Toward a Better Understanding of Electrocochleography: Analysis of Real-Time Recordings

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Objectives: Real-time electrocochleography (ECochG) has been used as a monitoring tool during cochlear implantation (CI), whereby, amplitude drops have been correlated with postoperative acoustic hearing results. However, no consensus has been reached as to how a single event of an amplitude drop should be characterized. The aim of this study was to identify ECochG events that predict loss of hearing 1 month after surgery.

Design: Fifty-five patients were included in this prospective cohort study. Real-time ECochG measurements were performed during CI electrode insertion. Single ECochG events were characterized according to their amplitude loss and slope steepness.

Results: Using receiver operating characteristic analyses, the most efficient cut-off criterion for a relative hearing loss of 25% was an amplitude loss of 61% at a fixed slope steepness of 0.2 µV/sec. Three-quarters of our population had at least one such event during implantation. Most events occurred shortly before full insertion. With increasing number of events, median residual hearing thresholds deteriorated for all frequencies. Larger amplitude drops trended toward worse hearing preservation. Signal recovery after an ECochG event could not be correlated to acoustic hearing outcomes.

Conclusions: Our data suggest that amplitude drops exceeding 61% of the ongoing signal at a slope steepness of 0.2 µV/sec are correlated with worse acoustic hearing preservation. Clearly defined ECochG events have the potential to guide surgeons during CI in the future. This is essential if a fully automated data analysis is to be employed or benchmarking undertaken.

Key words: Amplitude loss, Hearing preservation, Real-time electrocochleography.

(Ear & Hearing 2020;41;1560–1567)

INTRODUCTION

The measurement of acoustically evoked inner ear potentials, also called electrocochleography (ECochG), has been undertaken by clinicians for many decades (Ruben et al. 1961). Recordings were described to be a good predictor of peripheral hearing more than 30 years ago (Bellman et al. 1984). In recent years, the technique has been increasingly used during cochlear implantation (CI); intermittent or real-time measures are now used to monitor this surgery (Campbell et al. 2015; Harris et al. 2017; Dalbert et al. 2018).

During implantation, two main techniques for recording ECochG have been described. For the extracochlear technique, a recording electrode is introduced into the middle ear and positioned onto the promontory (Choudhury et al. 2012; Dalbert et al. 2016; Giardina et al. 2018). With intracochlear recordings, the electrode from the implant itself (or a temporarily introduced dummy electrode) is used (Campbell et al. 2015). The latter technique can be further subdivided into measurements taken during the insertion of the electrode (so-called "real-time" ECochG) and measurements taken after the electrode is in place.

Both, extra- *and* intracochlear recordings have been shown to predict postoperative preservation of residual hearing. Fluctuations of ECochG amplitude derived from *extracochlear* recordings, that occur before and after full electrode insertion, have been shown to correlate with hearing loss 4 weeks after implantation (Dalbert et al. 2018). However, other authors could not substantiate these findings (Adunka et al. 2016). During *intracochlear* real-time ECochG, manipulation of the electrode was shown to be reflected by amplitude decreases of the ECochG signal (Harris et al. 2017). Monitoring a drop in amplitude of the ECochG signal without recovery has been associated with poorer preservation of residual hearing (Campbell et al. 2016).

Whereas intra- *and* extracochlear recordings have been correlated with postoperative acoustic hearing results, only intracochlear real-time measurements have the potential to provide immediate feedback to surgeons during implantation. If we knew how to interpret ECochG signals, at the first sign of pending hearing loss a potentially traumatic insertion could be modified (e.g., correction of insertion trajectory, reduction of force, and partial instead of full electrode insertion). In current literature, a detrimental event during real-time ECochG is thought to be a reduction in response amplitude. This has been observed on the difference between responses evoked by alternating rarefaction and condensation polarity pure-tone pips (the "DIF" response) (Campbell et al. 2016; Harris et al. 2017; O'Connell et al. 2017) or on a combination of the summation and difference responses derived from these stimuli (Dalbert et al. 2018). However, no consensus has been reached on the definition of a clinically significant drop in ECochG amplitude. If ECochG measurements are to be used to guide surgeons in the future, a better definition and characterization of real-time recordings must be achieved. This is particularly essential if a fully automated data analysis is to be used to guide surgeons who are less experienced in interpreting ECochG results. The aim of this study was to better characterize changes in real-time ECochG recordings and relate them to postoperative hearing loss.

MATERIALS AND METHODS

Study Participants

The study was conducted in accordance with the Declaration of Helsinki (1975) and had been approved by the local ethical

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Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and text of this article on the journal's Web site (www.ear-hearing.com).

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<zdoi; 10.1097/AUD.0000000000000871>

committee (Human Research Ethics Committee, Royal Victorian Eye and Ear Hospital, project number 14/1171H). Written consent was given by all participants.

Fifty-five adults undergoing CI with a CI522 Slim Straight Electrode (Cochlear, Australia) were included in the study. All participants had postlingual hearing loss and a preoperative hearing threshold of 100 dB hearing level (HL) or less at 500 Hz. CI was performed by drilling a posterior tympanotomy and inserting the electrode through a round window membrane incision. Complete insertion of all electrodes was confirmed by neural response telemetry (NRT). The study was purely observational; during the insertion of the electrode, no feedback was given to the surgeons.

Data Collection

ECochG measurements were performed using the cochlear response telemetry (CRT) system, developed at our institution (Campbell et al. 2015). Acoustic stimuli were generated using a USB data acquisition card (DT9847, Data Translation, USA), produced by an Etymotics ER3A transducer (3M, USA), and supplied using insert E-A-RLINK Foam Ear Tips 3B (3M, USA). Acoustic stimuli with alternating polarities (condensation and rarefaction) were presented, identical with the ones used in our previous studies (Campbell et al. 2016). A tone pip at 500 Hz was used, 6 msec in length with an on-/off-set ramp of 1 msec and a 70 msec interstimulus interval. Stimulus intensity was at 100 dB HL for patients with a preoperative pure-tone hearing threshold of 70 dB HL or better at 500 Hz or 110 dB HL if the hearing threshold was worse. After conditioning of the electrode, responses from alternating polarity stimuli were saved in separate buffers, with an average of 100 samples taking approximately 5-sec. The sampling rate was 20 kHz, filtered with a 15th-order digital bandpass with a Hamming window from 450 to 550 Hz.

Recordings were processed by subtracting the alternating phase responses [DIF response, often referred as cochlear microphonic (CM)]. It must be stressed that, especially in low-frequency stimulation, DIF signals can also contain traces of the summation (SUM) signal (Forgues et al. 2013). The magnitude of the DIF response was calculated by using the fast Fourier transform (FFT) of the first harmonic (zero-padded to 1000 samples in length for a bin-width of 20 Hz, to ensure an integer-number of samples from the period of interest to prevent spectral smearing). System noise was calculated as the standard deviation of 6 FFT bins, 3 above and 3 below the 500-Hz bin, separated from 500-Hz by 3 bins. Figure 1 in the Supplemental Digital Content 1, http://links.lww.com/EANDH/A640, shows an example of a patient recording with a sudden drop and no recovery of the DIF signal. For further calculations, we used *relative* amplitude changes (i.e., percentage loss) of the DIF signal, because signal magnitudes differed greatly between individuals (median DIF magnitude at start of insertion 13.02 dB re: 1 μV, but ranged between –16.6 and 39.8 dB). Calculation of the relative amplitude changes has the advantage of normalizing changes in the response so that patients can be compared. Furthermore, relative changes are independent of stimulus intensity, which may differ between individuals with differing levels of preoperative hearing. Only real-time recordings were included in the analysis; however, for patients with no traceable ECochG signal during real-time measurements, postinsertion signals (500-Hz stimulus of 12 msec length and 50 msec interstimulus window, with an average of 100 measurements) were examined to gain a better understanding of why a signal could not be recorded during implantation.

Figure 1 shows pre- and postoperative hearing thresholds of all participants. As postoperative measure, we used the 4 weeks (or closest available) postinterventional hearing test. Relative hearing loss measures were calculated at different frequencies (250, 500, 1000, and 2000 Hz). This ratio was calculated as adaptation from the method of (Skarzynski et al. 2013) using following formula:

$$\frac{(\text{4 weeks postoperative hearing threshold @ f Hz- preoperative hearing threshold @ f Hz})}{(\text{120 dB - preoperative hearing threshold @ f Hz})}$$

Thereby, a value of 0 corresponds to no loss and a value of 1 to a complete loss of residual hearing.

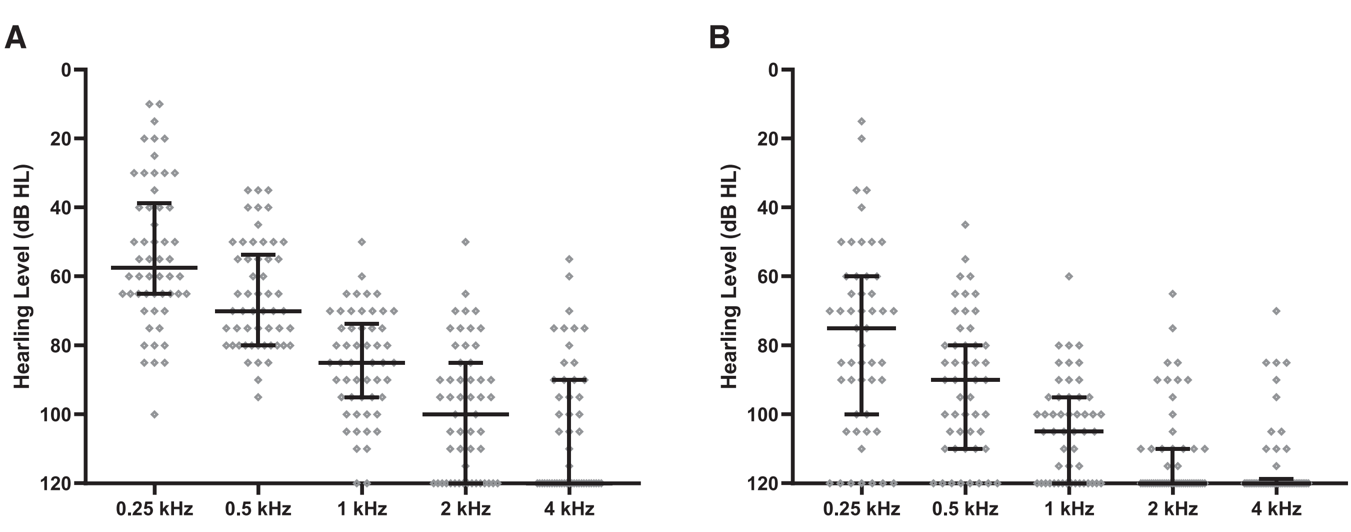

Fig. 1. Pre- (A) and 4 weeks postoperative (B) hearing tests for all included individuals. For all frequencies, the median and interquartile ranges are shown. The median hearing threshold at 500 Hz before surgery is 70 dB HL (53.75–80) and after surgery 90 dB HL (80–110).

Data Analysis

A DIF response was considered significant if the amplitude was three times greater than the calculated noise floor. Further, signal consistency was checked visually by three separate referees, experienced in reading and interpreting ECochG recordings. Only patients with valid ECochG signals were included in further analysis. For data analysis MATLAB (version 2017, MathWorks, USA) and GraphPad Prism (version 7, GraphPad Software, USA) were used. If required, nonparametric statistical tests were chosen to account for not-normally distributed data.

First, an ECochG event was defined requiring two characteristics: amplitude loss of the DIF signal and slope steepness. For the latter criterion, which indicates the rate of signal decay, the threshold was set at 0.2 µV/sec between two traces (which were acquired at 1 Hz). This ratio was chosen empirically (1) to exclude cases with a very slow signal decay and (2) to clearly define where an amplitude drop ends. To determine the cut-off amplitude loss of an ECochG event, for every individual, MATLAB calculated a bucket of DIF amplitude drops meeting the steepness criteria. We then put in the maximum DIF amplitude drop of each individual into a receiver–operator curve (ROC) analysis (n = 45, down from the possible 47 as 2 patients had incomplete audiometric data). As classifier, we used the binary "hearing preservation" metric of >25% loss of residual hearing at 500 Hz, 1 month after surgery (Skarzynski et al. 2013). Our rationale to set the classifier threshold at 25% relative hearing loss was to differentiate between patients who could keep (almost) all their residual hearing (atraumatic cases), and patients who lost part or all of their acoustic hearing. If an area under the curve of significantly greater than 0.5 was reached, resampling techniques (1000 bootstrap replicas) were used to estimate the sensitivity, specificity, and positive and negative predictive values. By calculating the Youden's J statistic, the most efficient cut-off criterion was determined (Youden 1950). ECochG DIF drops exceeding this threshold defined an "event" during real-time recordings. For every patient, the number, the relative amplitude loss (percent change of the ongoing DIF signal), and the recovery rate (percent recovery of the signal related to the predrop levels) of events were estimated and related to hearing loss.

RESULTS

Traceable ECochG Signal

To determine the noise floor of the system, we measured five responses with a clamped sound tube immediately after implantation. The mean measured noise amplitude was 0.1 µV with a standard deviation of 0.05.

Forty-seven patients out of 55 patients (85%) had useful and interpretable ECochG signals. In eight cases (15%), noise, but no significant DIF signals, were recorded. Hearing thresholds for these cases did not differ from the rest of the cohort; median hearing thresholds for the "nonresponder" cases were 55 dB HL at 250 Hz, 62.5 dB HL at 500 Hz, 77.5 dB HL at 1 kHz, 92.5 dB HL at 2 kHz and 97.5 dB HL at 4 kHz. In four of the eight cases, no traceable postinsertion measurements (i.e., measurements after achieving full insertion) were obtained. In the other four, postinsertion measurements were obtained, showing a valid DIF response. For further data evaluation, only cases with a detectable DIF signal during insertion were included.

Receiver-Operator Curve

In the receiver–operator curve calculation, a 61% amplitude DIF loss was the most efficient cut-off criterion for detecting detrimental ECochG drops, returning a good test with an area-under-curve of 0.81, significantly greater than 0.50 (95% CI from 0.60 to 0.93, $p < 0.0001$, shown in Fig. 2). With this criterion, calculated after 1000 bootstrap replicas, the statistics of the test are shown in Table 1. This threshold was used to define ECochG events in the subsequent analyses.

Number of ECochG Events

Twenty-three percent of all patients with traceable signals had no ECochG event with greater than a 61% drop of response during implantation (see Fig. 3A). Fifty-six percent of individuals showed 1 event, 17% showed 2 events, and 4% showed 3 events.

Individual patient data are presented in Figure 3B with medians and interquartile ranges (IQRs) depicted. A Kruskal–Wallis test was conducted to determine if there was a difference in hearing outcomes between the groups of 0, 1, and 2 drops, excluding the group of 3 drops because there were too few (2) patients. Preservation of residual hearing at 500 Hz was statistically different between the three subgroups ($\chi^2(2) = 8.48$, $p = 0.0144$). Post hoc Dunn's comparison showed a significant difference between 2 drops and 0 drop, but no significant difference for the other comparisons. Table 2 shows the distribution of number of drops and the corresponding relative hearing loss at different frequencies. With an increasing number of drops, relative median residual hearing loss increased for all frequencies.

Timing of ECochG Events and Amplitude Loss

In regard to the timing of the ECochG events, most events (54%) occurred when the electrode was being advanced from the first white electrode marker (20 mm) to full insertion (25 mm,

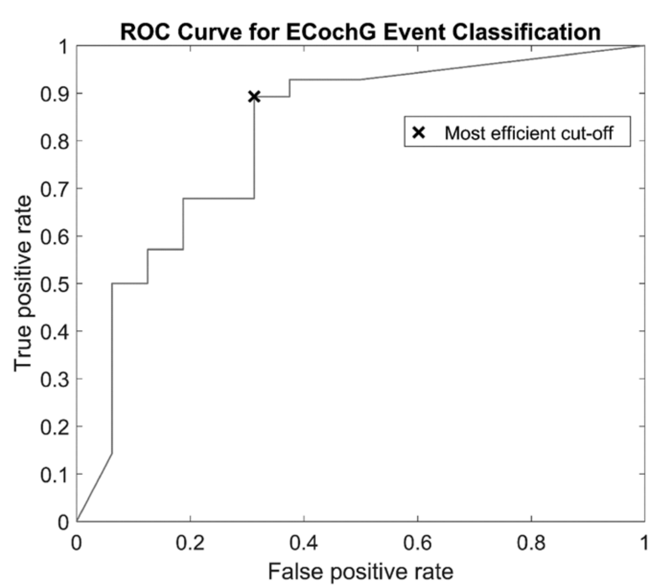

Fig. 2. Receiver–operator curve for the prediction of postoperative hearing loss as a function of DIF signal drop threshold. The point of maximum efficiency was defined by calculating the Youden's J statistic shown here as an X. DIF indicates difference; ECochG, electrocochleography; ROC, receiver–operator curve.

TABLE 1. Receiver–operator curve calculated for the prediction of postoperative hearing loss using the threshold of DIF signal drop for maximum efficiency, after 1000 bootstrap replicas to provide 95% CIs

	AUC	Sensitivity	Specificity	PPV	NPV
Mean	0.81	89%	69%	79%	82%
Upper limit 95% CI	0.93	97%	89%	79%	83%
Lower limit 95% CI	0.6	72%	40%	78%	81%

AUC indicates area under the curve; CI, confidence interval; DIF, difference; PPV, positive predictive value; NPV, negative predictive value.

Fig. 4). This was followed by placement of fascia to seal the round window when 28% of ECochG events occurred. Fewer patients had an event within the first 10 mm of the insertion, or between 10 and 20 mm (10 and 8%, respectively). The relations between the time when ECochG events occurred and preservation of residual hearing (again, just for with cases with one event), is shown in Figure 5. There were insufficient data in most groups to subject these to a statistical analysis. Although, in the few cases where ECochG events occurred during early electrode insertion, the relative hearing loss exceeded 0.5. In one of these cases, a translocation of the electrode was demonstrated on postoperative imaging (the only verified translocation in this study group).

To explore whether larger amplitude losses of ECochG events are associated with greater loss of residual hearing, the analysis was performed on patients with 1 drop only. There was a nonsignificant trend toward larger drops causing worse preservation of residual hearing (Fig. 6).

Maximal Signal Magnitude and Signal Recovery

In 15/47 patients (32%), maximal DIF amplitudes of the real-time recording were observed in the period *after* full insertion (see Fig. 7A). In four of these cases, ECochG event(s) had occurred before maximal signal amplitude was reached (median hearing loss at 500 Hz 45 dB, IQR 27.5 to 55). In 6 cases, events occurred after the maximum amplitude was seen (median hearing loss at 500Hz 30dB, IQR 30 to 55). And in five implant recipients, there was no ECochG event. In these cases, residual hearing was preserved much better (median hearing loss at 500 Hz 10 dB, IQR 5 to 12.5).

When comparing signal recovery following a single ECochG event (only including patients with 1 drop), no differences could be found between patients with and without signal recovery (Fig. 7B).

DISCUSSION

This study used an ROC analysis to define ECochG events in real-time measurements. Events were characterized by a required amplitude loss and slope steepness of the DIF signal. The so defined events were then further analyzed in relation to surgical progress and preservation of residual hearing.

To the best of our knowledge, no other study with real-time recordings has attempted to quantitatively describe single ECochG events. So far, one study correlated the DIF magnitude change between start of insertion, peak value, and end value to the pure-tone average shift [no significant correlation was found (O'Connell et al. 2017)]. Others have described if a drop recovered to predrop levels (Campbell et al. 2016). Finally, others have reported descriptive observations (Harris et al. 2017; Dalbert et al. 2018). If real-time recordings are to be used to guide surgeons in the future, understanding the ramifications of single events is mandatory and must be studied more carefully. Furthermore, better definition of the characteristics of ECochG events will allow for benchmarking and better comparison between studies.

Validity of Real-Time Responses

Valid real-time DIF responses can be measured in most of the cases. In our study cohort, an interpretable DIF signal could

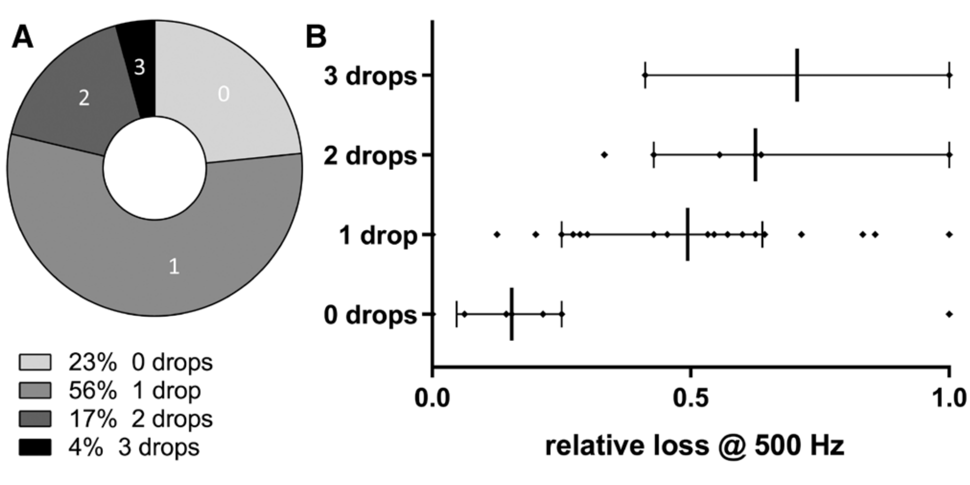

Fig. 3. A, Number of ECochG events in all participants. Twenty-three percent of patients showed no, 77% showed one or more ECochG events. B, The relative loss of residual hearing at 500 Hz (*x*-axis) is correlated to number of drops (*y*-axis). The median and interquartile ranges are shown. More ECochG events lead to an increase in the median relative hearing loss. For patients with one ECochG event, there is a large dispersion of data; some patients preserve their residual hearing, whereas others lose it completely. ECochG indicates electrocochleography.

TABLE 2. The distribution of number of events, patients in these subgroups, and the corresponding relative hearing loss at different frequencies

	n	250 Hz	500 Hz	1000 Hz	2000 Hz
0 events	10	0.0	0.2	0.3	0.4
1 event	27	0.3	0.5	0.4	0.8
2 events	8	0.4	0.6	0.9	0.8
3 events	2	0.7	0.7	1.0	1.0

With an increasing number of events, relative median residual hearing loss increases for all frequencies.

not be recorded 15% (8 patients). This stands in contrast with findings from Harris et al. (2017) where successful real-time measurement was possible in all cases (n = 14). In our series, lack of real-time signals might have been due to an unfavorable signal-to-noise ratio (SNR): in 4 patients, postinsertion measurements showed a valid DIF response. With the postoperative recordings, a different stimulation protocol was applied (Campbell et al. 2015), using longer stimulation periods and averaging more responses which would have improved the SNR. In the other half of patients with no valid ECochG traces, no real-time *and* no postinsertion measurements were measured. Here, the issue may have either been a technical problem with the system (e.g., interference with the lead or failure of the acoustic amplifier), the setup (e.g., kinked sound tube, fluid entering into the ear canal during the procedure), or a complete absence of functioning hair cells (which led to a lowered response amplitude, not significantly different from noise).

Cut-Off Criterion for ECochG Events

In our ROC analysis, a relative loss of 61% of the DIF signal was the most efficient cut-off criterion for association with a 25% postoperative hearing loss. This definition provided a good test for detecting approximately 80% of all patients with at least a moderate loss of residual hearing through a relatively straightforward monitoring paradigm. In a previous paper, Giardina et al. (2018) calculated the test-retest reliability of extracochlear ECochG drops. Strikingly, a signal loss exceeding 61% was statistically more likely to be caused by trauma to the inner ear and could not be explained by simple variability of the measurement.

It should be noted that the adoption of a 61% reduction in the DIF signal as an ECochG event was dependent upon the detection of a relatively small, 25% relative loss on the audiogram

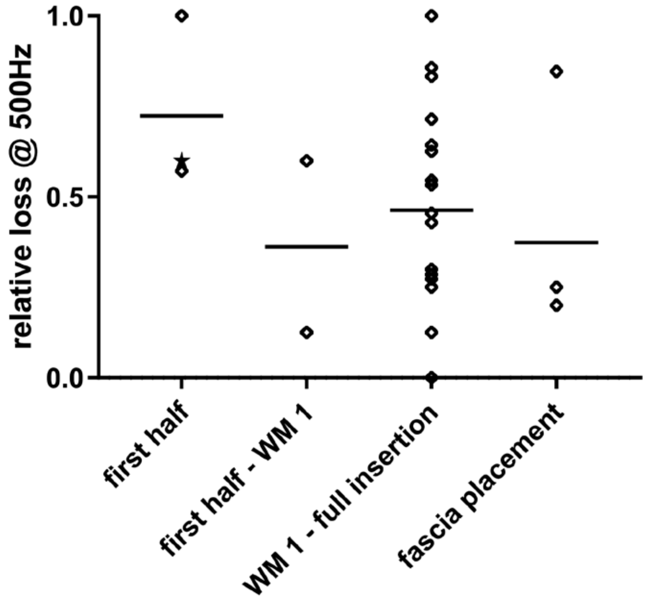

Fig. 5. The relations between the time when ECochG events occur (*x*-axis; WM) and the relative hearing loss at 500 Hz in dB (*y*-axis) is shown. In the few cases where ECochG events occur during early insertion, the relative hearing loss exceeds 0.5 (the case with electrode insertion into scala vestibuli is marked with a star symbol). ECochG indicates electrocochleography; WM, white marker.

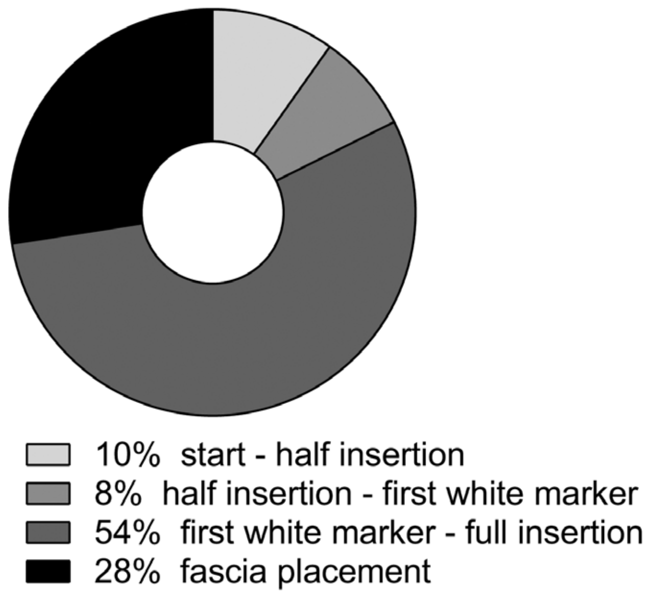

Fig. 4. Correlation of ECochG events to surgical progress. Most events occurred shortly before full insertion. ECochG indicates electrocochleography.

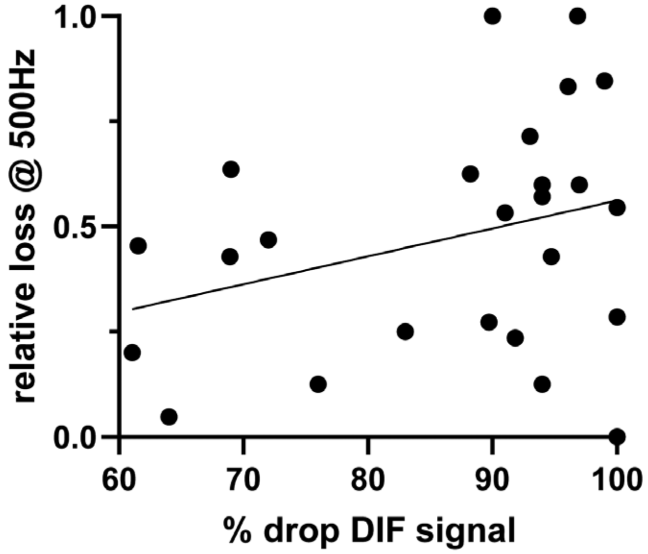

Fig. 6. For patients with 1 ECochG event, the percent amplitude loss (*x*-axis) is correlated to the relative loss of residual hearing at 500 Hz (*y*-axis). There is a nonsignificant trend toward larger drops causing worse preservation of residual hearing. DIF indicates difference; ECochG, electrocochleography.

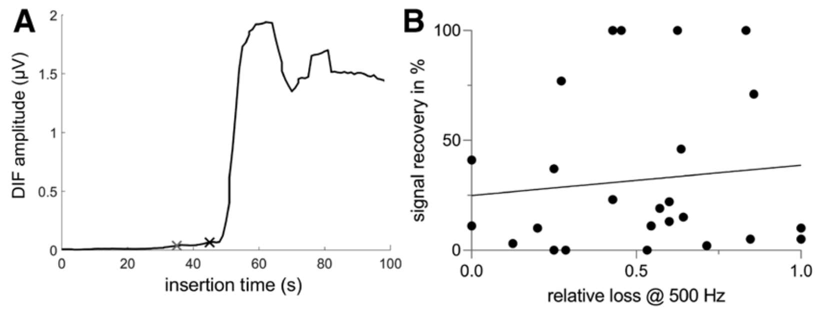

Fig. 7. A, In one-third of the patients, maximal DIF magnitudes are reached after full insertion. Here, an example is shown of a patient with no ECochG event during recordings. The gray cross signifies white marker 1, the black cross white marker 2. B, Relative hearing loss at 500 Hz (*x*-axis) is compared with signal recovery in percent after single ECochG events (*y*-axis). There was no statistical correlation. DIF indicates difference; ECochG, electrocochleography.

as defined by Skarzynski et al. (2013). Had the hearing-loss criterion been greater, for example, a "complete" loss of hearing, the DIF-signal cut-off would have differed. Furthermore, it is important to note that the relatively low specificity suggests that the state of the DIF signal during implantation does not capture all causes of postoperative hearing loss. Nor would this be expected, as postoperative hearing loss is presumed to be caused by intracochlear inflammation as suggested by its association with peaked electrode impedances (Choi et al. 2017; Scheperle et al. 2017; Chanan Shaul 2019). A holistic approach to cochlear health monitoring, that includes the perioperative condition of the DIF signal, as well as postoperative measures, such as electrode impedances, may be required to capture all hearing loss events.

Finally, if real-time ECochG signals are to be used in a surgical intervention, there is an argument that the surgeon should react to a less than 61% drop in the DIF signal. The observations made here reflect the ramifications of *passive observation* of DIF signal fluctuations when there is no surgical intervention. A similar analysis performed on data where surgeons had been given a chance to modify their surgical technique at the time may have led to a very different cut-off. Further studies must evaluate how quickly a surgeon can intervene to abort a traumatic implantation. Until further data are available, it would make sense from a surgical perspective to react as soon as a CM drop could be detected by a human observer, which we estimate to be a ≈30% reduction.

Number and Amplitude of ECochG Events

In our cohort, ECochG events occurred frequently (77% of patients showed at least one event). This number stands in accordance with an earlier study (Campbell et al. (2016) where 80% of the population showed a signal loss of the DIF trace during recordings.

In our analysis, the number of ECochG events correlated inversely with the degree of hearing preservation (Fig. 3B); patients with no ECochG event showed, in most cases, preserved acoustic hearing. While there was a large dispersion of data for patients with one ECochG event, with increasing numbers of events, the data clustered more closely together. In cases with two or more events, persistent hearing loss was more likely. In existing literature, Campbell et al. (2016) demonstrated that patients with amplitude loss of the DIF signal without recovery showed less hearing preservation than patients with no loss of the signal or lack of recovery after the ECochG event. However, in their study, not every amplitude drop was associated with a traumatic hearing loss; 2 out of 7 patients displaying a loss of the DIF signal without complete recovery, only lost very little of their acoustic hearing (Campbell et al. 2016). In our cohort, patients with one ECochG event displayed a wide variability of postoperative hearing outcome; some showed a complete loss of acoustic hearing, whereas others could preserve their inner ear function (Fig. 3B).

The positive predictive value of our ROC calculations computed 79% of correct detections of a significant postoperative hearing loss. We assume, that in falsely positive cases, the ECochG amplitude decreases due to mechanical changes within the inner ear without damaging the organ of Corti (DeMason et al. 2012). For example, the electrode might have contacted the basilar membrane only temporarily without damaging the epithelial lining of the scalar tympani. Furthermore, an atraumatic amplitude drop could also occur when the most apical electrode passes by the 500 Hz region. In the human cochlea, when considering individual variability in the length of the basilar membrane, the 500 Hz region for a cochlea with passive cochlear mechanics has been estimated to fall between 450° and 540° (Stakhovskaya et al. 2007). This is within the range of insertion angles reported with this electrode (e.g., 410.5° ± 77.6, range 282 to 585°; O'Connell et al. 2016), so the electrode tip may be expected to pass the 500 Hz region in some cases. The chances of this are heightened by the high levels of acoustic stimulation used here and hearing loss of the patients, both of which shift the excitation pattern of the cochlea basally (Eggermont 1979). on the other hand, our ECochG events were defined by the amplitude loss *and* the slope steepness. Later criterion was used to exclude cases with a slow signal decay. As during implantation electrodes are inserted very slowly, we assume that passing the 500 Hz point would lead to a gradual signal decrease, not fulfilling the criteria of an event.

There are also false-negative cases. The negative predictive value of our ROC analysis was estimated at 82%. One patient of our cohort with no ECochG event still suffered from a complete loss of acoustic hearing at 500 Hz (Fig. 3B). ECochG only detects cochlear injury directly impacting upon cochlear mechanics or outer hair cell function. Other potential injuries, such as damage to the endosteum away from the basilar membrane may not be detected by this method. Such incidents can have downstream effects, for example, bleeding may lead to increased inflammation and fibrosis, both of which are expected to cause a secondary loss of inner ear function (Radeloff et al. 2007).

In conclusion, it can be said that every ECochG event is a potential risk to lose acoustic hearing and multiple events make it statistically much more likely that (at least) one event will be detrimental to the inner ear.

Timing of ECochG Events

In our series, most ECochG events occurred during the last stages of the electrode insertion. This finding corroborates previous study results where most drops could either be found in the second half of implantation (Dalbert et al. 2018) or between the first and second white marker of electrode insertion (Campbell et al. 2016). Drops also often occurred during placement of fascia and placement of the electrode within the mastoid cavity. This has been well documented and described by Harris et al. (2017). When fascia is placed in the round window niche, there is a potential risk of electrode movement. The same applies to positioning of the electrode within the mastoid cavity. There, the electrode is often held with two electrode forceps, possibly leading to force transmission into the inner ear.

The timing of ECochG events also seems to have implications for preservation of acoustic hearing: all patients with an early drop showed a relative hearing loss greater than 50% (Fig. 5). However, the small sample size of this subgroup has to be taken into account. Early drops could be explained by an unfavorable trajectory of the electrode, leading to an early and traumatic signal loss. In accordance with that, in one patient of our cohort, a translocation of the electrode into scala vestibuli could be substantiated. ECochG drops that occurred as the electrode was advanced from its mid-point to the first white marker or drops that occurred during placement of fascia on the round window were associated with less relative loss of residual hearing. When the ECochG signal dropped as the electrode was advanced from the first white marker to full insertion, there was considerable dispersion in the postoperative acoustic hearing loss. As noted above, we hypothesize, that, as the diameter of the cochlea progressively narrows down, in some events the basilar membrane might have been contacted by the advancing electrode (leading to an ECochG event) without severely damaging the organ of Corti, whereas in other cases there was probably greater trauma.

Signal Recovery After ECochG Events and Maximal Signal Magnitude

In this series, recovery following single ECochG events did not correlate significantly with preservation of residual hearing. A previous study showed that patients with signal recovery had better acoustic hearing results compared with patients where DIF signals stayed low (Campbell et al. 2016). The observation that recovery of single events is not significant could be interpreted that attempts to recover ECochG amplitude are futile. However, it must again be emphasized that this is an observational study. In other words, the surgeon was not aware when the ECochG signal dropped and had no opportunity to respond. Whether immediate surgical intervention does indeed recover hearing remains to be proven.

In a third of patients, the peak amplitude of the real-time signal was seen after full insertion (Fig. 7A). The same findings were observed in extracochlear recordings (Adunka et al. 2016). A possible explanation for this effect may be the release of basilar membrane from fixation by a surgical manipulation of the electrode. If this is indeed the mechanism, then one might have expected signal recovery to better predict preserved acoustic hearing. However, as described above, it is not possible to detect certain types of inner injuries, such as abrasion and or bleeding of the endosteum which are likely to precipitate subsequent inflammation and hearing loss.

Limitations

We note that calculations used for our ROC analysis were measured from a dependant sample with limited size. Our results are a first step to define events during real-time recordings more clearly. Whether these values are predictive of hearing loss (rather than just being associated with it) must be validated against an independent and larger data set.

Regarding the degree of residual hearing, in this study, we also included patients which (preoperatively) were not eligible for electro-acoustic stimulation (Fig. 1). However, in our opinion, an atraumatic insertion technique is advisable in all implant patients to better preserve cochlear structures. In the future, new technologies and treatment options may arise requiring the exchange of the existing electrode and/or to combine the inserted electrode with biological treatments. We believe that a monitoring tool will be valuable in all patients with residual acoustic hearing.

We did not include phase shifts or absolute magnitudes of the DIF signal as a variable in our analysis. Other authors have shown that these parameters can provide relevant information on possible inner ear trauma during implantation (Koka et al. 2018; Giardina et al. 2019a). Phase shifts during DIF signal decays have been explained by differing signal generators indicating atraumatic ECochG events (Giardina et al. 2019b). Furthermore, other components of the ECochG signal might also be of interest as well [i.e., SUM signal, compound action potential (CAP), and summating potential]. The SUM signal is the summation of responses evoked by alternating rarefaction and condensation polarity pure-tone pip [often referred as auditory nerve neurophonic (ANN)]. However, the SUM response usually has a poorer SNR than the DIF signal. Mandalà et al. (2012) used CAP recordings to monitor CI and to guide surgeons during the procedure. However, compared with the CAP signal, the DIF trace has been shown to be more sensitive for detecting cochlear disturbance (Choudhury et al. 2014) and has a better SNR (Campbell et al. 2016). In our experience, and in accordance with previous literature (Scott et al. 2016; Abbas et al. 2017), the CAP is often exceptionally small in patients undergoing CI. In conclusion, taking into account multiple parameters may achieve higher positive predictive values.

Last, in this paper, we have solely described intracochlear real-time recordings. Other authors have argued that extracochlear measurements could be advantageous as they describe a whole-cochlear response (Dalbert et al. 2018). However, extracochlear signals have poorer a SNR and therefore require more averaging. This circumstance makes it difficult to use extracochlear recordings as real-time measures to guide surgeons with immediate feedback. Finally, the extracochlear response tends to be weighted toward hearing arising from more basal regions of the cochlea, which introduces its own set of complexities of interpretation.

CONCLUSION

In this study, real-time ECochG recordings were made during cochlear implant surgery, applying a passive observational protocol where surgeons were not informed of changes in the ECochG signal. On an ROC analysis, a drop of DIF amplitude exceeding 61% at a slope steepness of 0.2 μV/sec or higher was the most efficient cut-off for association with a 25% drop in residual hearing 1 month after surgery. Multiple such events put the acoustic hearing at greater risk. Signal recovery of the real-time signal was a poor predictor of hearing preservation. These results are a first step toward an automated intraoperative feedback tool to guide surgeons during electrode insertion. Furthermore, clearly defined ECochG events will allow a better comparison between studies.

ACKNOWLEDGMENTS

A.C.'s employer, the University of Melbourne, receives research grants from Cochlear. R.J.B. is a Consultant to Cochlear (Sydney, Australia). S.O.L. is funded by the National Health and Medical Research Council (Australia). His employer, the University of Melbourne, receives research grants from Cochlear.

All authors contributed equally to this work. S.W. analyzed the data and wrote the paper. C.B. designed the experiment and wrote the code for signal processing. A.C. wrote the code for signal processing. C.S. and R.J.B. provided interpretive analysis and critical revision. S.O.L. designed the experiment, analyzed the data, and provided interpretive analysis and critical revision.

The authors have no conflicts of interest to disclose.

Received April 18, 2019; accepted February 4, 2020.

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REFERENCES

Abbas, P. J., Tejani, V. D., Scheperle, R. A., et al. (2017). Using neural response telemetry to monitor physiological responses to acoustic stimulation in hybrid cochlear implant users. *Ear Hear, 38*, 409–425.

Adunka, O. F., Giardina, C. K., Formeister, E. J., et al. (2016). Round window electrocochleography before and after cochlear implant electrode insertion. *Laryngoscope, 126*, 1193–1200.

Bellman, S., Barnard, S., Beagley, H. A. (1984). A nine-year review of 841 children tested by transtympanic electrocochleography. *J Laryngol Otol, 98*, 1–9.

Campbell, L., Kaicer, A., Briggs, R., et al. (2015). Cochlear response telemetry: Intracochlear electrocochleography via cochlear implant neural response telemetry pilot study results. *Otol Neurotol, 36*, 399–405.

Campbell, L., Kaicer, A., Sly, D., et al. (2016). Intraoperative real-time cochlear response telemetry predicts hearing preservation in cochlear implantation. *Otol Neurotol, 37*, 332–338.

Shaul, C., Bester, C.W., Weder, S., et al. (2019). Electrical impedance as a biomarker for inner ear pathology following lateral wall and peri-modiolar cochlear implantation. *Otol Neurotol, 40, e518–e526*.

Choi, J., Payne, M. R., Campbell, L. J., et al. (2017). Electrode impedance fluctuations as a biomarker for inner ear pathology After Cochlear Implantation. *Otol Neurotol, 38*, 1433–1439.

Choudhury, B., Adunka, O.F., Awan, O., Pike, J.M., Buchman, C.A., Fitzpatrick, D.C. (2014). Electrophysiologic consequences of flexible electrode insertions in gerbils with noise induced hearing loss. *Otol Neurotol, 35*, 519.

Choudhury, B., Fitzpatrick, D. C., Buchman, C. A., et al. (2012). Intraoperative round window recordings to acoustic stimuli from cochlear implant patients. *Otol Neurotol, 33*, 1507–1515.

Dalbert, A., Huber, A., Veraguth, D., et al. (2016). Assessment of cochlear trauma during cochlear implantation using electrocochleography and cone beam computed tomography. *Otol Neurotol, 37*, 446–453.

Dalbert, A., Pfiffner, F., Hoesli, M., et al. (2018). Assessment of cochlear function during cochlear implantation by extra- and intracochlear electrocochleography. *Front Neurosci, 12*, 18.

DeMason, C., Choudhury, B., Ahmad, F., et al. (2012). Electrophysiological properties of cochlear implantation in the gerbil using a flexible array. *Ear Hear, 33*, 534–542.

Eggermont, J. J. (1979). Narrow-band AP latencies in normal and recruiting human ears. *J Acoust Soc Am, 65*, 463–470.

Forgues, M., Koehn, H. A., Dunnon, A. K., et al. (2014). Distinguishing hair cell from neural potentials recorded at the round window. *J Neurophysiol, 111*, 580–593.

Giardina, C. K., Brown, K. D., Adunka, O. F., et al. (2019). Intracochlear electrocochleography: Response patterns during cochlear implantation and hearing preservation. *Ear Hear, 40*, 833–848.

Giardina, C. K., Khan, T. E., Pulver, S. H., et al. (2018). Response changes during insertion of a cochlear implant using extracochlear electrocochleography. *Ear Hear, 39*, 1146–1156.

Harris, M. S., Riggs, W. J., Koka, K., et al. (2017). Real-time intracochlear electrocochleography obtained directly through a cochlear implant. *Otol Neurotol, 38*, e107–e113.

Koka, K., Riggs, W. J., Dwyer, R., et al. (2018). Intra-cochlear electrocochleography during cochear implant electrode insertion is predictive of final scalar location. *Otol Neurotol, 39*, e654–e659.

Mandalà, M., Colletti, L., Tonoli, G., et al. (2012). Electrocochleography during cochlear implantation for hearing preservation. *Otolaryngol Head Neck Surg, 146*, 774–781.

O'Connell, B. P., Holder, J. T., Dwyer, R. T., et al. (2017). Intra- and postoperative electrocochleography may be predictive of final electrode position and postoperative hearing preservation. *Front Neurosci, 11*, 291.

Radeloff, A., Unkelbach, M. H., Tillein, J., et al. (2007). Impact of intrascalar blood on hearing. *Laryngoscope, 117*, 58–62.

Ruben, R. J., Bordley, J. E., Lieberman, A. T. (1961). Cochlear potentials in man. *Laryngoscope, 71*, 1141–1164.

Scheperle, R. A., Tejani, V. D., Omtvedt, J. K., et al. (2017). Delayed changes in auditory status in cochlear implant users with preserved acoustic hearing. *Hear Res, 350*, 45–57.

Scott, W. C., Giardina, C. K., Pappa, A. K., et al. (2016). The compound action potential in subjects receiving a cochlear implant. *Otol Neurotol, 37*, 1654–1661.

Skarzynski, H., Van de Heyning, P., Agrawal, S., et al. (2013). Towards a consensus on a hearing preservation classification system. *Acta Oto-Laryngol, 133*, 3–13.

Stakhovskaya, O., Sridhar, D., Bonham, B. H., et al. (2007). Frequency map for the human cochlear spiral ganglion: Implications for cochlear implants. *J Assoc Res Otolaryngol, 8*, 220–233.