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A Method to Assess the Accuracy of Sonotubometry for Detecting Eustachian Tube Openings

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Abstract

Objective—Sonotubometry is a simple test for Eustachian tube opening during a maneuver. Different sonotubometry configurations were suggested to maximize test accuracy, but no method has been described for comparing sonotubometry test results with those for a definitive measure of Eustachian tube opening. Here, we present such a method and exemplify its use by an accuracy assessment of a simple sonotubometry configuration.

Methods—A total of 502 data-sequences from 168 test sessions in 103 adult subjects were analyzed. For each session, subjects were seated in a pressure chamber and relative middle ear over- and under-pressures created by changing chamber pressure. At each pressure, the test sequence of bilateral tympanometry, bilateral sonotubometry while the subject swallowed twice, and bilateral tympanometry was done. Tympanometric data were expressed as the fractional gradient equilibrated (FGE) by swallowing and sonotubometric signals were analyzed to record the shape of detected sound-signals. Tympanometric and sonotubometric tubal opening assignments were analyzed by cross-correlation.

Results—For the data-sequences with FGE=0 (n=32) evidencing no tubal opening and 1 (n=249) evidencing definitive tubal opening, detection of a sonotubometry sound-signal during a swallow had a sensitivity and specificity of 74.2% and 65.6% for identifying ET openings and an accuracy of 73.3% for assigning ET opening/non-opening by swallowing. Measures of sound-signal shape were significantly different between those groups.

Conclusions—This protocol allows a sonotubometry accuracy assessment for detecting Eustachian tube openings. For the test configuration used, accuracy was moderate, but this should improve as more sophisticated sonotubometry test configurations are evaluated.

Keywords

Eustachian tube; Adults; Sonotubometry; Methodology

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CONFLICT OF INTEREST STATEMENT

None of the authors has a real or potential conflict of interest to declare regarding the materials presented in this manuscript.

INTRODUCTION

The preservation of middle-ear (ME) health and “normal” hearing requires that ME pressure be maintained at near-ambient levels.[1] While, the ME-ambient pressure balance is continuously being disturbed by changes in atmospheric pressure attributable to changes in elevation and the movement of weather fronts and by physiologic process that cause a net decrease in ME pressure over time, periodic, active openings of the Eustachian tube (ET) re-set the extant ME-ambient pressure gradients to near 0 daPa.[2] Thus, active ET opening is the homeostatic process that maintains a semi-stable ME-ambient pressure balance and, as a consequence, ME health and “normal” hearing. This implies that there is a minimum ET opening efficiency required for ME-ambient pressure homeostasis with lesser efficiencies increasing the risk for ME disease and hearing loss.[2]

For these reasons, the development of a valid, broadly applicable test of ET opening function is a goal of current and past research. In theory, such a test would detect the transmission of a signal between the nasopharynx and ME if, and only if, the ET opens during a specified maneuver. For ears with non-intact tympanic membranes, ME-nasopharyngeal pressure gradients can be created and monitored easily by external instruments coupled to the ear-canal and ET openings can be accurately signaled by a change in that gradient caused by trans-ET gas flow. However, that type of test lacks broad applicability.[1] For MEs with an intact tympanic membrane, ME-ambient pressure gradients can be created within a pressure chamber and gradient change during ET openings measured by tympanometry or variations on that method [3], but that type of test cannot be practically instrumented in most research laboratories or clinical practices. As an alternative to these “manometric” test protocols, a number of investigators suggested that tests based on the detection of sound transmission across a transiently open ET would hold the advantages of being simple to perform, generalizable and easily instrumented in office practices.[4]

As early as 1869, the use of sound to detect ET openings was reported by Politzer who described holding a vibrating tuning fork in front of a person’s nose and hearing a weak tone in external ear that greatly increased in intensity during the act of swallowing.[5] Early attempts to develop this concept as a practical test of ET opening function were fraught with technical difficulties such as a significant sound-signal attenuation by the instrument’s “tubing” and an inability to record sound-signal waveforms, among others [6] but, by the 1950–60s, Perlman and colleagues reported that they had successfully recorded distinct sound envelopes during the act of swallowing when a sound was introduced into the nose. [7,8] Later technological advances in sound filters decreased ambient noise contamination obviating the need for testing in soundproof rooms and the development of smaller microphone and speaker sizes vastly improved the quality of subject-instrument coupling which increased the efficiency of sound-signal capture. [9] In 1978, Virtanen formalized a protocol and described an instrument to evaluate ET opening function by “sonotubometry”, presented as a mature ET function test.[4]

Over the years, sonotubometry has been used to: diagnose ET dysfunction [10,11,3]; assign individuals with respect to their risk for developing ME disease expressions [12,13], and predict the outcome (success/failure) of ME surgeries [14,15]. However, investigators have

continued to question the accuracy of sonotubometry for assigning ET openings/non-openings during a swallow or other maneuver based on theoretical considerations [4,16,11,17,18], and recommended various modifications to the core sonotubometry protocol intended to reduce false test results [16,18–20,14,21–25,11]. To date, there is no “accepted” protocol (configuration) for ET function testing using sonotubometry and no study has compared the accuracy of these different protocols for discriminating “true” ET openings. Moreover, while some studies have compared the results for sonotubometry with those for ET function tests done in a pressure chamber [3], the 9 Step test [16,26] and manometric tests [27,28], the results for the 2 tests were not recorded for the same swallow (i.e. done simultaneously), and, like sonotubometry, the accuracies of the comparator tests are not known.

To lay the groundwork for studies of the comparative accuracy of the different sonotubometry configurations, this study describes a methodology to estimate the accuracy of any specified sonotubometry configuration with respect to determining the “true” state of ET opening/non-opening during a swallow or other maneuver. The usefulness of that method is exemplified by an accuracy assessment for one sonotubometry configuration.

METHODS

The data for this analysis were abstracted from experiments on adult subjects focused on developing a standard test protocol to evaluate ET function within the environment of a hypo-hyperbaric pressure chamber. The differences between test protocols in those experiments included the magnitude and presentation order of the applied chamber pressures but, at each applied chamber pressure, a standard test sequence to evaluate ET openings was used. The experiments were approved by the IRB at the University of Pittsburgh, and all subjects provided written Informed consent for their participation.

On the day of testing, the subject presented to the Middle Ear Physiology Laboratory at the University of Pittsburgh. A brief medical history was taken, and the subject had a standard ENT examination done by a study physician that included pneumatic otoscopy and tympanometry. The subject was excluded from testing if he/she had a concurrent cold, signs and/or symptoms indicative of active allergic rhinitis, a non-intact tympanic membrane or evidence of extant ME effusion. If qualified for testing, the subject, accompanied by a technician who performed the test procedures, entered a hypo-hyperbaric pressure chamber (Hypertec 9100, Olney, Texas; modified during construction for hypo-hyperbaric applications), was seated on an exam chair and the chamber doors closed and secured. A member of the study staff located outside of the chamber monitored and controlled chamber pressures and recorded test data.

The protocol for all experiments consisted of: 1) “swallowing” at atmospheric pressure; 2) increasing chamber pressure at a rate of approximately 10 daPa/sec to a target pressure of atmospheric+200 or +400 daPa (as dictated by experiment) followed by completion of the standard test sequence; 3) reducing chamber pressure to atmospheric followed by repeated swallowing; 4) decreasing chamber pressure at a rate of approximately 10 daPa/sec to a target pressure of atmospheric-100 or -200 or -400 daPa (as dictated by experiment)

followed by completion of the standard test sequence; 5) increasing chamber pressure to atmospheric followed by repeated swallowing; 6) decreasing chamber pressure at a rate of 10 daPa/sec until passive ET openings were detected, or the chamber pressure achieved atmospheric-500 daPa, and 7) increasing chamber pressure to atmospheric followed by repeated swallowing.

The standard test sequence consisted of: 1) bilateral measurement of the ME-chamber pressure gradient by tympanometry (Titan, Interacoustics USA, Eden Prairie, MN), 2) placing the sonotubometry microphones into the bilateral ear-canals, 3) swallowing with the sonotubometry speaker probe in the right nostril and again with the probe in the left nostril, 4) removing the ear-canal microphones, and 5) bilateral measurement of the ME-chamber pressure gradient by tympanometry. This test sequence was completed in less than 3 minutes. At the end of the experimental protocol, the chamber doors (inner and outer) were opened, and the technician and subject exited. Subjects could be enrolled in more than 1 experiment.

The sonotubometer was a previously described instrument constructed in our laboratory [26]. Briefly, the core instrument consists of a proprietary circuit box linked to a PC that controls the sound characteristics delivered by the speaker (for these experiments; probe-tip sound pressure was 110 dB and sound frequency was a white noise, 2KHz to 20 KHz) and also amplifies/conditions the bilateral microphone signals for display as a sound intensity (dB, unfiltered) versus time function, with data storage within the memory of the PC. For each test, microphones (Knowles Electronic BT-21834-000-Itasca, Illinois, USA) fitted within an appropriate-sized plastic plug were inserted bilaterally into the ear-canals, and the external ears covered with a standard ear-protector (EARMUFF 1000-Aearo Technologies, Indianapolis, IN). A plastic nasal probe (2 cm in length, 8 mm in diameter) fitted to a hand-held plastic housing containing a speaker (Piezo Electric Tweeter SS-990-Herald Electronics, Lincolnwood, IL) was first inserted part-way into one nostril and then into the other for sound delivery. Synchronous data streams from both microphones, speaker state (on/off) and the chamber pressure were collected continuously during the test. For the analysis, these data streams were examined, and periods during which the speaker was active were excised and imported into an Excel file. For each swallow and ear, the sound intensity from the respective microphone was plotted as a function of time. Those plots were examined for a patterned increase in sound intensity (referenced to the baseline/background sound intensity) and 2 descriptive parameters of sound-signal shape, Signal Duration and Signal Amplitude (maximum), were measured and recorded (values of 0 were recorded for these parameters if no change in sound intensity was detected during the swallow). Area under the sound intensity versus time curve was estimated using a triangular area function; i.e. $\text{Area} = 1/2 \text{ Duration} \times \text{Amplitude}$.

The data for analysis consisted of the paired (pre-, post-swallow), bilateral ME-chamber pressure gradients measured by tympanometry (recorded as tympanometric pressures) and the 3 sound-signal shape parameters for the two swallows (left/right nostril) of the sonotubometry test for each chamber pressure during each experiment. These data for each ear are referred to as a data-sequence which is the experimental unit for this study. For each

data-sequence, the sonotubometric sound-signal shape parameters for the swallow with the highest Signal Area were used in the analysis.

This data analysis focuses on determining the accuracy of sonotubometry for assigning ET openings/non-openings to each data-sequence. This requires a simultaneously recorded “gold standard” measurement as to whether or not the ET had “truly” opened during the two swallows that were monitored for ET opening by sonotubometry. Under conditions of an extant ME-ambient (read ME-chamber) pressure gradient as can be created in a pressure chamber, an ET opening during a swallow or other maneuver will be accompanied by an air-flow between the nasopharynx and ME which will reduce (toward 0 daPa) the magnitude of the pre-maneuver ME-ambient pressure gradient. Therefore, a change in the ME-ambient pressure gradient after swallowing defines a “true” tubal opening during the swallows and, conversely, the lack of change in that gradient defines a “true” tubal non-opening during the swallows. In the context of the present study, the identification of a “true” ET opening/non-opening during the 2 swallows (sound source in right/left nostrils) for each data-sequence was based on the paired, pre/post-swallowing tympanometric measures of the ME-chamber pressure gradient. Specifically, the efficiency of tubal opening by the 2 swallows for ME pressure reduction was quantified as the fractional gradient equilibrated (FGE) which was calculated as the difference between the pre- and post-swallow ME-chamber pressure gradients divided by the pre-swallow gradient. Because the linear range for the pressure transducer within the tympanometer is approximately -300 to 300 daPa, those data-sequences with measurements outside of that range were excluded from the analysis. Also, to ensure that an adequate signal, indicative of an ET opening, was captured (i.e. conditions favoring a measurable gradient decrease after swallowing), only valid data-sequences where the absolute value of the pre-swallow ME-chamber pressure gradient was greater than 100 daPa were included in the analysis. For purposes of calculating accuracy measures for the sonotubometry results, a conservative “gold standard” assignment of a “true” ET opening/non-opening (high assurance of a valid assignment of test-sequences to ET opening/non-opening) based on the FGE was used. Specifically, each valid data-sequence (the population) was assigned to either a determinate ($FGE=0, 1$) or an indeterminate ($0<FGE<1$) group with respect to identifying a “true” ET opening/non-opening during the swallows. Then, the determinate group of data-sequences was partitioned into 2 subgroups, and a “true” ET opening assigned to test-sequences with $FGE=1$ (Subgroup 1, complete pressure equilibration with swallowing) and a “true” ET non-opening assigned to data-sequences with $FGE=0$ (Subgroup 2, no pressure equilibration with swallowing).

Prior to any statistical analyses of the sonotubometry data, the distribution of FGE values for all analyzed data-sequences was cast as the cumulative percent frequency of data-sequences in the population as a function of FGE, and the mean, standard deviation, median, mode and range for that distribution were calculated. For each determinate subgroup (yes/no “true” tubal opening), the frequency of sonotubometric recordings with an identifiable sound-signal indicative of a tubal opening ($Signal\ Area>0\ dB.sec$) during the swallow was calculated, and the between-subgroup difference in that frequency evaluated for statistical significance using a Chi-square test. A “Truth” table was constructed as the cross-tabulation of tubal opening assignments (yes/no) by sonotubometry and by tympanometry (i.e. $FGE=0,1$; the “gold standard”), and the sensitivity and specificity of sonotubometry sound-signal detection

for identifying a “true” tubal opening and the accuracy of that measure with respect to an agreement with the “gold standard” assignment were estimated using standard formulas. To determine if the shape of the sonotubometry sound-signals contains information useful in assigning “true” ET openings/non-openings, the average and standard deviations for the 3 sonotubometry sound-signal parameters were calculated for the 2 determinate subgroups and the between-subgroup difference in these distributions for each parameter was evaluated for significance using a normal approximation to the Mann-Whitney U test. In an attempt to minimize the biasing effect of an imbalance between subgroups in the frequency of 0 valued entries on distribution skewing, the calculations and comparisons were repeated on a restricted subset of the population of data-sequences defined by the presence of a detectable sonotubometry sound-signal with swallowing (restricted to: Signal Area>0 dB.sec).

Then, the population of test-sequences (all data-sequences defined by 0 FGE = 1) was examined for a patterned change in the frequency of sonotubometry assigned ET openings based on sound-signal detection during a swallow and in the average values of the 3 sound-signal shape parameters with increasing FGE. The frequency of sound-signals indicative of an ET opening (Signal Area>0) and the average and standard deviation for the 3 signal parameters were calculated for each of 5, 20% binned FGE values (e.g. 0 to 20%, 21–40%, 41–69%, ...). The frequencies of sound-signal detections and the average values of the sound-signal shape parameters were visually examined for a progressive increase with increasing binned FGE. To that end, Spearman-rank, correlation coefficients between FGE values and the values for each of the sound-signal parameters were calculated to explore the relatedness of those quantitative measures of ET opening efficiency. These calculations were repeated for the restricted subset of data-sequences and also after eliminating the boundary points for the FGE distributions (FGE=0,1).

Finally, the limits of the information contained in the continuous-measure, sound-signal shape parameters for accurately assigning ET openings/non-openings was explored using a Receiver Operating Characteristic (ROC) curve analysis operating on the determinate group of data-sequences (FGE=0,1) and on the subset of the determinate data-sequences with concurrent detection of a sonotubometry sound-signal (FGE=0,1; Signal Area > 0 dB.sec). Briefly, that analysis calculates the sensitivity and specificity for assignment to a “true” state/condition (e.g. ET opening) for each measured value of the parameter under consideration and then plots the sensitivities as a function of their paired 1-specificities (the ROC curve). A linear ROC curve with a slope of 1 (i.e. the identity diagonal) has an area under the ROC curve (AUROC) of 0.5 and is the expected result for chance assignment to the condition/state. For empirical data, the AUROC is a measure of the “amount of information” provided by the parameter with respect to condition/state assignment. To test if a significant “amount of information” for condition/state assignment is provided by each parameter, the empirical AUROC is compared with a value of 0.5 using a standardized “Z” statistic. The ROC curve also contains information for determining the cut-off value of a parameter that maximizes the desired sensitivity/specificity balance and for estimating the sensitivity/specificity of a test when evaluated at recommended or accepted parameter cut-offs.

All data analyses were done using the NCSS 2007 statistical software package (Kaysville, Utah). In describing the characteristics of data distributions, the format average $\pm$ standard deviation is used consistently and in describing the features of the AUROC, the format AUROC $\pm$ standard error is used.

RESULTS

A total of 691 data-sequences for individual ears were available for analysis. Of these, 502 obtained during 168 test sessions on 103 healthy, adult subjects satisfied the criteria for inclusion in this analysis. Sixty of the tested subjects were male and 43 female; their self-assigned race was 3 Asian, 25 Black, 61 White and 3 “mixed race” (11 subjects do self-report a racial assignment), and their average age was 30.4 $\pm$ 10.8 (range=18 to 54) years.

Figure 1 shows the cumulative percent frequency of data-sequences as a function of FGE. That distribution is skewed to higher FGEs, with an FGE value 0.9 recorded for the majority (62%) of data-sequences. The average FGE was 0.79 $\pm$ 0.32, the median value was 0.99 and the mode value was 1.00 (range=0 to 1.0). Of these data-sequences, no evidence of ET opening during the two swallows (FGE=0) was documented by repeat tympanometry for 32 (6.4%), and definitive ET opening during at least one the two swallows (FGE=1) was documented by repeat tympanometry for 248 (49.4%).

For the determinate group of data-sequences with an FGE of 0 or 1, the frequencies of ET openings identified by sonotubometry based on the presence of a detected sound-signal (Signal Area $>$ 0.0 dB.sec) were 34.5% and 74.2%, respectively, and the frequencies of ET non-openings based on the lack of a detected sound-signal (Signal Area=0.0 dB.sec) were 25.7% and 65.6%, respectively (Chi-Square=19.5, $p<0.001$). Relative to this data-sequence distribution, the sensitivity and specificity of the sonotubometry test for identifying a “true” ET opening were 74.2% and 65.6%, respectively. The accuracy of the measure (sound-signal detection) for identifying the “true” ET state during the swallows was 73.3%. Figure 2 shows the frequency of detected sonotubometric sound-signals as a function of FGE bins with 0.2 width for the population of data-sequences. There was a slight tendency for that frequency to increase with increasing FGE, but this was not impressive.

The Table reports the means and standard deviations of the 3 parametric descriptors of sonotubometry sound-signal shape, Signal Amplitude, Signal Duration and Signal Area, for the 2 determinate subgroups of data-sequences characterized by FGE=0 or FGE=1 and for the population of data-sequences (0 FGE 1) distributed into FGE bins 0.2 in width (Upper Rows). These summary statistics are also reported for the restricted subset of those data-sequences characterized by an identified sound-signal during the swallow (Lower Rows). For the population, the average values of all three signal parameters were significantly different between the determinate subgroups of data-sequences (for all parameters, $Z>3.6$, $p<0.001$). However, for the restricted subset of data-sequences, average Signal Duration was not significantly different between those subgroups ($Z=0.49$, $p=0.62$), but average Signal Amplitude ($Z=2.28$, $p=0.02$) and Signal Area ($Z=2.13$, $p=0.03$) were. For all significant comparisons, the average value of the parameter was higher when measured for the FGE=1 subgroup when compared to the value measured for the FGE=0 subgroup. With the

exception of Signal Duration for the restricted subset, average values of the signal parameters showed a tendency to increase with increasing binned FGE. Spearman rank order correlation coefficients between FGE and Signal Duration, Signal Amplitude and Signal Area, respectively, were: 0.27, 0.30 and 0.30 (all estimated $p < 0.001$) for the population and, 0.07 ($p > 0.20$), 0.13 ($p < 0.05$) and 0.14 ($p < 0.05$) for the restricted subset of data-sequences. Repeating those calculations while limiting the analysis to the indeterminate group (i.e. eliminating data-sequences with FGE=0 or 1) yielded correlation coefficients between FGE and Signal Duration, Signal Amplitude and Signal Area, respectively, of 0.13, 0.18 and 0.17 (all estimated $p \approx 0.10$) and, for the restricted subset of that group, of 0.09, 0.12 and 0.14 (all estimated $p > 0.20$).

Figure 3 shows the ROC curves for the 3 parametric descriptors of sound-signal shape when constructed using data-sequences in the determinate group (a) and when using the restricted subset of that group characterized by a detectable sonotubometry sound-signal (b). Those curves relate to the correct assignment of data-sequences to the FGE=1 subgroup. The respective AUROCs for Signal Amplitude, Duration, and Area were 0.69 ± 0.04 ($Z=5.25$, $p < 0.001$), 0.65 ± 0.04 ($Z=3.75$, $p < 0.001$) and 0.69 ± 0.03 ($Z=5.52$, $p < 0.001$) for the group, and 0.65 ± 0.06 ($Z=2.34$, $p=0.02$), 0.53 ± 0.07 ($Z=0.44$, $p=0.66$) and 0.64 ± 0.05 ($Z=2.67$, $p=0.008$) for the restricted subset of the group. With the single exception of the AUROC for Signal Duration developed using the restricted subset, all AUROCs were significantly different from chance assignment (chance AUROC=0.50), but the information provided by the parameters for accurate data sequence assignment to a “true” ET opening was quite limited (e.g. compare measured AUROC to a value of 1 representing 100% assignment accuracy). For example, stipulating that any useful cut-off value assigns a “true” ET opening with at a least 0.50 specificity and sensitivity, the best attainable sensitivity/specificity pairings for any cut-off value are 0.70/0.59 at a cut-off of 0.04 dB and 0.50/0.79 at a cut-off of 2.42 dB for Signal Amplitude. For completeness, a Discriminant Function Analysis for data-sequence assignment to ET opening/non-opening operating on the data-sequences for the determinate group using a combination of the 3 sound-signal shape parameters was done (data not shown). That analysis showed that those parameters share the majority of their predictive information such that combining the measures does not increase the sensitivity or specificity for correct data-sequence assignment to either subgroup.

DISCUSSION

Sonotubometry is a relatively simple test for the presence/absence of ET opening during swallowing (and other maneuvers) that could be implemented at low cost for “on-site” ET function testing in an office practice. Briefly, for testing, sound at a pre-defined frequency and intensity generated by an external speaker is channeled via the nose to the nasopharynx and “ME” sound pressure is continuously monitored by microphones in the ear-canals. If the ET opens during a maneuver associated with ET opening (e.g. swallowing), the presented nasopharyngeal sound is transmitted through the open ET to the ME and detected as an increase above baseline in the ear-canal sound pressure (i.e. the detected sound-signal). In contrast, if the ET fails to open during the maneuver, nasopharyngeal sound is not transmitted to the ME, and the baseline ME sound pressure is unchanged during the maneuver (i.e. no detected sound-signal). However, past reports identified a variety of

mechanisms that could downgrade the accuracy of ET opening assignments made using sonotubometry. These include detection by the ear-canal microphones, in the absence of a complete ET opening, of 1) typical sounds created by the maneuver itself [4,16]; 2) a patterned change in the presented nasopharyngeal sound pressure secondary to volume changes effected by raising and lowering the palate during a swallow [11,16] and 3) a patterned change in the ME sound pressure caused by increased trans-ET sound conductance with partial ET opening [4,17,29], among others. Conversely, a “true” ET opening may not be detected by sonotubometry if the presented nasopharyngeal sound is significantly attenuated [18], degraded and/or frequency-filtered on transmission through nose or the open ET[16] [22]. Suggestions to reduce the impact of these effects on test accuracy include: introducing large volume source speakers as components of the test system [16,26]; repeat testing while alternating nasal sides for sound presentation [16,26]; using a source sound with particular and/or unique characteristics (e.g. white noise [16,29,26], narrow band white noise [14,21,22], “perfect-sequence” sounds [23] [24], pure tones [18–20]) and selective frequency filtering of the signals outputted from the ear-canal microphones [16,14,23]. As yet, there is no accepted standard configuration for sonotubometric testing and the choice of a “best” (i.e. most accurate) test configuration reflects user preference without empirical support.

To date, there are no data on the accuracy of any sonotubometry test configuration for detecting a “true” tubal opening. Making this determination requires a cross-tabulation of the ET opening assignments made using a chosen sonotubometric test configuration with those made concurrently using a “gold standard” test that is characterized by near 100% accuracy. Physiologically, the ET is usually closed but opens transiently during swallowing, yawning and, less reliably, other maneuvers [1]. While there is no established non-invasive method to identify all ET openings with certainty, an ET opening at the time of an extant ME-ambient pressure gradient causes gas flow between the ME and nasopharynx and, consequently, a decrease in the pre-opening ME-ambient pressure gradient. Thus, measuring the ME-ambient pressure gradient before and after attempting to open the ET by a specified maneuver (e.g. a swallow) will yield data from which the gradient change can be calculated and then compared to the theoretical value of 0 daPa (no opening) to determine whether or not a functional ET opening actually occurred during the maneuver. From these considerations, a basic protocol to assess the accuracy of sonotubometric identification of the presence/absence of ET openings would include: 1) identifying MEs with a measurable extant pressure different from ambient; 2) accurately recording the ME-ambient pressure gradient immediately before and after a maneuver associated with ET opening, and 3) monitoring for ET openings during the maneuver by sonotubometry. The tubal opening (yes/no) assignments by sonotubometry could then be cross-tabulated with the “true” ET opening assignments defined by the post-maneuver change in pressure gradient to calculate the sensitivity and specificity (and other accuracy measures) for the tested sonotubometry configuration.

In practice, the ME-ambient pressure gradient can be measured non-invasively by tympanometry. However, that measurement has an intrinsic random error and the accuracy of tympanometric “pressure” measurements at high ME-ambient pressure gradients is a function of the response linearity for the particular instrument’s pressure transducer.

Therefore, in protocols that determine the presence/absence of “true” ET openings based on a change in a tympanometrically measured ME-ambient pressure gradient, the measured, pre-maneuver gradient needs to be at least two-fold greater than 2 times (to include the repeated measures) the approximate maximum error for tympanometric pressure measurements (e.g. a gradient of 100 or -100 daPa, as used here), but within the linear range for the instrument’s pressure transducer (e.g. a gradient of >-300 and <300 daPa, as used here). Such gradient magnitudes are not typical for MEs of individuals with even a moderate debility in ET opening efficiency, but specified ME-ambient (read chamber) pressure gradients can be created easily within the environment of a pressure-chamber as was done in the present study.

For this study, we identified pressure-chamber experiments conducted in our laboratory that included elements conforming to the requisite measures for evaluating the accuracy of sonotubometry as discussed above. Experiments that included the standardized test sequence of “tympanometry, sonotubometry during a swallow and tympanometry” within a short time interval at different chamber pressures satisfied those criteria. Because those protocols were not designed to address the accuracy of sonotubometry, it was necessary to abstract, from the available database, those data-sequences that conformed to the required range of pre-swallow ME-chamber pressure gradients (see above) for use in this analysis. While all conforming data-sequences were abstracted, the primary analysis focused on those sequences with high probability that the ET failed to open on both swallows as evidenced by a lack of gradient change (FGE=0) and on those sequences with a definitive ET opening on either of the 2 swallows as evidenced by complete gradient equilibration (FGE=1). Using a simple “truth” table analysis, a cross-tabulation of the presence/absence of detection of a sonotubometric sound-signal for either of the 2 swallows with an assignment of a “true” ET opening/non-opening based on gradient change (FGE=1 versus FGE=0) yielded a calculated sensitivity and specificity of the basic sonotubometry configuration used in those experiments for correctly assigning data-sequences to ET openings of 74% and 66%, respectively, and an accuracy for correct ET opening/non-opening assignments of 73%. To determine if the data available for the continuous measures of sound-signal shape provide additional information for data sequence assignment to “true” ET opening/non-opening, a ROC curve analysis was done. That analysis showed that at least 2 of the parametric descriptors (Signal Amplitude, Signal Area) contain significant, but limited and redundant information, with respect to correctly assigning a test-sequence to a tubal opening. Also, that analysis defined limiting bounds for the expected achievable sensitivity or specificity (approximately 0.08 for both) for tubal opening assignments based on those measures for the sonotubometry configuration used.

These results were all developed using data-sequences at the extremes of the FGE distribution (FGE=0 or 1) so as to apply a conservative “gold-standard” definition of ET opening/non-opening. While it is expected that intermediate values of FGE would also define a tubal opening, albeit less efficient than FGE=1, this could not be affirmed using the available data. Observed tendencies for the measures of ET opening by sonotubometry to increase with increasing FGE by visual inspection and the significant, positive correlations between the parametric values and FGE, support this possibility. However, that type of

analysis will need to be postponed until similar data are available for a more accurate sonotubometry configuration.

This data analysis shows that the described method for determining the accuracy of sonotubometric assessments with respect to whether the ET opens or not during swallowing is both feasible and practical for studies conducted within the environment of a pressure-chamber. Protocol modifications specific to that purpose would include: the enrollment of subjects with and without a suspected ET dysfunction (poor/good ET opening by swallowing) to achieve a more balanced data-sequence distribution for “true” ET opening/non-opening during a swallow; repeat tympanometry before and after each attempted (versus paired) ET opening maneuver, and targeted use of chamber pressures to achieve the desired (required) ME-chamber pressure gradients for the test as opposed to an application of standard pressures with secondary elimination of non-qualifying data-sequences as was done here. That type of protocol is adaptable to accuracy comparisons of different sonotubometry configurations using statistical tests for frequency data or statistical comparisons of the derived AUROCs for continuous data. In those protocols, ROC curves for the continuous measures of sonotubometry sound-signals can also be used to define empirically “reasonable” cut-off values with respect to a targeted sensitivity/specificity balance. For example, a sound-signal amplitude of at least 5 dB was used previously to assign an ET opening [26], but the data from this study using the same test configuration show that cut-off to have an estimated sensitivity of 0.30 and specificity of 0.91 for identifying a “true” tubal opening. Thus, the 5 dB cut-off accurately identifies most of swallows where the ET failed to open but miss-assigns a majority of the swallows where the ET had truly opened. A structured program of experiments developing these applications to the validation of different sonotubometry configurations is ongoing in our laboratories.

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Figure 1.
Cumulative percent frequency of data-sequences as a function of Fractional Gradient Equilibrated (FGE).

Figure 2. Frequency of sonotubometry sound-signal detection during swallowing (Signal Area>0 dB.sec) as a function of average Fractional Gradient Equilibrated (FGE) for bins of 0.2 width.

Figure 3.

Empirical Receiver Operating Characteristic (ROC) curves for the correct assignment of data-sequences to the FGE=1 subgroup based on each of the three sonotubometry sound-signal shape parameters, Signal Duration (dotted line), Signal Amplitude (dashed line) and Signal Area (solid line), constructed using the determinate group of data-sequences (a) and using the restricted subset of those data-sequences defined by detection of a sound-signal during swallowing (b). Solid diagonal line is that expected for chance assignment probability.

TABLE

Sample Size (N, data-sequences), Average (AVG) and Standard Deviation (STD) for the three sonotubometry sound-signal shape parameters, Signal Duration (sec), Signal Amplitude (dB) and Signal Area (dB.sec), calculated for the determinate subgroups (FGE=0,1) and the population of data-sequences subsetted into FGE bins of 0.20 width. These calculations were done for the population (POP) of data-sequences (upper grouping) and for a restricted subset defined by detection of a sound-signal during a swallow (lower grouping).

FGE	N	DURATION (sec)		AMPLITUDE (dB)		AREA (dB.sec)	
		AVG	STD	AVG	STD	AVG	STD
POP							
0	32	0.18	0.29	0.85	1.63	0.19	0.29
1	347	0.36	0.30	3.50	3.69	0.94	1.22
0.00–0.20	53	0.20	0.28	1.49	2.69	0.30	0.48
0.21–0.40	24	0.11	0.23	1.08	3.27	0.26	0.91
0.41–0.60	35	0.34	0.41	2.65	3.58	0.79	1.28
0.61–0.80	43	0.24	0.28	1.66	2.18	0.40	0.62
0.81–1.00	347	0.36	0.30	3.50	3.69	0.94	1.22
RESTRICTED							
0	11	0.54	0.22	2.49	1.95	0.55	0.22
1	243	0.51	0.23	5.00	3.45	1.34	1.26
0.00–0.20	22	0.48	0.21	3.59	3.17	0.73	0.48
0.21–0.40	6	0.46	0.25	4.31	5.69	1.05	1.66
0.41–0.60	20	0.60	0.38	4.63	3.64	1.38	1.44
0.61–0.80	22	0.48	0.19	3.24	2.03	0.79	0.67
0.81–1.00	243	0.51	0.23	5.00	3.45	1.34	1.26