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Effects of Otosclerosis on Middle Ear Function Assessed With Wideband Absorbance and Absorbed Power

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Abstract

Objective—Wideband absorbance and absorbed power were evaluated in a group of subjects with surgically confirmed otosclerosis (Oto group), mean age 51.6 years. This is the first use of absorbed power in the assessment of middle ear disorders. Results were compared with control data from two groups of adults, one with normal hearing, (NH group) mean age of 31 years, and one that was age- and sex-matched with the Oto group and had sensorineural hearing loss (SNHL group). The goal was to assess group differences using absorbance and absorbed power, to determine test performance in detecting otosclerosis, and to evaluate pre-operative and post-operative test results.

Design—Audiometric and wideband tests were performed over frequencies up to 8 kHz. The three groups were compared on wideband tests using analysis of variance to assess group mean differences. Receiver operating characteristic (ROC) curve analysis was also used to assess test accuracy at classifying ears as belonging to the Oto or control groups using the area under the ROC curve (AUC). A longitudinal design was used to compare pre- and post-operative results at 3 and 6 months.

Results—There were significant mean differences in the wideband parameters between the Oto and control groups with generally lower absorbance and absorbed power for the Oto group at ambient and tympanometric peak pressure (TPP) depending on frequency. The SNHL group had more significant differences with the Oto group than did the NH group in the high frequencies for absorbed power at ambient pressure and tympanometric absorbed power at TPP, as well as for the tympanometric tails. The greatest accuracy for classifying ears as being in the Oto group or a control group was for absorbed power at ambient pressure at 0.71 kHz with an AUC of 0.81 comparing the Oto and NH groups. The greatest accuracy for an absorbance measure was for the

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comparison between the Oto and NH groups for the peak-to-negative tail condition with an AUC of 0.78. In contrast, the accuracy for classifying ears into the control or Oto groups for static acoustic admittance (SAA) at 226-Hz was near chance performance, which is consistent with previous findings. There was good agreement between the present study and Keefe et al. (2017b) for absorbance peak-to-tail differences with high AUCs for both studies at 2.83 kHz for the peak-to-positive tail condition and at 4 kHz for the peak-to-negative tail condition. There were significant mean differences between pre- and post-operative tests for absorbance and absorbed power.

Conclusions—Consistent with previous studies, wideband absorbance showed better sensitivity for detecting the effects of otosclerosis on middle ear function than SAA at 226 Hz. This study showed that wideband absorbed power is similarly sensitive and may perform even better in some instances than absorbance at classifying ears as having otosclerosis. The use of a group that was age- and sex-matched to the Oto group generally resulted in greater differences between groups in the high frequencies for absorbed power, suggesting that age-related norms in adults may be useful for the wideband clinical applications. Absorbance and absorbed power appear useful for monitoring changes in middle ear function following surgery for otosclerosis.

INTRODUCTION

The etiology of an ossicular disorder leading to a conductive hearing loss in an ear with a normal tympanic membrane (TM) often proves difficult to diagnose. In the case of otosclerosis, there is an overlap in 226 Hz static acoustic admittance (SAA) between normal and otosclerotic ears such that ears with otosclerosis often have SAA in the normal range (Feeney et al. 2003; Rosowski et al. 2008). The patient's case history may not resolve the diagnostic dilemma, and the audiometric pattern of the hearing loss may be inconclusive. Although high resolution computerized tomography (CT) scans may be useful in the diagnosis of some middle ear (ME) disorders with a normal TM, such as otosclerosis (Curtin 2016), a systematic review questions the use of CT for the diagnosis of otosclerosis, with sensitivity to the disease ranging from 60 to 95% across 7 studies (Wegner et al. 2016). Definitive diagnosis with current methods may only be possible using exploratory ME surgery (Merchant & Rosowski 2008; Rosowski et al. 2008).

Wideband acoustic immittance (WAI) has been used to evaluate ears with otosclerosis. WAI refers to measures of ME function across a wide frequency range (0.25 to 8 kHz) that includes energy reflectance and absorbance (1-energy reflectance) (Keefe et al. 2015; Feeney et al. 2017). Stapes fixation caused by otosclerosis has been reported to decrease absorbance at frequencies below 1 kHz when measured at ambient pressure (Feeney et al. 2003; Allen et al. 2005; Shahnaz et al. 2009a; Nakajima et al. 2012; Nakajima et al. 2013). However, a recent study found no significant decrease in low-frequency absorbance at ambient pressure in the case of otosclerosis, rather a significant decrease at 4 kHz was observed (Keefe et al. 2017b).

Shahnaz et al. (2009a) reported a significantly higher mean energy reflectance (ER) at ambient pressure for one-third octave frequencies below 1 kHz in a group of 28 patients with surgically confirmed otosclerosis (28 ears) compared to a normal-hearing (NH) group (62

subjects, 115 ears). Using the area under the curve (AUC) for the receiver operating characteristic (ROC) analysis, Shahnaz et al. reported that the highest AUC of 0.86 for detecting otosclerosis was obtained using ER at ambient pressure at 0.4 and 0.5 kHz. That compared to an AUC of 0.5 for SAA for a 226 Hz probe tone. Shahnaz et al. (2009b) examined the change in ER at ambient pressure in 15 otosclerotic ears at times from 1 to 2 months following stapedectomy (ten of these were also subjects in Shahnaz et al. 2009a). Post-operative (post-op) ER at ambient pressure in these ears decreased in a low-frequency notch at frequencies below 1 kHz suggesting that ER may be useful in assessing post-operative changes in middle ear function. Feeney et al. (2003) presented data from a subject with otosclerosis whose abnormal post-operative middle-ear function (slipped prosthesis) was detectable by a decrease in reflectance similar to temporal bone cases of ossicular discontinuity (Feeney et al. 2009; Nakajima et al. 2012).

Nakajima et al. (2012) obtained measurements of ER at ambient pressure in adults with otosclerosis, disarticulation and superior semicircular canal dehiscence. They reported that when combined with the average audiometric air-bone gap (ABG) from 1 to 4 kHz, ER at ambient pressure averaged from 0.6 to 1 kHz successfully separated 28 of 31 cases into the 3 pathologies. This approach takes advantage of the smaller ABGs observed at high frequencies for patients with superior semicircular canal dehiscence compared to patients with otosclerosis.

Keefe et al. (2017b) applied a wideband test battery for auditory assessment for classifying ears as NH or with a diagnosis of otosclerosis and described results for ears that received surgery to remedy otosclerosis. The tests included a wideband acoustic stapedius reflex threshold (ASRT) test, a chirp-evoked transient otoacoustic emission (TEOAE) test, and WAI measures of absorbance and group delay. Responses were evaluated from 23 ears with NH, 12 ears with a diagnosis of otosclerosis, and 13 ears that previously had surgical intervention for otosclerosis. Subjects with a diagnosis of otosclerosis had lower mean absorbance at ambient pressure at 4 kHz with no significant difference between groups at lower frequencies. However, the otosclerosis group had lower absorbance at 0.7 and 1 kHz when measured at the tympanometric peak pressure (TPP). Ears with surgical intervention for otosclerosis generally had greater absorbance and group delay at or below 1 kHz than for the NH group or the group with a diagnosis of otosclerosis.

The purpose of the present study was to evaluate the use of wideband absorbance and wideband absorbed power to assess middle ear function in patients with otosclerosis. Absorbed power has not previously been used to assess middle ear disorders. However, we reported on absorbed power at ambient pressure to assess middle ear function in NH adults and to measure the acoustic reflex and acoustic reflex threshold (Feeney & Keefe, 1999; Keefe et al. 2017a). The absorbed sound power W_a is proportional to the product of the squared magnitude of the forward pressure P_f , the cross-sectional area A of the ear canal, and the absorbance α of the ear canal terminated by the middle ear at the TM (Keefe & Schairer, 2011):

$$W_a = \alpha \frac{|P_f|^2 / 2}{\rho c} A,$$

with a proportional constant of the product of two times the equilibrium density (ρ) of air and the phase velocity (c) of air. In the limit that the small losses of sound power at the ear-canal walls between the probe and TM are neglected, the absorbed sound power is equal at the probe tip and TM by conservation of energy. It follows that absorbed sound power controls for ear-canal acoustics via the use of forward pressure and for middle-ear power absorption via the use of absorbance. The inclusion of cross-sectional area controls for its spatial variation between the probe tip and TM. Spatial variations in ear-canal area produce concomitant spatial variations in the calculated forward pressure magnitude and absorbance at each location between the probe tip and the TM. In contrast, absorbed power in a loss-less ear canal is invariant across all locations in the approximate of one-dimensional acoustics. Thus, absorbed power may provide a measure of the effect of middle-ear disorders that is less affected than absorbance or forward pressure level by spatial variations in the sound field within the ear canal.

The corresponding absorbed power level is calculated as 10 times the common logarithm of the ratio of absorbed sound power to 4×10^{-18} Watts. With this normalization, an absorbed power level of 0 dB occurs for a sinusoidal tone at 0 dB sound pressure level (SPL) that delivers power into an acoustic conductance of one mmho, which is the centimeter-gram-second (CGS) unit of acoustic admittance magnitude commonly used in acoustic immittance measurements at 226 Hz.

The present study used wideband ambient pressure and tympanometric absorbance and absorbed sound power measures to evaluate three groups of adult subjects: a group with surgically confirmed otosclerosis, and two comparison groups, one with NH with a mean age 20 years younger than the Oto group, and one that was age and sex-matched with the Oto group. The present study also assessed pre-and post-surgical ambient and tympanometric absorbance and absorbed power for participants who underwent stapes surgery to determine the extent to which post-surgical changes in middle ear function could be detected with longitudinal wideband tests. The methods and equipment used in this study were the same as those used in Keefe et al. (2017b), but the data were collected at a different location with unique subjects for the two studies.

MATERIALS AND METHODS

Subjects

Subjects with Otosclerosis—The otosclerosis (Oto) group consisted of a total of 17 adults (23 ears), 13 female, 4 male [mean age of 51.6 year (y), range 25 to 71 y]. Thirteen of these subjects had surgically confirmed otosclerosis in the test ear with two subjects contributing data from both ears (15 ears, 9 female, 7 right). Data from the remaining 8 ears from subjects with a diagnosis of bilateral otosclerosis (6 female, 3 right) were obtained for ears with surgical confirmation of otosclerosis in the opposite ear.

Control Subjects—Adult subjects with NH served as one control group. The general inclusion criteria for these subjects consisted of 1) pure-tone air-conduction (AC) thresholds 20 dB HL at frequencies ranging from 0.25 to 8 kHz with an audiometric ABG 10 dB at octave frequencies from 0.25 to 4 kHz; 2) a negative history of hearing loss or ear surgery; 3) normal otoscopy, 4) a peak-compensated SAA magnitude at 226 Hz (Y_{tm}) from 0.3 to 1.7 mmho, and ME pressure within ± 100 daPa. The NH group included a total of 46 adults, 17 males and 29 females, ranging in age from 18 to 54 y, with a mean age of 32.1 y. Note that the mean difference in age between this control group and the Oto group was 20 years, the same as the mean age difference between the control and otosclerosis groups in Keefe et al. (2017b).

This study was part of a larger study evaluating a wideband acoustic test battery for hearing assessment including absorbance, wideband acoustic reflex thresholds, and TEOAEs in adults and children (Keefe et al. 2015; Hunter et al. 2016; Keefe et al. 2017a; Feeney et al. 2017). As part of the larger study, a group of adult participants with SNHL were recruited to examine the detection of SNHL with TEOAEs (Putterman et al. 2017). Based on previous findings of an age effect in wideband absorbance with older subjects having higher absorbance in the 2–4 kHz frequency range (Feeney and Sanford, 2004), a subset of subjects from Putterman et al. was used as a second control group for the present study that was age- and sex-matched to the subjects in the Oto group of the present study. Subjects in this group had SNHL, but otherwise the same inclusion criteria as the NH controls. These subjects make an appropriate Oto comparison group as they are matched for age and sex, and we would expect no effect of SNHL on their middle-ear function measured by absorbance (Cetin et al. 2019). A total of 23 adults with SNHL served as the second control group. There were 8 males and 15 females, the same sex breakdown as ears within the Oto group, with a mean age of 51.2 y compared to 51.6 y for the Oto group.

Across all groups the percentage of each reported race was: 87% White, 7% Asian, 2% Black or African American, 1% American Indian or Alaska Native, and 1% no report. The ethnicity composition across all groups was 90% not Hispanic, 9% Hispanic, and 1% no report.

Instrumentation

Clinical—A Grason-Stadler Inc. (Eden Prairie, MN), GSI-61 audiometer with ER-3A insert earphones and a B-71 oscillator calibrated to ANSI standard S3.6 (2010) was used for pure-tone AC and bone-conduction (BC) audiometry. A GSI Tymptstar tympanometer calibrated to ANSI standard S3.39 (2012) was used for 226-Hz tympanometry and clinical ASRTs.

Experimental—The hardware for the wideband experimental tests was an Interacoustics (Middlefart, Denmark) Wideband Tympanometry research system with custom software (Liu et al. 2008; Keefe et al. 2015). The experimental probe assembly contained 2 receivers: one was a wide-bandwidth receiver used to generate clicks (0.2 to 8 kHz) as a probe stimulus; and the second had the same bandwidth but allowed higher levels to generate acoustic reflex activator signals. A modified Interacoustics AT235 tympanometer and a sound card (CardDeluxe) located in a 32-bit computer were controlled by custom software.

The computer sound card had 2 digital-to-analog converters to drive a pair of receivers in the probe. An analog-to-digital converter was used to change the microphone output of the probe to a digital signal at a sampling rate of 22.05 kHz. Additionally, a controller in the AT235 was modified to allow computer control of the air pressure generated by the tympanometry pump via a serial port (RS-232).

Procedures

All procedures were approved by the Institutional Review Board of the Oregon Health & Science University and subjects signed informed consent prior to study participation. Clinical audiometric and immittance tests were completed prior to the wideband experimental tests at each visit. Acoustic reflex and otoacoustic emission data were also collected but not reported on here. All testing was completed in a double-walled sound treated booth. NH and SNHL control subjects underwent the same testing protocol on both ears during their initial visit, and at a follow-up visit scheduled approximately 1 month later. The first ear tested at each visit was determined by a random order function. One ear from each control subject was randomly selected for inclusion in the study, typically from the first-visit data, or from the second visit in the case that the ear chosen did not meet inclusion criteria for visit 1, or was not usable due to equipment issues. Individual wideband data obtained with the same equipment and similar procedures have been reported in Keefe et al. (2015).

Subjects diagnosed with otosclerosis in the Oto group were tested at a single visit. When possible, those subjects who subsequently underwent stapes surgery had follow-up visits scheduled at approximately 3 and/or 6 months post treatment.

Clinical tests—After the otoscopic examination, the following clinical audiologic tests were administered for both ears using previously described equipment: 1) pure-tone AC audiometry at frequencies from 0.25 to 8 kHz; 2) pure-tone BC audiometry from 0.25 to 4 kHz; 3) tympanometry using a 226-Hz probe tone with a pressure sweep from +200 to – 200 daPa. Acoustic reflex thresholds were subsequently obtained, but not reported here.

For subjects seen for 3- or 6-month post-op testing, the clinical assessment included AC and BC testing, but did not include 226-Hz tympanometry to reduce the number of tympanograms in post-operative ears.

Wideband Experimental Tests—The WAI test system was calibrated for reflectance measurements by recording the pressure response to a click stimulus with a spectrum of 0.2 to 8 kHz in a pair of hard-walled cylindrical tubes with a diameter of 7.94 mm, similar to an average adult ear canal, and with nominal lengths of 292 and 8.2 cm. The calibration tubes were closed at one end and the probe was inserted in the opposite end using a tympanometry probe tip. The incident pressure spectrum and the source reflectance of the Interacoustics probe were calculated using these measured data and an acoustical model of sound propagation in cylindrical tubes with viscothermal loss (Keefe & Simmons 2003). The software determined when a valid calibration was obtained. This calibration was performed daily before measurements were obtained.

WAI test procedures were the same as those described in Feeney et al. (2017) except that the wideband tympanometry pressure range was ± 200 daPa in the present study compared to +200 to -300 daPa in Feeney et al. The pressure range was restricted in the present study for the purpose of testing patients at 3 and 6 months following surgery for otosclerosis. The stimulus used to measure WAI at ambient pressure was a repeating broadband click presented at a rate of 11.7/s and a total SPL of 60 dB as measured in a Brüel and Kjær (Nærum, Denmark) model 4157 artificial ear simulator. Prior to measurements, the ear canal pressure was automatically adjusted to ambient pressure by the pump circuit with the probe inserted into the ear canal. Synchronous time averaging of the microphone response to the sound stimulus was employed, with a length of 1024 samples lasting 46 ms. Several buffers were discarded at the beginning of the test, and then 32 synchronous buffers were acquired by the software over a duration of 1.49 s. For wideband tympanograms, the rate of the pressure sweep was approximately 100 daPa/s. At this sweep rate, the static pressure varied by about 4.6 daPa between adjacent click responses. If a pressure leak was detected, the software presented a message to the user to re-fit the probe and restart the test. The WAI test order started with a down-swept tympanogram (+200 to -200 daPa) followed by a measurement at ambient pressure and then a final measurement in an up-swept tympanogram (-200 to +200 daPa). The TPP was calculated as the pressure at which the maximum of the low-frequency averaged absorbance occurred for the down-swept tympanogram over the frequency range from 0.376 to 2 kHz. This frequency range excluded the somewhat noisier data below 0.376 kHz related to the lack of averaging across click responses during the tympanometric sweep (Liu et al. 2008). The initial down-swept tympanogram starting with positive ear canal pressure was highly effective at detecting a leaky probe fit through an inability to pressurize the ear canal to +200 daPa. This and subsequent test recordings were monitored by a researcher during data collection to ensure that the probe insertion was maintained. Furthermore, the researcher was alerted by the software to the possibility of a leaky probe fit (Keefe et al. 2015). If this occurred, then the measurement was repeated.

Data Analyses

A one-way analysis of variance (ANOVA) was used for mean comparisons of NH, SNHL and Oto groups for WAI measurements as a function of frequency. The measurements included $\frac{1}{2}$ octave-averaged absorbance and absorbed power. Independent one-way ANOVAs comparing group means were obtained at ambient pressure, and for pressurized measurements. Results were similar for up-swept and down-swept tympanograms, and so only results for down-swept tympanograms are reported. These were obtained at TPP, at the positive and negative tympanometric tails, and for peak-to-tail differences for positive and negative pressures. A Bonferroni correction for an alpha level of 0.05 was used for comparison of means at each frequency. Separate within-subjects repeated measures ANOVAs were used to evaluate responses from a subset of Oto subjects who had pre-operative (pre-op) tests and/or 3- and 6-month post-operative (post-op) tests for the WAI measures. Paired *t* tests were used to compare means between pre-op and 3-month and 6-month post-op tests to test the hypothesis whether a test variable such as absorbance differed on average between the pre-op and post-op conditions.

ROC curve analysis was also conducted, including the non-parametric AUC to assess the accuracy of each test at classifying ears as belonging to the Oto group compared to either the NH or SNHL groups. The AUC was calculated for each test type independently at each ½-octave frequency. Statistical analyses were generated with IBM SPSS 22 software.

RESULTS

Audiometric Data

One ear from each of the 46 subjects in the NH group was selected at random for inclusion in the study with equal numbers of right and left ears. One ear from each of the 23 subjects from the SNHL group was also randomly selected for inclusion in the study with a total of 11 right ears and 12 left ears. The mean AC thresholds for the audiometric frequencies in dB HL $\pm$ 1 standard error (SE) of the mean for the NH and SNHL groups are shown in the top panel of Figure 1 along with the mean and SE for the AC and BC thresholds for the Oto group. The mean 3-frequency (0.5, 1 and 2 kHz) pure-tone average (PTA) AC threshold was 6 dB HL for the NH group and 12 dB HL for the SNHL group. The SNHL group on average had a mild high-frequency loss. This compares to a 3-frequency PTA for AC for the Oto group of 56 dB HL with a mean 3-frequency ABG of 28 dB. The mean BC thresholds for the ears with otosclerosis were borderline normal at around 25 dB HL or better from 0.5 to 4.0 kHz except at 2 kHz where the mean BC threshold was 36.5 dB HL demonstrating a BC “Carhart notch” often associated with otosclerosis (Wegner et al. 2013). These BC thresholds were within 5 dB of the mean BC thresholds at each frequency from 0.5 to 4.0 kHz in preoperative audiograms from 83 patients with otosclerosis aged 50–60 years reported by Vartiainen and Karkalainen (1992).

The bottom panel of Figure 1 shows the mean and SE of pre-op and post-op AC and BC thresholds at 3 months for 12 ears. Values were similar for the 10 ears available for the 6-month pre-op/post-op comparison (not shown). The 3-frequency pure-tone AC average improved from 59 to 36 dB HL, and the 3-frequency pure-tone BC average improved slightly from 32 to 28 dB HL.

Absorbance

Group Differences—Absorbance at ambient pressure (A_a) was compared for the NH, SNHL, and Oto groups as shown in Figure 2, top panel. An ANOVA showed a significant difference among mean absorbance values at 2 and 2.83 kHz. Post hoc comparison with a Bonferroni correction revealed a significant difference between means for the NH and SNHL groups at 2 kHz and 2.83 kHz and between the means for the Oto and SNHL group at 2.83 kHz. Tympanometric absorbance (A_t) at TPP was also compared for the three groups as shown in the bottom panel of Figure 2. An ANOVA showed a significant difference among means at 2.83 and 4 kHz. Post hoc tests revealed a significant difference between the means for the Oto and SNHL groups at 2.83 kHz and between the means for the Oto and NH groups at 4 kHz.

For A_t at the positive tympanogram tail (+200 daPa) (PT) an ANOVA showed a significant difference among mean absorbance values at 0.25, 2 and 2.83 kHz (top panel, Figure 3).

Post hoc testing revealed a significant difference between the means for NH and Oto groups at 0.25 kHz, between the means for NH and SNHL groups at 2 kHz and between the means for NH and Oto groups and NH and SNHL groups at 2.83 kHz. For A_t at the negative tail (NT) an ANOVA showed a significant difference among mean absorbance values at 0.25, 0.35, 0.5, 2 and 2.83 kHz (bottom panel, Figure 3). Post hoc testing revealed a significant difference between means for the NH and Oto groups at 0.25, 0.35 and 0.5 kHz, and between the means for NH and SNHL groups at 2 and 2.83 kHz.

An ANOVA for the A_t peak-to-tail difference for the PT showed a significant difference among means at 2.83 and 5.66 kHz. Post hoc testing revealed a significant difference between the means for the NH and Oto groups at 2.83 kHz and between the means for the NH and SNHL groups at 5.66 kHz (Figure 4, top panel). An ANOVA for the peak-to-tail differences in A_t for the NT for the three groups showed a significant difference among the means at 2.83 and 4 kHz. Post hoc testing revealed a significant difference between the means for the NH and Oto groups for both frequencies (Figure 4, bottom panel).

ROC Analyses for Absorbance—AUCs were calculated to quantify the accuracy of absorbance to classify ears in the Oto, NH or SNHL groups. Table 1 shows AUCs 0.70 for each absorbance measurement type and frequency for the comparison of Oto to NH or Oto to SNHL groups. The greatest AUC for absorbance for the Oto and NH group comparison was 0.78 for the Peak-to-NT absorbance difference at 4 kHz. The only AUC 0.70 for the Oto and SNHL comparison was 0.74 at 2.83 kHz for the TPP condition.

Absorbance Pre- and Post-Op Comparisons—Of the 23 ears from subjects in the Oto group, both pre-op and 3-month post-op data were obtained for a subset of 12 ears (see audiogram, bottom panel Figure 1). Nine of those 12 ears plus one additional ear provided post-op data for a total of 10 ears at 6 months. Figure 5 shows the pre- and post-op absorbance results at 3 months (top row) and 6 months (bottom row) for A_a (left column) and A_t at TPP (right column). The mean ($\pm$ SE) pre- and 3-month post-op A_a results are shown for 12 ears in the top left panel. A frequency by test (pre-op versus post-op) within-subjects ANOVA revealed a significant main effect for test and a significant test by frequency interaction. Paired samples t tests revealed that the 3-month post-op mean A_a was significantly greater than pre-op at 0.71 and 1 kHz. A similar pattern was observed for A_a for the 10 ears that had pre- and post-op tests at 6 months as shown in the bottom left panel of Figure 5. A frequency by test within-subjects ANOVA for the 6-month comparison revealed a significant main effect for test and a significant test by frequency interaction. Paired samples t tests revealed that A_a at the 6-month post-op visit was significantly greater than pre-op at 0.71 and 1 kHz, and was significantly lower than pre-op at 2 kHz.

The mean pre- and post-op A_t at TPP at 3 and 6 months (Figure 5, right column) were similar to the mean results for A_a (Figure 5, left column), but the differences between pre- and post-op absorbance tests were somewhat smaller for A_t . For the pre-op to 3-month mean comparison (Figure 5, top right panel), a frequency by test within-subjects ANOVA failed to show a significant main effect of test. However, there was a significant test by frequency interaction. The 3-month post-op A_t at TPP was significantly lower than pre-op at 2.83 kHz. For the 6-month comparison (bottom right panel, Figure 5), a frequency by test within-

subjects ANOVA did not show a significant main effect of test. However, there was a significant test by frequency interaction. Paired samples t tests revealed that A_t at 6 months was greater than pre-op at 0.71 and 5.66 kHz.

Absorbed Power

Group Differences—The mean $\frac{1}{2}$ octave ambient absorbed power spectrum level (L_{Wa}) in dB ± 1 SE is shown in the top panel of Figure 6 for the NH, SNHL and Oto groups. An ANOVA showed a significant difference among group means at 0.71, 1, 4 and 5.66 kHz. Post hoc comparisons revealed a significant difference between means for the NH and Oto groups at 0.71 and 1 kHz and between the means for the Oto and SNHL groups at all four frequencies. Tympanometric absorbed power spectrum level (L_{Wt}) at TPP was compared for the three groups as shown in the bottom panel of Figure 6. An ANOVA showed a significant difference among means at 0.71, 4 and 5.66 kHz. Post hoc tests revealed a significant mean difference in L_{Wt} between NH and Oto groups at 0.71 and 4 kHz, between SNHL and Oto groups at 4 and 5.66 kHz, and between NH and SNHL groups at 4 kHz. Note that for both plots in Figure 6, the absorbed power for the SNHL group was higher than for the other two groups at 4 and 5.66 kHz.

For L_{Wt} at the PT, an ANOVA showed a significant difference among mean absorbance values at high frequencies: 2.83, 4 and 5.66 kHz (top panel, Figure 7). Post hoc analysis revealed a significant difference between the means for NH and SNHL groups at 2.83 kHz, and between the means for the SNHL and Oto groups at 4 and 5.66 kHz. An ANOVA for L_{Wt} for the NT showed a significant difference among groups at 1.41, 2.83, 4 and 5.66 kHz. Post hoc tests revealed a significant difference between means for the SNHL and Oto groups at 1.41, 4 and 5.66 kHz and between the SNHL and NH groups at 2.83, 4 and 5.66 kHz.

For the peak-to-tail difference for L_{Wt} at the PT, an ANOVA showed a significant difference among means at 2.83 and 5.66 kHz. Post hoc testing revealed a significant difference between the means for the NH and Oto groups at 2.83 kHz and between the means for the NH and SNHL groups at both 2.83 and 5.66 kHz (top panel, Figure 8). An ANOVA for the peak-to-tail differences in L_{Wt} for the NT showed a significant difference among the means for the three groups at 1.41, 2.83 and 4 kHz. Post hoc testing revealed a significant difference between the means for the SNHL and Oto groups at 1.41 kHz, between the NH and Oto groups at 2.83 and 4 kHz, and between the NH and SNHL groups at 4 kHz.

ROC Analyses for Absorbed Power—AUCs were calculated to quantify the accuracy of absorbed power to classify ears selected from various pairs of NH, SNHL and Oto groups. There were 10 cases in which the AUCs for measures of absorbed power were > 0.70 for comparisons of the Oto group with either the NH or SNHL groups or both, compared with 6 cases for absorbance measures (Table 1). L_{Wa} at 1.71 kHz had the largest AUC of 0.81 for the comparison of NH and Oto groups followed by L_{Wt} at 4 kHz for the peak-to-NT difference with an AUC of 0.80 for the comparison of NH and Oto groups. The highest AUC for the SNHL and Oto group comparison was also for L_{Wa} at 0.71 kHz with an AUC of 0.75.

Absorbed Power Pre- and Post-Op Comparisons—For the subset of 12 ears from the Oto group with pre- and post-op tests, the post-op mean L_{Wa} for the 3-month comparison

was greater than the pre-op mean at 1 kHz as shown in Figure 9 (upper left panel). An ANOVA revealed no significant main effect for the pre-op/post-op tests, but there was a significant test by frequency interaction. Paired samples t tests revealed that the 3-month post-op mean L_{Wd} was significantly greater than the pre-op mean at 1 kHz. A frequency by test ANOVA for L_{Wd} in the 10 subjects with pre-op and post-op data at 6-months (Figure 9, bottom left panel) did not show a significant main effect of test. However, there was a significant test by frequency interaction. Paired samples t tests revealed that the mean L_{Wd} at 1 kHz was greater for the post-op test at 6-months.

The pre- and post-op L_{Wt} data at 3 and 6 months at TPP are shown in the right column of Figure 9. The results were similar to the pre- and post-op L_{Wd} with greater post-op absorbed power around 1 kHz, but with somewhat smaller mean differences between groups compared to L_{Wd} in both cases. An ANOVA for the 12 subjects with a 3-month comparison to pre-op did not show a significant main effect of test or a significant test by frequency interaction. An ANOVA for the 6-month comparison of L_{Wt} at TPP with pre-op failed to show a significant effect of test, but there was a significant test by frequency interaction. Paired samples t tests for the 6-month L_{Wt} comparison revealed that the post-op mean L_{Wt} was greater than the pre-op mean at 1 kHz.

226 Hz Y_{tm}

The mean 226 Hz Y_{tm} for the three groups was similar: for the NH group, 0.69 mmho (SE=0.04 mmho), for the SNHL group, 0.67 (SE=0.07), and for the Oto group, 0.70 mmho (SE=0.08 mmho). An ANOVA revealed that these means were not significantly different. An ROC analysis for Y_{tm} for a comparison of the NH group and the Oto group resulted in an AUC of 0.53. A similar comparison between the SNHL and Oto groups resulted in an AUC of 0.49, both of which are indicative of chance performance.

DISCUSSION

Absorbance

Several previous studies have reported lower A_d in the frequencies below 1 kHz for ears with otosclerosis compared to NH ears in a small number of cases (Feeney et al. 2003; Allen et al. 2005) or in group data (Shahnaz et al. 2009a; Nakajima et al. 2012). The Oto group in the present study had lower absorbance for A_d than either control group from around 0.71 to 5.66 kHz, but this was only significant at 2.83 kHz in comparison with the SNHL group. This result was similar to the findings of Keefe et al. (2017b), who reported significantly lower A_d for their otosclerosis groups at 4 kHz. Interestingly, the only frequency where there was an AUC = 0.70 for A_d in the present study was at 0.71 kHz. However, group mean differences did not reach statistical significance at that frequency. Overall, the findings in the present study were similar to Keefe et al. 2017b, which did not show significantly lower A_d for subjects with otosclerosis in the frequencies below 1 kHz.

For A_t at TPP the Oto group had lower mean absorbance than the control groups from 2 to 4 kHz. However, the difference was only significant between the Oto and SNHL groups at 2.83 kHz, the same finding observed for A_d . Keefe et al. (2017b) is the only previous study

to evaluate ears with otosclerosis with A_t at TPP. That study reported lower A_t at TPP at 0.71 and 1 kHz for their otosclerosis group, similar to previously reported low-frequency group findings for A_a (Shahnaz et al. 2009a; Nakajima et al. 2012). AUCs for A_t at TPP were similar for the present study and Keefe et al. (2017b). Both studies also showed greater mean A_t peak-to-tail differences at high versus low frequencies. Keefe et al. reported an AUC of 0.87 for the peak-to-PT difference at 2.8 kHz, which was larger than for any other tympanometric condition in that study. Similarly, in the present study the peak-to-PT condition for 2.83 kHz was the second-highest AUC for absorbance variables at 0.73. There was also agreement between the studies for the peak-to-NT condition, with both studies having AUCs > 0.75 at 4 kHz.

Keefe et al. (2017b) used the same wideband absorbance method employed in the present study, but with a wider tympanometric pressure range of +200 to -300 daPa compared to ± 200 daPa in the present study. The otosclerosis and NH groups in Keefe et al. had similar age and sex distributions as in the present study, but with a smaller sample size: 23 NH ears and 12 ears with otosclerosis in their diagnosed group compared with 46 NH, 23 SNHL, and 23 Oto ears in the present study. Thus, differences in sample size may have contributed to group differences. The AC PTA for the Oto group in the present study was 57 dB HL with an average ABG of 28 dB, compared to Keefe et al. with an average AC PTA of 43 dB HL and an average ABG of 20 dB. This difference between otosclerosis groups, with greater hearing loss and ABGs in the present study, does not appear to account for differences between the studies. The absorbance results obtained by the present study and by Keefe et al. (2017b) may differ from other previously reported studies due to differences in equipment, probe design and processing software. Previous results obtained at ambient pressure may vary from findings at TPP due to the effect of middle ear pressure on the absorbance. Finally, the present study used $\frac{1}{2}$ octave measures of absorbance and absorbed power as was used by Keefe et al. (2017b). The data from the present study were also analyzed using $\frac{1}{6}$ octave averaging (not shown), and the findings between groups were similar to those obtained with $\frac{1}{2}$ octave averaging. This is consistent with the findings of Shahnaz and Bork (2006) who examined group differences in energy reflectance (1-absorbance) between Caucasian and Chinese subjects and reported that group differences observed with 248 frequencies between 0.25 and 6 kHz were replicated when the data were re-analyzed using $\frac{1}{6}$ and $\frac{1}{3}$ octave averaging.

Figure 10 shows mean absorbance at ambient pressure (top row) and TPP (bottom row) for the current study and for Keefe et al. (2017b) for the NH and SNHL groups (left column) and Oto groups (right column). The top left panel in Figure 10 shows that means for A_a for the NH and SNHL groups of the current study are greater than the means for Keefe et al. from 0.25 to 2.83 kHz. The differences between groups are reduced except at 8 kHz when measured at TPP as shown in the bottom left panel of Figure 10. This suggests that group differences based on measures at ambient pressure might be affected by differences in tympanometric pressure between groups. This is also demonstrated in Figure 2 for absorbance measures in which group differences between 0.5 and 1 kHz are reduced at TPP compared to ambient pressure. Similarly, for the right column of Figure 10, there are greater differences between the otosclerosis groups of the present study and that of Keefe et al. at 2 and 2.83 kHz compared to other frequencies. However, for the TPP measure (bottom right

panel) the SE bars overlap for the two groups at every frequency. For clinical practice, testing at TPP would eliminate the middle ear pressure bias for comparison with normative data.

Absorbed Power

This paper presented the first use of wideband absorbed power to evaluate ears with a ME disorder. Absorbed power shares a property with absorbance in that the value measured at the probe tip is equivalent to that measured at the TM assuming minimal losses at the ear canal, which generally holds for adult ears. This is an advantage in middle ear measurements that is not shared with admittance at the probe tip or group delay, which must be corrected for ear canal properties in order to evaluate ME status. Moreover, as described above, absorbed power may provide a means of assessing the effect of middle-ear disorders that is less affected than absorbance or forward pressure level by spatial variations in the sound field within the ear canal. As shown in Table 1, there were more instances where absorbed power performed better in detecting ears with otosclerosis than the corresponding absorbance values. There were only two instances of AUCs > 0.80 in the present study and they were both for comparisons of absorbed power between the Oto and NH groups: L_{Wa} at 0.71 kHz and L_{Wt} at TPP at 4 kHz. These findings are encouraging for including absorbed power in future WAI studies for the assessment of middle ear disorders.

Pre- and Post-op Comparisons

Following stapes surgery for otosclerosis at 3 and 6 months, there were increases in A_a and L_{Wa} at frequencies around 1 kHz. Similar results for longitudinal comparisons of A_a in pre- and post-op otosclerosis have been reported (Shahnaz et al. 2009b). This was also reported for absorbance and group delay in a group of patients who had stapes surgery compared to a group with a diagnosis of otosclerosis who did not have surgery (Keefe et al. 2017b).

The post-op pattern in WAI variables may provide useful information in assessing surgical outcome or changes in function following surgery. For example, if the connection between the incus and the prosthesis becomes loose, one might expect a larger absorbance or absorbed power peak near 1 kHz or below, or perhaps a shift of the absorbance peak to a lower frequency as in the case of a disarticulation (Feeney et al. 2009; Nakajima et al. 2013). The consistent trend in the mean absorbance and absorbed power data over the first 6 months is encouraging especially when assessed at TPP to offset ME pressure effects.

Age-related normative data

In general, the SNHL control group that was matched in age and sex to the Oto group had higher absorbance and absorbed power in the high frequencies than the NH group. This resulted in more significant differences between SNHL and Oto groups for ambient and TPP measures in the high frequencies. This was more pronounced for the absorbed power measures L_{Wa} and L_{Wt} at TPP than for absorbance. This high frequency effect is somewhat consistent with age effects in wideband absorbance data reported by Feeney & Sanford (2004) that showed high-frequency absorbance differences between a group of young adults with a mean age of 21.4 years compared to a group of older adults with a mean age of 71.6 years. In that study, the older group had higher absorbance at frequencies between around .8

to 2 kHz, but lower absorbance at 4 kHz. These findings suggest that improved test performance in detecting middle ear disorders with WAI may be obtained using age-related normative data.

Clinical Implications

The data from the present study on the detection of otosclerosis using absorbance measures is generally in agreement with data from Keefe et al. (2017b) that used the same equipment and procedures. The pattern of lower absorbance at frequencies below 1 kHz as reported in some previous studies using different equipment and procedures was not supported (e.g., Shahnaz et al. 2009a). One implication for clinical use given these findings is to obtain normative data for each clinic with the system employed locally rather than relying on published norms. Although more normative data are needed, it appears that it may be useful to use age-related norms for adults, as discussed in the previous section. Finally, an innovative approach for diagnosing ossicular disorders by combining information from absorbance with the audiogram is promising for improving test sensitivity and specificity (Nakajima et al. 2012).

Conclusions

The greatest difference between groups for wideband absorbance and absorbed power measures was observed for a comparison of the NH and Oto groups for L_{Wa} at 0.71 kHz with an AUC of 0.81 and for L_{Wt} for the peak-to-NT difference at 4 kHz with an AUC of 0.80. There was generally good agreement between the present study and Keefe et al. (2017b) for A_t peak-to-tail differences with high AUCs for both studies at 2.83 kHz for the peak-to-PT condition and at 4 kHz for the peak-to-NT condition. However, relative to the Oto group, the present study showed absorbance at TPP to be higher for the NH group at 4 kHz and for the SNHL group at 2.83 kHz, whereas Keefe et al. reported higher absorbance for the NH group at 0.7 and 1 kHz. Wideband assessment at TPP in ears with otosclerosis, especially in ears with excessive middle ear pressure, should result in improved comparisons with normative data. The use of a group that was age- and sex-matched to the Oto group generally resulted in greater differences between groups in the high frequencies for both absorbance and absorbed power at ambient pressure and TPP. This suggests that the use of age-related normative data for adult WAI may improve the effectiveness of these measures to assess middle ear disorders given the observed age-related increase in high-frequency absorbance and absorbed power consistent with previous findings. This study suggests that post-op absorbance and absorbed power are useful measures for monitoring changes in middle ear function. This property may be useful in monitoring the status of ears following stapes surgery.

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MPF, DHK and LLH collaborated on study design. DHK and DFF developed software for data collection and analysis and participated in data analysis. ACG and DBP collected data. MPF, ACG, DBP participated in data analysis, and MPF wrote the paper. All authors discussed the results and commented on the manuscript at all stages.

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Conflicts of Interest/Sources of Funding

This work was supported by NIH, NIDCD Grant DC010202. Douglas Keefe has an interest in the commercial development of devices to assess middle-ear function and measure otoacoustic emissions.

LIST OF ABBREVIATIONS

ABG	air-bone gap
AC	air conduction
ANOVA	analysis of variance
ASRT	acoustic stapedius reflex threshold
AUC	area under the ROC curve
BC	bone conduction
CGS	centimeter-gram-second
CT	computerized tomography
ER	energy reflectance
ME	middle ear
NH	normal hearing
NT	negative tail of the tympanogram at –200 daPa
Oto	otosclerosis group
post-op	post-operative
pre-op	pre-operative
PT	positive tail of the tympanogram +200 daPa
PTA	pure-tone average
ROC	receiver operating characteristic
SE	standard error
SNHL	sensorineural hearing loss
SPL	sound pressure level
SAA	static acoustic admittance
TEOAE	transient evoked otoacoustic emission

TPP	tympanometric peak pressure
TM	tympanic membrane
WAI	wideband acoustic immittance

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Figure 1.

Top panel: Mean pure-tone AC thresholds ± 1 SE for the 46 NH ears (open diamonds), the 23 ears with SNHL (open squares), and 23 ears of Oto subjects (filled triangles). Mean BC thresholds ± 1 SE of Oto subjects are also shown (filled inverted triangles, dashed line). Bottom panel: Pre-operative (PreOp) mean pure-tone AC thresholds (filled circles) and BC thresholds (filled triangles, dashed line) ± 1 SE for 12 Oto subjects who returned for a 3-month post-operative test. Also shown are mean 3-month post-operative (PostOp) AC

thresholds (open circles) and BC thresholds (open triangles, dashed line) ± 1 SE for the same 12 subjects for the 3-month post-operative test.

Figure 2.

Mean $\frac{1}{2}$ -octave absorbance ± 1 SE at ambient pressure (top panel) and tympanometric peak pressure (TPP, bottom panel) for the NH group (open circles) SNHL group (filled squares) and Oto group (open triangles). Symbols represent a significant difference between the NH and Oto groups (+), between the SNHL group and the Oto groups (*) and between the NH and SNHL groups (^).

Figure 3.

Mean $\frac{1}{2}$ -octave absorbance ± 1 SE at +200 daPa (PT, top panel) and -200 daPa (NT, bottom panel) for the NH group (open circles) SNHL group (filled squares) and Oto group (open triangles). Symbols represent a significant difference between the NH and Oto groups (+), between the SNHL group and the Oto groups (*) and between the NH and SNHL groups (^).

Figure 4.

Mean $\frac{1}{2}$ -octave absorbance ± 1 SE at TPP minus PT at +200 daPa (Peak-to-PT, top panel) and TPP minus NT at -200 daPa (Peak-to-NT, bottom panel) for the NH group (open circles) SNHL group (filled squares) and Oto group (open triangles). Symbols represent a significant difference between the NH and Oto groups (+), between the SNHL group and the Oto groups (*) and between the NH and SNHL groups (^).

Figure 5. Mean $\frac{1}{2}$ -octave Pre-op (open circles) and Post-op (filled squares) absorbance ± 1 SE at ambient pressure (left column) and tympanometric peak pressure right column at 3 months (top row, N=12) and 6 months (bottom row, N=10) for the Oto group. Asterisks signify significant differences between mean $\frac{1}{2}$ -octave measures for Pre-Op and Post-Op.

Figure 6.

Mean $\frac{1}{2}$ -octave absorbed power spectrum level ± 1 SE at ambient pressure (top panel) and tympanometric peak pressure (TPP, bottom panel) for the NH group (open circles), SNHL group (filled squares) and Oto group (open triangles). Symbols represent a significant difference between the NH and Oto groups (+), between the SNHL group and the Oto groups (*) and between the NH and SNHL groups (^).

Figure 7.

Mean $\frac{1}{2}$ -octave absorbed power spectrum level ± 1 SE at +200 daPa (PT, top panel) and -200 daPa (NT, bottom panel) for the NH group (open circles), SNHL group (filled squares) and Oto group (open triangles). Symbols represent a significant difference between the NH and Oto groups (+), between the SNHL group and the Oto groups (*) and between the NH and SNHL groups (^).

Figure 8.

Mean $\frac{1}{2}$ -octave difference in absorbed power ± 1 SE at the tympanometric peak pressure (TPP) minus PT at +200 daPa (Peak-to-PT, top panel) and TPP minus NT at -200 daPa (Peak-to-NT, bottom panel) for the NH group (open circles), SNHL group (filled squares) and Oto group (open triangles). Symbols represent a significant difference between the NH and Oto groups (+), between the SNHL group and the Oto groups (*) and between the NH and SNHL groups (^).

Figure 9.

Mean $\frac{1}{2}$ -octave Pre-op (open circles) and Post-op (filled squares) absorbed power spectrum level ± 1 SE at ambient pressure (left column) and TPP (right column) at 3 months (top row, N=12) and 6 months (bottom row, N=10) for the Oto groups. Asterisks signify significant differences between mean $\frac{1}{2}$ -octave measures for the two sub-groups.

Figure 10.

Mean 1/2-octave absorbance ± 1 SE for three groups from the current study and two groups from Keefe et al. (2017b). The left column represents results for both studies for the NH groups and for the current study for the SNHL group. The right column represents results for both the current study and the Keefe et al. study for the two groups with otosclerosis. The top row is for results at ambient pressure and the bottom row is for results at TPP.

Table 1.

Measurement variables with AUC values ≥ 0.70 for classifying ears as Oto or NH and Oto or SNHL for absorbance at ambient pressure (A_a); pressurized absorbance (A_p) at TPP, Peak-to-tail differences for the positive tail (Peak-to-PT) and negative tail (Peak-to-NT), and measures of ambient absorbed power (L_{Wa}) or pressurized absorbed power (L_{Wp}).

Measure	Frequency (kHz)	AUC NH	AUC SNHL
A_a	0.71	0.70	
A_p TPP	4.0	0.70	
A_p TPP	2.83		0.74
A_p Peak-to-PT	2.83	0.73	
A_p Peak-to-NT	2.83	0.70	
A_p Peak-to-NT	4.0	0.78	
L_{Wa}	0.25		0.71
L_{Wa}	0.71	0.81	0.75
L_{Wa}	1.0	0.77	0.73
L_{Wa}	5.66		0.70
L_{Wp} TPP	4.0		0.71
L_{Wp} Peak-to-PT	0.71	0.70	
L_{Wp} Peak-to-PT	2.83	0.72	
L_{Wp} Peak-to-NT	1.41		0.71
L_{Wp} Peak-to-NT	2.83	0.70	
L_{Wp} Peak-to-NT	4.0	0.80	0.72