Detecting changes in intracranial pressure using ear-canal reflectance and otoacoustic emissions

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Abstract

Intracranial pressure (ICP) monitoring is currently an invasive procedure that requires access to the intracranial space through an opening in the skull. Noninvasive monitoring of ICP via the auditory system is theoretically possible because changes in ICP transfer to the inner ear through connections between the cerebral spinal fluid and the cochlear fluids. In particular, measures of middle-ear transmission, including low-frequency distortion-product otoacoustic emissions (DPOAEs) and reflectance, measured noninvasively in the external ear canal, appear to depend on ICP. Postural changes in healthy humans cause systematic changes in ICP. Here, we demonstrate the effects of postural changes, and presumably ICP changes, on DPOAE magnitude, DPOAE angle, and the reflectance measures of power reflectance and transmittance. In general, DPOAE magnitudes decrease with increased ICP at frequencies from 500 to 2000 Hz, and the corresponding angle shows systematic changes in a given individual. Low-frequency power reflectance appears to increase systematically with increased ICP, while the corresponding transmittance decreases systematically. Preliminary results on intensive-care unit (ICU) patients undergoing medically necessary ICP monitoring demonstrate that repeated measurements on an ICU population have similar standard deviations to repeated measurements in the lab setting with healthy volunteer subjects.

Keywords: Intracranial pressure, Distortion product otoacoustic emissions, Reflectance

Abbreviations: DPOAE distortion product otoacoustic emissions; ICP intracranial pressure; TPP tympanic peak pressure; ICU intensive-care unit; MEP middle ear pressure.

1 Introduction

Noninvasive ear-canal based acoustical measurements have diagnostic potential in the area of neurology. A wide range of devastating brain pathologies (e.g., head injury, stroke, hydrocephalus, and brain surgery) cause brain swelling or bleeding. Because the skull is fixed in volume, increases in the volume of its contents result in increases in intracranial pressure (ICP). Elevations of ICP can lead to worsening brain injury or death by compressing blood vessels supplying the brain or vital brain structures themselves. Current tools used to evaluate ICP objectively (e.g., epidural transducers or intraventricular catheters) are invasive and require direct entry of a probe system through the skull, introducing risks that include infection, intracerebral hemorrhage, and direct brain injury (Filbotte, Lee, Koroshetz, Rosand, & McDonald, 2004). A noninvasive method for monitoring ICP would eliminate these risks.

The auditory system is sensitive to changes in ICP because the cochlear aqueduct connects the cerebral spinal fluid to the cochlear fluid; increases in ICP are transferred to increases in intracochlear pressure, which results in outward static displacements of the compliant oval and round windows. These ICP increases are most likely to be detected as reductions in middle-ear transmission that result from an increased stiffness of the annular ligament, which connects the stapes to the oval window (Büki et al., 2000; Büki, de Kleine, Wit, & Avan, 2002; Voss, Horton, Tabucchi, Folowosele, & Shera, 2006), with the effects of increased stiffness most prominent at frequencies below the middle ear's resonant frequency (< 2000 Hz).

Theoretically, different middle-ear transmission measurements could be used to detect ICP changes, including otoacoustic emissions (Büki et al., 1996; de Kleine, Wit, Van Dijk, & Avan, 2000; Frank et al., 2000; de Kleine, Wit, Avan, & Van Dijk, 2001; Büki et al., 2002; Voss et al., 2006), changes in middle-ear impedance (Magnano et al., 1994) and other related quantities such as reflectance, and changes in displacement patterns of the tympanic membrane (Marchbanks, 1984), which were later shown to be too variable to monitor ICP (Rosingh, Wit, & Albers, 1998; Shimbles, Dodd, Mendelow, & Chambers, 2005). An advantage of evoked otoacoustic emissions is that they are affected by two reductions in middle-ear transmission:

one in the forward direction as the stimulus and one in the reverse direction as the emission (Voss & Shera, 2004); a limitation is that the emissions may be weak or absent in individuals with a hearing loss. Thus, the potential for monitoring changes in ICP through concomitant changes in middle-ear transmission should be evaluated using multiple measures, and here we quantify how both distortion product otoacoustic emissions (DPOAEs) and reflectance, which is related to impedance measures (e.g., Voss & Allen, 1994; Allen, Jeng, & Levitt, 2005), are affected by changes in ICP.

Recent work demonstrates systematic effects of postural changes, which induce ICP changes (Chapman, Cosman, & Arnold, 1990), on low-frequency DPOAE magnitudes when measured on normal-hearing subjects (Voss et al., 2006). This preliminary work from Voss et al. (2006) is the basis for the more detailed set of measurements presented in the current paper, where the effects of postural changes, and presumably ICP changes, are studied for DPOAE magnitudes, DPOAE angles, power reflectance and transmittance measured in the ear canal. Here, the intra-subject variability of these measures is also compared to the variability of the measurements when they are made in a hospital intensive-care-unit (ICU) setting.

2 Material and Methods

2.1 Overview

Measurements of DPOAE magnitudes, DPOAE angles, power reflectance, and transmittance were made to characterize how posture, and presumably intracranial pressure (ICP), affects these three measures. Additionally, the intra-subject variability for all three measures is quantified through repeated measurements on both lab-based subjects and ICU hospital patients undergoing invasive and medically necessary ICP monitoring.

2.2 Human Subjects

Measurements are reported from two sets of subjects: "Lab" and "ICU". The "Lab" group includes 12 normal-hearing healthy subjects (24 ears), ages 19 to 42 years, all with a negative history for middle-ear problems, hearing thresholds below 20 dB HL at 500, 1000, 2000, and 4000 Hz, and normal tympanograms. Eight additional subjects were recruited but did not complete five measurement sessions because of the time required or discomfort with being tilted at −45 degrees. The "ICU" group includes four subjects (6 ears) selected from a larger population of subjects recruited through the Neurocritical Care Unit at the Massachusetts General Hospital. These ears were selected as the subset of ears with the largest number of repeated measurements on subjects with the least variation in middle-ear pressure and intracranial pressure. Auditory testing was not available for the ICU subjects. Both sets of subjects were given an otoscopic examination to ensure no excessive ear wax was present in the ear canal. The measurements were approved by the Smith College and Massachusetts General Hospital Institutional Review Boards, and informed consent was obtained from all subjects or their surrogates.

2.3 Acoustic Measurement Equipment

DPOAE magnitudes and angles and reflectance measurements were made with an Etymotic ER-10c probe using software and hardware developed by Mimosa Acoustics (HearID v4.0.13). To maximize the DPOAE magnitude response at the frequency $f_{\mathrm{dp}} = 2f_1 - f_2$ at the lower frequencies, we fixed $f_2/f_1 = 1.25$ and $L_1 = L_2 = 75$ dB SPL (Lim, Bauer, Horton, & Voss, 2007); DPOAEs were measured at 13 log-spaced frequencies from approximately 500 to 4000 Hz. Response magnitudes were obtained from the discrete Fourier transform of the time-domain average of N responses. The number of responses N varied with noise level, with a maximum N=420. The artifact rejection algorithm with HearID was used so that noisy buffers were not included in the averaging; averaging was automatically stopped before N=420 when the signal-to-noise ratio exceeded 15 dB. The noise floor was estimated from a narrow frequency band surrounding the response measured at $f_{\rm dp}$, and data that fell less than 6 dB above the estimated noise floor were eliminated (Roede, Harris, Probst, & Xu, 1993). Reflectance and impedance quantities were calculated, as described in the HearID users manual or in Voss and Allen (1994) or Allen et al. (2005), from pressure measurements made in the ear canal at a level of 75 dB SPL across a broad-band frequency range. Briefly, pressure reflectance R is calculated directly from the impedance, and the pressure reflectance is the complex ratio between the reflected pressure and the incident pressure. The power reflectance is the square of the magnitude of the pressure reflectance $|R|^2$, and the power reflectance can be interpreted as the fraction of power reflected in the ear canal and at the tympanic membrane. Transmittance T in units of dB was calculated from pressure reflectance R as

$$T = 10\log(1 - |R|^2). \quad (1)$$

As described by Allen et al. (2005), the transmittance is a useful quantity because its dB scale reduces the variability in power reflectance at the lower and higher frequencies and also provides a measure that might best relate to hearing levels.

2.4 Measurement Protocol: "Lab" Subjects

Subjects were placed on a tilting table (Hangups®II Inversion Table) at two postural positions: upright (90° relative to the horizontal) and tilted (−45° relative to the horizontal). The estimated ICPs of the subjects at these two positions are 0 mmHg at 90° and 22 mmHg at −45°(Chapman et al., 1990; de Kleine et al., 2000; Voss et al., 2006). Each subject participated in a total of five measurement sessions across five different days. During each session, measurements of DPOAEs and reflectance were made in each of the left and right ears at both upright and tilted positions. Thus, a total of 20 measurements of DPOAEs and reflectance were made on each of the 12 subjects (5 sessions ×2 ears ×2 positions) for a total of 240 measurements. For each ear, measurements were made in the following order. First, the subject was placed on the tilt table in the upright position. Tympanometry (Earscan, Micro

Audiometrics Corp., ES-T) was used to monitor middle-ear pressure MEP (assumed equal to the tympanic peak pressure TPP). In order to maintain the MEP as close to zero as possible, the subject was asked to swallow; in cases where MEP differed by more than ± 25 kPa from zero, subjects were encouraged to continue swallowing until either the MEP was within ± 25 kPa of zero or the subject demonstrated an inability to equalize his or her MEP to zero. Once the MEP was documented and as close to zero as possible, the ER-10c's foam plug was placed in the ear canal and consecutive measurements of DPOAEs and reflectance were made. Next, the subject was tilted to the $-45°$ position. After tilting, emission measurements reach stability (presumably a stable ICP) within 30 seconds (de Kleine et al., 2000), so subjects were tilted for one minute before additional measurements were made. At this position, the MEP sequence described above was repeated, and followed by measurements of DPOAEs and reflectance at the tilted position.

2.5 Measurement Protocol: "ICU" Subjects

Subjects recruited through the ICU were being monitored for medical reasons for changes in ICP. Tympanometry (as described above), DPOAEs, and reflectance were measured repeatedly on these subjects over time periods of several hours that spanned up to three days. In order to compare the intra-subject variation in our lab-based, normal-hearing subjects to this hospital population, we have selected six ears with multiple measurements of DPOAEs and reflectance and with limited variations in MEP and ICP. Specifically, for each of the six subjects, we analyze the subset of the individual's DPOAE and reflectance measurements that had a corresponding MEP within ± 25 daPa of that subjects median MEP and an ICP within ± 3mmHg of that subjects median ICP. Given these constraints, the number of measurements on each of the six ears is: 6 (Subject 38), 8 (Subject 41), 5 (Subject 44 left), 6 (Subject 44 right), 8 (Subject 45 left), and 18 (Subject 45 right).

2.6 Data Analysis

All DPOAE data within 6 dB of the noise floor were removed (Roede et al., 1993). Additionally, some measurements from the lab subjects were discarded for artifactually high levels. After all measurements were made, some measurements were observed to have much higher DPOAE magnitudes (> 30 dB SPL) than a typical measurement. These measurements were outliers in both DPOAE magnitudes (much higher than other measurements) and phase (nearly constant phase across most frequencies). These measurements were reproduced in a cavity by making many repeated measurements of DPOAEs in a cavity; most DPOAE measurements were within the noise (low distortion), but occasionally, a high level of distortion was measured in the cavity with characteristics similar to what we observed in our outlier data. It appears that the PC-card used during these measurements could enter an unstable mode. We systematically swapped out pieces of the HearID system and discovered that the distortion only appeared with this particular card. Once the card was retired, no more measurements with high levels of distortion were observed. None of the hospital-based measurements were made with the unstable PC-card. Of the 240 measurements made on the lab-based subjects, we eliminated 24 measurements (10%). Of the 240 measurements, the number of measurements discarded for high distortion levels is indicated in parenthesis for the specific situation: Left ear upright (one measurement on each of six subjects, N=6), right ear upright (one measurement on each of four subjects and two on one subject, N=6), left ear tilted (one measurement on each of six subjects, N=6), and right ear tilted (one measurement on each of four subjects and two on one subject, N=6). Generally, when one measurement of an upright / tilted combination showed distortion, the other measurement also showed distortion; there were only two exceptions to this generalization.

2.7 Statistical Analyses

Descriptive statistics (means, medians, standard deviations) are computed to describe the data. These quantities are calculated for cases when three or more data points exist. For fewer than three data points, no mean, median, or standard deviation is reported. (Fewer than three data points can result in cases where data were eliminated due to noise floors or distortion.)

The null hypothesis that data collected at the two postural positions are different was tested by calculating p values with a permutation test with 10,000 iterations (and replacement), as described by Efron and Tibshirani (1993). The test used distances calculated between mean values for the data collected at each of the two postures. Individual p values were calculated for each subject at each frequency for the four quantities: DPOAE magnitudes, DPOAE angles, power reflectance, and transmittance.

3 Results

3.1 Middle-ear pressures

The tympanic peak pressure or middle-ear pressure (MEP) was measured before each DPOAE and reflectance measurement session. Figure 1 reports these MEPs for each ear at each of the two postural positions. The MEP from 23 of the 24 ears is always within ± 30 daPa of zero when the subject is in the upright position; the exception is the left ear of Subject 9, which ranges from -66 to -30 daPa in the upright position. When the subject is tilted, 14 of these 23 ears remain within ± 30 daPa of zero. The ten ears that are not always within ± 30 daPa of zero tend to show increases in MEP between the upright position and the tilted position.

There are a total of 108 pressure measurements in the upright position and 108 measurements in the tilted position; 106 of these measurements are common to measurements made consecutively in the upright and tilted position, resulting in the ability to calculate 106 changes in pressure between the upright and tilted position. If we define ΔMEP as $\Delta\text{MEP} \equiv \text{MEP}_{\text{upright}} - \text{MEP}_{\text{tilted}}$, then of the 106 measurements of ΔMEP, 7 cases have $\Delta\text{MEP} = 6$ daPa, 13 cases have $\Delta\text{MEP} = 0$ daPa, 53 cases have $-30 \leq \Delta\text{MEP} < 0$ daPa, 21 cases have $-60 \leq \Delta\text{MEP} < -30$ daPa, and 12 cases have $-90 \leq \Delta\text{MEP} < -60$.

3.2 Measurements on "Lab" subjects: Upright and Tilted

Distortion product otoacoustic emissions (DPOAE) and reflectance were measured on 24 ears from 12 subjects. Figure 2 shows an example of these measurements from Subject 4 (chosen at random from the 12 subjects, using the "rand" function in Matlab). The results from this example (Subject 4) are comparable with those from the other 11 subjects (not shown). Figure 2 (left column) plots the DPOAE magnitude results. The upper and middle plots show the DPOAE magnitudes measured on the left and right ears with the subject in the upright position (left at the top in blue and right in the middle in red) and the tilted position (green). The lower plot shows the differences for each ear between the DPOAE magnitudes in the upright and tilted positions. Both here and in the other 11 subjects, the low-frequency DPOAE magnitudes systematically decrease when the subject is tilted. For frequencies above 1500 to 2000 Hz, the differences between upright and tilted position decrease substantially and are not generally systematically different from zero.

Figure 2 (left-middle column) plots the DPOAE angle results. The upper and middle plots show the DPOAE angles measured on the left and right ears with the subject in the upright position (left at the top in blue and right in the middle in red) and the tilted position (green). Across all frequencies, there are systematic changes between the upright and the tilted positions. For most frequencies the tilted position leads to increases in the angle, which vary from a small fraction of a cycle to more than a quarter of a cycle. The change in angle depends on both frequency and the specific ear. This observation of a systematic change in angle between the upright and tilted positions seen here for Subject 4 is consistent with the measurements on all other ears. In some of the other ears, the change in angle is a reduction in angle instead of an increase in angle when tilted; however, the repeatable and steady change between the two positions occurs across all ears.

Figure 2 also plots the power reflectance (right-middle column) and the transmittance (right column). Here, below 1500 Hz there are systematic changes in power reflectance and transmittance between the upright and tilted positions; when the subject is tilted, the power reflectance increases at these lower frequencies and the transmittance decreases. Above about 1500 Hz, changes are less apparent. These systematic changes in the power reflectance and transmittance between the upright and tilted positions generally occurs on the ears from the other 11 subjects. However, there are six cases (from 24 ears) in which some (but not all) of the tilted reflectance and transmittance measurements overlap at low frequencies with the upright measurements; in these cases, there is more variation in the repeated measurements than what is shown by Subject 4 in Fig. 2.

3.3 Changes in DPOAE and reflectance measurements with changes in ICP

For each measurement session on each ear, the difference between the DPOAE magnitude, DPOAE angle, power reflectance and transmittance in the upright and tilted positions was calculated, and the mean difference for each ear is plotted (Fig. 3 upper row). The upper-left plot shows that the median of the mean DPOAE magnitude differences increases from about 10 dB at 500 Hz to 13 dB at 1000 Hz, decreases to 7 dB at 1400 Hz, and then decreases to nearly zero above 2000 Hz. All measurements on all ears show this general pattern of larger low-frequency differences and small to nearly no differences above about 2000 Hz. Thus, DPOAE magnitudes are systematically reduced at frequencies below 1500 Hz when a subject is tilted, and presumably experiences an increase in ICP. The middle-left plot (Fig. 3) shows that the median of the mean DPOAE angle differences is systematically different from zero. For most subjects at most frequencies, the angle difference is on the order of -0.10 to -0.25 cycles. Thus, DPOAE angles appear to be systematically changed from normal at all frequencies in the 500 to 4000 Hz range when a subject it tilted, and presumably experiences an increase in ICP. The middle-right plot shows that the median of the mean power reflectance differences is systematically different from zero at lower frequencies; below 1500 Hz, most ears show mean changes that range from -0.05 to -0.25. Above 1500 Hz, the changes are smaller and are both positive and negative, with a median that hovers near zero. The transmittance has a corresponding change for frequencies below 1500 Hz (right plot). In summary, changes in reflectance measures between the upright and tilted positions appear to be systematically different from zero at frequencies below 1500 Hz.

Figure 3 (lower row) plots p values computed to test whether or not the data collected at the two positions (upright and tilted) are different. The p values support the hypothesis that systematic changes occur in DPOAE magnitudes and angles and reflectance measures when the subject is tilted and presumably experiences an increase in ICP. The DPOAE magnitudes show their strongest changes at the lowest frequencies, with a median p value below 0.01 for frequencies below about 1500 Hz. Above about 2000 Hz, the DPOAE magnitudes become more similar between the two conditions and the p values associated with DPOAE magnitudes measured at the two positions increase above 0.05. In contrast to the DPOAE magnitudes, the DPOAE angles have a median p value below 0.05 across the entire frequency range of 500 to 4000 Hz; above 3000 Hz the 25 to 75% range approaches 0.5, but below 3000 Hz the p values associated with DPOAE angles are generally below 0.05. Thus, the DPOAE angle may include important information up to at least 3000 Hz for distinguishing changes in ICP. The reflectance measures (power reflectance and transmittance) show their smallest p values at the lowest frequencies. Below about 1000 Hz, the majority of p values associated with changes in reflectance measures are well below p=0.05. However, above 1000 Hz the median p value exceeds 0.05 and it seems that reflectance measures are not a reliable measure for distinguishing between the postures of the subjects, and presumably their corresponding ICP.

The pink dashed lines in all of the plots of Fig. 3 correspond to three ears that include 10 of the 12 largest changes in middle-ear pressure (ΔMEP). There is no evidence that the results from these ears with larger ΔMEP changes differ systematically from ears with smaller changes in ΔMEP.

3.4 Intra-subject variability of measurements

Multiple measurements of DPOAE magnitudes, DPOAE angles, and reflectance were made on each subject for three measurement conditions: lab subjects (upright), lab subjects (tilted), and hospital-based intensive-care-unit (ICU) patients. Figure 4 plots the standard deviations of the multiple measurements for each individual ear for each condition. For the lab subjects in the upright position, DPOAE magnitudes have standard deviations between about 1 and 2 dB SPL (25 to 75% range) for the frequency range of 500 to 4000 Hz (Fig. 4, upper left). The tilted condition for the lab subjects (Fig. 4, upper-middle row) and the ICU subjects (Fig. 4, upper right) have a slightly larger 25 to 75% range of about 1.5 to 3 dB SPL for frequencies below 2000 Hz and have a similar range to the upright condition above 2000 Hz. The standard deviations for the DPOAE angles (Fig. 4 upper-middle row) are the smallest for the lab subjects in the upright position, with a 25 to 75% range generally within about 0.01 to 0.04 cycles (depending on frequency). The range for the tilted lab subjects and the ICU patients is somewhat larger, ranging from about 0.02 to 0.06 cycles at most frequencies. The standard deviations for the power reflectance (Fig. 4, lower-middle row) have medians that hover near 0.05 for all three conditions, with a 25 to 75% range that is smaller for the upright lab subjects and the ICU patients than for the tilted lab subjects. For frequencies below about 2000 Hz, the tilted lab subjects have a larger range of standard deviations that approach 0.1 for some frequencies. The standard deviations for the transmittance (Fig. 4, lower row) have medians that are generally between 0 and 1 dB, but are larger in the tilted condition for frequencies below 1000 Hz.

We note that for all lab subjects plots (upright and tilted) in Fig. 4, individual standard deviations that fall outside of the gray shaded regions are not dominated by ears with larger ranges in middle-ear pressure (Fig. 1).

4 Discussion

4.1 Summary of Results

DPOAE magnitudes, DPOAE angles, power reflectance, and transmittance all showed systematic changes with posture, and presumably with ICP (Figs. 2 and 3). DPOAE magnitudes had the strongest separation between upright and tilted positions: for frequencies below 1500 Hz the DPOAE magnitudes resulted in the smallest p values of all measurements for the range of $500 < f_2 < 1500$. Considering all four measures, DPOAE angles showed consistent separation between the postures across the largest frequency range, with the majority of measurements having p values below 0.05 from $500 < f_2 < 3000$. The reflectance measures (power reflectance and transmittance) show systematic changes that are statistically significant with $p < 0.05$ only for the lowest frequencies: below about 1000 Hz the median and the majority of measurements have $p < 0.05$, however, just above 1000 Hz, the number of ears for which the p value exceeds 0.05 increases to more than half. Thus, reflectance measures appear to provide meaningful information regarding posture, and presumably ICP, for frequencies below about 1000 Hz.

Multiple measurements on the same ear, repeated during different sessions on different days, provide data regarding the variability of DPOAE magnitudes, DPOAE angles, and reflectance. We report standard deviations as a measure of repeatability of these measurements (Figure 4). In general, the DPOAE magnitude standard deviations in the upright position appear lower than or comparable to other reports in the literature (Franklin, McCoy, Martin, & Lonsbury-Martin, 1992; Roede et al., 1993; Zhao & Stephens, 1999; Beattie, Kenworthy, & Luna, 2003; Wagner, Heppelmann, Vonthein, & Zenner, 2008). Here, the standard deviations in the tilted position and the ICU environment are generally slightly larger than those in the upright position but are still comparable to standard deviations reported in the literature. Similarly, the standard deviations for the DPOAE angles and reflectance measures are somewhat smaller for the upright position, as compared to the tilted position and the ICU environment; nonetheless, it appears that measurements in the ICU environment do not have dramatically different levels of variability than those in the lab setting.

4.2 Interpretation of the standard deviations

The reported standard deviations in the measured quantities provide a metric to determine if a change in DPOAE is a true change or a random variation. For example, if one starts with a good estimate for the mean of either the DPOAE magnitude, DPOAE angle, or reflectance (perhaps obtained from multiple measurements when the subject is known to be in a normal state), then a change in condition (e.g., increase in ICP) can be suspected at a 95% chance if a new measurement of the same quantity differs from the original estimate by more than two times the standard deviation. As an example, consider the median standard deviation data in Fig. 4 for the normal upright subjects. Here, the median of the standard deviations of the DPOAE magnitudes is between 1 and 2 at all frequencies; thus, for a subject with a similar standard deviation, changes in DPOAE magnitude between 2 and 4 dB would suggest a change in condition for that subject. Similarly, the mean DPOAE angle standard deviation is between 0.02 and 0.03, leading to changes on the order of 0.04 to 0.06 in angle required to suggest a change in condition. The power reflectance standard deviation median is about 0.05 at most frequencies, requiring a change on the order of 0.1 required to suggest a change in condition, and the transmittance standard deviation median is about 0.5 dB, requiring a change on the order of 1 dB to suggest a change in condition.

4.3 Effects of middle-ear static pressure

Changes in middle-ear static pressure present a complication to our use of middle-ear transmission to monitor changes in ICP. It is widely recognized that static pressure differences across the tympanic membrane, with either positive or negative middle-ear pressures, affect middle-ear function and thus DPOAEs (e.g., Huttenbrink, 1988; Hauser, Probst, & Harris, 1993; Osterhammel, Nielsen, & Rasmussen, 1993; Plinkert, Bootz, & Voßieck, 1994; Sun & Shaver, 2009) and reflectance (e.g., Keefe & Levi, 1996; Feeney, Grant, & Marryott, 2003; Voss, Moonshiram, & Horton, 2008). Specifically, for low frequency DPOAEs, the DPOAE magnitude has been shown to decrease with nonzero middle-ear pressures (e.g., Huttenbrink, 1988; Hauser et al., 1993; Osterhammel et al., 1993; Plinkert et al., 1994; Sun & Shaver, 2009). Sun and Shaver (2009) provide the most systematic data related to the effect of middle-ear pressure on DPOAE magnitude, showing that middle-ear pressures of -40 to -65 daPa lead to low-frequency reductions in DPOAE magnitudes of 4 to 6 dB, and as middle-ear pressures decrease below -65 daPa, the DPOAE magnitudes are reduced further at low frequencies. Work from our group on human cadaver ears shows that middle-ear pressures as small as ± 50 daPa lead to frequency-dependent changes in reflectance that are largest at lower frequencies, and can affect the reflectance from at least 200 to 6000 Hz (Voss et al., 2008).

In the measurement protocol here, the subjects went from an upright to a tilted position, and this change in position appears to sometimes lead to increases in middle-ear pressure (Fig. 1), resulting in the change in pressure being negative (upright pressure minus tilted pressure). We hypothesize that as a subject is tilted, and the ICP increases, the stapes equilibrium position shifts so that the stapes is pushed into the middle ear by the increased ICP and corresponding increased intracochlear pressure. This shift in the stapes has at least two effects: (1) the volume of the middle-ear air space is reduced, which leads to an increase in the pressure within the air space, and (2) the stiffness of the annular ligament is changed (presumably increased) as the stapes is pushed out of its normal equilibrium position. In our protocol, subjects were asked to swallow multiple times after being tilted, so that any increase in middle-ear pressure would be eliminated via opening of the Eustachian tube. We assessed middle-ear pressure via the TPP from tympanometry, which reports the ear-canal static pressure for which the admittance is a maximum; this assumption that TPP is equivalent to middle-ear pressure when the stapes is not beginning in its equilibrium position at ambient pressure has not been tested. Thus, our measured changes in middle-ear pressure between the upright and tilted position could occur (1) because the subject was unable to equalize his or her middle-ear pressure via the Eustachian tube and a true pressure differential exists or (2) the measure of TPP could be inaccurate in some subjects when the stapes is not in its equilibrium position at an ambient middle-ear pressure.

In our data set of 106 sequences (from 24 ears) of measurements with the subject first upright and then tilted, the change in middle-ear pressure between the two positions was between −30 and +6 daPa for 72 of the 106 measurements; thus, in 68% of our cases the middle-ear pressure changes were minimal. An additional 21 cases had changes between −30 and −60 daPa, and 12 cases had changes between −60 and −90 daPa. The reasons for these larger changes might be one of the two reasons hypothesized above: either the subject was unable to equilibrate his or her pressure or the measure of TPP is an inaccurate measure of middle-ear pressure. Nonetheless, the changes in pressure we estimate are generally small. As a further test of the effect of changes in middle-ear pressure, we highlight the three ears that include 10 of the 12 largest pressure differences measured via TPP. As shown in Fig. 3, these ears are not outliers in the measures of mean changes (between upright and tilted) or p values for any of the measured quantities (DPOAE magnitudes, DPOAE angles, power reflectance, and transmittance).

4.4 Clinical application of monitoring ICP with ear-canal based measurements

Changes in middle-ear transmission appear to offer a noninvasive method to monitor ICP changes. Systematic changes in both DPOAEs and reflectance measures occur with posture changes (and presumably increases in ICP); in normal-hearing patients, a combination of DPOAE and reflectance measures are a candidate for noninvasive detection of changes in ICP. (DPOAE measures require a functioning inner ear, while reflectance measures require a normal middle ear.) The work here demonstrates the ability to measure DPOAEs and reflectance in a noisy hospital setting with standard deviations (and noise floors) comparable to those obtained in the controlled and quiet lab environment. The method of detecting changes in middle-ear transmission as an indicator for changes in ICP will not lead to numerical estimates for ICP, but instead will provide a metric for detecting changes in ICP; this method therefore requires at least one and preferably a series of baseline measurements from each patient in a particular state. In the long term, the DPOAE and reflectance measurement system might be designed with a built-in tympanometric measurement system that could monitor and compensate for middle-ear pressure. Situations where this method to monitor ICP might be particularly useful include long-term monitoring of patients with potential for changes in ICP (e.g., hydrocephalus, brain tumors), post-surgical monitoring of ICP, and monitoring of ambulatory patients during transport to medical facilities (e.g., traumatic injuries such as acquired via traffic accidents or in the military field).

4.5 Unanswered Questions

The use of a metric that uses changes in middle-ear transmission to detect changes in ICP requires more work. Future work might explore methods to combine (1) the information from DPOAE magnitudes and angles and reflectance measures into a single metric and (2) a magnitude and angle analysis in the complex plane (Adegoke, Voss, Horton, Raza, & Shera, 2008) to determine how points affected by noise might be identified in ways different than imposing an elimination of points with DPOAE magnitudes within 6 dB of the noise floor. Current measurements on ICU patients have demonstrated that DPOAE and reflectance measurements can be made in the noisy ICU environment with standard deviations similar to those in the lab; however, it is not possible to correlate most of these measurements with changes in ICP because the ICP of the patients in the ICU is medically controlled, leading to minimal changes in ICP. Future measurements will need to focus on additional populations with more variability in ICP (e.g., pseudotumor celebri and hydrocephalus patients would be good candidate populations).

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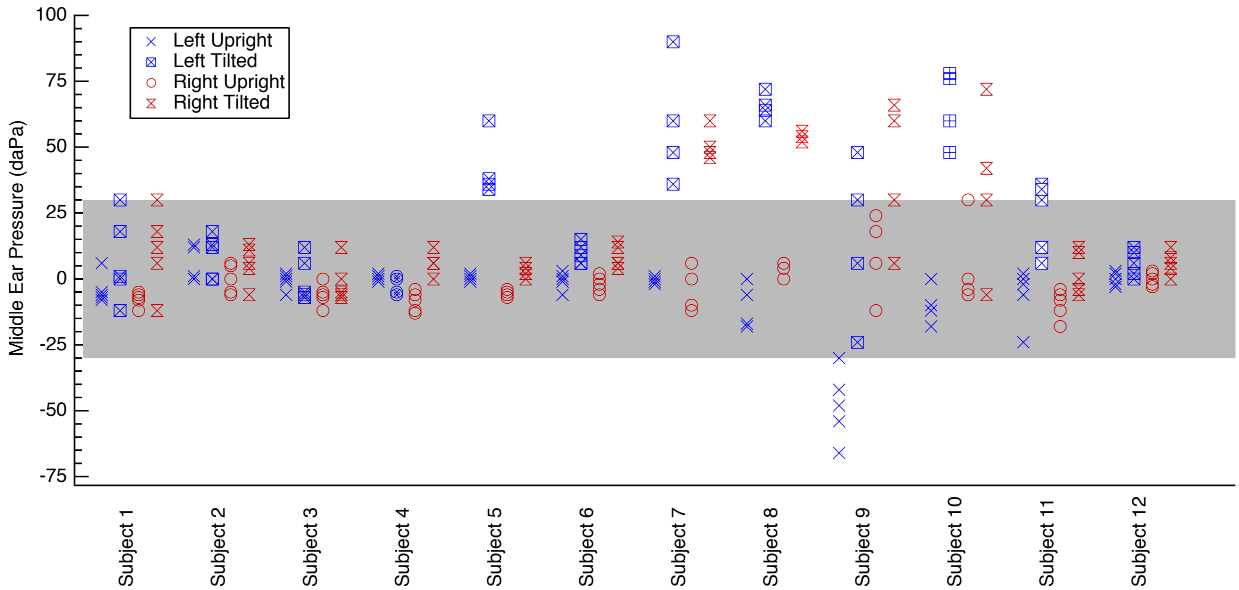
List of Figures


Left Upright
Left Tilted
Right Upright
Right Tilted
Middle Ear Pressure (daPa)
100
75
50
25
0
-25
-50
-75
Subject 1
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Subject 3
Subject 4
Subject 5
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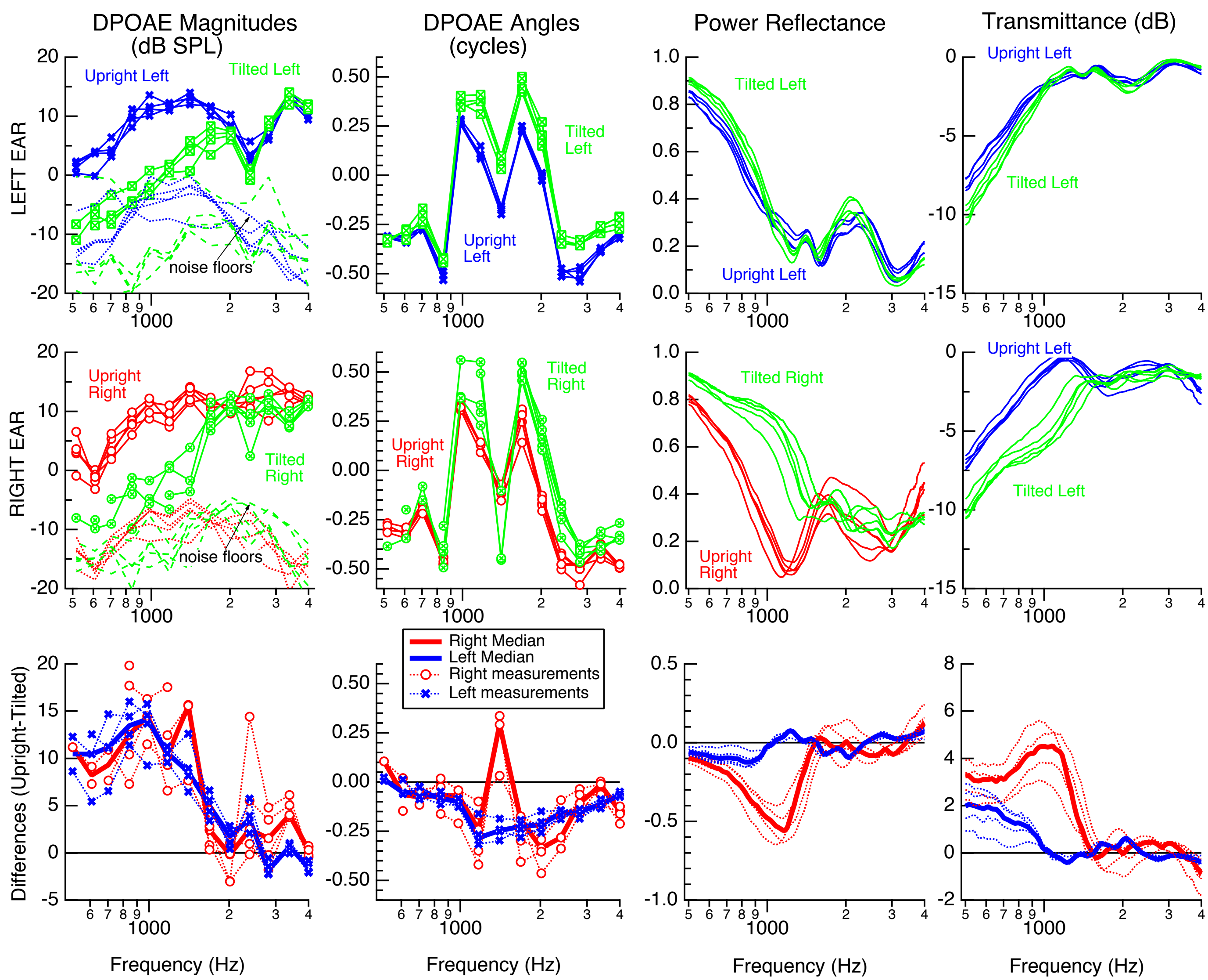
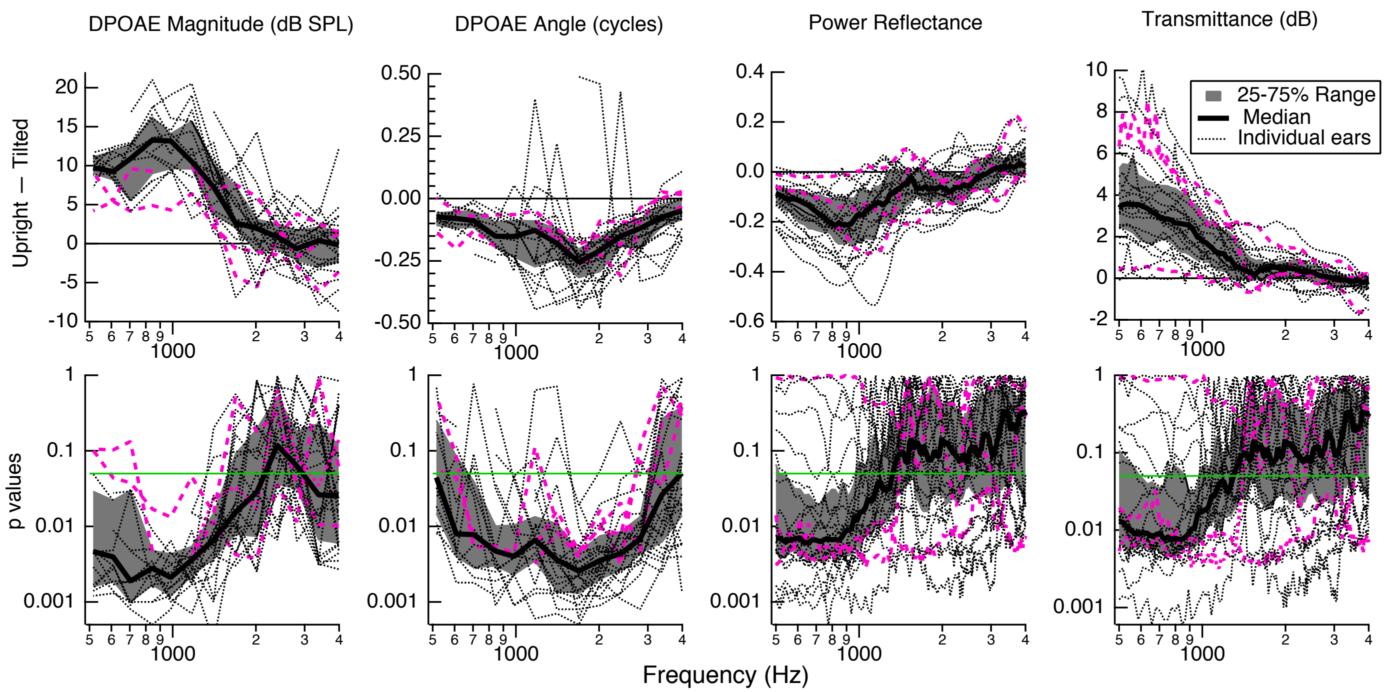
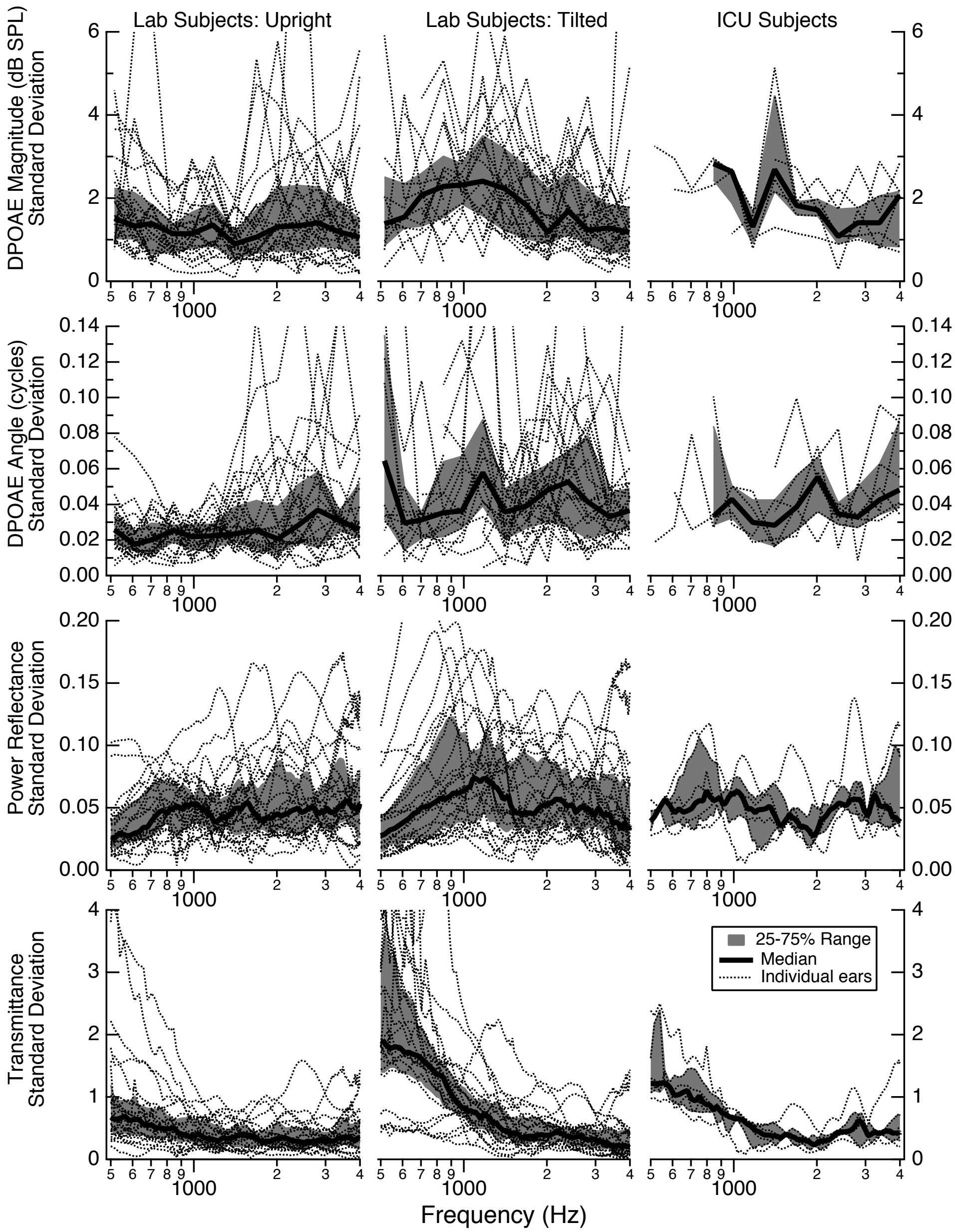
Subject 9
Subject 10
Subject 11
Subject 12


DPOAE Magnitudes (dB SPL)
DPOAE Angles (cycles)
Power Reflectance
Transmittance (dB)
LEFT EAR
RIGHT EAR
Differences (Upright-Tilted)
Upright Left
Tilted Left
noise floors
Upright Right
Tilted Right
Right Median
Left Median
Right measurements
Left measurements
Frequency (Hz)



DPOAE Magnitude (dB SPL)
DPOAE Angle (cycles)
Power Reflectance
Transmittance (dB)
25-75% Range
Median
Individual ears
Upright — Tilted
p values
Frequency (Hz)
1000


Lab Subjects: Upright
Lab Subjects: Tilted
ICU Subjects
DPOAE Magnitude (dB SPL) Standard Deviation
DPOAE Angle (cycles) Standard Deviation
Power Reflectance Standard Deviation
Transmittance Standard Deviation
25-75% Range
Median
Individual ears
Frequency (Hz)