1990) screening criteria for normal auditory function and middle ear status.

2. Pass a Transient-evoked otoacoustic emission (TEOAE) screening in a particular ear, in order to assure healthy middle ear status and cochlear integrity.

3. Negative middle ear pressure measured with low frequency tympanometry did not exceed -99 daPa.

4. Age within the range of 5 years, 0 months to 6 years, 11 months.

5. No apparent disease of either the outer or middle ear upon otoscopic examination.

6. No reported history of head trauma or hospitalization for an illness.

2.1.4 Inclusion and exclusion criteria for diseased group subjects

1. Evidence of middle ear effusion or negative middle ear pressure. Presence of middle ear effusion was determined by decreased hearing thresholds, absent TEOAEs and flat tympanograms at 226 and 1000 Hz, and/or surgical confirmation by a pediatric otolaryngologist for the subjects who were patients of Dr. Kozak's. Negative middle ear pressure was determined by a Jerger Type C tympanogram measured with low and high frequency tympanometry, using a positive to negative pressure sweep direction. Negative middle ear pressure was classified as either severe (-200 daPa or

more negative) or mild (between -100 and -199 daPa). The static admittance of the tympanometric measures was not directly considered, but was ranged from normal to abnormally low within each group.

2. Age ranging from 4 to 12 years. The age range for the diseased group subjects was extended to include the patients of Dr. Kozak's who wished to participate in the study.

3. No otoscopic evidence of outer or middle ear pathology, with the exception of visualizing a retracted tympanic membrane or middle ear effusion.

4. No reported history of head trauma or hospitalization for an illness.

2.2 Instrumentation

2.2.1 Otoscopy, audiometry, transient-evoked otoacoustic emissions and tympanometry

Otoscopy was performed using a Welch-Allen clinical otoscope. Pure tone audiometry was conducted using a portable audiometer (Maico MA 40, calibrated July 2006) for the control subjects and the study subjects who were tested at the hospitals. A GSI 61 audiometer (calibrated July 2006) was used for those subjects tested at the School of Audiology and Speech Sciences. The audiometers were calibrated according to ANSI standards (re: S3.6.1989), and a biological listening check was performed each day prior to testing. Supra-aural headphones (TDH-39) were used to screen the hearing of control subjects and to obtain the audiometric thresholds of study subjects. A bone oscillator was used to confirm normal cochlear function among the study subjects tested at the School of Audiology and Speech Sciences. Testing was conducted in a sound-treated booth or a quiet

room of the hospital for the study subjects. The control subjects were tested in a quiet room of the school, such as the counselor's office or the library.

Transient-evoked otoacoustic emissions (TEOAE) were tested using an ILO-292 Analyzer (Otodynamics, Ltd., Hatfield, England), which was calibrated based on the instructions provided in the operator's manual from the manufacturer. Transient-evoked otoacoustic emissions are an established component of the audiologic test battery. A commercially available immittance system, Grason –Stadler Tympstar version 2, was used to conduct tympanometry. The Tympstar was calibrated according to manufacturer recommendations.

2.2.2 Wideband reflectance (WBR)

The wideband reflectance equipment used for this study was from Mimosa Acoustics (RMS-system, version 4.03). The components of the system include an IBM compatible laptop computer with a Type II PCMCIA slot for delivering and acquiring audio data, as well as for digital signal processing. The system also includes a DSP-card, an ER-10CP acoustical probe, made up of two output transducers and one input transducer (microphone), and a probe interface cable which connects the probe to the PC board of the laptop and serves as a pre-amplifier for the probe. Calibration of the individual probe tips was done using the four-cavity calibration device, which is also provided by the manufacturer. Probe tips were required to pass the calibration process with an overall calibration value of at least 90%.

When a new patient is entered into the WBR system and the appropriate probe tip is selected and calibrated, there are four windows that can be used to display the subject data. The windows can show data from the left, right or both ears, and data from one of fourteen y-axis variables is be displayed graphically as a function of frequency. The variables of middle

ear transmission are: Sound pressure level, Sound pressure level (Group Delay), Power Reflectance, Reflectance (Group Delay), Power Absorption, Impedance (Real Part) - resistance, Impedance (Imaginary Part) - reactance, Impedance (Magnitude), Impedance (Group Delay), Admittance (Real Part) - conductance, Admittance (Imaginary Part) - susceptance, Admittance (Magnitude), Admittance (Group Delay), and Sound intensity level. The four middle ear variables selected for the current study are Power Reflectance, for continuity with the literature, and Impedance (Real Part), Impedance (Imaginary Part) and Impedance (Magnitude), which represent resistance, reactance and impedance, respectively, for generation of an optimally complete measure of middle ear sound transmission.

2.3 Ethics approval

2.3.1 Ethics approval

Approval from the University of British Columbia ethics board was obtained (CREB file number H03-70209), which permitted testing at the University of British Columbia School of Audiology and Speech Sciences, B.C. Children's and Women's Hospital, and Richmond Hospital for the diseased group subjects, and at elementary schools for the control subjects (Appendix I).

2.3.2 Consent retention

All of the signed consent forms and printed subject data are kept locked in the Middle Ear Laboratory. Computer records of subject data are coded, and do not reveal any identifying information.

2.4 Recruitment

2.4.1 Recruitment of control subjects

Subjects were recruited from five elementary schools in the Greater Vancouver Area: Harbourview Elementary, Ranch Park Elementary and Porter Street Elementary in Coquitlam (school district number 43) and Blair Elementary and Blundell Elementary in Richmond (school district number 38). Permission was obtained from each of the school boards. Packages consisting of the Invitation letter, the Consent form and the Case History form were distributed to the parents of the Kindergarten and Grade 1 students. Copies of these forms can be found in Appendices II, III and IV. These forms were accompanied by a letter from the school principal indicating that the students would be eligible to participate in the study if the case history form was completed and returned to the school along with the signed consent form.

2.4.2 Recruitment of diseased group subjects

Eleven of the subjects with OME were recruited through Dr. F. Kozak, head of pediatric otolaryngology at B.C. Children's Hospital in Vancouver. These subjects were scheduled to receive myringotomy and tympanostomy surgeries, and were tested prior to surgery. An introductory letter was mailed home to the patients several weeks prior to the surgery date, which provided an explanation of the study goals and test procedures. This letter also included the contact information of the principal investigator, and parents were encouraged to contact Dr. Shahnaz with any further questions. The introductory letter was followed by a telephone call to schedule test times. Subjects were either tested at the UBC School of Audiology and Speech Sciences on the day prior to surgery or were tested at the hospital (either BC Children's Hospital or Richmond Hospital) approximately an hour prior

to the surgery time. The consent form was provided and explained at the time of testing, and informed consent was obtained before the testing commenced. A copy of this form and the introductory letter, can be found in Appendices V and VI. The remainder of the study subjects were recruited through testing at the elementary schools. Students who did not meet the inclusion criteria for the control group were included in one of the study groups if they met those inclusion criteria.

2.5 Procedure

2.5.1 Testing conducted prior to subject inclusion

An otoscopic examination was performed to rule out any gross abnormalities of the external ear, ear canal or eardrum. Standard 226-and multi-frequency tympanometry was performed to obtain an estimate of middle ear pressure and tympanic membrane mobility. A soft probe tip was inserted into the outer ear canal, which formed a seal with the walls of the canal. Pressure was swept from a positive to negative direction, and tympanograms were generated using probe tones of 226, 678 and 1000 Hz. The equivalent ear canal volume and middle ear pressure values were recorded and the data was printed for later reference. An estimate of resonant frequency was obtained, both manually and automatically by the Tympstar machine. Hearing thresholds were screened at 20 dB_{HL} for 500, 1000, 2000 and 4000 Hz, according to the ASHA (1990) guidelines to determine normal auditory function. Subjects were required to give a clear hand raise response twice at each of the test frequencies in each ear, in order for the data from that ear to be included in the study.

A transient-evoked otoacoustic emission (TEOAE) screening was conducted to verify normal middle ear status and cochlear function at the level of the outer hair cells. Otoacoustic emission testing is a non-invasive and safe measure of outer hair cell function in

young children, as well as in newborns (NIH, 1993). A soft hypoallergenic probe tip, containing a microphone and receiver, was inserted into the ear canal. A series of non-linear clicks was presented through the probe tip, at a level roughly equivalent to that of average conversational speech. The responses from the cochlea were measured and averaged by a laptop computer over a 20 ms time window. A pass was achieved when an emission-to-noise ratio of at least 6 dB was measured at any four out of the five test frequency bands (1000, 1500, 2000, 3000 and 4000 Hz). The absolute amplitudes of the emissions were also required to be greater than 0 dB_{SPL} to confirm that a response was in fact present. If the subject did not pass the TEOAE criteria, the testing was conducted a second time. If the subjects met the inclusion criteria outlined in section 2.1.3, their data was included in the control group subject pool. If the subject did not meet the control group criteria, but met the criteria outlined in section 2.1.4, then the data was included in the appropriate study group.

Letters were sent home to the parents explaining the test results. Any abnormalities found at the time of testing were conveyed in the letter. The parents were encouraged to telephone or email the researchers with any questions or concerns regarding the test results. In the cases where the results were not all normal, the parents were given the opportunity to have their child re-tested, either another day at their elementary school or at the School of Audiology and Speech Sciences.

2.5.2 Testing conducted following study subject inclusion

The Mimosa Acoustics WBR system collected energy reflectance data as a function of frequency, which was displayed graphically as a percentage. During data collection the four windows of the software were set to show power reflectance and power absorption in the right and left ears. These parameters were selected so that the normative data provided

by Mimosa Acoustics could be visualized during data acquisition. From the reflectance data, the WBR program computed the three other middle ear parameters: impedance, reactance and resistance.

Different sized disposable foam and plastic probe tips are available. Only foam tips were used for this study. Each tip was calibrated prior to use, and was selected based on the size of the patient's ear canal. The tips were rolled in a uniform fashion and inserted into the subject's ear canal, where, once expanded, they were required to form a seal with the canal walls.

A new window opens for each WBR measurement. This window shows the response spectrum and the noise levels as a function of frequency. The WBR response can be re-measured until a smooth curve is obtained and the levels of the signal are clearly higher than the levels of the noise at all frequencies. Figure 2.1 below represents an optimally quiet WBR measurement, where Figure 2.2 represents one with a high degree of low frequency noise. When a WBR response is accepted, the measurement window closes and the results are displayed graphically on the four-window screen. Significant visual overlap of at least two measurement curves was required in order to ascertain test-retest reliability.

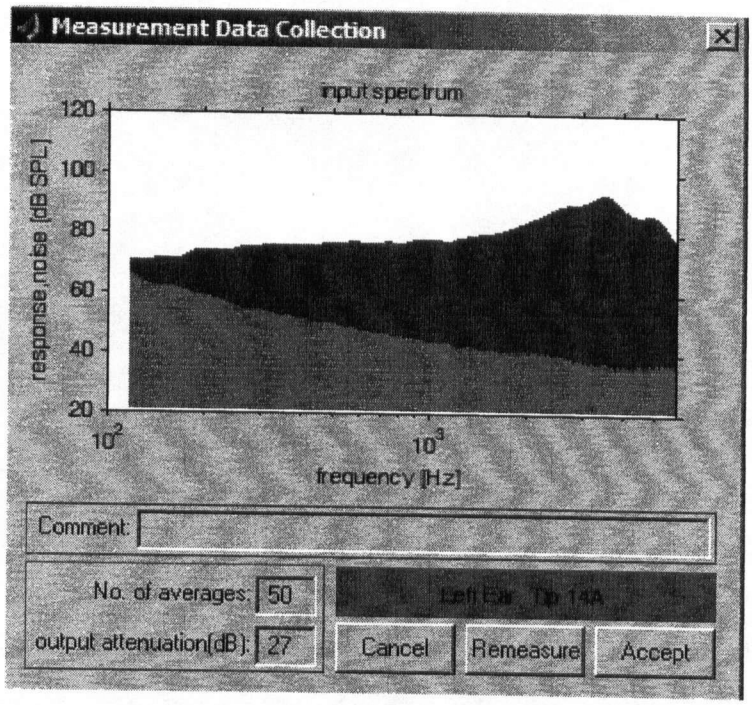


Figure 2.1 Measurement collection window used to view subjects' results in the Mimosa Acoustics (RMS system, version 4.03) wideband reflectance software. The lower shaded region depicts the noise level and the upper shaded region depicts the signal level, both as a function of frequency. This is an example of an optimally quiet measurement.

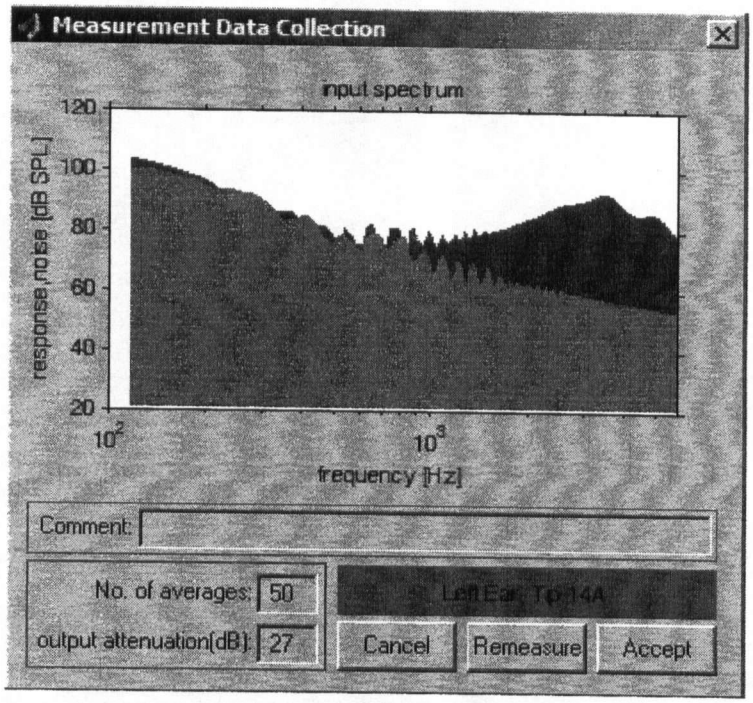


Figure 2.2 Measurement collection window used to view subjects' results in the Mimosa Acoustics (RMS system, version 4.03) wideband reflectance software. The lower shaded region depicts the noise level and the upper shaded region depicts the signal level, both as a function of frequency. This is an example of a noisy measurement.

In order to obtain numeric values for the WBR data, the most representative curve for each of the four variables was exported from the software, saved as a text file and imported into a Microsoft Excel spreadsheet for further analysis. The WBR data from each subject was compiled into the appropriate Excel database, determined by the inclusion criteria met. Each of the four middle ear variables was analyzed across the test frequency range (211 to 6000 Hz) and according to subject group.

2.6 Data analysis

A mixed-model analysis of variance (ANOVA) was used to analyze the pediatric control data. For this model, the four middle ear variables (energy reflectance - ER, normalized impedance, normalized reactance and normalized resistance) were measured on

three different between-group factors: ethnic origin (Caucasian versus Chinese), gender (male versus female) and ear (right versus left). The between-group factors were measured across 248 frequencies (repeated measures factor frequency with 248 levels). This resulted in a mixed-model ANOVA design of 2 x 2 x 2 x 248, where the first three factors were the between-group factors and the fourth was the repeated measure factor.

The pediatric control ER data were then compared to the adult control ER data obtained by Shahnaz and Bork (2006) using a mixed model ANOVA. Energy reflectance was measured on two between group factors: age (child versus adult) and race (Caucasian versus Chinese). The between group factors were measured across 248 frequencies, resulting in a mixed-model ANOVA design of 2 x 2 x 248.

The data from the pediatric control subjects were then compared to the three study subject groups. As this study was exploratory, the data were compiled across gender and race to increase the number of subjects in each group. The four middle ear variables (ER, normalized impedance, normalized reactance and normalized resistance) were measured on one between group factor: middle ear condition (normal, clinically insignificant negative pressure, clinically significant negative pressure, middle ear effusion). The between group factor was measured across 248 frequencies, which resulted in a mixed-model ANOVA design of 4 x 248.

The Greenhouse-Geisser (1959) approach was used in all cases to compensate for inflated Type I error, which can exist among a large number of repeated measures. A p-value of less than 0.05 was set a priori to determine significance.

Chapter III Results

3.1 Control subject data

The energy reflectance (ER), normalized impedance (Z), normalized reactance (X), and normalized resistance (R) variables were tested separately in a mixed-model ANOVA, with ethnic origin, gender and ear (each with two levels) as a between subject factor, and frequency (with 248 levels) as a within subject factor.

3.1.1 Energy reflectance (ER) data

The ER data were explored for differences between Caucasian and Chinese, male and female, and right and left ears. The main effects of race [$F(1,76) = 0.10$, $p = 0.752$], gender [$F(1,76) = 0.58$, $p = 0.500$] and ear [$F(1,76) = 0.02$, $p = 0.885$] were not significant. There were no significant interactions between race, gender and ear. The interactions between frequency and race [$F(247, 18772) = 5.43$, $p = 0.000$], frequency and ear [$F(247, 18772) = 2.21$, $p = 0.000$], and frequency, gender and race [$F(247, 18772) = 2.52$, $p = 0.000$] were significant. The ER ANOVA table is summarized in Appendix VII, where the bolded data represents significant interactions. Following the Greenhouse-Geisser (G-G) adjustment method, the interaction between frequency and race [$F(247, 18772) = 5.43$, $p = 0.004$] was the only interaction that remained significant, indicating that ER varies differently as a function of frequency between the Caucasian and Chinese groups.

The mean ER data is shown in Figure 3.1, which varies as a function of frequency (211 to 6000 Hz) between the Caucasian and Chinese children. The vertical bars denote the 0.95 confidence intervals (CI) for both racial groups. Energy reflectance is represented as a percentage value, where 100% indicates that all of the energy has been reflected and 0% indicates that all of the energy has been absorbed by the middle ear system. The ear canal

walls are also responsible for a small amount of sound energy absorption. The mean ER value is high for both the Caucasian and Chinese groups at low and high frequency values. Over the mid-frequency range (between approximately 1000 and 5000 Hz), where middle ear sound transmission is most efficient, the mean ER values fall closer to 0%. The mean ER reaches a different minimum value for each racial group. The Caucasian mean ER is lowest at approximately 3492 Hz, where the lowest mean ER value for the Chinese group occurs at approximately 2367 Hz. The shape of the ER curve is different between the two subject groups. To determine the frequency range over which group differences exist, a post hoc Tukey Honestly Significantly Different (HSD) test was performed, but the results were not significant at any frequencies; however, there was overlap between Caucasian and Chinese groups' 0.95 CI for the frequency range between approximately 1617 and 2450 Hz (Figure 3.1).

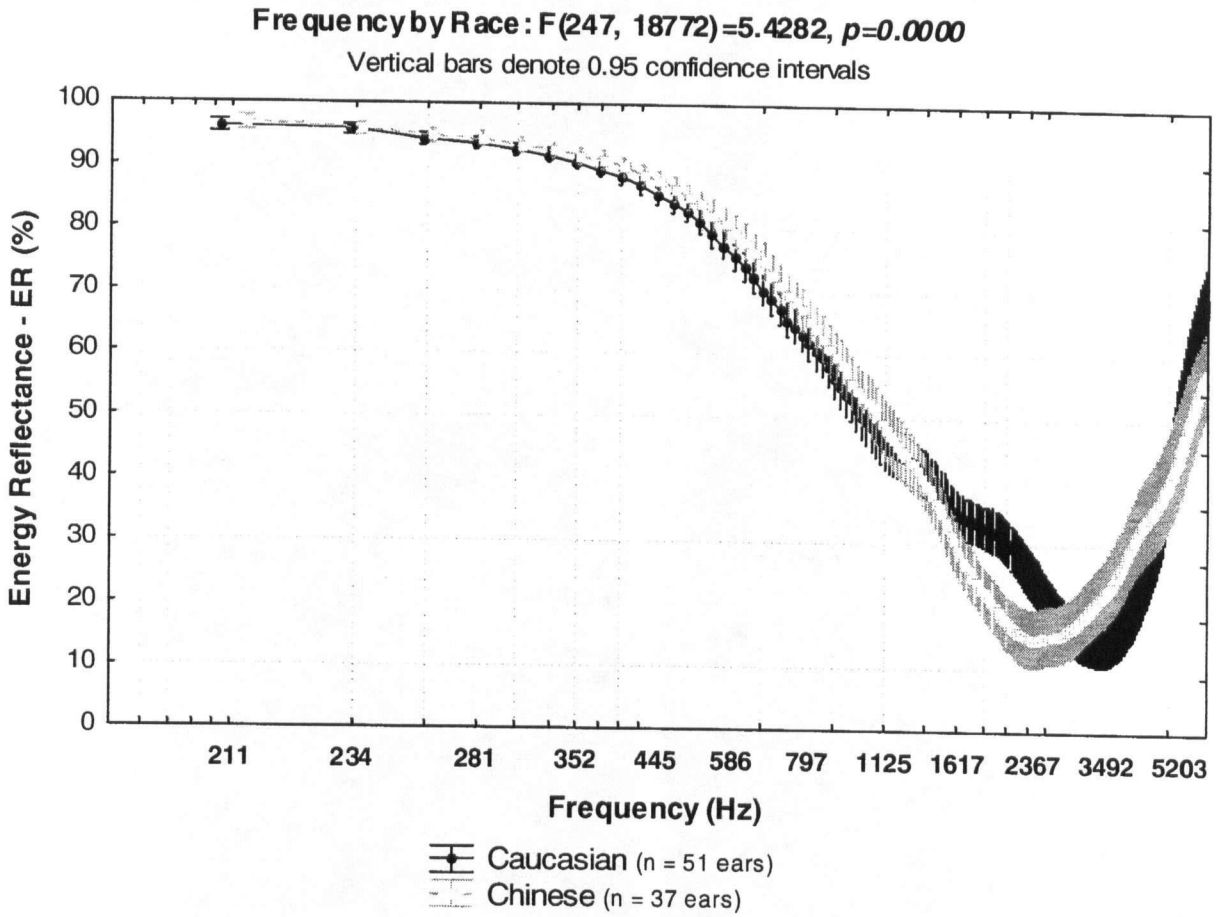


Figure 3.1. Mean energy reflectance as a function of frequency for Caucasian and Chinese pediatric control groups. Vertical bars denote 0.95 CI.

3.1.2 Impedance, reactance and resistance data

The data for the remaining three variables (Z, X and R) were also explored for differences between Caucasian and Chinese, male and female, and right and left ears. A main effect of race was significant for impedance [F (1,76) = 15.48, p = 0.000], reactance [F (1,76) = 11.41, p = 0.001] and resistance [F (1,76) = 15.59, p = 0.000]. The main effects of gender and ear were not significant and there were no significant interactions between race, gender and ear, for Z, X or R. Frequency and race was the only significant interaction following the G-G adjustment for normalized impedance [F (247, 18772) = 5.60, p = 0.006],

normalized reactance [F (247, 18772) = 4.73, p = 0.010], and normalized resistance [F (247, 18772) = 6.25, p = 0.003]. The ANOVA tables are summarized in Appendix VI, where the bolded data represents significant interactions.

The mean impedance data, in addition to the 0.95 CI are shown in Figure 3.2 which vary as a function of frequency (211 to 6000 Hz) between the Caucasian and Chinese children. The mean normalized impedance value is highest for low frequencies, for both the Caucasian and Chinese groups. Impedance reaches a minimum value for the Caucasian group at approximately 3400 Hz and for the Chinese group at approximately 2200 Hz. The variation of Z as a function of frequency is different between the two subject groups. The mean impedance curve for the Chinese group was higher than that of the Caucasian group between approximately 3400 and 5300 Hz, where the 0.95 CI of the two groups do not overlap. To determine the frequency range over which group differences exist, a post hoc Tukey HSD test was performed, but the results were not significant at any frequencies tested.

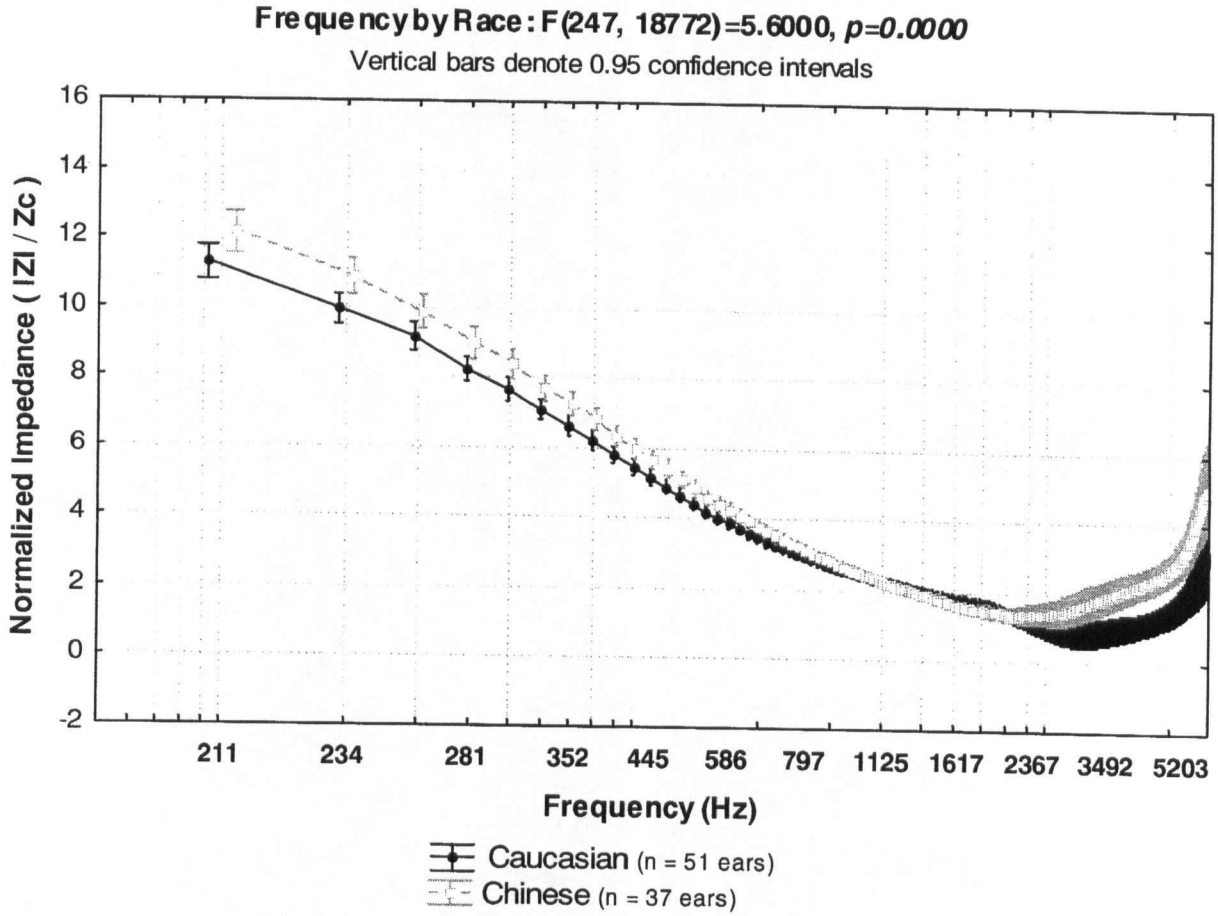


Figure 3.2. Mean normalized impedance as a function of frequency for Caucasian and Chinese pediatric control groups. Vertical bars denote 0.95 CI.

The mean reactance data, in addition to the 0.95 CI are shown in Figure 3.3, which vary as a function of frequency (211 to 6000 Hz) between the Caucasian and Chinese children. The mean normalized reactance value is highest for low frequencies, for both the Caucasian and Chinese groups. Reactance reaches a minimum value for the Caucasian group at approximately 3400 Hz and for the Chinese group at approximately 3100 Hz, which represents the frequency at which the middle ear transitions from a stiffness-dominated to a mass-dominated system. This may indicate that the resonant frequency of the middle ear differs between the two racial groups. The variation of X as a function of frequency is

different between the two subject groups. The mean normalized reactance curve for the Chinese group was higher than that of the Caucasian group between approximately 3400 and 5200 Hz. This was considered to be significant because the 0.95 CI of the two groups do not overlap. A post hoc Tukey HSD test was performed, but the results were not significant.

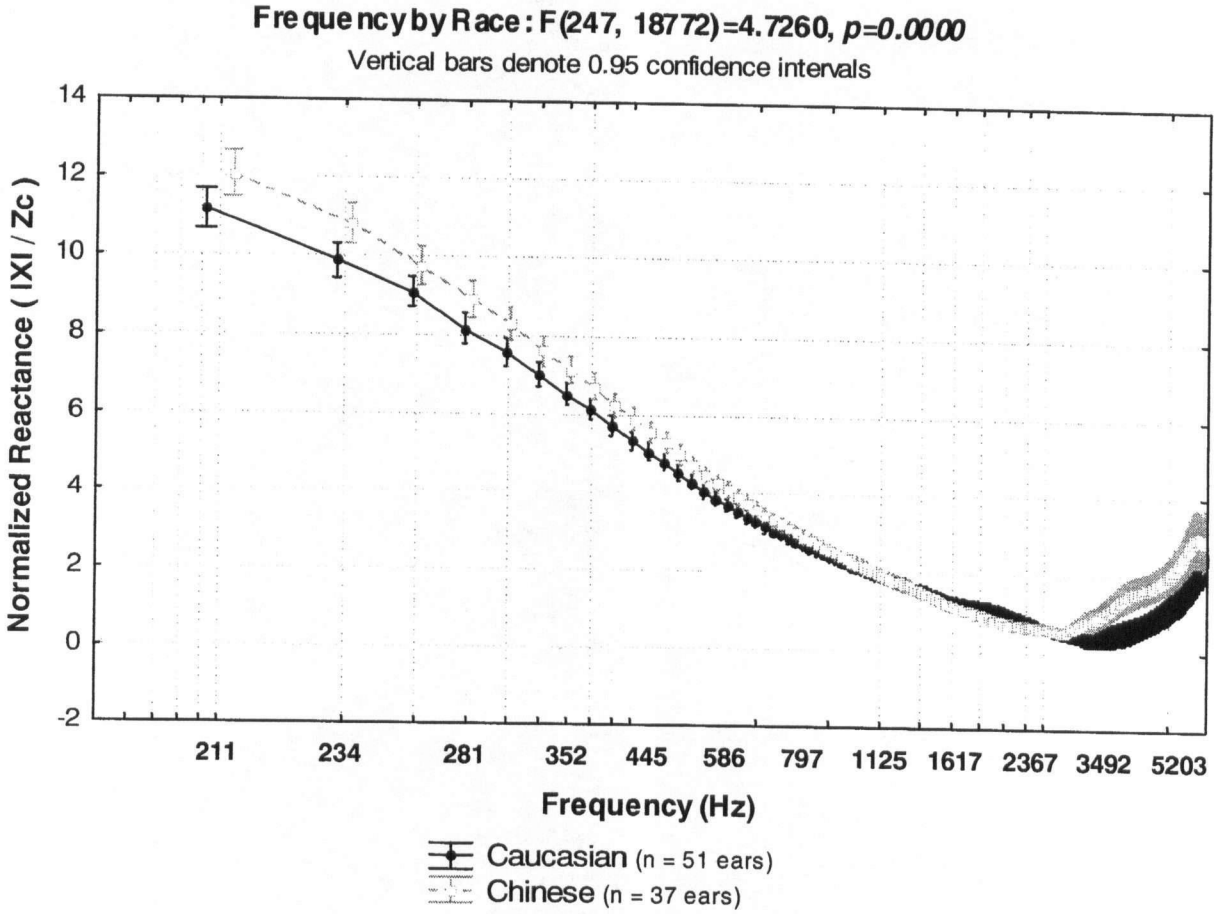


Figure 3.3. Mean normalized reactance as a function of frequency for Caucasian and Chinese groups. Vertical bars denote 0.95 CI.

The mean R data, in addition to the 0.95 CI are shown in Figure 3.4, which vary as a function of frequency (211 to 6000 Hz) between the Caucasian and Chinese children. The mean normalized resistance value is highest for high frequencies, for both the Caucasian and

Chinese groups. Resistance is different between the two subject groups. The mean resistance curve for the Chinese group was higher than that of the Caucasian group between approximately 3400 and 5500 Hz, where the 0.95 CI of the two groups do not overlap. To determine the frequency range over which group differences exist, a post hoc Tukey HSD test was performed, which indicated that significant group differences exist between 5320 and 6000 Hz.

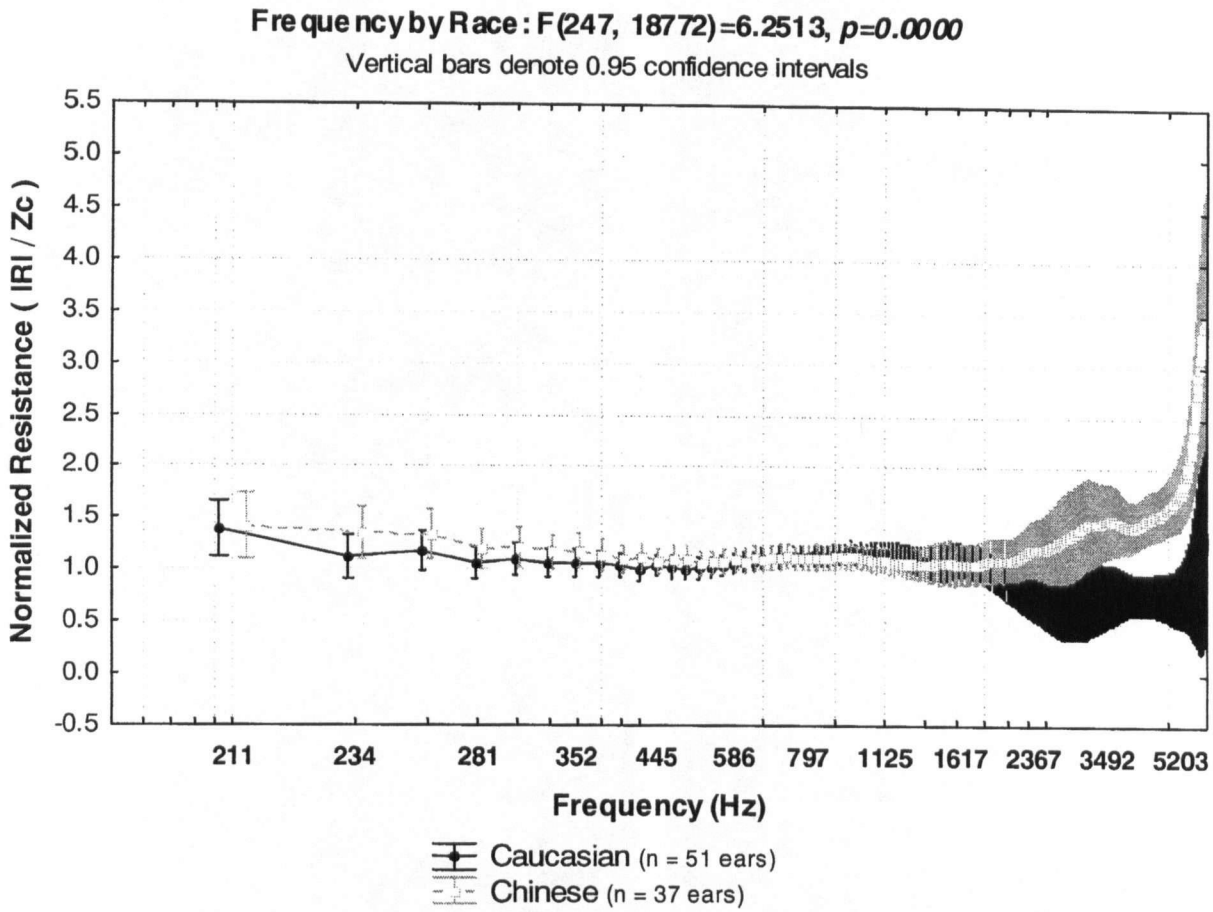


Figure 3.4. Mean normalized resistance as a function of frequency for Caucasian and Chinese pediatric control groups. Vertical bars denote 0.95 CI.

Energy reflectance differences exist between the two racial groups through the mid-frequency range (1617 and 2450 Hz), while impedance differences (Z, X and R) occur at higher frequencies (3350 to 5500 Hz). Table 3.1 summarizes the frequency ranges over which differences exist between the Caucasian and Chinese children, which were determined by the frequency ranges over which the 0.95 CI do not overlap.

Summary of the frequency ranges over which group differences exist.

Variable	Range	
Energy reflectance - ER	1617 to 2450 Hz	Chinese curve above Caucasian curve
Normalized impedance - Z	3400 to 5400 Hz	Caucasian curve above Chinese curve
Normalized reactance - X	3400 to 5200 Hz	Caucasian curve above Chinese curve
Normalized resistance - R	3350 to 5500 Hz	Caucasian curve above Chinese curve

Table 3.1. Summary of the frequency ranges over which racial group differences existed for energy reflectance, normalized impedance, normalized reactance and normalized resistance control data.

3.2 Pediatric versus adult energy reflectance data

The pediatric control subject ER data was compared to the adult normative ER data collected by Shahnaz and Bork (2006) to determine whether differences exist between middle ear transmission properties at different ages. The data were explored using a mixed-model ANOVA. In this model age, Adults versus Children, served as the between subject factor and frequency served as a within subject factor. This model was conducted separately for each ethnicity, Caucasian and Chinese.

3.2.1 Caucasian data

The Caucasian ER data was explored for differences between children and adults using a similar mixed model ANOVA design to the one explained in section 3.1. There was

a main effect of age [F (1,161) = 9.96, p = 0.002]. The interaction between frequency and age [F (247, 39767) = 17.43, p = 0.000] was also significant. Following the G-G adjustment to guard against inflated Type I error, the interaction between frequency and race [F (247, 39767) = 17.43, p = 0.010] remained significant.

The mean Caucasian ER data is shown in Figure 3.5, which varies as a function of frequency (211 to 6000 Hz) between the adults and children. The vertical bars denote the 0.95 CI for both groups. The mean ER value is high for both children and adults at low and high frequency values. Through the mid-frequency range, where middle ear sound transmission is most efficient, the mean ER values fall closer to 0%. The mean ER reaches different minima values for each age group. The mean ER for the pediatric group is lowest at approximately 3492 Hz, and only one minimum point is notable from the figure. The mean reflectance pattern of the adult group had two minima points, where the lower frequency minimum was shallower than the one occurring at a higher frequency. The frequencies of the two minima points were approximately 1617 and 3164 Hz (Shahnaz & Bork, 2006). A post hoc Tukey HSD test was performed to determine the frequencies over which group differences existed. The Tukey test revealed that between 516 and 984 Hz, the children have significantly higher ER values. This means that at low frequencies sound transmission through the middle ear is less effective in children than it is in adults. At higher frequencies (between 2719 and 4992 Hz) the Tukey test revealed that the pediatric middle ear system absorbed significantly more energy than did the adult middle ear system.

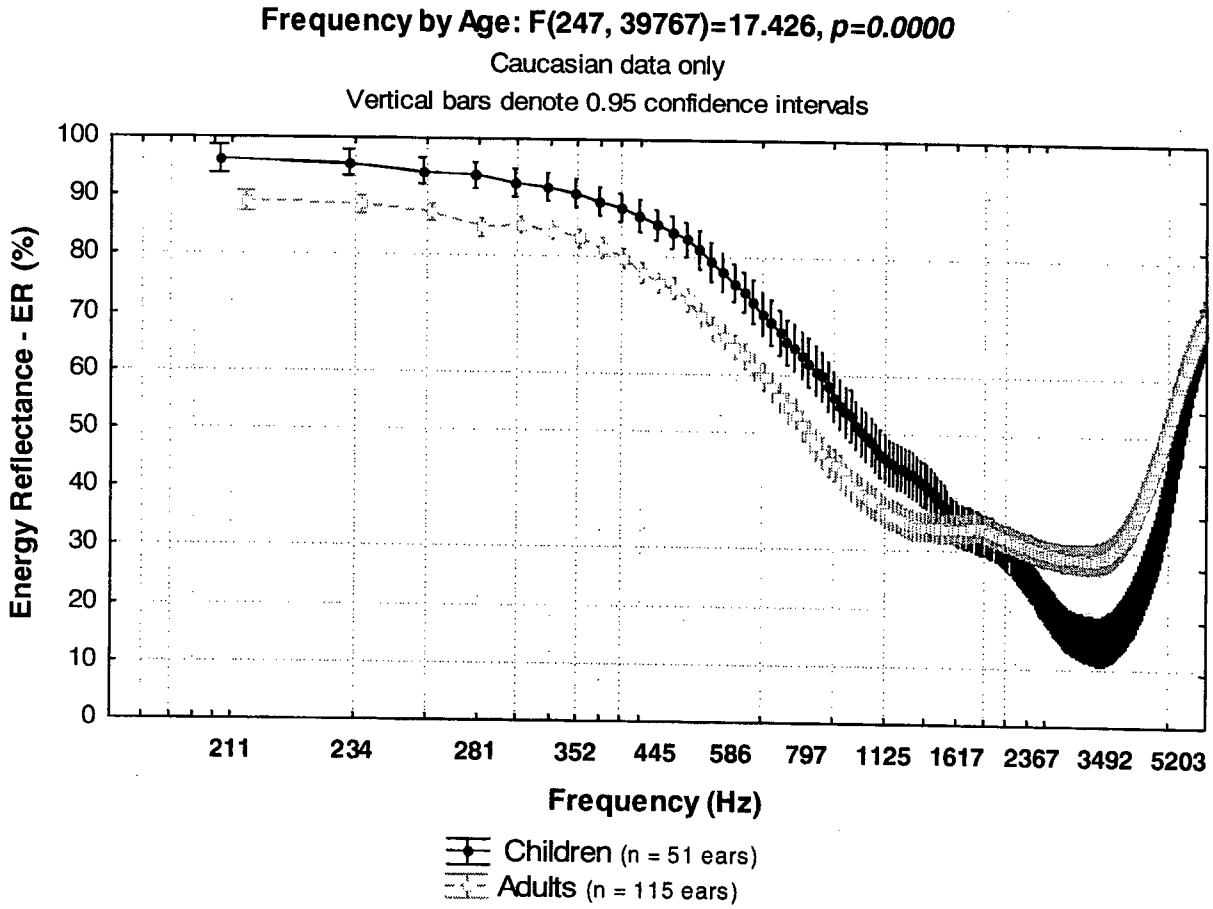


Figure 3.5. Mean energy reflectance as a function of frequency for pediatric and adult groups, Caucasian subjects only. Vertical bars denote 0.95 CI

3.2.2 Chinese data

The Chinese ER data were explored for differences between children and adults. The main effect of age [F (1,151) = 0.55, p = 0.459] was not significant. The interaction between frequency and age [F (247, 37297) = 10.28, p = 0.000] was significant. Following the G-G adjustment, the interaction between frequency and age [F (247, 37297) = 10.28, p = 0.000] remained significant, indicating that energy reflectance varies differently as a function of frequency between children and adults.

The mean Chinese ER data is shown in Figure 3.6, which varies as a function of frequency (211 to 6000 Hz) between the adults and children. The vertical bars denote the 0.95 CI for both groups. The mean ER value is high for both children and adults at low and high frequency values, but over the mid-frequency range the mean ER values fall closer to 0%. The mean ER reaches different minima values for each age-group, but only one minimum point exists for each group. The mean ER for the pediatric group is lowest at approximately 2367 Hz, and for the adult group at approximately 3141 Hz (Shahnaz & Bork, 2006). A post hoc Tukey HSD test was performed to determine the frequencies over which age-group differences exist. The Tukey test revealed that between 1711 and 2719 Hz, the adults have significantly higher ER values than the children. This means that for this range of mid-frequencies, sound transmission through the middle ear is less effective for an adult population compared to a pediatric population.

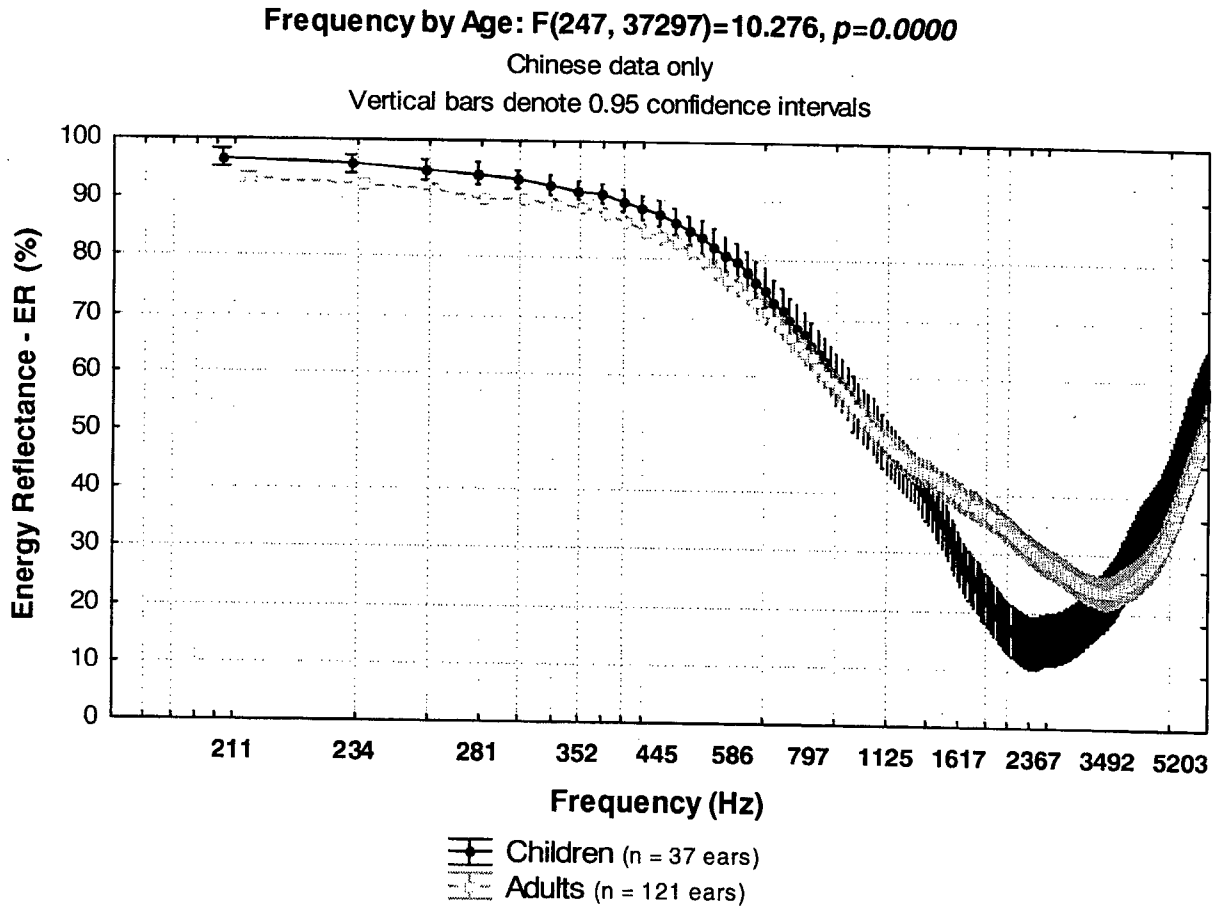


Figure 3.6. Mean energy reflectance as a function of frequency for pediatric and adult groups, Chinese subjects only. Vertical bars denote 0.95 CI.

3.3 Data analyzed by middle ear condition

The data from the control subjects was analyzed against the data from the three groups of subjects with suspected middle-ear pathology. This aspect of the study was exploratory, as there were not equal numbers of ears in each of the diseased groups and the control group. There were three groups of diseased subjects: those with middle ear effusion, those with severe negative middle ear pressure, and those with mild negative middle ear pressure. Subject data from children of all races and both genders was combined. A mixed-

model ANOVA was used to examine the potential differences between the diseased groups and the control group for each of the following variables, ER, Z, X, and R. In this model condition (4 levels) served as a between subject factor and frequency served as a between subject factor. The ANOVA tables are summarized in Appendix VIII, where the bolded data represents significant interactions

3.3.1 Energy reflectance data

The data for the middle ear variable ER was explored for differences between middle ear conditions. The main effect of condition [$F(3,150) = 60.51, p = 0.000$] was significant. The interaction between frequency and condition [$F(247, 37050) = 4.99, p = 0.000$] was also significant. Following the G-G adjustment, the interaction between frequency and condition [$F(247, 37050) = 4.99, p = 0.000$] remained significant.

The mean ER data is shown in Figure 3.7, which varies as a function of frequency (211 to 6000 Hz), and is broken down by middle ear condition. The vertical bars denote the 0.95 confidence intervals (CI) for each of the four middle ear condition groups. The mean ER minima values exist at approximately the same frequency value (3400 Hz) for each condition group; the minimum ER value attained, however, differs with middle ear status. The minimum ER value ranges from the value of approximately 15% reached by the control group to approximately 62% for the group with middle ear effusion. The variance pattern of ER as a function of frequency is grossly consistent among the four groups.

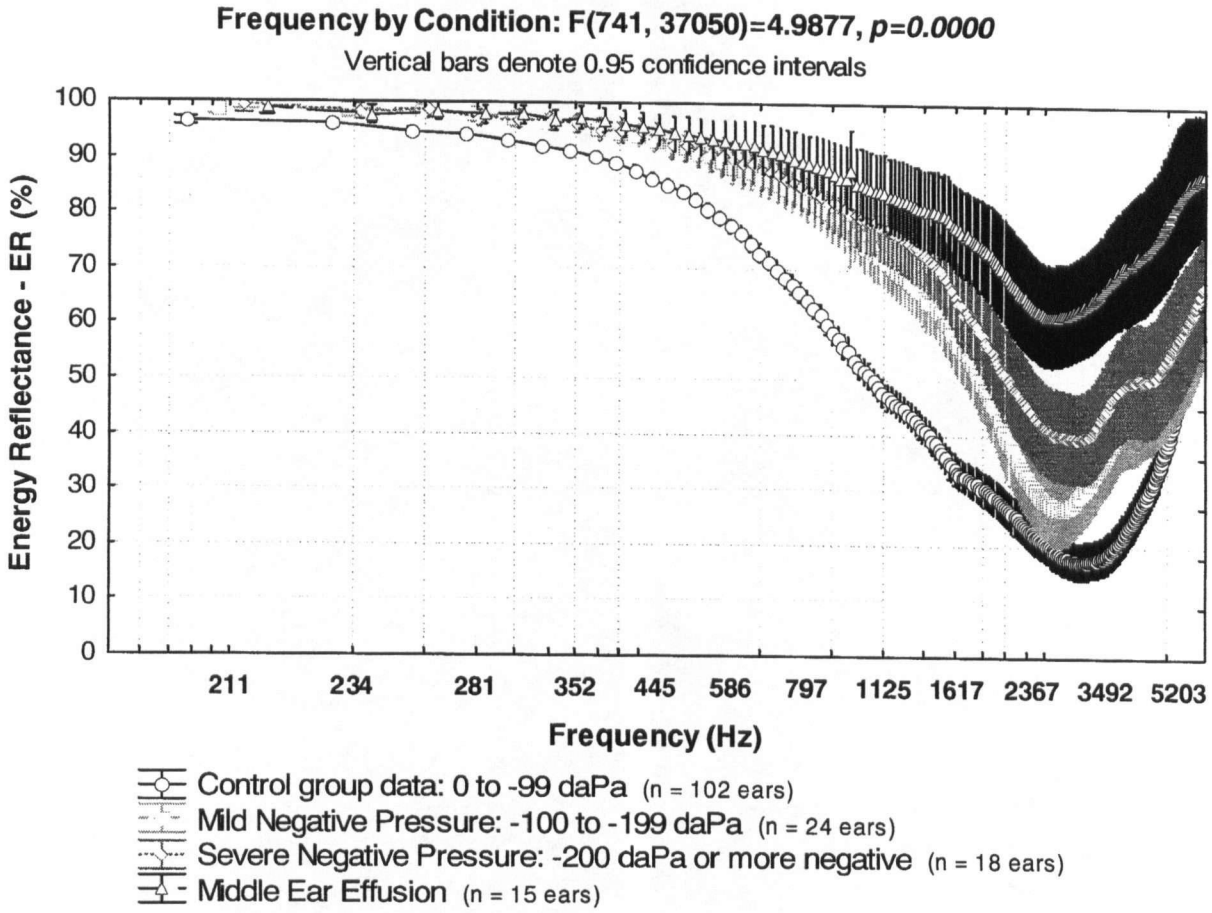


Figure 3.7. Mean energy reflectance as a function of frequency for different middle ear condition groups. Vertical bars denote 0.95 CI.

Several post hoc Tukey HSD tests were performed to determine the frequency ranges over which significant group differences exist. The Tukey tests revealed that the ER of the control subjects was significantly different from that of all three study subject groups. The frequencies over which ER differed from that of the control group were 727 to 6000 Hz for the middle ear effusion group, 797 to 4453 Hz for the clinically significant negative middle ear pressure group, and 797 to 1852 Hz for the clinically insignificant negative middle ear pressure group. The ER values for the middle ear effusion group were significantly higher

than the clinically insignificant negative pressure group between 1875 and 6000 Hz. The Tukey test revealed no significant group differences between the insignificant and significant negative middle ear pressure groups, and between the significant negative middle ear pressure and middle ear effusion groups. See Table 3.2 for a summary of the ER results.

Summary of the post hoc Tukey HSD tests for ER data sorted by subject condition

Comparison groups	Frequency range of significant ER differences
Normal subjects vs. Mild middle ear pressure	**797 - 1852 Hz**
Normal subjects vs. Severe middle ear pressure	**797 - 4453 Hz**
Normal subjects vs. Middle ear effusion	**727 - 6000 Hz**
Mild vs. Severe negative middle ear pressure	No significant differences
Mild middle ear pressure vs. Middle ear effusion	**1875 - 6000 Hz**
Severe middle ear pressure vs. Middle ear effusion	No significant differences

Table 3.2. Summary of the post hoc Tukey HSD tests for energy reflectance data as a function of middle ear condition.

3.3.2 Impedance, reactance and resistance data

The data for the remaining three middle ear variables were also explored for differences between middle ear status groups. A main effect of condition was significant for reactance [F (3,155) = 5.65, p = 0.001] and resistance [F (3,150) = 4.66, p = 0.004], but not for impedance [F (3,155) = 1.24, p = 0.298]. There were significant interactions between frequency and condition for impedance [F (247,38285) = 3.70, p = 0.000], reactance [F (247, 38285) = 3.90, p = 0.000] and resistance [F (247,37050) = 1.84, p = 0.000]. Following the G-G adjustment, impedance [F (247,38285) = 3.70, p = 0.001] and reactance [F (247,38285) = 3.90, p = 0.000] remained significant, but resistance [F (247, 37050) = 1.84, p = 0.075] was no longer significant.

The mean impedance data is shown in Figure 3.8, which varies as a function of frequency (211 to 6000 Hz), and is broken down by middle ear condition. The vertical bars denote the 0.95 CI. The mean impedance value is highest at low frequencies for all four groups. Impedance reaches a minimum value for the middle ear effusion group at approximately 3400 Hz and for the other three groups at a slightly lower frequency (approximately 3000 Hz). Both the impedance curve variance as a function of frequency and the minimum level value of impedance attained are grossly equivalent between the four condition groups.

Several post hoc Tukey HSD tests were performed to determine the frequency ranges over which significant group differences exist. The Tukey tests revealed that the impedance of the control subjects was significantly lower than that of all three study subject groups. The frequencies over which impedance differed from that of the control group were 211 to 258 Hz and 305 to 328 Hz for the middle ear effusion group, 211 to 375 Hz for the clinically significant negative middle ear pressure group, and 211 to 469 Hz for the clinically insignificant negative middle ear pressure group. The impedance values for the three study subject groups did not differ significantly from each other.

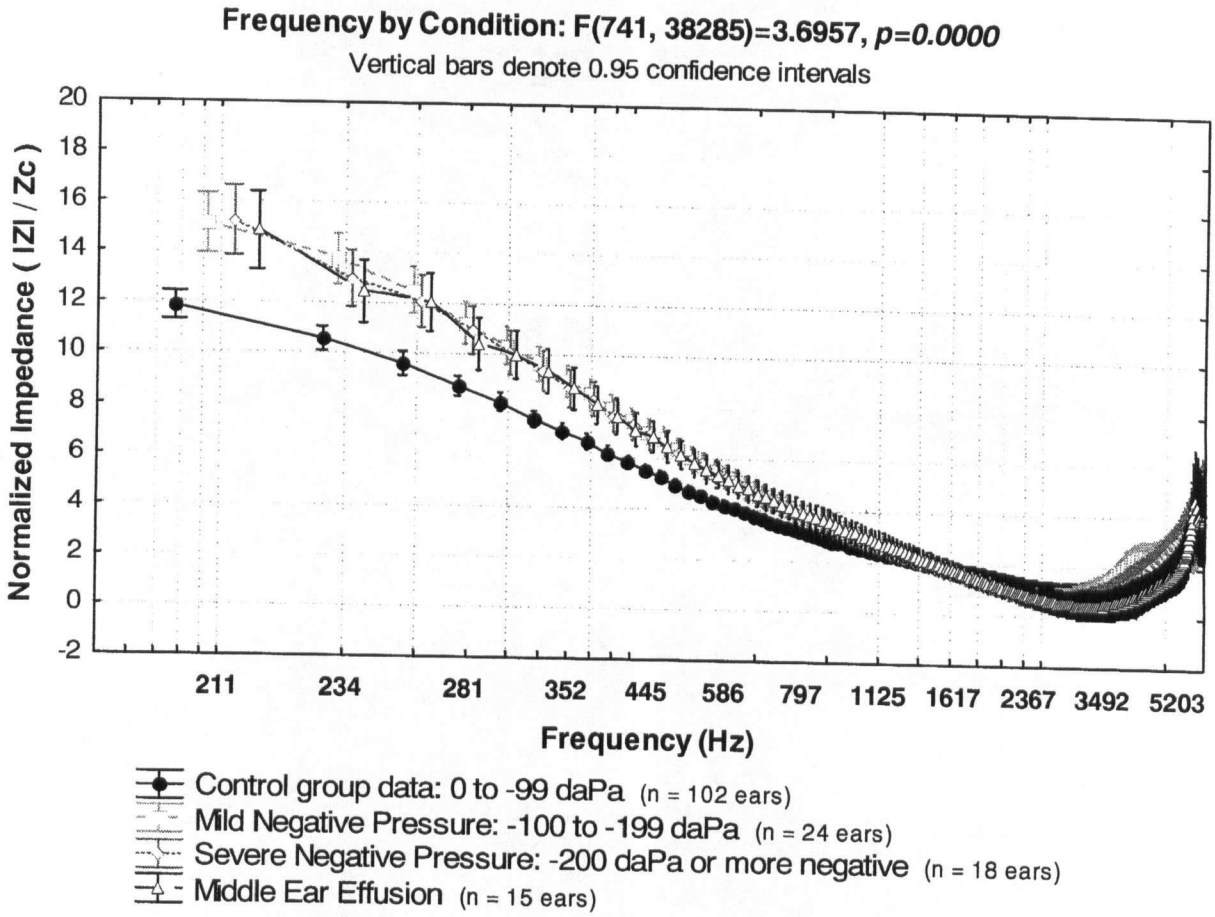


Figure 3.8. Mean normalized impedance as a function of frequency for different middle ear condition groups. Vertical bars denote 0.95 CI.

The mean reactance data is shown in Figure 3.9, which varies as a function of frequency (211 to 6000 Hz), and is broken down by middle ear condition. The vertical bars denote the 0.95 CI. The mean reactance value is highest at low frequencies for all four groups. Reactance reaches a minimum value for the middle ear effusion group at approximately 3400 Hz and for the other three groups at a slightly lower frequency (approximately 3000 Hz). Both the reactance curve variance as a function of frequency and

the minimum level value of reactance attained are grossly equivalent between the four condition groups.

Several post hoc Tukey HSD tests were performed to determine the frequency ranges over which significant group differences exist. The Tukey tests revealed that the reactance of the control subjects was significantly lower than that of all three study subject groups. The frequencies over which reactance differed from that of the control group were 211 to 398 Hz for the middle ear effusion group, 211 to 492 Hz for the clinically significant negative middle ear pressure group, and 211 to 609 Hz for the clinically insignificant negative middle ear pressure group. The reactance values for the three diseased subject groups did not differ significantly from each other.

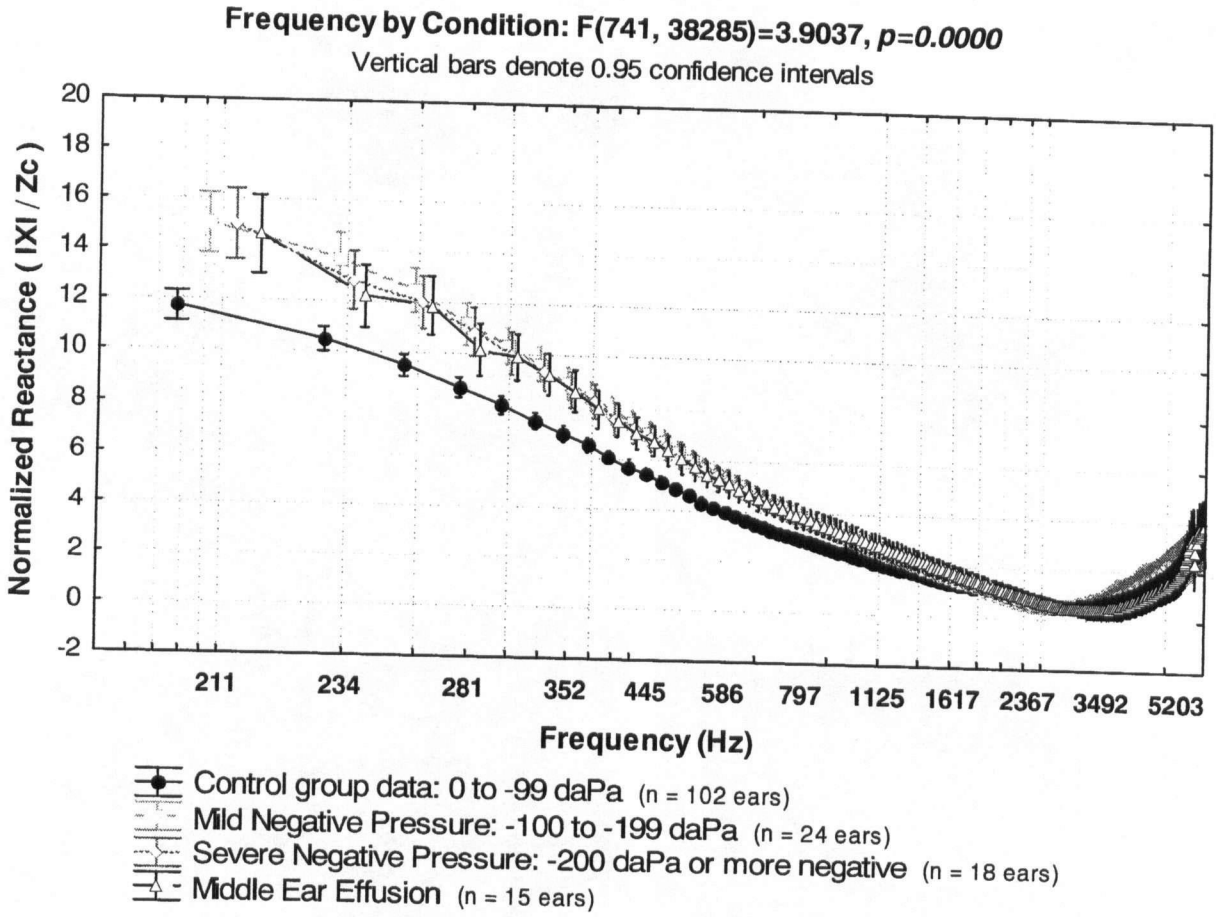


Figure 3.9. Mean normalized reactance as a function of frequency for different middle ear condition groups. Vertical bars denote 0.95 CI.

3.4 Comparing data from ears with middle ear effusion to the control data

The mean and 90% range (from the 5th to the 95th percentiles) of the pediatric control group ER data is shown in Figure 3.10, along with the data from the 15 children's ears with either highly suspected or surgically confirmed middle ear effusion (MEE). The normative data includes all of the ER measures from all ethnic groups. Test sensitivity and specificity were estimated. All fifteen of the MEE subjects' ER measures fell outside of the 90% range between approximately 1266 and 2578 Hz.

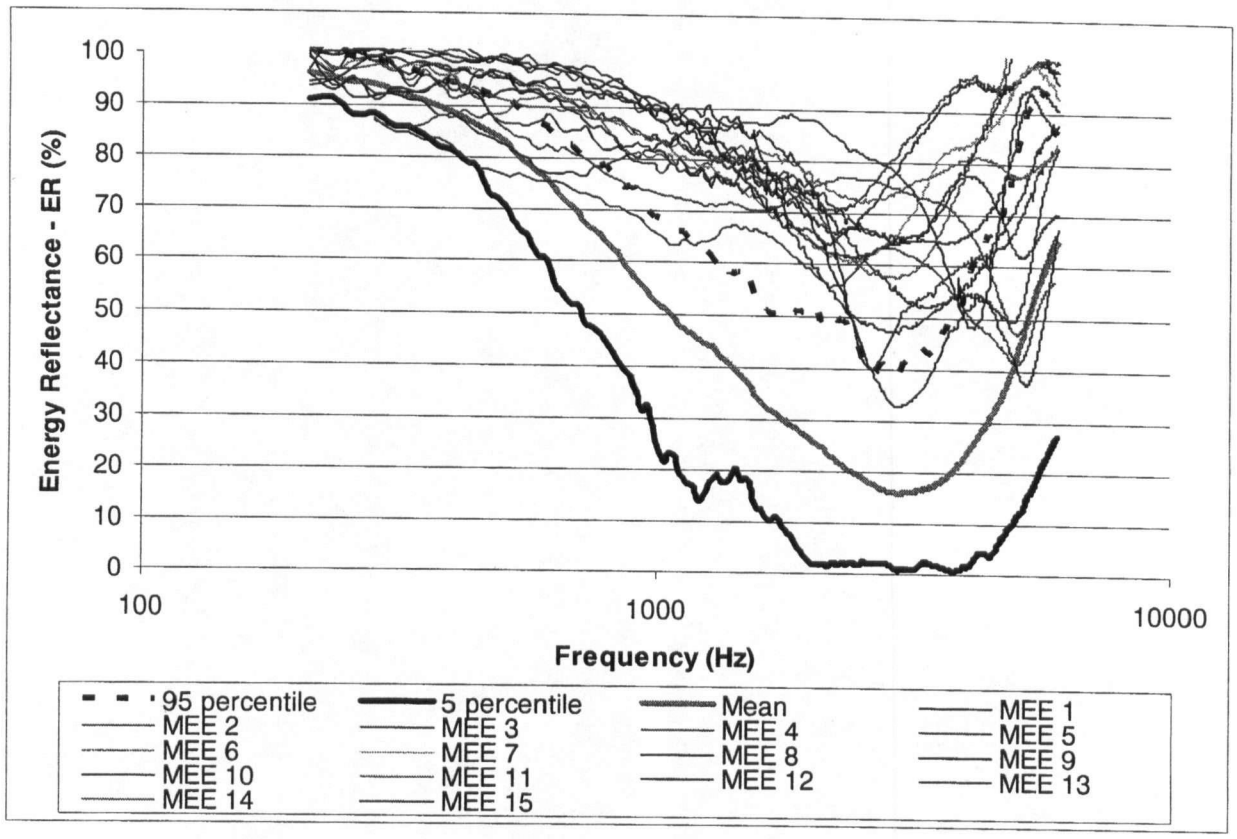


Figure 3.10. Mean and 90% range (5th and 95th percentiles) of the pediatric control energy reflectance (ER) data, along with the ER data from the 15 ears with suspected or surgically confirmed middle ear effusion (MEE). The normative data includes both the Caucasian and Chinese data.

The mean and 90% range (from the 5th to the 95th percentiles) of the pediatric control group ER data is shown in Figure 3.11, along with the data from the 11 children's ears with surgically confirmed middle ear effusion (MEE). The normative data includes all of the ER measures from all ethnic groups. All eleven of the MEE subjects' ER measures fell outside of the 90% range between approximately 1266 and 3961 Hz. The low frequency ER values for MEE subjects 5 and 11 are low, which is consistent with a poor probe tip seal with the ear canal walls. Despite the imperfect measurement technique used, the ER pattern of these two subjects falls above the 90% range of the control subjects through the mid-frequency range.

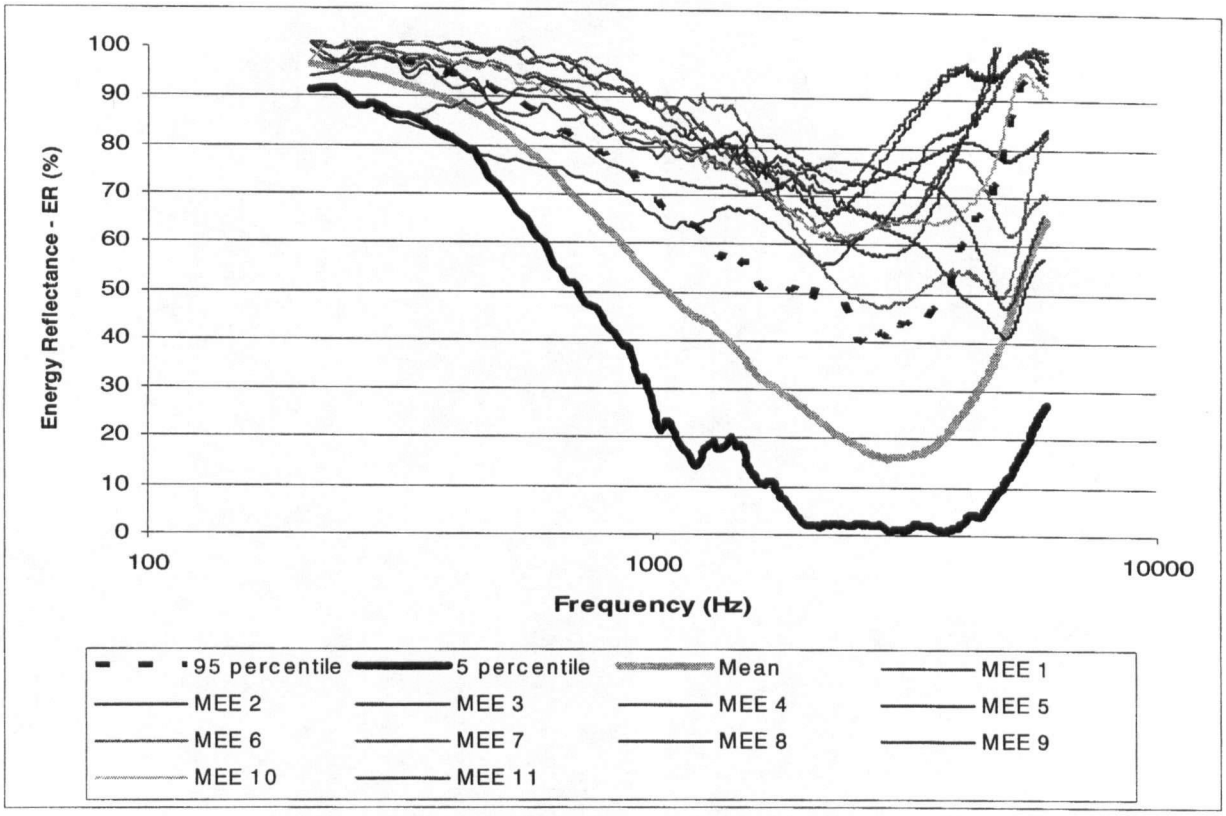


Figure 3.11. Mean and 90% range (5th and 95th percentiles) of the pediatric control energy reflectance (ER) data, along with the ER data from the 11 ears with surgically confirmed middle ear effusion (MEE). The normative data includes both the Caucasian and Chinese data.

Subjects MEE 5 and MEE 11 were omitted from the subsequent analysis due to a potentially inaccurate WBR measure, resulting from a poor probe seal. Figure 3.12 below shows the mean and 90% range of the pediatric control ER data, along with the data from the 9 ears with surgically confirmed middle ear effusion (MEE) and accurate WBR measures. All nine of the MEE subjects' ER measures fell outside of the 90% range between approximately 609 and 3961 Hz.

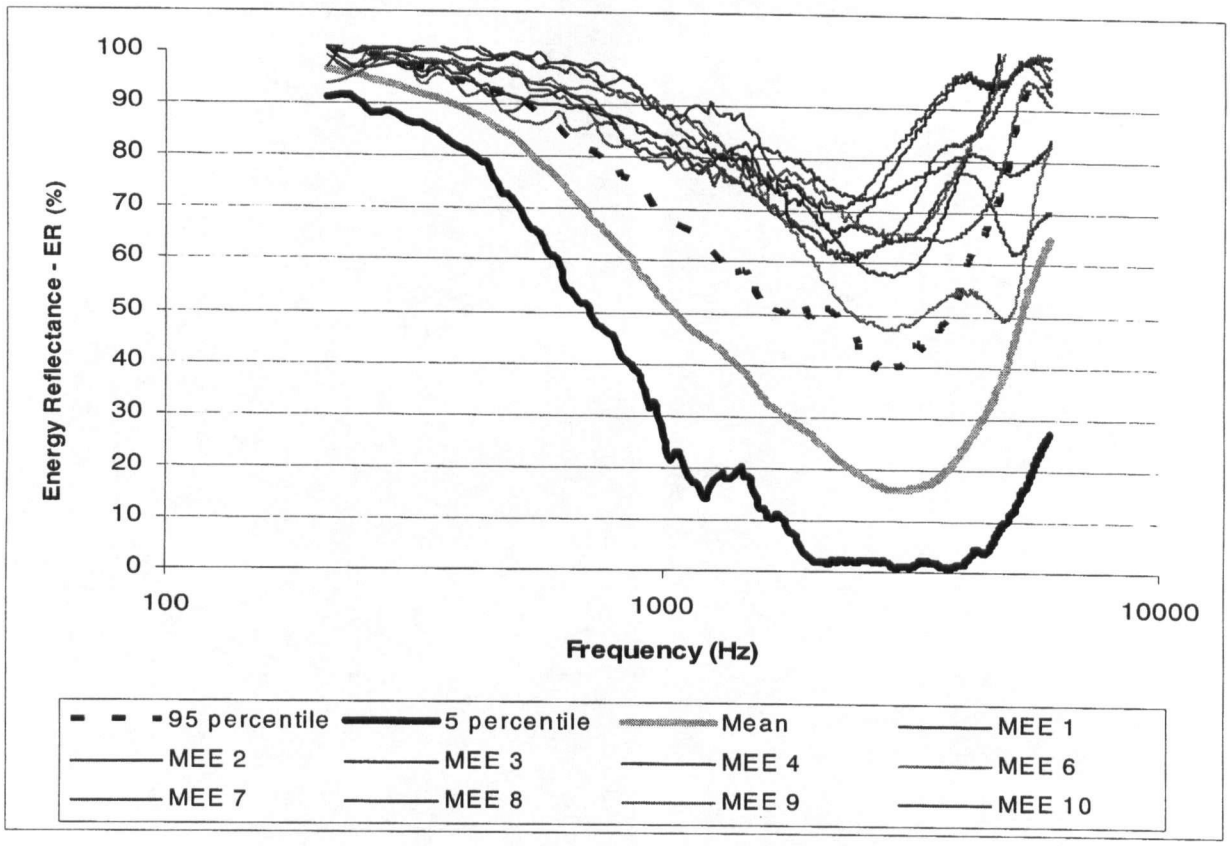


Figure 3.12. Mean and 90% range (5th and 95th percentiles) of the pediatric control ER data, along with the ER data from the 9 ears with surgically confirmed middle ear effusion (MEE) and accurate WBR measures. The normative data includes both the Caucasian and Chinese data.

There were three subjects (four ears) where middle ear effusion was suspected, based on elevated hearing thresholds, absent OAEs and abnormal acoustic immittance measures at both 226 and 1000 Hz. In these children the presence of fluid in the middle-ear cavity was not surgically confirmed. The data from these subjects were not included in Figures 3.11 and 3.12 above. Two of the three subjects (three ears) were retested approximately six weeks following their initial test. In all three cases, the effusion was no longer suspected to be present at the time of the retest. The initial and follow-up test ER data for each of the three ears is represented in Figures 3.13, 3.14, and 3.15 below, along with the 90% range of the

normative pediatric data. In all three cases, a much larger proportion of the ER pattern falls within the 90% range at the time of the follow-up test compared to the ER measure obtained on the initial test date.

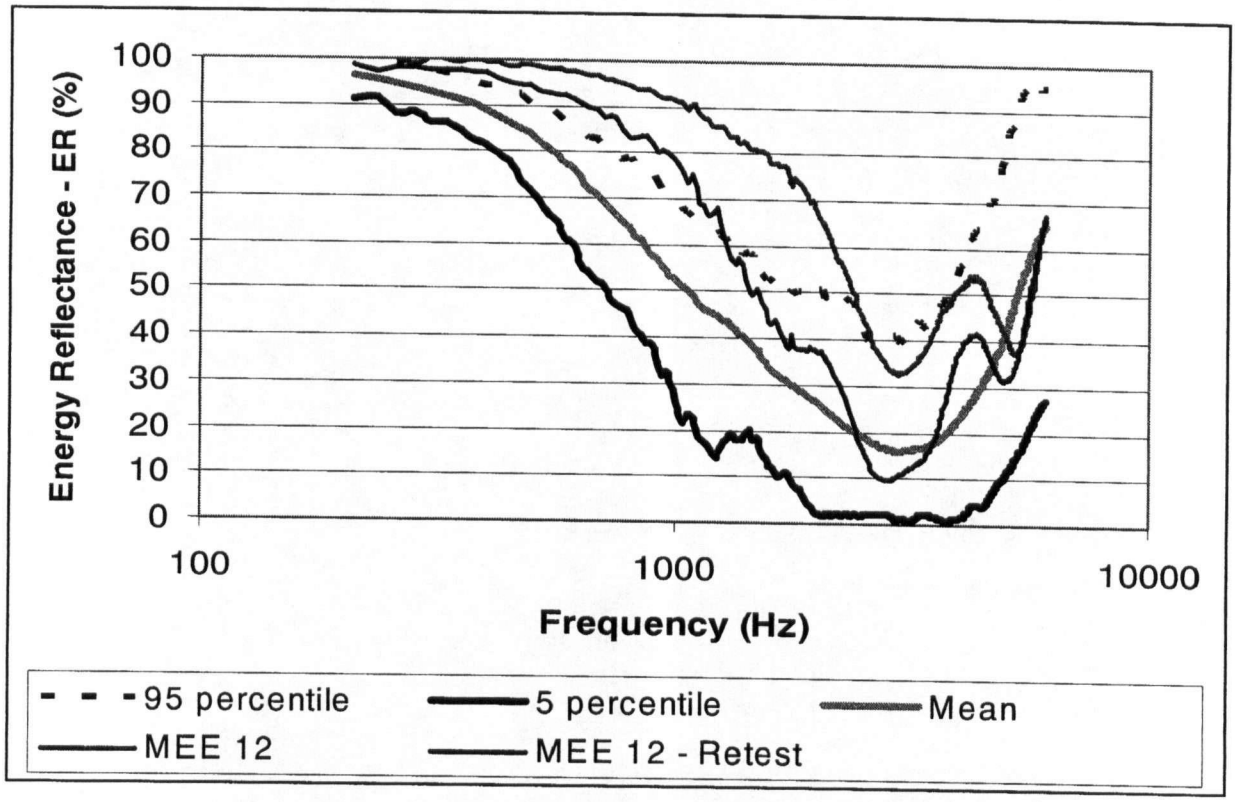


Figure 3.13. Mean and 90% range (5th and 95th percentiles) of the pediatric control ER data, along with the initial and follow-up ER data from subject MEE 12, where middle ear effusion was suspected to be present at the time of the initial test and to have resolved by the time of the follow-up test. The normative data includes both the Caucasian and Chinese data.

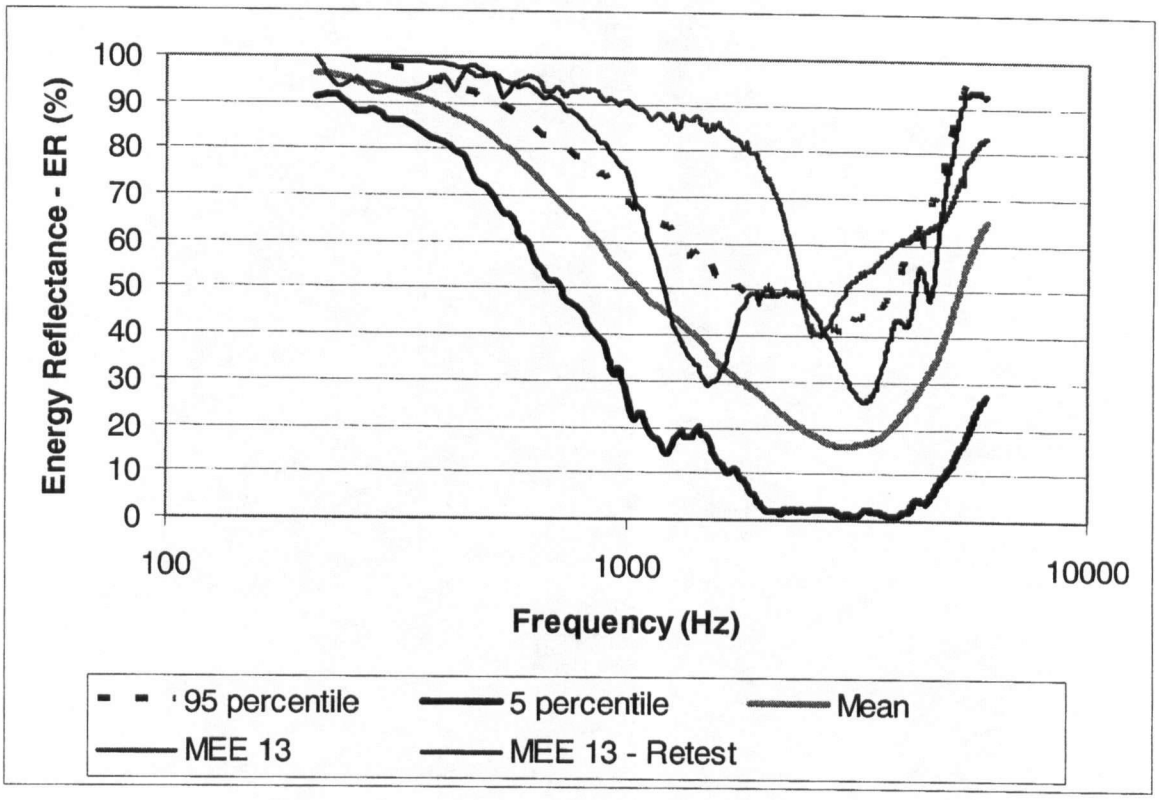


Figure 3.14. Mean and 90% range (5th and 95th percentiles) of the pediatric control ER data, along with the initial and follow-up ER data from subject MEE 13, where middle ear effusion was suspected to be present at the time of the initial test and to have resolved by the time of the follow-up test. The normative data includes both the Caucasian and Chinese data.

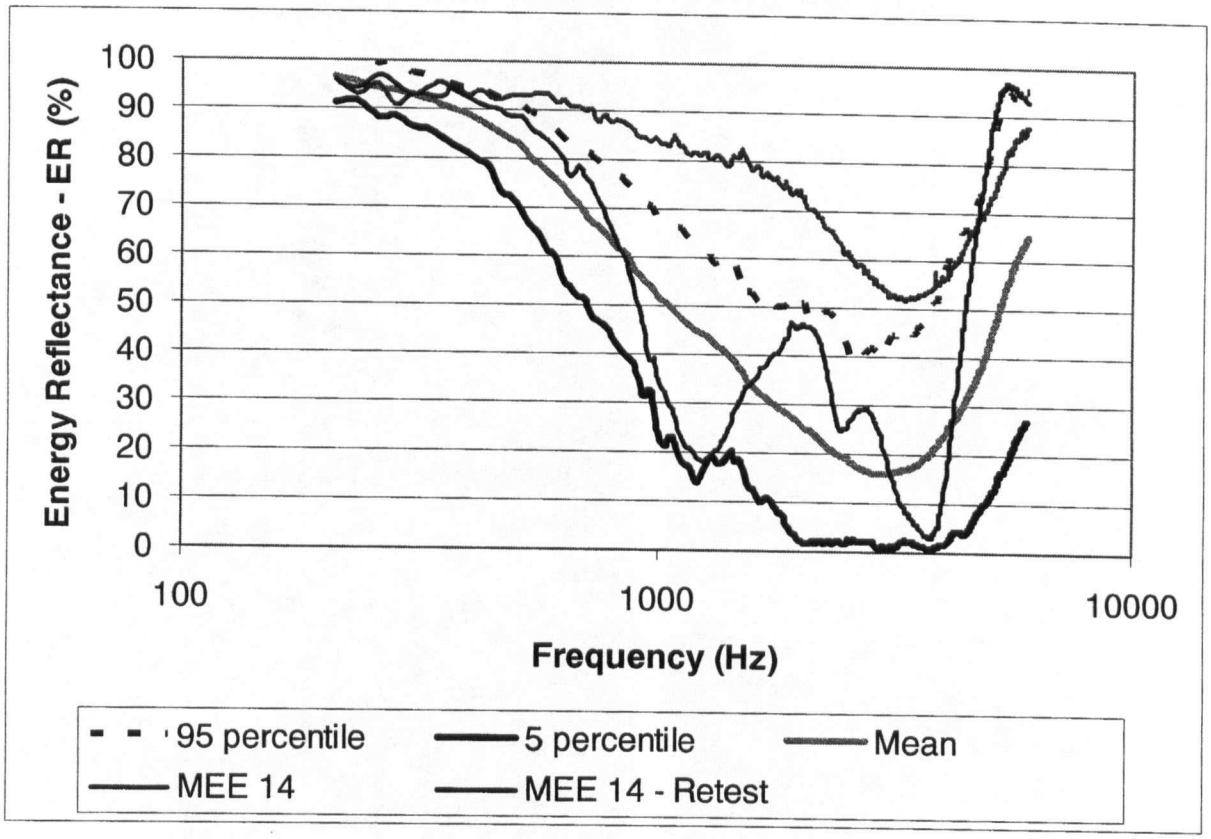


Figure 3.15. Mean and 90% range (5th and 95th percentiles) of the pediatric control ER data, along with the initial and follow-up ER data from subject MEE 14, where middle ear effusion was suspected to be present at the time of the initial test and to have resolved by the time of the follow-up test. The normative data includes both the Caucasian and Chinese data.

Standard 226-Hz tympanometry is currently being used in the clinic to differentiate normal middle ears from those with effusion. Figure 3.16 below illustrates the low frequency tympanometry results from the fifteen ears where middle ear effusion was either surgically confirmed or suspected based on the synthesis of the test battery results. Of the middle ears where effusion is likely present, only nine generated flat tympanograms. Four ears generated Jerger Type C tympanograms (Figure 3.17). This indicates that middle ear pressure is significantly negative, but that an admittance peak can still be determined. Two of the ears

were measured to have clinically insignificant negative middle ear pressure, and produced Jerger Type A/C tympanograms. See Figure 3.18 for an example of this. It should be noted that the Type C and Type A/C tympanograms all had low static admittance and wide tympanometric width, and that three of the ears generated flat tympanograms when a 1000 Hz probe tone was used.

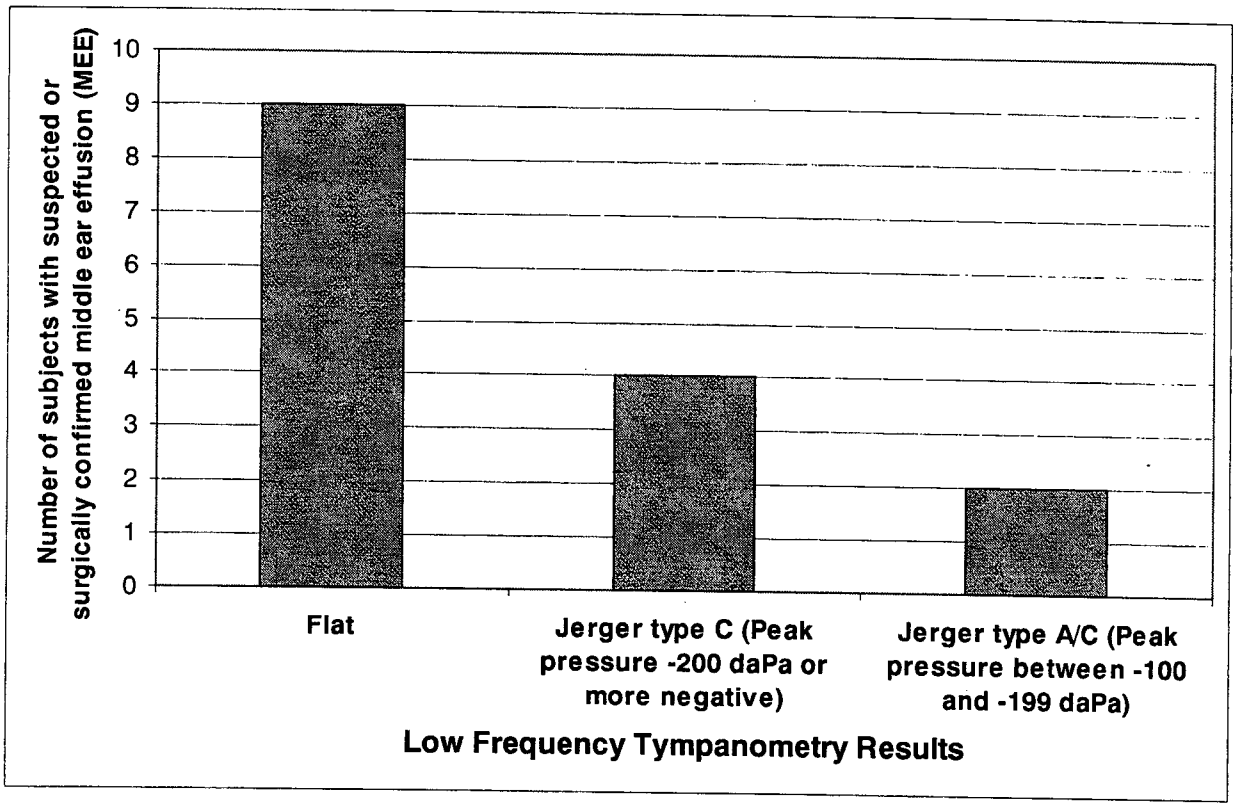
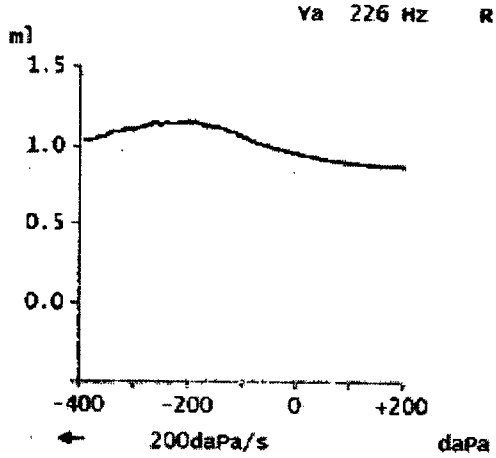


Figure 3.16. Low frequency tympanometry results for the fifteen subjects with either surgically confirmed or highly suspected middle ear effusion.

DATE/TIME: 01/17/2007 03:55 pm
GSI TYMPSTAR MIDDLE EAR ANALYZER
PROBE S/N: 20062388

TYMP DIAGNOSTIC TEST 1

Ya 226 Hz R

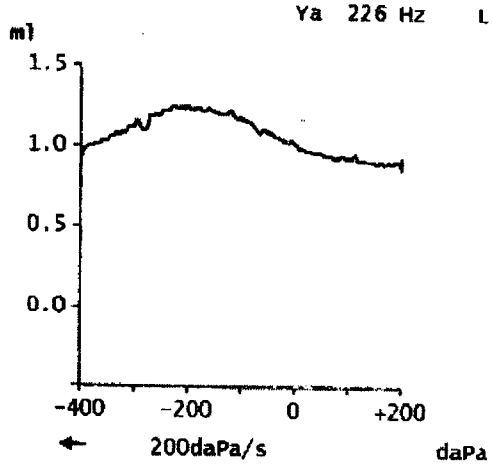


Cl: 0.9

	daPa	ml
TYMP 1:	-200	1.2
TYMP 2:		
TYMP 3:		
GRADIENT:		

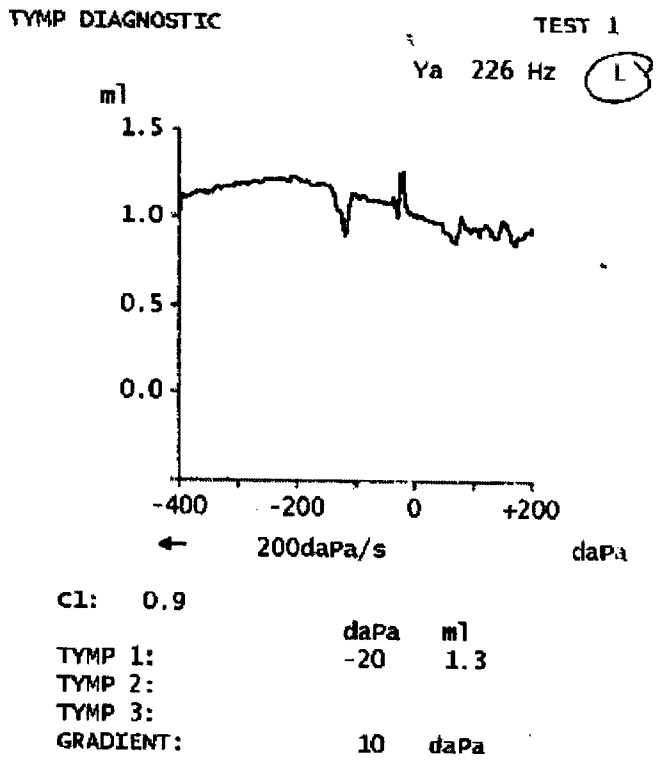
TYMP DIAGNOSTIC TEST 12

Ya 226 Hz L



Cl: 0.9

	daPa	ml
TYMP 1:	-205	1.3
TYMP 2:		
TYMP 3:		



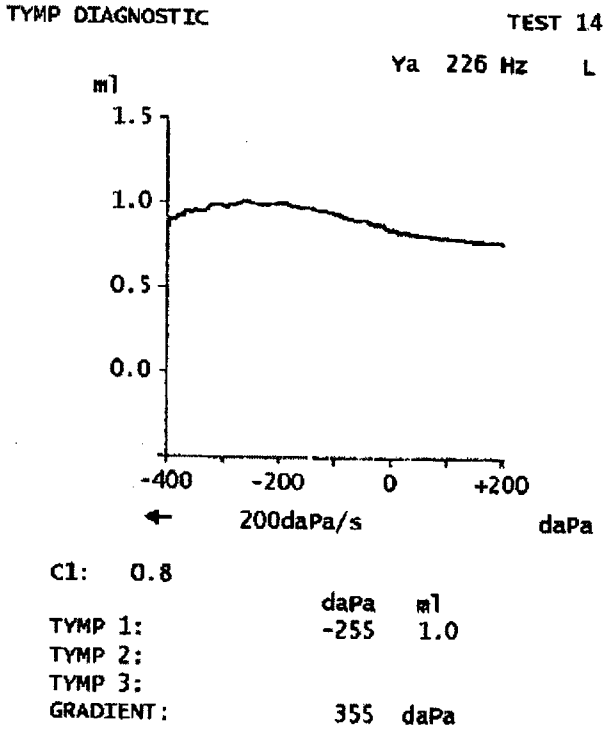


Figure 3.17. The four standard (226 Hz) tympanometry Jerger Type C results for subjects with highly suspected or surgically confirmed middle ear effusion.

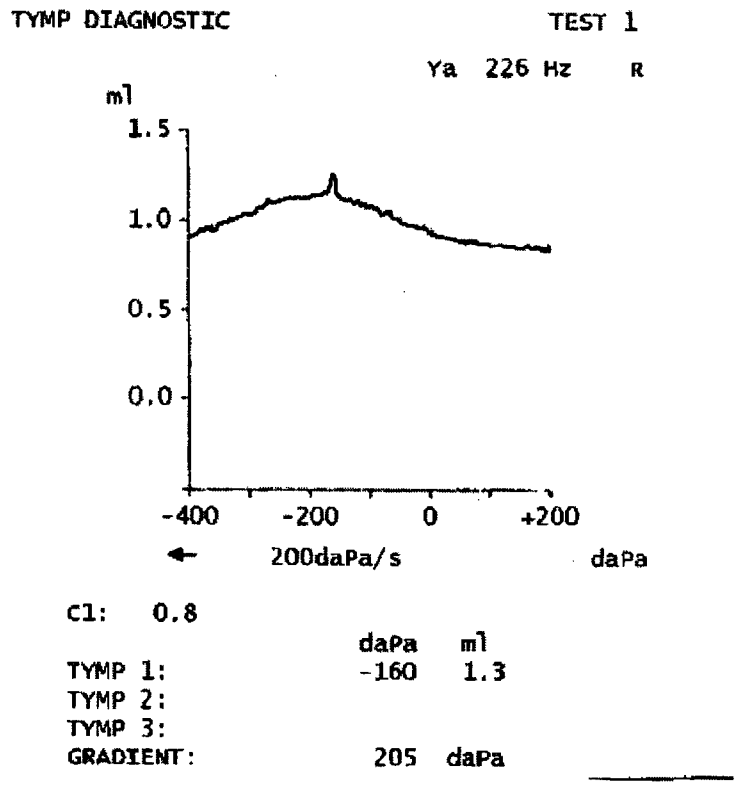


Figure 3.18. Example of a standard (226 Hz) tympanometry Jerger Type A/C result for a subject with suspected or surgically confirmed middle ear effusion.

3.5 Test-retest reliability

Analyses were performed to assure that the ER differences observed between the control subjects and those with middle ear effusion were in fact due to presence of the middle-ear effusion rather than variability in test measurement techniques, such as the reinsertion of the ear tips or the test variability between two normal ears. Ten ears were randomly selected during testing to serve as an estimate of probe tip reinsertion test-retest reliability. Following the collection of the WBR data, the probe was removed for 1-2 minutes, reinserted into the same ear canal, and the ER was re-measured. The difference between the initial and secondary insertion ER values was calculated at each of the 248

frequencies, and the mean insertion difference was calculated. Mean ER differences were also calculated between ten pairs of control subject ER tests to provide an estimate of the variability that can be expected between tests of normal middle ears. Differences between normal middle ears were calculated by selecting twenty control subject ER measures at random, irrespective of ear, race and gender, and by calculating the mean of the ten difference measures.

The differences of principle interest in this section of the study are those between ears with healthy middle ear status and those with effusion present. The ER measures from ten healthy ears and ten with middle ear effusion were selected at random. For each of the ten cases, the ER values of the healthy ears were subtracted from the ER values of those with effusion at each of the 248 frequencies. A mean value was calculated. Figure 3.19 illustrates this mean value, the mean insertion difference, and the mean difference between normal subjects. As can be seen in this figure, both the mean insertion difference and difference between normal subjects are negligible compared to the difference that was measured between children with normal middle ear status and those with middle ear effusion.

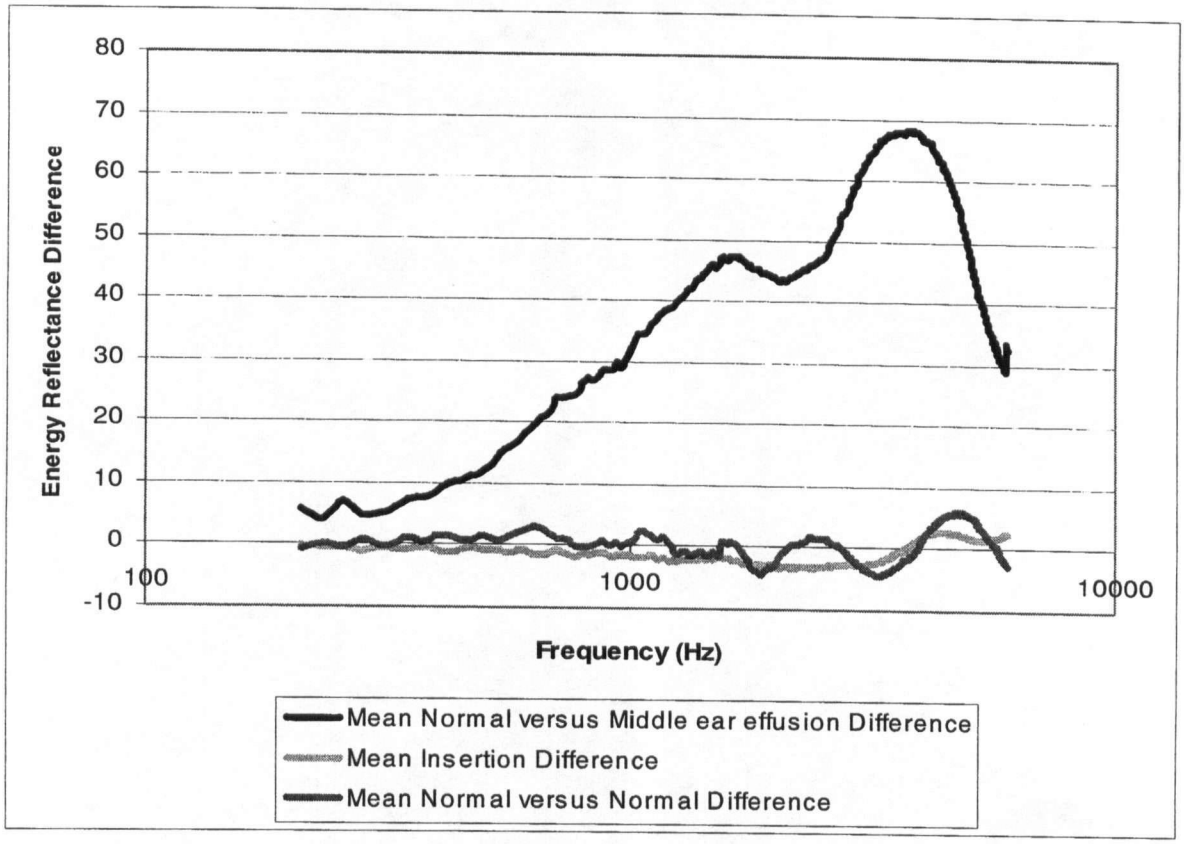


Figure 3.19. Mean difference between normal and middle ear effusion ears versus the mean difference between two normal ears and probe tip re-insertion as a function of frequency. Each mean value is an average of 10 ER differences.

Chapter IV Discussion

Several studies have provided normative WBR adult data, but there has been relatively little published pediatric data. The purpose of this study was to gather WBR data from early school-aged children in order to begin forming a normative database for this population, to determine whether acoustic power reflectance differs significantly between Caucasian and Chinese male and female children, and to compare the WBR patterns obtained from those with healthy middle ear status to those with varying degrees of middle ear pathology.

Wideband reflectance measurements have been found to differ between normal middle ears and those with various pathologies, such as otosclerosis, tympanic membrane perforation, ossicular discontinuity, and otitis media with effusion (Allen, Jeng & Levitt, 2005; Feeney, Grant & Marryott, 2003; Jeng, Levitt, Lee & Gravel, 1999). The number of children tested with OME was limited to 3 subjects (5 ears) in the Jeng, Levitt, Lee and Gravel study and 1 subject (1 ear) in the Allen, Jeng and Levitt study, but both concluded that power reflectance is significantly elevated when fluid is present in the middle ear cavity. The acoustic energy reflected was close to 100% for frequencies up to 1000 Hz and the largest discrepancy between the normal and otitis media with effusion WBR curves occurred for the 1000 to 2500 Hz range (Jeng, Levitt, Lee & Gravel, 1999). In the present study the WBR curves between normal subjects and those with OME were investigated among a larger sample of children and the diseased group criteria was expanded to include subjects with varying degrees of OME pathology in order to determine whether WBR can be a clinically useful measure of middle ear status for children with OME and whether WBR can provide more information than or complementary information to traditional tympanometric measures.

Middle ear transmission properties have been proposed to vary with gender and/or race. Margolis and Heller (1987), Roup, Wiley, Safady and Stoppenbach (1998), Shahnaz and Davies (2006), and Wan and Wong (2002) have found that middle ear tympanometric measures differed either in terms of race, gender or both. It is for this reason Shahnaz and Davies (2006) suggested that gender-specific and race-specific (Caucasian and Chinese) normative data be used for low frequency and multifrequency tympanometry. A recent study by Shahnaz and Bork (2006) evaluated WBR patterns in Caucasian and Chinese young adults with normal middle ear function and found evidence of both gender and racial differences in middle ear function. The authors proposed that body size may have contributed to some of this variation between the subject groups. The pediatric data gathered in this study was analyzed for effects of gender and race in order to determine whether the acoustical transmission differences evident between male and female, Caucasian and Chinese adult middle ears exist among a younger population as well.

4.1 Discussion of results section

4.1.1 Control subject data

The control subject data consisted of energy reflectance ER, normalized impedance Z, normalized reactance X and normalized resistance R measures, and was analyzed on three between subject factors (ear, gender and race) and within subject factor (frequency). The Analysis of Variance (ANOVA) summary tables in Appendix VII reveal that the only significant main effect was that of race, which was significant for middle ear impedance, reactance and resistance, but not significant for energy reflectance. This means that when the normalized impedance (Z), reactance (X) and resistance (R) data were compiled across all 248 frequencies, the net Z, X and R values were significantly different between Caucasian

and Chinese children. The values for Z, X and R are significantly greater among the Caucasian compared to the Chinese child data through the frequency range of approximately 3350 to 5500 Hz (Figures 3.2, 3.3 & 3.4). This is the only range of frequencies where separation is evident between the 0.95 CI of the two racial groups. The overall measures of normalized impedance, normalized reactance and normalized resistance, irrespective of their values at individual frequencies, are significantly higher for the Caucasian than for the Chinese children's middle ears through the frequency range 3350 to 5500 Hz.

The main effect of race was not significant for the energy reflectance data. This means that when the ER data was compiled across the range of test frequencies to generate a net ER value for the Caucasian children and a net ER for the Chinese children, the values did not significantly differ from each other. Figure 3.1 shows that the Chinese mean ER is greater than the Caucasian mean ER for both low (approximately 280 to 1300 Hz) and high (approximately 3492 to 5000 Hz) frequency values, but through the mid-frequency range (approximately 1600 to 2500 Hz) the Chinese mean ER curve is lower than that of the Caucasian children. Through the range of mid-frequencies, not only is the Chinese mean ER lower that the Caucasian mean ER, but the 0.95 CI do not overlap between 1617 and 2450 Hz.

The data were then explored for significant interactions of the three between-subject factors (ear, gender and race) with frequency. In these cases, the ER, Z, X and R data were not complied across the range of frequencies, but were analyzed as a function of frequency. The only significant interaction was that between frequency and race, which was significant for all four of the variables: ER, Z, X and R, which indicates that all four variables differ between Caucasian and Chinese subjects as a function of frequency.

From the graphically presented results, the ER is lower for the Chinese children through the mid-frequency range (approximately 1617 – 2367 Hz) and the minimum value attained by the mean ER occurs at a lower frequency in Chinese children (roughly 2367 Hz) than it does in Caucasian children (roughly 3492 Hz). This suggests that acoustical transmission of mid-range frequency sounds is more efficient through the Chinese middle ear than it is through the Caucasian middle ear. There is currently no published pediatric WBR literature of this sort. Child WBR studies to date have been limited to case studies or a sample size. It is for this reason that the pediatric WBR measures will be compared to the normative adult WBR data.

The differences that exist between Caucasian and Chinese energy reflectance are much more pronounced within an adult population. The data presented by Shahnaz and Bork (2006) reveals that up to 1500 Hz the Caucasian ER is significantly lower than the Chinese ER, but that above 3891 Hz the 0.95 CI of the Caucasian ER lies above that of the Chinese group. The range of frequencies over which the Caucasian and Chinese ER 0.95 CI do not overlap is much greater among an adult population compared to a child population. The frequency corresponding to the minimal amount of energy reflection is lower for the Chinese children than it is for the Caucasian children. This suggests that among the pediatric population the characteristic frequency of the Chinese middle ear is lower than that of the Caucasian middle ear.

There is significant overlap of the Caucasian and Chinese 0.95 CI on the impedance, reactance and resistance graphs up to approximately 3492 Hz. Above 3492 Hz, however, the Chinese mean impedance, reactance and resistance curve is higher than the Caucasian curve. This suggests that for higher frequency sound transmission (above 3492 Hz) the Chinese

middle ear has more impedance from both the reactance and resistance components. This may be due to the Chinese middle ear having a lower resonant frequency than that of the Caucasian middle ear, which will lower the efficiency with which high frequency sounds are transferred through to the inner ear. This may be reflective of anatomical differences between the middle ears of the two races. Greater middle ear ossicle mass in Chinese children compared to Caucasian children may be associated with increased high frequency impedance and increased mass-reactance. More efficient middle ear mass distribution among Caucasian children compared to Chinese children may be consistent with a greater amount of high frequency resistance in the Chinese middle ear system, due to increased energy dissipation at the ossicular joints.

As was suggested by Shahnaz and Bork (2006), body size may play a factor in the measured middle ear differences between male and female Caucasian and Chinese individuals. Around 5 to 6 years-of-age, females are comparable in size to their male peers. Table 4.1 summarizes the mean values for length, mass and body mass index (BMI) for children aged 5.5 years and 20 years (National Center for Health Statistics, 2007). A relatively uniform body size between males and females at 5.5 years of age may be the reason for the lack of significant gender differences measured from the pediatric middle ear.

Summary of length, mass and BMI for male and female children aged 5.5 and 20 years

	Mean values at 5.5 years		Mean values at 20 years	
	MALES	**FEMALES**	**MALES**	**FEMALES**
Length (cm)	112	118	177	164
Mass (kg)	20	19	70	58
BMI (kg/m^2)	15.50	15.25	23.00	21.75

Table 4.1. Summary of length, mass and body mass index for male and female children aged 5.5 and 20 years.

Shahnaz and Bork (2006) attributed a portion of the Caucasian versus Chinese WBR differences to the general discrepancy in body size between the two races. In order to compare the WBR patterns between racial groups, the authors attempted to control for the effect of body size by comparing the energy reflectance patterns between Chinese males and Caucasian females. The same comparison was made with the pediatric data (Appendix IX). When the ER patterns between Chinese male children and Caucasian female children are compared, the interaction between race and frequency was no longer significant ($p = 0.111$). It is not known how well Chinese males compare in height and weight to Caucasian females. Additionally, all of the children in the Chinese subject group were included because parental report indicated that the child was of Chinese descent. It may be presumed, however, that the majority of these Chinese children had been born and raised in Canada. In which case, if they are reared in a similar fashion to Caucasian children the Caucasian versus Chinese body size discrepancy may be less evident than it would be had we been comparing Chinese children living in China with age-matched Caucasian children from Canada. Further investigation is required before the source of the frequency-specific racial differences can be determined.

4.1.2 Pediatric versus adult energy reflectance data

The pediatric data from children with normal middle ear function were compared to the normative adult data gathered by Shahnaz and Bork (2006) to determine whether the WBR patterns differ among these two populations, and whether it is in fact important to establish separate norms for younger age-groups. Children are known to have immature outer and middle ear systems until adolescence (Dallos, 1973; Djupesland & Zwislocki, 1973; Northern & Downs, 1974; Wright, 1997). The ear canal develops until a child has

reached 7 years of age, and upon maturity, the canal is longer in length, larger in diameter, more round in shape, and less compliant (Northern & Downs, 1974). The resonant frequency of an adult ear canal is typically 3000 Hz (Djupesland & Zwislocki, 1973), where the average canal resonant frequency in newborns is 3800 Hz. This indicates that there is a decrease in the resonant frequency of the external canal as an individual develops. Also, the 10- 12 dB_{SPL} gain provided by an adult ear canal is largely due to its diameter and compliance. Due to the smaller diameter and larger amount of sound absorption by the soft cartilage of the walls, this gain is not provided by immature ear canals (Dallos, 1973).

The mass and stiffness elements of the middle ear system determine its sound transmission across the frequency range. Middle ear volume, for example, contributes significantly to the stiffness of the system; stiffness decreases as middle ear volume increases. Growth of the temporal bone and pneumatization of the mastoid space also increase middle ear volume as a child develops (Anson & Donaldson, 1981). The use of animal models has revealed that a positive correlation exists between mass of the middle ear ossicles and body size (Werner & Igic, 2002). If this model holds true for humans, and increasing body size (as an individual develops from childhood to adulthood) is related to an increase in the size and mass of the ossicles, then a larger mass of the middle ear system among an adult population could reduce its efficacy in the acoustic transfer of high frequency sounds. Several structural changes have been documented to occur within the outer and middle ear systems as an individual develops from infancy, through childhood to adulthood. It is not known, however, how the mechanico-acoustical properties differ between a pediatric and adult population.

The ER data was analyzed on one between group factor (age: child versus adult) and one within subject factor (frequency). The data was analyzed separately for Caucasian and Chinese subjects. The Caucasian data shows that for low frequency sound transmission, up to approximately 1400 Hz, the 0.95 CI of the mean adult ER data curve is below the pediatric curve. This indicates that the adult middle ear is capable of more efficient sound transmission for low frequency sounds. At higher frequencies (between roughly 2400 and 5200 Hz) the mean pediatric ER curve is lower than the adult curve, which is indicative of a more efficient middle ear system above 2400 Hz in children. The pediatric versus adult data is summarized in Figure 4.1 below.

The differences in middle ear function may be attributable to the discrepancy in body size between adults and children. If adults are larger in size, which includes larger middle ear volume, their middle ear systems will have a lower resonant frequency and be better able to transfer low frequency sounds. This is consistent with the data from the present study. Children, on the other hand, who have a smaller body size and consequently, smaller volume middle ear cavities, will have a higher middle ear resonant frequency and a better system for the acoustical transmission of high frequency sounds. The resonant frequency of the middle ear system has been estimated to be 1003 Hz in children aged 6-15 years (Hanks & Rose, 1993). Within an adult population the middle ear resonant frequency has been estimated at 894 Hz for individuals aged 20 to 43 years (Shahnaz & Polka, 1997) or 817 Hz among individuals ranging between 20 and 40 years (Shanks, Wilson & Cambron., 1993). Additionally, if children have reduced middle ear ossicle mass compared to adult subjects, this may also contribute to their improved ability to transfer high frequency sounds through the middle ear system. Another factor affecting the acoustic transfer of the middle ear may

be the difference in ear canal structure between children and adults. The resonant frequency of the ear canal is known to decrease as a child develops (Djupesland & Zwislocki, 1973), which can also degrade the acoustic transfer of high frequency sounds. The compliant nature of the immature ear canal decreases the acoustic transfer of high frequency sounds to a lesser extent than low frequency sounds (Keefe & Levi, 1996).

The Chinese pediatric versus adult data followed a similar trend as the Caucasian data, but the age-related differences were less pronounced at low frequencies. There is marginal separation of the pediatric and adult 0.95 CI curves up to approximately 500 Hz, which is unlike the clear separation of the curves from the Caucasian data. This borderline child versus adult discrepancy in low frequency sound transmission may be due to several factors. Looking solely at the adult data, the Chinese ER curve attains a minimum value at a higher frequency than does the Caucasian ER curve. This may be indicative of the Chinese adult having a higher frequency at which maximal acoustic energy is transferred through the middle ear (analogous to resonant frequency) compared to the Caucasian adult, which leads to the decreased efficiency of the Chinese adult middle ear at transmitting low frequency sounds. In this case the Chinese adult middle ear is acting more like the middle ear system of a child, which also has a higher resonant frequency than the system of a Caucasian adult. If the mean body size of the Chinese adults falls in between the mean body sizes of the children and the Caucasian adults, and middle ear volume varies with body size, then the resonant frequency of the Chinese adults should also fall in between that of the children and the Caucasian adults. This is consistent with the data presented in this study. Alternatively, there were fewer Chinese children tested than Caucasian children or either Caucasian or Chinese adults. This reduced number of subjects may have lead to an increase in variability

among Chinese children, leading in turn to smaller differences between Chinese adults and children.

At high frequencies there is a clear distinction between the mean ER curves of the Chinese children and adults, which is similar to the differences observed between the Caucasian pediatric and adult data. Between approximately 1400 and 3200 Hz, the Chinese adult ER curve is significantly above that of the children. This suggests that within this frequency range, the pediatric middle ear systems are more efficient at transmitting sounds than are the adult systems. This supports the theory stating that because children have smaller body sizes and presumably smaller volume middle ear cavities, their middle ear systems will achieve resonance at a higher frequency and will be more efficient at conducting high frequency sounds compared to an adult middle ear system.

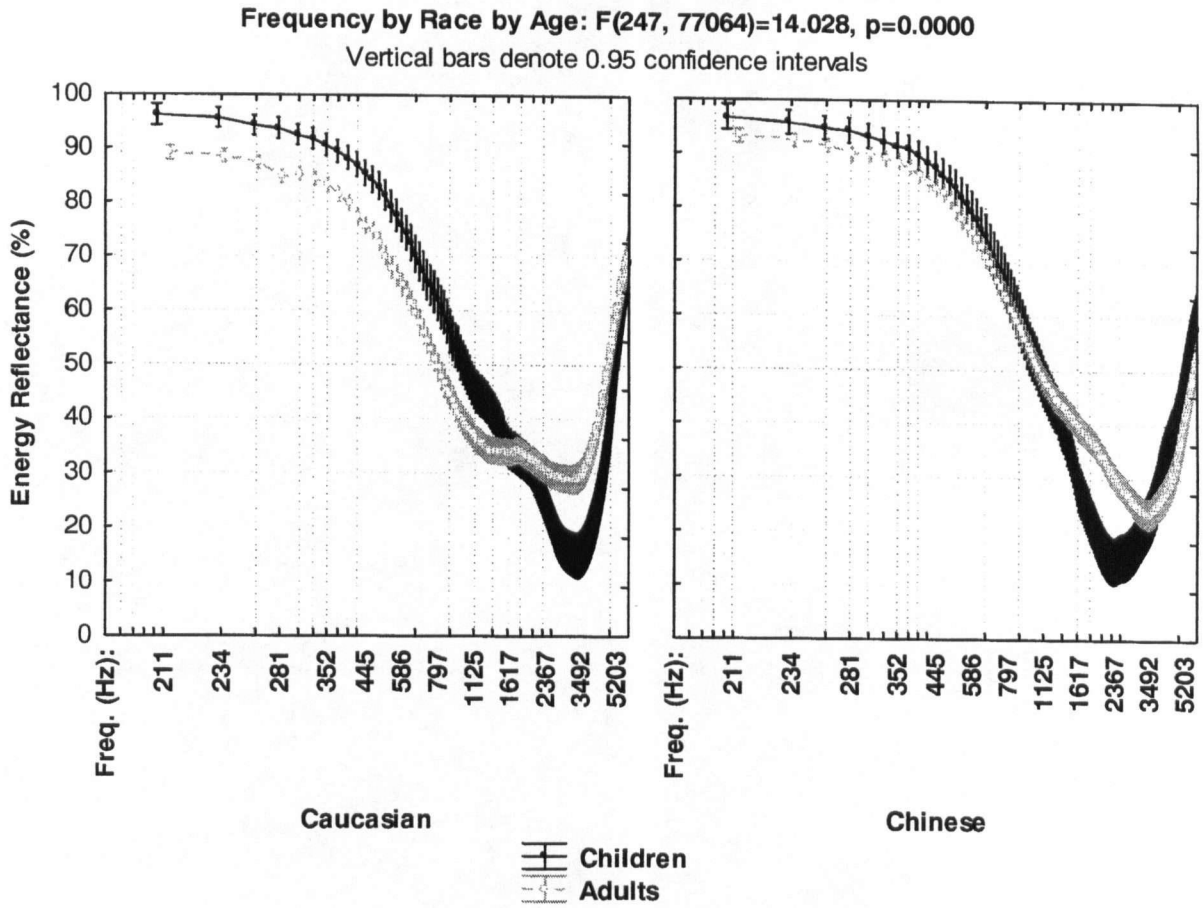


Figure 4.1. Mean energy reflectance as a function of frequency and age for Caucasian and Chinese groups. Vertical bars denote 0.95 CI.

4.1.3 Wideband reflectance data for different middle ear conditions

The clinical utility of WBR was explored by comparing the data from children with healthy middle ear status to those with varying degrees of middle ear pathology. Middle ear status was classified as having a mild degree of negative pressure (-100 to -199 daPa), a severe degree of negative pressure (-200 daPa or more negative) or effusion present. This component of the study was exploratory in nature, because the number of ears tested was not equivalent among each of the diseased groups and the control group. In this section the data

for both genders and all races was compiled in order to increase the number of ears within each subject group.

The energy reflectance data revealed several significant differences of condition as a function of frequency. The data from all three diseased groups differed from the control group data, and the measures from those with a mild degree of negative middle ear pressure differed from those with middle ear effusion. There were no significant ER differences between middle ears with a mild and a severe degree of negative pressure or between severe negative middle ear pressure and middle ear effusion. The energy reflectance measures were sensitive to varying degrees of middle ear pathology, despite the large variability of the 0.95 CI for the three diseased groups due to the smaller number of ears tested. Even a mild degree of negative middle ear pressure significantly increased the ER over the frequency range from 797 to 1852 Hz. A clear trend of decreased energy transmission through the middle ear is evident as its status progresses from normal through the three pathological conditions.

The impedance-based measures revealed significant interactions between condition and frequency. At low frequencies (up to approximately 600 Hz), the impedance and reactance of children with normal middle ear status was significantly lower than from those with mild and severe negative middle ear pressure, as well as those with middle ear effusion. The data from the three diseased groups did not differ significantly from each other. There were no significant interactions between condition and frequency for the resistance data, which was evident because of the large amount of overlap between the 0.95 CI for all four groups. This suggests that middle ear pathology, ranging from a mild degree of negative pressure to effusion, increases the net impedance of the middle ear system up to 600 Hz by increasing the reactance component at these frequencies and does not add much to the

resistive element of the system. This is consistent with the findings from the Jeng, Levitt, Lee and Gravel (1999) study, where middle ear reactance was significantly elevated in the three children (5 ears) with OME compared to the control group at low frequencies. The authors attributed this to an increase in the stiffness of the middle ear system when middle ear effusion is present.

Wideband reflectance, particularly reflectance-based measurements, are sensitive to minimal changes in middle ear status and provide estimates of acoustic transfer over a large range of frequencies. A single WBR measure can be manipulated to generate several values for middle ear energy reflectance and impedance, making this technique a highly useful diagnostic tool for assessing the mechano-acoustical properties of middle ear function and for differentiating between healthy and varying degrees of pathological middle ears. This exceeds the information that is able to be provided by traditional tympanometric measures.

4.2 Limitations of the study

One limitation of this study was the sample size, particularly within the three diseased groups. A larger number of subjects is required before the data can be considered representative of early school-aged children with either normal or pathological middle ears. An increased sample size is especially warranted for the diseased subject groups, as their 0.95 CI were large compared to those of the normal subjects. A larger number of subjects may reduce the variability of the WBR data within the diseased groups and reveal even greater ER differences as a function of middle ear condition. Further experimentation with WBR is needed before it can be used clinically as a diagnostic tool. Testing more subjects, with both normal and pathological middle ears is required before these findings can be generalized. Wideband reflectance data from pathological ears of several different races is

needed. With data from enough Caucasian and Chinese subjects with either negative middle ear pressure or middle ear fluid, the pathological data can be compared to the normative data within a particular ethnic group. This would determine whether race-specific norms are necessary for differential diagnosis of middle ear pathology. It may be that the acoustic transfer function differences between a normal middle ear and one with a mild degree of negative pressure are larger than the differences in middle ear transmission properties between races within a pediatric population. This would argue against the development of race-specific normative data for children. Once the optimal level of normative data homogeneity is determined, it will only be valid for children of this age-group with otitis media with effusion. As other middle ear pathologies may manifest themselves differently, normative data for these children must be independently established.

It is not known whether the effect of age confounded the WBR data of the diseased group subjects. The age range for the normal subjects and the diseased group subjects recruited through the elementary schools was strictly limited to 5 and 6 year-old children, but the patients who were recruited through B.C. Children's Hospital and tested prior to their tube-placement surgeries were between the ages of five and twelve years. A looser age criterion was utilized to increase the number of pathological ears tested.

The middle ear impedance variables (impedance, reactance and resistance) are mathematically altered by the WBR system to normalized values in order to reduce between-subject and between-test variation (Allen et al., 2005). The formula by which these values are normalized includes the area of the ear canal as a variable. Using an average ear canal size introduces potential error, as this is not consistent between subjects. In addition to differences in the physical size of the ear canal, the depth of probe tip insertion and the

amount of cerumen present can also affect its size at the time of the WBR measurement. Of greatest concern in this study is that the average adult ear canal size was used by the WBR machine, while our testing occurred within a pediatric population. It is not known whether this has shifted the impedance-based measurements.

Another limitation of WBR in general is that due to its recent development there is not yet consensus regarding the best way to represent measurement results (Energy Reflectance, Power Absorption, Transmittance, Impedance, Reactance or Resistance). The pediatric data analyzed in this study reveals that ER is more sensitive than impedance, reactance or resistance to varying degrees of otitis media with effusion. This is consistent with the case study of a child with OME by Allen, Jeng and Levitt (2005), where the reactance-based measures revealed greater deviation of the pathological WBR patterns from the normative data compared to the impedance-based measures. Future research may determine that another middle ear variable may provide more information when other types of middle ear pathologies exist. For example, in the presence of a mass-loading pathology such as a cholesteatoma, a more accurate middle ear analysis may be provided by impedance or reactance data.

A potential source of variability in the WBR data is that two different probe tip sizes were used. Four of the control group subjects with small ear canals were tested with a 14B sized probe tip, not the 14A sized tip that was used for the remainder of the subjects. The smaller tips used with the four subjects were able to form a seal with the canal walls. As the number of subjects tested with a smaller sized probe tip is small and each of the 14B tips were properly calibrated as such, the confounding effect of probe size was considered to be negligible and was not considered in the analysis of the data.

4.3 Test-retest reliability

In order to show that the differences observed between normal and pathological ears are in fact due to the differences in middle ear status and not an artifact of the testing procedure, differences in probe tip insertion were measured and compared to the differences measured between middle ear conditions. Figure 3.19 illustrates the mean difference of probe tip re-insertion and the mean difference between two normal WBR patterns were evaluated against to the mean difference between normal and middle ear effusion ears as a function of frequency. The confidence intervals are not shown, but there is a clear separation of the mean values. Re-insertion data from subjects with normal middle ear status, severe negative middle ear pressure and effusion were compiled. The differences between the initial and second probe insertion measurements were negligible, as were the differences between WBR measures from two normal middle ears.

4.4 Implications of the study

Wideband reflectance shows great promise as a diagnostic tool for middle ear analysis. It is able to generate frequency-specific measures of middle ear acoustic transfer through the middle ear and provide information regarding the impedance components of the system. Contrary to tympanometry, the generation of standing waves within the ear canal is not of concern and the depth of probe tip insertion is not critical. Additionally, because pressure is maintained at an ambient level, the highly compliant ear canals will not confound measurements.

The results of this study provide evidence that the mechanico-acoustical transmission properties of a healthy middle ear system differ between pediatric and adult populations, and also between Caucasian and Chinese children. Acoustic transfer through the middle ear

decreases with varying degrees of middle ear pathology, which is best represented by reflectance-based as opposed to impedance-based measures.

In order to increase the differential diagnosis capability of WBR measures, normative pediatric data must be established. The adult middle ear is less efficient than a child's middle ear at transmitting sound energy through the mid-frequency range (Figure 4.1). Energy reflectance among an adult population with healthy middle ear status is not increased to the same degree as is the ER measured from an ear with middle ear effusion. It is for this reason that normative adult data may effectively identify pediatric middle ears with effusion. However, the lesser degree of reduced energy transmission (evident in the groups with mild and severe negative middle ear pressure) may not be identified as abnormal using adult norms.

Figure 3.12 depicts the mean and 90% range (5th and 95th percentiles) of the pediatric control ER data, along with the ER data from the 9 ears with surgically confirmed middle ear effusion (MEE). From this data we see that above approximately 1875 Hz there is considerable variability among the ER patterns of the 9 ears. This may be due to individual variability in middle ear transmission properties, or it may be reflective of subtle differences in middle ear status. Surgical confirmation of middle ear effusion did not specify volume or viscosity of the fluid. Further investigation into the WBR patterns generated from specific middle ear statuses may lead to an increasingly specific diagnostic tool.

Wideband reflectance may have the ability to identify the volume and/or viscosity of middle ear effusion. It is known that as the duration for which middle ear fluid is present increases, the effusion becomes more mucoid. The ability of a non-invasive measurement technique to determine the precise nature of the middle ear fluid could assist medical

professionals in assessing the possible long-term damage (such as ossicle erosion) that can occur as a result of chronic viscous effusion and could prepare otolaryngologist surgeons as to the precise state of the middle ear prior to tympanostomy and myringotomy surgeries.

4.5 Directions for future research

Wideband reflectance measures must be evaluated in terms of sensitivity and specificity against the other available measures of middle ear status, such as otoacoustic emissions and standard 226-Hz and multi-frequency tympanometry, in order to determine which middle ear measure or combination of measures are able to provide the most information with the highest degree of accuracy. This will also determine which middle ear assessment methods should be utilized prior to surgery and may alter the methods used for screening school-aged children.

It may be possible to employ WBR as a pre-operative screening tool. As waiting lists to receive myringotomy and tympanostomy surgeries are lengthy, it is possible that middle ear effusion may resolve prior to the surgery. Once reliable normative data is established, further experimentation can be conducted to determine sources of WBR differences among patients with middle ear effusion.

It is necessary to collect WBR data for individuals of different ethnic backgrounds, with both normal and pathological middle ears. The WBR test performance for identifying various middle ear pathologies must be analyzed within specific racial and age groups in order to determine the extent to which normative data should be homogeneous. It is possible that OME, for example, reduces acoustic transmission differently across the frequency range among individuals of different races.

Hearing sensitivity was screened for this study at 20 dB_{HL} at 500, 1000, 2000 and 4000 Hz, and was classified as either normal or abnormal. Energy reflectance measures suggest that with even a mild degree of negative middle ear pressure, an individual's access to sound is significantly reduced. These changes should be tracked in terms of hearing thresholds, both air conduction and bone conduction, in order to determine whether the changes in ER are also reflected in an individual's hearing sensitivity.

4.6 Conclusions

A preliminary set of normative WBR data has been generated for a pediatric population between the ages of 5 and 6 years. The data was compared to previously collected adult WBR data (Shahnaz & Bork, 2006). It was found that both Caucasian and Chinese data differed between children and adults. The normative pediatric data was compared to measurement from middle ears with varying degrees of pathology. Energy reflectance measures were more sensitive to changes in middle ear status than were the impedance-based measures. Wideband reflectance must be further explored within a pediatric population before results can be generalized, but this measurement technique shows promise of providing a better understanding of the mechanico-acoustic properties of the middle ear and the changes to the system's functioning with middle ear pathology.

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Appendix I Ethics Approval

The University of British Columbia
Office of Research Services
Clinical Research Ethics Board – Room 210, 828 West 10th Avenue,
Vancouver, BC V5Z 1L8

ETHICS CERTIFICATE OF EXPEDITED APPROVAL: RENEWAL

PRINCIPAL INVESTIGATOR:	DEPARTMENT:	UBC CREB NUMBER:
Navid Shahnaz	UBC/Medicine, Faculty of/Audiology & Speech Sciences	H03-70209

INSTITUTION(S) WHERE RESEARCH WILL BE CARRIED OUT:

Institution	Site
UBC	Point Grey Site
Vancouver Coastal Health (VCHRI/VCHA)	Richmond Health Services
Children's and Women's Health Centre of BC (incl. Sunny Hill)	Children's and Women's Health Centre of BC (incl. Sunny Hill)

Other locations where the research will be conducted:
Prince George Regional Hospital (Subjects) Elementary Schools (controls)

CO-INVESTIGATOR(S):
Brian D. Westerberg
Osama Marglani
Shahnaz Atashband
Alison Beers
Frederick K. Kozak

SPONSORING AGENCIES:
Unfunded Research - "Advanced Middle Ear Analysis Techniques for Diagnosis of Middle Ear Effusion"

PROJECT TITLE:
Advanced Middle Ear Analysis Techniques for Diagnosis of Middle Ear Effusion

EXPIRY DATE OF THIS APPROVAL: April 19, 2008

APPROVAL DATE: April 19, 2007

CERTIFICATION:
In respect of clinical trials:
1. The membership of this Research Ethics Board complies with the membership requirements for Research Ethics Boards defined in Division 5 of the Food and Drug Regulations.
2. The Research Ethics Board carries out its functions in a manner consistent with Good Clinical Practices.
3. This Research Ethics Board has reviewed and approved the clinical trial protocol and informed consent form for the trial which is to be conducted by the qualified investigator named above at the specified clinical trial site. This approval and the views of this Research Ethics Board have been documented in writing.

The Chair of the UBC Clinical Research Ethics Board has reviewed the documentation for the above named project. The research study, as presented in the documentation, was found to be acceptable on ethical grounds

Study Procedures:

If you agree to participate in this project three tests will be conducted at your child's school or at the School of Audiology & Speech Services at UBC. First, a hearing test will be performed. The three tests are: 1) Transient Otoacoustic emissions (TOAE), 2) Multifrequency tympanometry (MFT), and 3) Wide band reflectance (WBR). The first two tests are commonly used in infants and young children for detection of middle ear and inner ear problems and pose no risk to your child's ear or to your child's hearing. The third test, wide band reflectance, is not a routine clinical test, however, it is using the same probe as otoacoustic emission (OAE) machines which have been used extensively in universal newborn hearing screening programs and pose no risks or danger to your child's ear or hearing. The three tests together take approximately twelve to fifteen minutes depending on your child's state. This will be in addition to the 10-15 minutes that it normally takes to screen your child's hearing. In the first test, TOAE, a soft disposable probe tip will be inserted into your child's ear. The probe tip is hypoallergenic, which means that it has a decreased tendency to provoke an allergic reaction. Through the probe a click-like sound will be presented (the level of click like sound is the same as normal conversational speech) and the echoes that are emitted from the inner ear will be measured automatically by a computer. The purpose of this test is to further verify the condition of your child's middle ear and inner ear. This test will take 2-3 minutes for each ear.

The remaining two tests, MFT and WBR, are being evaluated as methods to distinguish middle ear problems in newborns, young children, and adults. For these two tests a different soft, delicate hypoallergenic probe tip will be inserted into your child's ear. For the MFT test, a tone will be presented through the probe and at the same time the air pressure in the ear canal will change. When the air pressure changes there will be an increase in pressure followed by a decrease. While the pressure is changing your child will be asked to refrain from talking or swallowing. The pressure changes will be repeated several times and a different tone will be presented during each pressure change. Each pressure change will take approximately 5 seconds. Two additional pressure measurements will be made in which a set of tones is presented with each step of pressure change. These pressure changes will take about 100 seconds. This test will take about 5 minutes for each ear. For the last test, WBR, a different soft disposable hypoallergenic probe tip will be inserted into your child's ear. A series of chirping sounds will be presented through the probe into the ear canal. This test measures the response of the middle ear to a wide range of sounds, with an emphasis on the frequency range of human speech. WBR testing takes about 2-3 seconds for each ear.

The presence of the probe during the above tests may be uncomfortable but it is not painful. However, some children may fuss throughout testing. You may be present throughout all of the testing. If your child fusses there will be a pause in testing. We will terminate testing at any time at your request. All testing will be conducted by Dr. N. Shahnaz, M.Sc., and Ph.D., who is a certified audiologist or by his research assistant (graduate audiologist student) under his supervision.

You have been invited to participate in this study because your child has no history of middle ear problems. As a volunteer for this study, your child will attend one session of 30-35 minutes in duration. Testing will be carried out at your child's school or at the School of Audiology & Speech Services at UBC. Should there be any findings that may be useful to your child's doctor; this information will be communicated to them with your permission. You may withdraw from this study at any time. Withdrawal will in no way jeopardize your child's present or future clinical care.

Advantages:

This is a test of middle ear function; it is not a treatment. It is hoped that the information obtained will help refine the assessment of middle ear disease. There are no direct benefits to your child for participating in this research, but in the long run the results may improve the diagnosis and treatment of people with middle ear disease.

Disadvantages:

Tympanometry is a well-established clinical technique with a long track record as a safe procedure. Your child's participation in this study does expose her/him to small pressure changes in her/his ear and to a low volume tone. The tones are presented at a safe level and the pressure changes occur well below levels that may do any damage to the eardrum or middle ear. Under these conditions there are no known complications arising from tympanometry or wide band reflectance.

How the data will be used:

Your child's data will be compared to data from children who have confirmed middle ear disease. We will examine the results to determine whether the new procedure is a better technique for distinguishing normal and diseased middle ears. Your child's results will be compared to the children who will undergo middle ear surgery to determine whether the severity of middle ear disease can be predicted from the new test procedure.

Confidentiality:

Your child's identity will be coded using a code known only to the researchers, and all information that is collected from your child will remain confidential. Only group results or coded individual results will be given in any reports about the study. Coded results only (no personal information) will be kept in computer files on a password protected hard drive.

Your child's confidentiality will be respected. No information that discloses your child identity will be released or published without your specific consent to the disclosure. However, research records and medical records identifying your child may be inspected in the presence of the Investigator or his designate by representatives of Health Canada, and the UBC Research Ethics Board for the purpose of monitoring the research. However, no records which identify your child by name or initials will be allowed to leave the Investigators' offices.

Compensation for Injury:

Signing this consent form in no way limits your legal rights against the sponsor, investigators, or anyone else.

Consent:

I, _____, have read the above test protocol and I consent for my child to participate in this study undertaken by Drs. Navid Shahnaz, Frederick K. Kozak, and Brian David Westerberg at the child's school or School of Audiology & Speech Sciences. The researcher assures me that my participation in this experiment is completely voluntary and that I may withdraw from this research at any time without consequences.

The parent(s)/guardian(s) and the investigator are satisfied that the information contained in this consent form was explained to the child to the extent that he/she is able to understand it, that all questions have been answered, and that the child assents to participating in the research.

Tympanometry (MFT), and 3) Wide Band Reflectance (WBR). The first two tests are commonly used in infants and young children for detection of middle ear and inner ear problems and pose no risk to your child's ear or to your child's hearing. The third test, wide band reflectance, is not a routine clinical test, however, it is using the same probe as otoacoustic emission (OAE) machines which have been used extensively in universal newborn hearing screening programs and pose no risks or danger to your child's ear or hearing. The three tests together take approximately twelve to fifteen minutes depending on your child's state. This will be in addition to the 20-30 minutes that it normally takes to test your child's hearing. This time estimate takes into account frequent breaks that will be taken as needed to avoid child fussiness. In the first test, TOAE, a soft disposable probe tip will be inserted into your child's ear. The probe tip is hypoallergenic, which means that it has a decreased tendency to provoke an allergic reaction. Through the probe a click-like sound will be presented (the level of click like sound is the same as normal conversational speech) and echoes that are emitted from the inner ear will be measured automatically by a computer. The purpose of this test is to further verify the condition of your child's middle ear and inner ear. This test will take 2-3 minutes for each ear.

The remaining two tests, MFT and WBR, are being evaluated as methods to distinguish middle ear problems in newborns, young children, and adults. For these two tests a different soft, delicate hypoallergenic probe tip will be inserted into your child's ear. For the MFT test, a tone will be presented through the probe and at the same time the air pressure in the ear canal will change. When the air pressure changes there will be an increase in pressure followed by a decrease. While the pressure is changing your child will be asked to refrain from talking or swallowing. The pressure changes will be repeated several times and a different tone will be presented during each pressure change. Each pressure change will take approximately 5 seconds. Two additional pressure measurements will be made in which a set of tones is presented with each step of pressure change. These pressure changes will take about 100 seconds. This test will take about 5 minutes for each ear. For the last test, WBR, a different soft disposable hypoallergenic probe tip will be inserted into your child's ear. A series of chirping sounds will be presented through the probe into the ear canal. This test measures the response of the middle ear to a wide range of sounds, with an emphasis on the frequency range of human speech. WBR testing takes about 2-3 seconds for each ear.

The presence of the probe during the above tests may be uncomfortable but it is not painful. However, some children may fuss throughout testing. You will be present throughout all of the testing. If your child fusses there will be a pause in testing. We will terminate testing at any time at your request. All testing will be conducted by Dr. N. Shahnaz, M.Sc., and Ph.D., who is a certified audiologist or by his research assistant (certified audiologist) under his supervision.

You have been invited to participate in this study because your child has medically confirmed middle ear effusion. As a volunteer for this study, your child will attend one session of 45 minutes in duration. Testing will be carried out in paediatric otolaryngology clinic at BC Children's hospital or at the School of Audiology & Speech Services at UBC. Should there be any findings that may be useful to your child's doctor, this information will be communicated to them with your permission. You may withdraw from this study at any time. Withdrawal will in no way jeopardize your child's present or future clinical care.

Advantages:

This is a test of middle ear function; it is not a treatment. It is hoped that the information obtained will help refine the assessment of middle ear disease. There are no direct benefits to your child for participating in this research, but in the long run the results may improve the diagnosis and treatment of people with middle ear disease.

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

_____	_____
Parent name (please print) Date	Parent signature
_____	_____
Witness name (please print) Date	Witness signature
_____	_____
Name of principal/co-investigator Date	Signature of principal/co- investigator

Appendix VII Analysis of Variance (ANOVA) tables for Control Group subjects.

	Repeated measure analysis of variance energy reflectance					
Effect	SS	Degree of freedom	MS	F	p	G-G Adj. p
Intercept	**29401725**	**1**	**29401725**	**1542.883**	**0.000000**	
Ear	404	1	404	0.021	0.884691	
Gender	11006	1	11006	0.578	0.449621	
Race	1910	1	1910	0.100	0.752426	
Ear*Gender	13	1	13	0.001	0.979608	
Ear*Race	9071	1	9071	0.476	0.492338	
Gender*Race	41579	1	41579	2.182	0.143775	
Ear*Gender*Race	13276	1	13276	0.697	0.406527	
Error	1448283	76	19056			
Frequency	**8227794**	**247**	**33311**	**177.872**	**0.000000**	**0.000000**
Frequency*Ear	**102273**	**247**	**414**	**2.211**	**0.000000**	0.108735
Frequency*Gender	31467	247	127	0.680	0.999964	0.518550
Frequency*Race	**251093**	**247**	**1017**	**5.428**	**0.000000**	**0.004217**
Frequency*Ear*Gender	49738	247	201	1.075	0.200474	0.347285
Frequency*Ear*Race	49531	247	201	1.071	0.213972	0.348877
Frequency*Gender*Race	**116748**	**247**	**473**	**2.524**	**0.000000**	0.078981
Frequency*Ear*Gender*Race	36471	247	148	0.788	0.993732	0.464831
Error	3515521	18772	187			

Table A1: Summary of ANOVA for energy reflectance data, where bold data represents statistical significance.

Effect	Repeated measure analysis of variance impedance					G-G Adj.
	SS	Degree of freedom	MS	F	p	p
Intercept	**106138.0**	**1**	**106138.0**	**583.7111**	**0.000000**	
Ear	249.3	1	249.3	1.3710	0.245294	
Gender	557.9	1	557.9	3.0680	0.083884	
Race	**2815.6**	**1**	**2815.6**	**15.4843**	**0.000183**	
Ear*Gender	138.2	1	138.2	0.7600	0.386074	
Ear*Race	291.0	1	291.0	1.6005	0.209701	
Gender*Race	166.4	1	166.4	0.9150	0.341812	
Ear*Gender*Race	11.7	1	11.7	0.0641	0.800747	
Error	13819.3	76	181.8			
Frequency	**44638.7**	**247**	**180.7**	**134.6696**	**0.000000**	**0.000000**
Frequency*Ear	**458.9**	**247**	**1.9**	**1.3845**	**0.000067**	0.253615
Frequency*Gender	286.4	247	1.2	0.8640	0.939000	0.416728
Frequency*Race	**1856.2**	**247**	**7.5**	**5.6000**	**0.000000**	**0.005559**
Frequency*Ear*Gender	**394.8**	**247**	**1.6**	**1.1909**	**0.021990**	0.304732
Frequency*Ear*Race	316.9	247	1.3	0.9561	0.678320	0.381412
Frequency*Gender*Race	**587.9**	**247**	**2.4**	**1.7736**	**0.000000**	0.175916
Frequency*Ear*Gender*Race	91.3	247	0.4	0.2754	1.000000	0.743700
Error	25191.6	18772	1.3			

Table A2: Summary of ANOVA for impedance data, where bold data represents statistical significance.

Effect	Repeated measure analysis of variance reactance					G-G Adj.
	SS	Degree of freedom	MS	F	p	p
Intercept	**62159.28**	**1**	**62159.28**	**763.0492**	**0.000000**	
Ear	80.03	1	80.03	0.9824	0.324759	
Gender	113.66	1	113.66	1.3952	0.241204	
Race	**929.14**	**1**	**929.14**	**11.4059**	**0.001157**	
Ear*Gender	91.33	1	91.33	1.1212	0.293018	
Ear*Race	94.41	1	94.41	1.1589	0.285091	
Gender*Race	129.96	1	129.96	1.5953	0.210429	
Ear*Gender*Race	0.09	1	0.09	0.0011	0.973523	
Error	6191.09	76	81.46			
Frequency	**49899.57**	**247**	**202.02**	**251.3067**	**0.000000**	**0.000000**
Frequency*Ear	**266.17**	**247**	**1.08**	**1.3405**	**0.000307**	0.264856
Frequency*Gender	108.55	247	0.44	0.5467	1.000000	0.583754
Frequency*Race	**938.40**	**247**	**3.80**	**4.7260**	**0.000000**	**0.009696**
Frequency*Ear*Gender	226.59	247	0.92	1.1412	0.064373	0.322916
Frequency*Ear*Race	150.39	247	0.61	0.7574	0.998166	0.473250
Frequency*Gender*Race	**389.00**	**247**	**1.57**	**1.9591**	**0.000000**	0.143454
Frequency*Ear*Gender*Race	86.47	247	0.35	0.4355	1.000000	0.652075
Error	15090.59	18772	0.80			

Table A3: Summary of ANOVA for reactance data, where bold data represents statistical significance.

	Repeated measure analysis of variance resistance					
Effect	SS	Degree of freedom	MS	F	p	G-G Adj. p
Intercept	**28067.42**	**1**	**28067.42**	**252.0457**	**0.000000**	
Ear	146.86	1	146.86	1.3188	0.254405	
Gender	363.60	1	363.60	3.2652	0.074723	
Race	**1735.55**	**1**	**1735.55**	**15.5852**	**0.000175**	
Ear*Gender	41.15	1	41.15	0.3695	0.545079	
Ear*Race	168.29	1	168.29	1.5113	0.222740	
Gender*Race	14.75	1	14.75	0.1324	0.716956	
Ear*Gender*Race	2.75	1	2.75	0.0247	0.875464	
Error	8463.24	76	111.36			
Frequency	**1644.33**	**247**	**6.66**	**7.2068**	**0.000000**	**0.001438**
Frequency*Ear	148.29	247	0.60	0.6499	0.999995	0.511398
Frequency*Gender	188.94	247	0.76	0.8281	0.976748	0.430391
Frequency*Race	**1426.32**	**247**	**5.77**	**6.2513**	**0.000000**	**0.003256**
Frequency*Ear*Gender	187.87	247	0.76	0.8234	0.979798	0.432334
Frequency*Ear*Race	214.99	247	0.87	0.9422	0.732706	0.385727
Frequency*Gender*Race	**528.26**	**247**	**2.14**	**2.3152**	**0.000000**	0.106886
Frequency*Ear*Gender*Race	129.73	247	0.53	0.5686	1.000000	0.553694
Error	17340.49	18772	0.92			

Table A4: Summary of ANOVA for resistance data, where bold data represents statistical significance.

Appendix VIII Analysis of Variance (ANOVA) by middle ear condition

	Repeated measure analysis of variance energy reflectance					
Effect	SS	Degree of freedom	MS	F	p	G-G Adj. p
Intercept	66304538	1	66304538	2346.123	0.00	
Condition	**5130145**	**3**	**1710048**	**60.508**	**0.00**	
Error	4239198	150	28261			
Frequency	**5170372**	**247**	**20933**	**106.358**	**0.00**	**0.000000**
Frequency*Condition	**727393**	**741**	**982**	**4.988**	**0.00**	**0.000010**
Error	7291926	37050	197			

Table A5: Summary of ANOVA for energy reflectance data, where bold data represent statistical significance.

	Repeated measure analysis of variance impedance					
Effect	SS	Degree of freedom	MS	F	p	G-G Adj. p
Intercept	**128600.3**	**1**	**128600.3**	**658.0064**	**0.000000**	
Condition	725.9	3	242.0	1.2381	0.297862	
Error	30293.1	155	195.4			
Frequency	**89655.3**	**247**	**363.0**	**227.9570**	**0.000000**	**0.000000**
Frequency*Condition	**4360.6**	**741**	**5.9**	**3.6957**	**0.000000**	**0.000758**
Error	60961.3	38285	1.6			

Table A6: Summary of ANOVA for impedance data, where bold data represent statistical significance.

	Repeated measure analysis of variance reactance					
Effect	SS	Degree of freedom	MS	F	p	G-G Adj. p
Intercept	**96626.08**	**1**	**96626.08**	**942.7157**	**0.000000**	
Condition	**1736.53**	**3**	**578.84**	**5.6474**	**0.001067**	
Error	15887.13	155	102.50			
Frequency	**90251.80**	**247**	**365.39**	**379.8969**	**0.000000**	**0.000000**
Frequency*Condition	**2782.22**	**741**	**3.75**	**3.9037**	**0.000000**	**0.000340**
Error	36823.22	38285	0.96			

Table A7: Summary of ANOVA for reactance data, where bold data represent statistical significance.

	Repeated measure analysis of variance resistance					
Effect	SS	Degree of freedom	MS	F	p	G-G Adj. p
Intercept	**15181.84**	**1**	**15181.84**	**139.6554**	**0.000000**	
Condition	**1521.36**	**3**	**507.12**	**4.6649**	**0.003804**	
Error	16306.40	150	108.71			
Frequency	**3574.04**	**247**	**14.47**	**13.7986**	**0.000000**	**0.000000**
Frequency*Condition	1431.43	741	1.93	1.8422	0.000000	0.075261
Error	38852.20	37050	1.05			

Table A8: Summary of ANOVA for resistance data, where bold data represent statistical significance.

Appendix IX Analysis of Variance (ANOVA) for Caucasian females versus Chinese males

	Repeated measure analysis of variance energy reflectance					
Effect	SS	Degree of freedom	MS	F	p	G-G Adj. p
Intercept	**16370818**	**1**	**16370818**	**1478.830**	**0.000000**	
Race	2730	1	2730	0.247	0.621807	
Error	509225	46	11070			
Frequency	**5558740**	**247**	**22505**	**133.755**	**0.000000**	**0.000000**
Frequency*Race	**92352**	**247**	**374**	**2.222**	**0.000000**	0.110548
Error	1911713	11362	168			

Table A9: Summary of ANOVA for energy reflectance data, where bold data represent statistical significance.