OtoID: New extended frequency, portable audiometer for ototoxicity monitoring

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Abstract—Portability of equipment is an increasingly important component in the practice of audiology. We report on a new device, the OtoID, that supports evidence-based ototoxicity testing protocols, provides capability for hearing testing on the hospital treatment unit, and can automate patient self-testing. The purpose of this article is to report on the validation and verification of the OtoID portable audiometer in 40 subjects both young and old, with and without hearing impairment. Subjects were evaluated by an audiologist using the manual hearing test program and then self-tested via an automated testing program. Testing was done in a sound booth and on a hospital treatment unit. Therefore, data were collected in four conditions (booth vs hospital unit and automated vs manual testing) and analyzed for testing bias, repeatability, and American Speech-Language-Hearing Association-significant ototoxicity false-positive rate. Repeatable hearing threshold results were obtained on all subjects who performed the test, regardless of hearing status or testing location.

Key words: audiometer, chemotherapy, cisplatin, hearing loss, monitoring, OtoID, ototoxicity, rehabilitation, tinnitus, Veterans.

INTRODUCTION

One source of acquired hearing loss is the use of ototoxic medications for the treatment of cancer. The standard of care for detecting ototoxic hearing loss is the behavioral hearing test. Since ototoxic damage generally occurs near the high-frequency–coded base of the cochlea and progresses apically, capitalizing on this progression using the sensitive range for ototoxicity (SRO) procedure is both a time-efficient and sensitive technique [1]. The SRO is a pure tone screening procedure in which a one-octave individualized (by ear) range of frequencies at the high-frequency limit of hearing is monitored for change during treatment. Testing these seven frequencies, spaced one-sixth octave apart, identifies 94 percent of initial ototoxic hearing shifts [2]. Further, this screening procedure reduces testing time by two-thirds in comparison with full frequency testing. In most patients, the SRO extends above the conventional testing range (>8.0 kHz), but for Veterans, who often enter treatment

with preexisting hearing loss, the lower frequencies of the SRO frequently include the conventional (0.5–8.0 kHz) and sometimes even speech frequency (0.5–4.0 kHz) ranges. Therefore, hearing change from chemotherapeutic treatment can cause abrupt communication difficulties for these patients if early changes go undetected. Early detection of an ototoxic-based hearing shift is important and provides the best opportunity to preserve communication during and after treatment.

Cisplatin, the most ototoxic chemotherapeutic medication, can cause hearing loss and tinnitus in 40 to 50 percent of adults [3–5]. Cisplatin-related ototoxicity is dose dependent, with initial hearing shifts in average hearing adults (SRO pure tone average = 70 decibels sound pressure level [dB SPL]) occurring at approximately 350 mg [6–7]. This dose-hearing relationship is moderated by preexposure hearing loss such that those adults with better than average hearing in the SRO (50 dB SPL) sustain hearing shifts at lower cumulative doses (190 mg) [6]. Knowing the planned cumulative dose of cisplatin and the extent of hearing loss prior to treatment allows relatively precise predictions regarding the inevitability of hearing shift and may prove to be an effective tool for oncology treatment planning. Effective chemotherapeutic medicines and treatment strategies have greatly improved cancer survivability, making quality of life following cancer a principal treatment goal. The perspective of the World Health Organization is that quality of life is one of two main goals in cancer treatment, with prolonging life being the other. If changes in cisplatin dose or regimen or substitution to a less ototoxic medication can be made without compromising effective treatment, a patient's hearing can be preserved, especially in the frequencies relevant to speech understanding, thereby maintaining the highest quality of life for these patients following cancer.

Despite the potential to minimize or prevent communicatively important hearing loss, ototoxicity monitoring practices have not been implemented as a standard of care in most medical centers largely because of practical limitations. Accessing and testing patients in a sound booth of an audiology clinic prior to or during treatment is a major logistical barrier. Further, cancer patients are often too ill or fatigued to tolerate the comprehensive audiometric testing typically done. And finally, many audiology clinics do not have access to extended high-frequency audiometry (>8.0 kHz) and/or the capability to test in one-sixth octave steps, a requirement of the time-efficient

SRO protocol. Use of a portable device combined with the capability to accurately test using time-efficient and highly sensitive protocols during treatment on a hospital unit ensures success of a monitoring program.

In this article, we describe a portable audiometric device, the OtoID, capable of chairside hearing testing during treatment. This device has the capability to adjust test frequencies in fine one-sixth octave steps across the entire frequency test range of 0.5 to 20.0 kHz and has an output capability of −10 through 105 dB SPL. The OtoID has both manual (audiologist-directed testing) and automated (patient self-test) modes. The automated testing mode was designed specifically to support ototoxicity monitoring. The OtoID is a sturdy, easy-to-use device designed so that patients undergoing chemotherapy can test themselves either on the chemotherapy unit during treatment or at home prior to treatment. A comparison of the OtoID to a commercially available clinical audiometer (Grason-Stadler GSI 61) using 10 young normal hearing subjects has previously been reported [8]. There were two purposes for this project. The first was to determine whether the OtoID provided equivalent thresholds from subjects varying in age, sex, and hearing status when done by an audiologist using the manual test mode versus when done by the subjects using the automated test mode. The second purpose was to determine whether the OtoID provided equivalent results regardless of test site (sound booth vs hospital treatment unit).

METHODS

Subjects

Healthy, volunteer subjects were recruited from the Portland Department of Veterans Affairs (VA) Medical Center (PVAMC), the local community, and from a database of research subjects maintained by the National Center for Rehabilitative Auditory Research (NCRAR). All subjects were consented to participate in the study following the guidelines of the PVAMC Institutional Review Board and were compensated for their time. All subjects met the following criteria: (1) no history of ear disease and (2) normal tympanometry and otoscopy at the time of testing. In order to achieve a balance of important patient characteristics, we based recruitment on three factors: age, hearing status, and sex. Age was defined as <40 or ≥40 yr of age, while hearing was divided into normal (≤25 decibels hearing level [dB HL]

at 0.5–8.0 kHz) and hearing impaired (>25 dB HL for at least one frequency). Criteria for excluding potential subjects from this study were (1) cognitive, physical, or psychological inability to participate; (2) inability to provide reliable behavioral threshold responses (patient did not meet intrasession reliability of ±5 dB using the manual testing mode); and (3) subject or medical record report of Ménière's disease, retrocochlear disorder, or active or recent history of middle ear disorder.

Instrumentation

The OtoID device, shown in **Figure 1** during subject self-testing, is comprised of an ARM-based processor with a touch-screen monitor running Microsoft Windows CE (Microsoft; Redmond, Washington) and OtoID firmware, a custom audiometer circuit board with extended high-frequency audiometer (HFA) capability and Sennheiser HDA200 circumaural headphones (Sennheiser Electronic Corp; Old Lyme, Connecticut). The OtoID is ergonomically designed to be sturdy and comfortable to use by both professional and nonprofessional personnel.

In the development of the OtoID, demanding acoustic performance was required such that each one-sixth octave frequency (0.5–20.0 kHz) had a dynamic range of 115 dB (−10 to 105 dB SPL). A specification summary comparing the OtoID with the American National Standards Institute (ANSI) S3.6-2010 standard for audiome-

Figure 1.
View of OtoID screen. Subject was presented with listening interval and required to make behavioral response (yes or no) regarding whether tone was heard. Presentation intervals contain "catch" trials (interval with no stimulus) to determine threshold reliability.

ters is shown in **Table 1**. The OtoID meets all ANSI S3.6-2010 class type 4 and HFA specifications for reference equivalent SPL, frequency accuracy and purity, attenuator accuracy and linearity, tone switch characteristics, and absence of unwanted acoustic signals. A fully detailed description of the technologies employed in the OtoID device and performance of the device is available elsewhere [8]. Full calibration of the OtoID was done annually with intensity verification checks performed weekly at 0.5 to 20.0 kHz in one-sixth octave intervals, using a Brüel and Kjær (B&K) 2250 sound level (Brüel and Kjær; Nærum, Copenhagen, Denmark) and a B&K model flat-plate coupler equipped with a B&K 4192 microphone. The Grason-Stadler Tymp Star middle ear analyzer (Grason-Stadler; Eden Prairie, Minnesota) and MAICO EasyTymp (MAICO Diagnostic, GmbH; Eden Prairie, Minnesota) used in the study were calibrated annually.

Procedures

Procedures for all subjects included (1) a brief hearing history questionnaire, (2) otoscopy, (3) tympanometry, (4) pure tone air conduction thresholds obtained by a licensed audiologist using the modified Hughson-Westlake procedure [9], and (5) pure tone air conduction thresholds in the SRO frequency range obtained by each subject using the automated self-testing mode. Tympanometry was measured on all subjects using the previously mentioned Grason-Stadler immittance screening devices, and results were required to be normal. Tympanometric measurements were considered to be normal when compliance ranged within 0.2 to 1.8 cm^3 and peak pressure ranged within −150 to +100 daPa.

All testing occurred on three separate days within 1 month and was done in a sound-attenuated booth and in a quiet area of a hospital treatment unit on each day. All manual-mode testing in both ears was done by the same licensed audiologist. Self-testing of the seven individualized SRO frequencies using the automated mode was done by the subjects. All initial evaluations by the audiologist included behavioral hearing testing (0.5–20.0 kHz) and subsequent determination of the individualized SRO, defined as the uppermost frequency, R, with a threshold of ≤100 dB SPL followed by the next adjacent six lower frequencies in one-sixth octave steps, R-1 through R-6, all <100 dB SPL. Initial testing location (hospital treatment unit vs sound suite) was counterbalanced for each subject. The 3-day testing sequence was kept the same, including

Table 1.
OtoID performance specification comparison with ANSI S3.6-2010 standard, type 4 HFA. Measurements obtained from OtoID meet or exceed standard. All dB SPL re: 20 μPa.

Measurement	Standard	Finding
Output Level	−10 to 100 dB HL	−10 to 105 dB SPL 0.5
Frequency Range (Hz)	Type 4, 0.5 to 8.0 kHz	0.5 to 20.0 kHz
	HFA >8.0 to 16.0 kHz[*]	
Frequency Accuracy/Resolution	±3%	±1%/5.0 Hz
Harmonic Distortion	<2%	<0.1%
Attenuator Accuracy/Resolution	±3 to 5 dB	±4%/0.1 dB
Attenuator Rise/Fall Characteristics	20 to 200 ms	45 to 60 ms
Ambient Room Noise Monitor	N/A	20 to 100 dB SPL

[*]When equipped with extended frequency testing package.
ANSI = American National Standards Institute, db HL = decibels hearing level, dB SPL = decibels sound pressure level, HFA = high-frequency audiomemter, N/A = not applicable.

test location and order of testing (e.g., audiologist testing then self-test).

Figure 1 also provides a view of the OtoID screen during self-testing in the automated test mode. Prior to the subject self-test, the audiologist provided a brief explanation and orientation to the OtoID device and indicated the behavioral response required. The subject then began the automated SRO threshold program, which used the modified Hughson-Westlake threshold procedure [9]. Subjects were first alerted (with "Listen Now" on the screen) to an upcoming listening interval in which a tone may or may not be presented. After the trial, the subject was required to indicate whether a tone was heard (yes/no). If the subject reported hearing the tone when the tone was presented, the level of the tone was decreased by 10 dB. If the subject reported that no tone was heard when a tone was presented, the tone was increased by 5 dB. This continued until a threshold was obtained (two out of three ascending behavioral responses at the lowest decibel level) for each of the SRO frequencies. Ten percent of the presentations were randomly presented "catch" trials to detect false-positive behavioral responses. If the subject reported hearing the tone during a catch trial, the screen message read, "Listen carefully for the tone." At this point, a tone may or may not (presentation of another catch trial) be presented. If the subject reported that no tone was heard during a catch trial, the testing continued.

Data Analysis

To determine whether the OtoID was accurate for serial self-testing regardless of sex, age, and hearing status, a comparison was necessary between pure tone results obtained from serial automated testing and serial manual testing across testing environments and test frequencies. The assessment was made by contrasting the automated mode OtoID results with the manual mode OtoID results under various conditions. In order to be clinically recommended, automated testing must perform no worse than manual testing by an audiologist, considered for this analysis to be the gold standard.

While frameworks for assessing a new device are varied, in this analysis, we used three metrics to assess the accuracy and reliability of the OtoID automated testing procedure compared with the manual testing procedure: bias, repeatability, and false-positive rate.

Bias

Bias was defined as the percentage of thresholds measured by the subject (automated mode) that were >5 dB different from the thresholds obtained in the same ear and frequency of each subject when tested by the audiologist in the same session and location (booth vs ward). Bias <10 percent indicates that patients evaluating their own thresholds using the automated mode of the OtoID give functionally equivalent thresholds to those obtained by an audiologist under the same conditions.

Repeatability

Repeatability is a measure used to determine whether hearing thresholds are functionally equivalent when the threshold test is performed multiple times under identical conditions. To be deemed repeatable, ≥90 percent of tests must achieve retest results within 5 dB for all conditions. Repeatability was derived from an estimate of the variance of the difference between retests and assumed no true

change in pure tone thresholds between tests. The variance of the difference between retests was estimated from twice the residual variability of a one-way analysis of variance model, with subject × ear as the factor, fit separately to each frequency, location, and subject hearing level [10]. The percentage of retests within 5 dB was computed from percentages of the cumulative normal distribution with zero mean and variance defined previously.

False-Positive Rate

False-positive tests are retests that indicate a clinically significant shift in pure tone thresholds when no true hearing shift should occur. Recall that all subjects are healthy volunteers. A clinically significant shift indicating ototoxicity has been defined by the American Speech-Language-Hearing Association (ASHA) [11] as (1) a ≥20 dB increase in threshold at any SRO frequency, (2) a ≥10 dB increase at any two adjacent SRO frequencies, or (3) loss of behavioral response at any three adjacent SRO frequencies at which responses were initially obtained. In this analysis, the set of threshold measurements taken on the first study visit constituted the baseline test, and false-positive rates were computed for the second and third follow-up visits.

Throughout this analysis, statistical hypothesis tests were avoided for three important reasons. First, multiple threshold measurements obtained from the same subject must be addressed using multiplicity adjustment, such as Bonferroni testing, resulting in extremely low test power. Second, each subject provided an automated and a manual measurement over seven SRO frequencies for both ears in two locations (booth and ward) on 3 days of testing, or 84 measurements per subject. This induced a complex correlation structure that must be accurately estimated for any of the *p*-values to be correct. Finally, all tests must be equivalence-type tests, requiring sufficient evidence to reject the null hypothesis that the manual and automated methods gave different results. Under some limited circumstances, equivalence testing methodology is well developed. However, similar methodology for the instrument testing conducted here is not available. In the end, hypothesis testing was not done in favor of more easily interpretable outcomes.

RESULTS

Forty subjects (80 ears), 19 females and 21 males, ranging in age from 18 to 74 yr with normal hearing or sensorineural hearing loss were recruited for participation. **Table 2** shows the number of ears used in the analysis, organized by age, sex, and hearing impairment. The groups were roughly equivalent across sex. However, younger cochlear subjects and older normal hearing ears were underrepresented compared with the other groups, typical for these groups of subjects.

Bias is an indication of measurement similarity between the two testing modes, in this case automated and manual. **Figure 2** illustrates the percentage of automated pure tone thresholds that deviated more than 5 dB from thresholds obtained by the audiologist as a function of frequency. The four panels represent the type of subject (cochlear, normal hearing) and location of test (booth, hospital ward). The numbers in each panel are the number of tests at each one-sixth octave frequency ranging from 1 to a maximum of 120. Fewer tests were done at frequencies ≤6.0 kHz than frequencies >6.0 kHz. This is particularly true for the normal hearing group of subjects, because the individualized SRO for this group is primarily in the extended frequency range (above >8.0 kHz). Only one frequency (20.0 kHz) exceeded 10 percent bias. This occurred for the normal hearing subject group when tested in the sound booth. However, apart from this condition, the automated OtoID thresholds did not exhibit bias (better or poorer) compared with the manually obtained OtoID results, and in fact, results were very similar.

Figure 3 shows the estimated repeatability of test results across test site, test mode, and 3 days of testing as a function of frequency for each group. Repeatability was the estimated percent of retests with thresholds that were within 5 dB, the standard definition of a reliable measure in clinical auditory testing. Repeatability was high (>90%) under all test conditions, except for subjects with

Table 2.
Number of ears measured by age, sex, and hearing status.

| Participant	Age (yr)	Cochlear	Normal	Total
Female	≥40	14	6	20
	<40	4	14	18
Male	≥40	14	6	20
	<40	7	15	22
Total	—	39	41	80
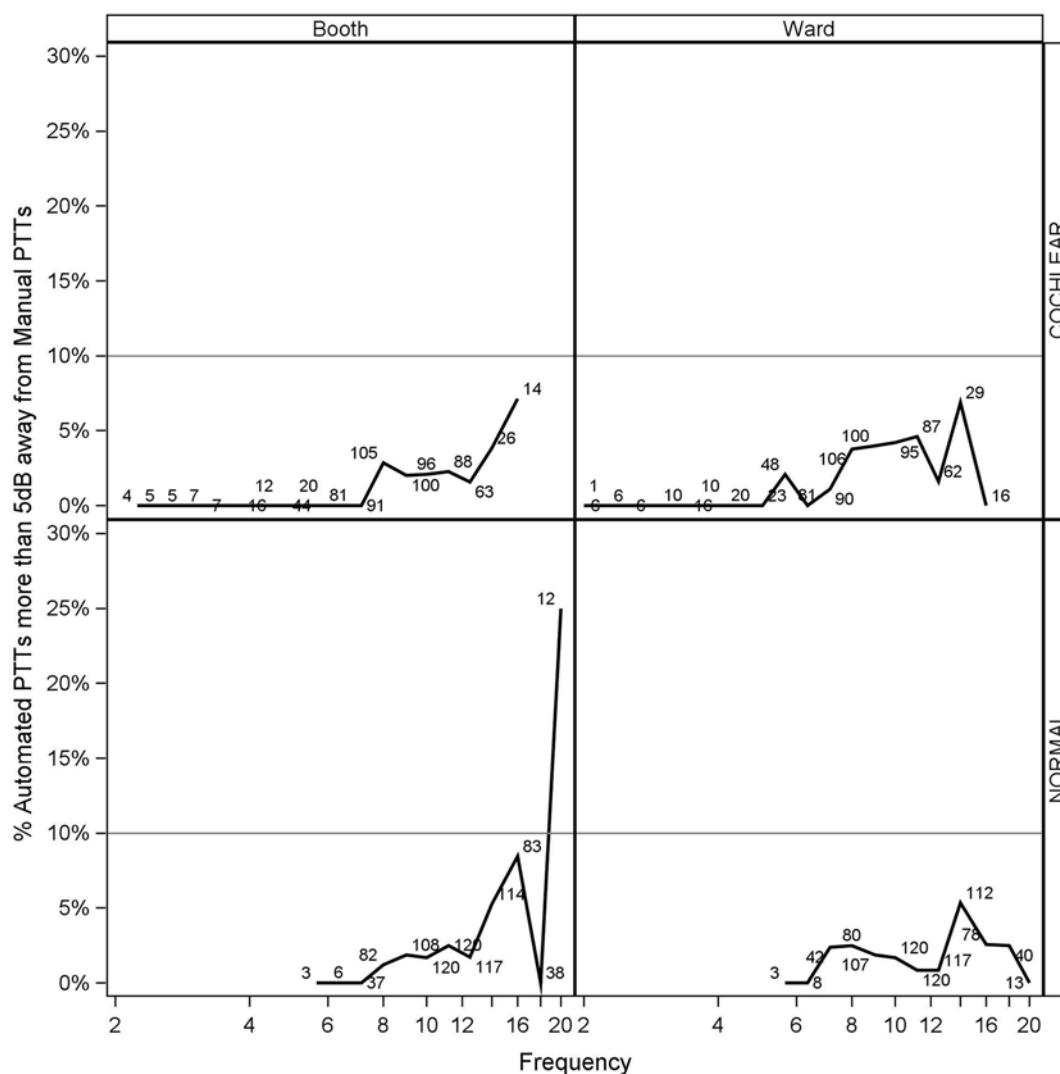
Figure 2.
Bias plot of percent of automated (self-test) OtoID pure tone threshold (PTT) tests that are more than 5 dB from manual (audiologist) test measurement taken on same ear at same time and place as function of test frequency. Numbers in each panel indicate number of separate visit measurements taken at each frequency.

normal thresholds at 16.0 kHz in the sound suite. This is indicated by the star in the bottom left panel and points to repeatability of about 85 percent for that frequency. When tested using normal hearing subjects in a sound booth, this frequency gives unacceptably low retest accuracy using the automated mode. Note also that the automated test gives lower repeatability throughout the extended frequencies (>8.0 kHz), though the difference was generally within the standard (±5 dB) across tests and/or subjects.

Table 3 shows the false-positive rates of hearing shifts. Hearing shifts that meet or exceed the ASHA hearing change criteria are considered false positives when found in subjects not in treatment. It was not uncommon for the SRO frequency range to vary. This situation, uncommon clinically, is one in which the SRO frequencies established at the first visit changed because of retest variability. This may be the result of the definition of "high frequency limit of hearing." This highest frequency showed an inherent fluctuation in our groups. However, in
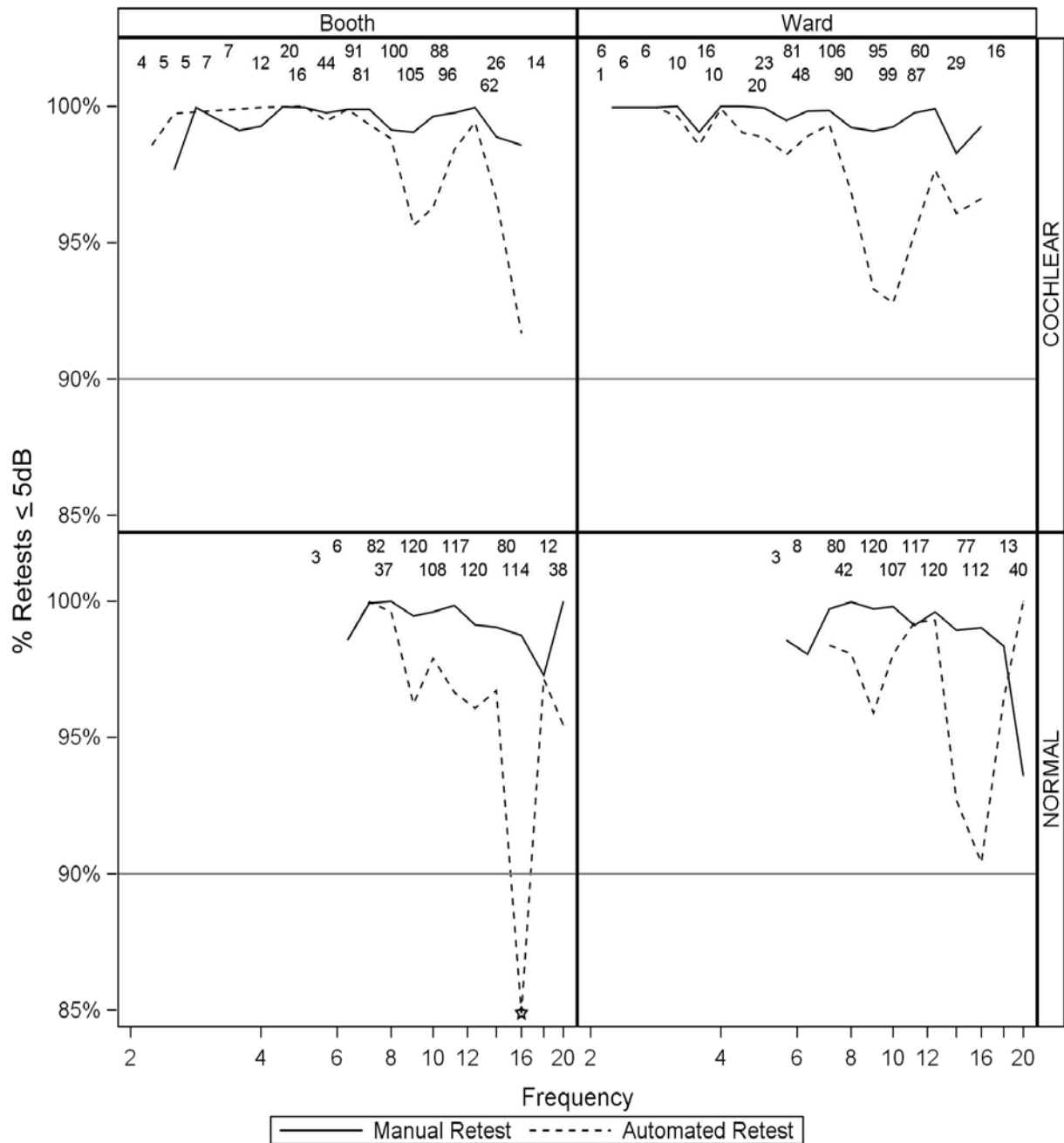
Figure 3.
Repeatability of manual (solid line) and automated (dashed line) OtoID protocols. Numbers in each panel indicate number of separate measurements by ear taken at each frequency and range from minimum of 1 to maximum of 120 individual tests.

practice, the SRO frequency is established at baseline and does not fluctuate, since this is the standard to which all subsequent tests are compared. The measurements in which the SRO did vary were not included in the analysis.

Manual testing yielded uniformly small false-positive rates of 0 percent under all conditions except for measurements of cochlear subjects tested on the ward (3.8%; two tests). The automated false-positive rates were somewhat

Table 3.
Estimated false-positive rates among normal and cochlear subjects in both locations using each testing protocol. First visit was used as baseline measure against which sensitive range for ototoxicity pure tone thresholds taken at second and third follow-up visits were compared. (*N* = number of tests).

Hearing	Location	*N*	Automated		Manual	
			n Shifted	False-Positive Rate (%)	*n* Shifted	False-Positive Rate (%)
Cochlear	Booth	55	3	5.5	0	0.0
	Ward	52	3	5.8	2	3.8
Normal	Booth	66	2	3.0	0	0.0
	Ward	64	0	0.0	0	0.0

higher for normal subjects tested in the booth (3%; two tests) and cochlear subjects tested in the booth (5.5%; three tests) and ward (5.8%; three tests). While the automated tests gave slightly higher false-positive rates, the actual number of tests was few and within acceptable limits. It should be kept in mind that, in actual practice, when an ASHA-significant shift in hearing occurs, regardless of the mode of testing, thorough retesting after repositioning the headphones is done by the audiologist to validate the findings.

DISCUSSION

Hearing impairment is the second most frequently awarded Veteran service-connected disability. Therefore, preservation of residual hearing is of primary importance. The current standard of care for ototoxicity monitoring is a cumbersome audiological evaluation in a sound booth, where logistical issues such as coordinated scheduling quickly become a hindrance to service delivery. A technology that can enable accurate ototoxicity monitoring with little-to-no disruption in treatment was needed. The OtoID adeptly provides "chairside" testing with extended frequency capability that capitalizes on the efficient and accurate SRO protocol. In those instances when audiology services are scarce, the OtoID automated mode accommodates reliable and accurate hearing self-monitoring.

Using a young normal–hearing cohort, a previous report showed that results obtained from the manual and automated OtoID test programs compared favorably with results from a commonly available clinical audiometer [8]. In this article, we present results evaluating the OtoID using subjects young and old both with and without cochlear (permanent-type) hearing loss. Subjects were tested across 3 days in both a sound booth and on a busy hospital treatment unit. When compared, the OtoID automated and manual modes of testing provided equiva-lent and repeatable results in a group of subjects who varied in age and in hearing status when tested in both locations. Further, there was little potential for false positive (for ototoxicity) findings, which is particularly important since no difference was expected.

There was high bias at 20.0 kHz (25%) and reduced repeatability at 16.0 kHz (≤85%) when testing young normal-hearing listeners in the sound booth using the automated mode. These findings are rather difficult to explain. The expectation is that listeners might have greater difficulty establishing threshold on a noisy hospital treatment unit than in a quiet test booth. Further, it might be expected that subjects with cochlear hearing loss would have more difficulty establishing threshold in a quiet test booth given their theoretically higher rates of interfering tinnitus. However, that is not what we found. Since we performed a complete calibration prior to initiation of the project, we do not believe that spurious distortion was present and audible to this subgroup of listeners in the automated mode. Therefore, the most plausible explanation is that for a percentage of time some listeners failed to attend to the task. Cooperating with four hearing tests across two locations in 1 day may have proved too difficult for some portion of listeners at some frequencies. It should be kept in mind that these highest frequencies (16.0–20.0 kHz) have been reported as a pressure sensation rather than tonal. Momentary inattention to subtle sensations of pressure seems likely. If this is true, this finding does not reflect on the device but rather on the hearing test task. Veterans often do not have hearing in these highest frequencies so for this population, the device seems well suited. However, for young subjects with better hearing, these highest frequencies may be part of the SRO but are at their hearing limit as well. Further, the number of tests with high bias ($n = 3/12$) or reduced repeatability ($n = 12/80$) was very small.

Though within tolerance for repeatability, automated threshold testing tended to result in greater variability

than when an audiologist directed the testing. This finding was likely the result of the algorithm directing the threshold procedure. Audiologists frequently resolve even minor changes between tests that are only weeks apart, especially when there is no reason to expect a hearing shift. This works well when a patient can tolerate extended testing such as with the majority of the subjects in this study. However, this might not work as well when sick patients are being tested. Resolution of minor threshold differences (±5 dB) would fatigue a sick patient unnecessarily, compromising the more important goal of a complete hearing test. This sort of "human discretion" is hard to code in a computer-driven automated test algorithm. Importantly, there was no bias in the automated mode testing, indicating that the algorithm is expedient and accurate.

CONCLUSIONS

The mean age of Veterans across our ototoxicity studies is 62 yr. Most Veterans entering treatment have significant histories of noise exposure such that even small decrements in hearing result in large changes in communication ease with family and with the oncology team. Ototoxicity monitoring has the potential to minimize debilitating postchemotherapy hearing loss if treatment can be changed. Cancer survivability is improving such that quality of life after treatment is emerging as an important treatment goal. An easy-to-use, sturdy device that allows hearing testing during treatment either professionally or through self-testing is available. In tight budgetary times such as these, husbanding professional resources by using automated testing strategies is an idea whose time has come. After testing, if hearing is found to be stable, no action is necessary. If, however, hearing has shifted, the audiologist can inform the Veteran and the oncology team of the change so that (1) treatment options can be discussed with the patient and (2) auditory assistive devices can be considered.

Currently, the OtoID is undergoing improvements to add remote data transfer via SMS (simple messaging system) so that testing can be done at home by chemotherapeutic patients. Data transfer capabilities will allow the audiologist to monitor hearing thresholds in real time from a central location and provide the opportunity for the audiologist to contact the patient for a professional hearing assessment prior to the next treatment if there is

evidence of hearing changes. The OtoID device will enable the widespread implementation of ototoxicity monitoring best practices and provide clinicians the critical information and opportunity to minimize or prevent the progression of hearing loss, ultimately preserving a high quality of life for Veterans following treatment.

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