Author/s:
O'Leary, S;Mylanus, E;Venail, F;Lenarz, T;Birman, C;Di Lella, F;Roland, JT;Gantz, B;Beynon, A;Sicard, M;Buechner, A;Lai, WK;Boccio, C;Choudhury, B;Tejani, VD;Plant, K;English, R;Arts, R;Bester, C

Title:
Monitoring Cochlear Health with Intracochlear Electrocochleography during Cochlear Implantation: Findings from an International Clinical Investigation

Date:
2023-03-01

Citation:
O'Leary, S., Mylanus, E., Venail, F., Lenarz, T., Birman, C., Di Lella, F., Roland, J. T., Gantz, B., Beynon, A., Sicard, M., Buechner, A., Lai, W. K., Boccio, C., Choudhury, B., Tejani, V. D., Plant, K., English, R., Arts, R. & Bester, C. (2023). Monitoring Cochlear Health with Intracochlear Electrocochleography during Cochlear Implantation: Findings from an International Clinical Investigation. Ear and Hearing, 44 (2), pp.358-370. https://doi.org/10.1097/AUD.0000000000001288.

Persistent Link:
https://hdl.handle.net/11343/327346

HHS Public Access

Author manuscript

*Ear Hear*. Author manuscript; available in PMC 2023 February 25.

Published in final edited form as:

*Ear Hear*. 2023 ; 44(2): 358–370. doi:10.1097/AUD.0000000000001288.

# Monitoring Cochlear Health With Intracochlear Electrocochleography During Cochlear Implantation: Findings From an International Clinical Investigation

**S. O'Leary**[1,2], **E. Mylanus**[3], **F. Venail**[4], **T. Lenarz**[5], **C. Birman**[6], **F. Di Lella**[7], **J. T. Roland Jr**[8], **B. Gantz**[9], **A. Beynon**[3], **M. Sicard**[4], **A. Buechner**[5], **W. K. Lai**[6], **C. Boccio**[7], **B. Choudhury**[8], **V. D. Tejani**[9], **K. Plant**[10], **R. English**[10], **R. Arts**[11], **C. Bester**[1,2]

[1]Royal Victorian Eye and Ear Hospital, Melbourne, Australia;

[2]The University of Melbourne, Melbourne, Australia;

[3]Department of Otorhinolaryngology and Head and Neck Surgery, Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behaviour, Nijmegen, The Netherlands;

[4]University Hospital of Montpellier & Institute of Neurosciences of Montpellier INSERM U1298, Montpellier, France;

[5]Department Otolaryngology, Hannover Medical School, Hannover, Germany;

[6]Cochlear Implant Program, NextSense, Sydney, Australia;

[7]Hospital Italiano de Buenos Aires, Argentina;

[8]NYU Grossman School of Medicine, New York, USA;

[9]University of Iowa Carver College of Medicine, Iowa City, Iowa, USA;

[10]Cochlear Limited, Sydney, Australia;

[11]Cochlear Benelux NV, Mechelen, Belgium.

## Abstract

**Objectives:** Electrocochleography (ECochG) is emerging as a tool for monitoring cochlear function during cochlear implant (CI) surgery. ECochG may be recorded directly from electrodes on the implant array intraoperatively. For low-frequency stimulation, its amplitude tends to rise or may plateau as the electrode is inserted. The aim of this study was to explore whether compromise of the ECochG signal, defined as a fall in its amplitude of 30% or more during insertion, whether transient or permanent, is associated with poorer postoperative acoustic hearing, and to examine how preoperative hearing levels may influence the ability to record ECochG. The specific hypotheses tested were threefold: (a) deterioration in the pure-tone average of low-frequency hearing at the first postoperative follow-up interval (follow-up visit 1 [FUV1], 4 to 6 weeks) will



Address for correspondence: Dr. Christofer Bester, Dept Surgery - Otolaryngology, University of Melbourne, 5th Floor, Peter Howsen Wing, RVEEH, 32 Gisborne St, East Melbourne 3002, Australia. christofer.bester@unimelb.edu.au.

be associated with compromise of the cochlear microphonic (CM) amplitude during electrode insertion (primary hypothesis); (b) an association is observed at the second postoperative follow-up interval (FUV2, 3 months) (secondary hypothesis 1); and (c) the CM response will be recorded earlier during electrode array insertion when the preoperative high-frequency hearing is better (secondary hypothesis 2).

**Design:** International, multi-site prospective, observational, between groups design, targeting 41 adult participants in each of two groups, (compromised CM versus preserved CM). Adult CI candidates who were scheduled to receive a Cochlear Nucleus CI with a Slim Straight or a Slim Modiolar electrode array and had a preoperative audiometric low-frequency average thresholds of ≤80 dB HL at 500, 750, and 1000 Hz in the ear to be implanted, were recruited from eight international implant sites. Pure tone audiometry was measured preoperatively and at postoperative visits (FUV1 and follow-up visit 2 [FUV2]). ECochG was measured during and immediately after the implantation of the array.

**Results:** From a total of 78 enrolled individuals (80 ears), 77 participants (79 ears) underwent surgery. Due to protocol deviations, 18 ears (23%) were excluded. Of the 61 ears with ECochG responses, amplitudes were <1 μV throughout implantation for 18 ears (23%) and deemed "unclear" for classification. EcochG responses >1 μV in 43 ears (55%) were stable throughout implantation for 8 ears and compromised in 35 ears. For the primary endpoint at FUV1, 7/41 ears (17%) with preserved CM had a median hearing loss of 12.6 dB versus 34/41 ears (83%) with compromised CM and a median hearing loss of 26.9 dB ($p < 0.014$). In assessing the practicalities of measuring intraoperative ECochG, the presence of a measurable CM (>1 μV) during implantation was dependent on preoperative, low-frequency thresholds, particularly at the stimulus frequency (0.5 kHz). High-frequency, preoperative thresholds were also associated with a measurable CM > 1 μV during surgery.

**Conclusions:** Our data shows that CM drops occurring during electrode insertion were correlated with significantly poorer hearing preservation postoperatively compared to CMs that remained stable throughout the electrode insertion. The practicality of measuring ECochG in a large cohort is discussed, regarding the suggested optimal preoperative low-frequency hearing levels (<80 dB HL) considered necessary to obtain a CM signal >1 μV.

### Keywords

Cochlea health; Cochlear implant diagnostics; Cochlear implant electrophysiology; Residual hearing preservation

## INTRODUCTION

Preservation of cochlear function and structure is an important goal during cochlear implant (CI) surgery. Hearing preservation can be facilitated through atraumatic electrode insertion and electrode placement that does not impede normal cochlear function. When successful, this can increase the likelihood of preserving any acoustic hearing present at the time of surgery. The preservation of acoustic hearing provides many benefits, particularly when combined with electrical hearing. Retaining acoustic hearing postoperatively, in addition to the benefits provided by electrical stimulation, has been shown to improve speech recognition in quiet and noise and music perception (Turner et al. 2004; Gfeller et al. 2006;

Gifford et al. 2013; Incerti et al. 2013; Lenarz et al. 2013; Roland et al. 2016; Sheffield et al. 2015; Loiselle et al. 2016) access to interaural timing cues (Gifford et al. 2013; Loiselle et al. 2016) and access to spectral/temporal cues needed for complex listening tasks (Golub et al. 2012; Tejani et al. 2021). Furthermore, fear of the loss of acoustic hearing may be a barrier to cochlear implantation (Rapport et al. 2019). Another potential benefit of attempting to preserve hearing is minimization of cochlear trauma. This may make the surgery for CI explantation and reimplantation, if needed, potentially easier and may enable future regenerative therapies in that ear. In the case of CI recipients of all ages, in particular in elderly CI recipients, the possibility of vestibular disturbance postsurgery may be reduced if hearing is preserved (Sosna-Duranowska et al. 2021).

Intraoperative, intracochlear monitoring of the cochlear response to acoustic stimulation during cochlear implantation shows promise as a tool to assist with hearing preservation (Campbell et al. 2016; Giardina et al. 2019; Dalbert et al. 2021). Electrocochleography (ECochG) records electrical potentials generated by the inner ear and auditory nerve in response to acoustic stimulation. The cochlear microphonic (CM) potential is generated primarily by transduction currents in outer hair cells as soon as mechanically gated ion channels open at the tip of stereocilia when the basilar membrane is displaced (Ruben et al. 1961; Dallos & Santos-Sacchi 1983; Patuzzi et al. 1989). Therefore, the CM is well placed to detect any disturbance of cochlear mechanics, such as fixation of the basilar membrane by the electrode array (Kiefer et al. 2006). When ECochG is recorded from the apical electrode of the array during implantation, the signal amplitude tends to rise continuously or plateau for low-frequency stimulation. Observational studies report that even a transient fall in amplitude at any time during implantation results in poorer residual hearing levels postoperatively (Weder et al. 2020). Patients with a preserved CM during implantation have been shown to retain more residual hearing for up to 12 months after surgery when compared to patients with an intraoperative CM drop (O'Leary et al. 2020). However, not all studies investigating the relationship between ECochG and hearing preservation have reported a negative association. Studies that exclusively used extra-cochlear ECochG are divided on its utility for predicting hearing preservation. One research group has consistently reported predictive value (Dalbert et al. 2015, 2016, 2020, 2021). In contrast, other research groups have not replicated these findings (Adunka et al. 2016; Haumann et al. 2019). Regarding intracochlear ECochG and published studies with greater than 10 subjects, there is not consensus on whether CM amplitude fluctuations are sufficient to predict hearing preservation (Dalbert et al. 2020). Researchers, Campbell et al. (2016) found that only permanent changes in CM amplitude (i.e., a CM drop that remained <70% of the previous maximum CM amplitude throughout implantation) were associated with poorer hearing preservation postoperatively. In contrast, Giardina et al. (2019) found an association with hearing preservation was only achieved when phase changes and auditory nerve neurophonic (ANN)/CM ratios were taken into consideration.

## PRIMARY OBJECTIVE

The primary aim of the present investigation was to examine whether a reduction in CM amplitude, termed a CM drop, is associated with poorer acoustic hearing preservation at 4 to 6 weeks postoperatively compared to individuals with a preserved CM.

## SECONDARY OBJECTIVES

A secondary aim was to determine whether compromised CM during surgery is associated with poorer acoustic hearing preservation 3 months postoperatively compared to preserved CM. In addition, the study examined how low- and high-frequency preoperative hearing thresholds may affect the presence and onset of the CM during electrode array insertion. This could help determine the profile of CI candidates for whom a surgeon could anticipate ECochG to be elicited, and at which point during implantation a response is likely to be detected. Finally, the association between hearing preservation and the nature of CM drops was investigated, specifically CM drops that are transient in nature (i.e., recover without surgical intervention) versus CM drops that are permanent (i.e., do not recover).

Since initiation of the present study, evidence is building that indicates other components of the ECochG response may also be important in detecting potential loss of hearing. These include latency of the CM and the amplitude of the ANN, a component of the ECochG response that is thought to derive from the auditory nerve (Palmer & Russell 1986; Forgues et al. 2014; Giardina et al. 2019). These aspects were not explored in the present investigation.

## MATERIALS AND METHODS

### Participants and Study Design

This international, multicenter, prospective, clinical study included two sites in Australia, two in the United States, three in Europe (Germany, France, and the Netherlands), and one in Latin America. The research was conducted under the auspices of the local human research and ethics committees as follows: Melbourne: RVEEH The Royal Victorian Eye and Ear Hospital Human Research Ethics Committee (HREC Number 17/1338H); Buenos Aires: Comite de Etica de Protocolos de Investigacion del Hospital Italiano de Buenos Aires (IRB 00010193); Sydney: RPAH The Royal Prince Alfred Research Ethics and Governance Office, (HREC/17/RPAH/524); NYU: NYU School of Medicine: Office of Science and Research Institutional Review Board (Study ID i17–00928); Nijmegen: Commissie Mensgebonden Onderzoek Radboud Universitair Medisch Centrum (NL61426.091.17); Hannover: Ethikkommission Medizinische Hochschule Hannover (7621MPG-LKP mono); Montpellier: Comité de Protection des Personnes SUD-EST IV (2017-A01149-44). The conduct of the commercially-sponsored study conformed in all respects to the Declaration of Helsinki (Association, 2013). Written informed consent was obtained from all participants prior to enrollment.

Potential participants were included if they met the following criteria: 18 years of age or older, a CI candidate based on local criteria, recommended for implantation with a flexible straight or perimodiolar electrode (Cochlear Nucleus CI models: CI522, CI532, CI622, CI632), and a preoperative, 500 Hz pure-tone threshold <80 dB HL under headphones in the ear to be implanted.

Potential participants were excluded for the following reasons: prior cochlear implantation in the ear to be implanted, ossification or any cochlear anomaly that might prevent

complete electrode array insertion, abnormal cochlear, or cochlear nerve anatomy on preoperative CT or MRI (excluding a mild Mondini malformation or large vestibular aqueduct syndrome), deafness due acoustic nerve or central auditory pathway lesions, diagnosis of auditory neuropathy, active middle ear infection, additional handicaps that would prevent participation in study evaluations, and unrealistic expectations from the participant regarding the possible benefits, risks, and limitations inherent to the CI procedure and investigational ECochG recording device.

## Patient Flow

Potential participants were recruited after a screening visit to confirm eligibility for study enrollment; thereafter, data were collected according to the evaluation schedule outlined in Table 1.

## Objectives

**Primary Aims •—**To examine whether a compromised CM at any time during CI surgery, that is a drop in CM amplitude from a previous maximum of at least 30%, is associated with greater postoperative low-frequency acoustic hearing deterioration at FUV1. Specifically, to compare mean low-frequency, postoperative hearing threshold deterioration at follow-up visit (FUV1) for the compromised CM and preserved CM groups. While a prior study separated transient and permanent reductions in CM amplitude (Campbell et al. 2015), in our study, both patterns are combined. This is based on more recent observations with larger patient cohorts indicating that a CM drop at any time during surgery, with or without recovery, is associated with loss of residual hearing postoperatively (Weder et al. 2020). Results from these studies also form the basis for the 30% CM drop threshold criterion used in the present work (Campbell et al. 2015; Weder et al. 2020). Methods for measuring CM amplitude and drop detection are described in the Electrocochleography section below. Participants were categorized as having an 'unclear' CM response if their CM was below 1 μV throughout the electrode insertion.

## Secondary Aims

**FUV2 Hearing Preservation •—**To test the longer duration hearing outcome of preoperative to follow-up visit 2 (FUV2), the primary aim is repeated with the only change of comparing groups to low-frequency acoustic hearing deterioration at FUV2.

**Preoperative Hearing and Stage of Implantation at Which the CM was Detected •—**To investigate whether preoperative acoustic hearing influences the point during insertion when the CM response was detected, the high-frequency average (HFA) of 2, 4, and 8 kHz from preoperative visit 1 (POV1) is calculated for the CM compromised and preserved groups. Point of insertion is derived from the impedances measured from every second electrode during implantation. The insertion depth at the point where the CM exceeded 1 μV is defined as the number of electrodes that were inserted into the cochlea before the CM exceeded 1 μV. Therefore, if the CM appeared when two electrodes were inserted, it was deemed to have been present at the beginning of the insertion. If 22 electrodes were inserted, then the CM exceeded the 1 μV threshold after all electrode contacts were inserted.

## Exploratory Analyses

**Transient or persistent CM amplitude drop associated with hearing loss •—**CM drops are transient in nature, that is, the amplitude decreases by 30% or more but then recovers to within 30% of the prior maximum CM amplitude. To determine whether these "transient" drops are as predictive of postoperative hearing loss as 'permanent' CM drops, participants from the primary outcome group with CM drops detected during insertion will be further categorized into permanent (CM amplitude remained <30% of the prior maximum), or as transient (CM amplitude recovered to within 30% of the prior maximum without surgical intervention). The low-frequency average (LFA) hearing loss at FUV1 for transient and persistent drops in CM amplitude will be compared.

**Preoperative Audiometric Thresholds Associated With CM Detection •—**To determine the effect of POV1 audiometric thresholds on the presence or absence of CM during the implantation, CMs were categorized as present (>1 μV) during insertion, or absent, with a response ≤1 μV throughout the electrode insertion. Then, the overall detectability of the CM and its relationship to hearing loss will be tested using the Kruskal Wallis test for medians.

**Audiometry •—**Unaided audiometric thresholds were obtained for each ear using the standard audiometric technique (ISO 8235–1 [ISO, 1992]) for pure-tone testing at POV1, FUV1, and FUV2.

Testing for both ears included air conduction thresholds (125, 250, 500, 750, 1000, 1500, 2000, 3000, 4000, 6000, 8000 Hz), bone conduction thresholds (250, 500, 750, 1000, 1500, 2000, 3000, 4000 Hz), and tympanometry.

Postoperative threshold shifts were calculated only at frequencies with preoperative thresholds <80 dB HL, using the LFA threshold for 500, 750, and 1000 Hz between the preoperative baseline and FUV1 (4 to 6 week postoperative visit). For this LFA, 250-Hz was excluded due to the vibrotacile response (@ 80 dB HL) was limiting for the calculation for threshold shift. Threshold shift calculations for any participant excluded frequencies where the preoperative threshold was >80 dB HL; these were also excluded from the pre and postoperative LFA value. Nonmeasurable postoperative acoustic thresholds were assigned a value of 126 dB HL, regardless of frequency. Vibrotactile responses at any frequency were not included in the analysis of threshold shifts. By default, 250 Hz was excluded to avoid confounding threshold shift results for all participants.

**Electrocochleography •—**ECochG was recorded using the University of Melbourne's Cochlear Response Telemetry (CRT) investigational system (Campbell et al. 2016), developed in collaboration with Cochlear Ltd. The system is designed to record electrical potentials from the cochlea using acoustic stimulation. The acoustic stimuli for ECochG were generated by a USB DAC (DT9847, Data Translation, MA, USA) at 192 kHz. The pure tones were presented closed-field to the ear canal via an ER3C insert earphone (Etymotics, IL, USA) using silicone tubing and foam ear tips (sterilized according to local hospital protocols if required). The acoustic output was calibrated with peak-to-peak amplitudes equal to the dB HL scale for insert earphones (ISO 389-2:1994). The calibration

procedure used a Sound Level Meter (Type Class 1) with a ½ inch microphone connected to a 2 cc coupler stud. The insert earphone (ER-3C) was connected to the stud via the insert earphone silicon tubing. The acoustic output level from the insert earphone was measured at a number of frequencies and checked against a specified tolerance range. Every center applied the same calibration procedure. Responses were analyzed off-line, with the CM derived by taking the difference of the rarefaction and condensation responses, divided by two. The amplitude of the CM was taken by applying a 15th order digital bandpass filter around the stimulus frequency (0.9*F to 1.1*F), then using a fast-Fourier transform (FFT) by first zero-padding the signal to 1000 for a 20 Hz bin size (by appending zeros to the end of the signal until a sample length of 1000 is reached), and then taking the bin at the stimulus frequency (i.e., 500 Hz).

The most apical electrode (E22) was introduced into the cochlea via the round window or cochleostomy, where it was conditioned and impedances stabilized for a total conditioning time of 10 to 30 sec; then the CRT operator indicated that electrode array insertion could begin. During insertion via the round window or cochleostomy, intraoperative ECochG recordings were obtained on E22 with the extracochlear plate electrode as reference, using a 500 Hz acoustic tone burst (6 msec duration, including 1 msec linear rise/fall times) presented at 100 dB HL with a repetition rate of 14 Hz. Stimuli were presented with alternating rarefaction and condensation polarities and responses saved to separate buffers as a simple moving average of the last 20 samples. During insertion and throughout implantation, the ongoing averaged CM and ANN and their amplitudes were shown to the observer. Monitoring of the CM continued throughout the procedure until closure of the deep subcutaneous/muscle layer. During the implantation of the array, surgeons did not receive feedback regarding any changes to the CM; thus, surgical intervention was not influenced by ECochG outcomes. Surgeons were instructed to perform their standard implant procedure, with insertion speed and depth as per their surgical routine. Throughout insertion of the array, common ground impedances were monitored on every second electrode along the array, beginning from the most apical to intracochlear electrode E2.

The operative microscope imaging system recorded video of the entire insertion, beginning just before cochlear opening and ending after closure of the deep subcutaneous/muscle layer. The surgeon signified the end of surgery on the video by clicking surgical tweezers in front of the microscope three times; then the CRT software operator recorded the current timestamp on the software. This footage was necessary to analyze the CRT in response to specific surgical events. Therefore, surgical events were synchronized with the ECochG recordings using event-related time stamps on the videos and, likewise, recording a corresponding index in the CRT software. At this stage, insertion depth at each ECochG sample could be derived from the timing of each electrode reaching a closed circuit, assumed to be the timing of the electrode contacting cochlear perilymph.

Surgeons documented surgical approach, use of corticosteroids, and ease and depth of electrode insertion.

**Sample Size •—**Prospective sample size estimation for a two-sample *t* test was conducted, given that the study used a between-groups design to investigate its primary hypothesis.

The sample size was calculated for a 0.80 power, one-tailed α of 0.05, for >15 dB HL deterioration in low-frequency average acoustic hearing threshold (500, 750, and 1000 Hz) for participants with compromised CM compared to those with preserved CM. This difference was based on prior experience with ECochG fluctuations (Campbell et al. 2016) and indicates a change in hearing loss classification (Van Abel et al. 2015), as well as being greater than the clinically acceptable test-retest difference margin for pure tone audiometry of 10 dB based on a 5 dB step size. The expected SD was set to 25 dB HL, which is conservative based on clinical experience.

Based on the above assumptions, it was expected a minimum sample size of 36 participants with preserved and 36 with compromised CMs would be required to reject a false null hypothesis of equivalent or worse hearing preservation for participants with preserved CM (using Sigma Plot 13.0). This minimum sample size was increased for the following reasons: (1) to allow for the possibility that the hearing threshold data were not normally distributed and that a nonparametric statistical analysis would be required, and the sample size was increased by 15% to 41 participants per group, which should achieve the equivalent power; and (2) to allow for the prediction that approximately 5% of CI recipients would not exhibit an intraoperative CM response (Dalbert et al. 2015), and the sample size was increased to a total of 43 participants per group.

## RESULTS

Seventy-eight participants, representing data from 80 ears, were enrolled in the study, two patients were bilaterally implanted. The average age at the time of enrollment was 59.7 years (SD 22.2 range: 19 to 87). One subject withdrew before undergoing surgery (data reduced to 79 ears) due to unrelated medical complications. Surgeries in all 77 participants were reported as uneventful. Recruitment was halted at 78 patients, as an interim analysis at 60 patients demonstrated that the 50:50 breakdown of CM status was not satisfied, with a substantially larger number of patients showing lost CM; however, the primary outcome LFA threshold shift, between POV1 and FUV1 was achievable with a substantially smaller data set.

From 79 ears, 18 ears (23%) were excluded from data analysis due to protocol deviations. These included the following: the surgeon had received feedback regarding the CM status (n = 3, 17%); the electrode array was not selected according to the protocol (n = 3, 17%); the preoperative 500 Hz threshold was poorer than 80 dB HL (n = 5, 28%); no ECochG was recorded during insertion (n = 5, 28%); and no pre or postoperative follow-up suitable to assess the primary and secondary endpoints (n = 2, 10%).

Sixty-one ears had sufficient data collected for the Primary outcome. The majority (85%, 52/61) received a Cochlear Nucleus Profile with a Slim Straight Electrode (CI522) or Cochlear Nucleus Profile Plus with a Slim Electrode (CI622). A few ears (15%, 9/61) were implanted with a Cochlear Nucleus Profile with a Slim Perimodiolar Electrode (CI532).

Figure 1 shows the participant pathway followed in the investigation. Table 2 shows the measures at each interval and the available datasets for analysis for study endpoints.

ECochG responses were available from 61 ears, n = 31 left, and n = 34 females. In 18 ears, the ECochG amplitude remained <1 μV throughout insertion; classified as "unclear" as it was impossible to discern a trend in change over electrode implantation. In the remainder (43 ears), responses were categorized as CM preserved or CM compromised.

Figure 2 shows examples of two participants for whom the CM was classified as preserved; of note, small CM fluctuations of less than 30% of the prior maximum occurred frequently. Figure 3 shows examples of two participants with substantial CM drops during implantation, one early during array insertion and one late after full insertion. In Figure 4, examples of two participants are shown, considered to have borderline CM drops, one with a CM drop that just exceeds the 30% criteria, and another with a transient CM drop that recovers after insertion was complete. Participants for whom the CM could not be classified because the CM amplitude never exceeded 1 μV (N = 18) at any point during the insertion were excluded from the primary outcome analysis.

## Primary Outcome

LFA threshold shift, between POV1 and FUV1, was calculated for 41 ears in 40 participants. Of these, 34 ears (83%) were categorized as having a compromised CM and seven ears (17%) as having preserved CM. The compromised CM group exhibited significantly poorer LFA preservation compared to the preserved CM group, with mean threshold deteriorations of 26.9 and 12.6 dB HL, respectively (Fig. 5 Mann–Whitney U test, Z = −2.46, $p$ = 0.0137). The preserved CM (no drop) group (N = 7) had only one participant with a low-frequency threshold shift greater than 15 dB HL (red cross outlier on Figs. 5 and 6). In some participants, these threshold shifts were substantial, typically reflecting participants with very good preoperative thresholds losing enough hearing to reach the limits of the audiometer (e.g., two participants with preoperative LFA of 60 and 71.67 dB shifting to 113.33 dB and 126 dB, respectively). There was no significance difference between preoperative LFA in the two groups (medians of 66.67 dB for CM preserved and 65 dB for CM loss, $p$ = 0.74 on Kruskal-Wallis test).

We also investigated whether the LFA threshold shift from POV1 to FUV1 was ≤15 dB HL or >15 dB HL depending on if the CM was compromised or preserved, with a comparison to the individuals with unclear CM response (Table 3). The compromised CM group demonstrated poorer average postimplantation acoustic hearing preservation compared to the preserved CM group (Fisher's exact test, $p$ = 0.0094).

## Secondary Objective Analyses

**FUV2 Hearing Preservation •—**Thirty-eight ears (38/43, 88%) in 37 participants were included in this secondary endpoint analysis (FUV2). Data were missing for five ears. In 30 ears (30/38, 79%), a compromised CM was exhibited and eight ears (8/38, 21%) displayed a preserved CM. Analysis indicated that a compromised CM was associated with a poorer mean LFA hearing preservation compared to when CM was preserved, with mean threshold deteriorations of 31.52 and 13.23 dB, respectively (Fig. 6 Mann–Whitney U test, Z = −2.61, $p$ = 0.0089).

**Preoperative Hearing and Stage of Implantation at Which the CM was Detected** •—The high-frequency average (HFA – average of 2, 4, and 8 kHz) from POV1 was calculated from datapoints for 36 ears (36/43, 84%), consisting of 29 ears (81%) with a compromised CM and seven ears (19%) with a preserved CM. Seven participants were excluded from this analysis because impedances were not recorded during the insertion (n = 3), or the impedances changed in a manner inconsistent with the surgical description (n = 4), likely due to additional liquid present in the middle ear. The absence of accurate impedance measurements prevented the derivation of insertion depth. A moderate positive correlation was found between high-frequency hearing thresholds and the number of electrodes inserted when the CM was detected (Fig. 7 Pearson's $r^2 = 0.60$, $p < 0.001$).

## Exploratory Analyses

**Transient or Persistent CM Amplitude Drop Associated With Hearing Loss** •—The 34 participants from the primary outcome group with CM drops were further categorized into those with permanent CM drops (CM amplitude remained <30% of the prior maximum, n = 26), or as transient (CM amplitude recovered to within 30% of the prior maximum without surgical intervention n = 8). The LFA hearing loss at FUV1 for transient and persistent drops in CM amplitude are shown in Figure 8. Mean postoperative hearing loss did not differ significantly between participants with transient CM drops (n = 8 ears, median LFA hearing loss of 23.83 dB) and those with persistent CM drops (n = 26 ears, median LFA hearing loss of 21.83 dB; Mann–Whitney U Test, $p = 0.90$).

**Preoperative Audiometric Thresholds Associated with CM Detection** •—Out of all ears with ECochG recorded during implantation and available POV1 hearing thresholds (n = 61), a robust CM could be detected in 70% of ears (43/61); in 30% (18/61) ears, CM responses were categorized as unclear, with a response ≤1 μV throughout the electrode insertion. This analysis explored whether CM detection might relate to the preoperative audiometric results. Given the significant number of unclear responses, we analyzed the overall detectability of the CM and its relationship to the degree of hearing loss. Using the Kruskal Wallis test for medians, the preoperative pure-tone audiometric thresholds in participants with a detected CM was compared to those with an unclear CM and no technical issues during insertion (n = 18 ears). The participants with unclear CM responses had significantly poorer mean audiometric thresholds at 250 Hz ($p = 0.03$), 500 Hz ($p < 0.001$), 750 Hz ($p < 0.001$), 1 kHz ($p < 0.001$), and 2 kHz ($p = 0.022$) compared to the participants with detectable CMs. There was no significant difference between the two groups at 4 kHz ($p = 0.129$) and 8 kHz ($p = 0.164$) (Fig. 9).

**Surgery** •—A total of 72 out of 79 surgeries (n = 72 ears, 91%) had surgical questionnaires completed (n = 3 no intraoperative measures, n = 3 incorrect implant, n = 1 missing data). In most cases, the cochlea was opened via the round window (86%), with only a few cases through an extended round window (8%) or cochleostomy (6%). The mean time to insert the electrode was 141 seconds (SD 118 range: 5 to 802, n = 69). During surgery, most participants (77%) received a systemic antibiotic and/or steroid.

## DISCUSSION

This multi-region, multi-center clinical investigation provides further evidence that a reduction in CM response amplitude during cochlear implantation is associated with a greater loss of acoustic hearing thresholds postoperatively, at both 4 to 6 weeks postoperatively and 3 months postactivation. A CM amplitude drop, even if transient, is associated with a detrimental effect on hearing, supporting the notion that monitoring must be continuous throughout electrode insertion to be predictive of postoperative hearing. This observation may help explain why some studies that have recorded ECochG intermittently (O'Connell et al. 2017) or at the end of implantation (Haumann et al. 2019) failed to find an association with residual hearing loss, although some researchers have found these measures adequate for the prediction of hearing preservation (Adunka et al. 2016; Dalbert et al. 2016).

CM amplitude drops reflect either an interruption of cochlear mechanics or cochlear trauma. The transient nature of some drops suggests that this may be reversible in some situations. Recent research has demonstrated that surgical intervention can recover the CM amplitude after it has dropped (Bester et al. 2021), by withdrawing the electrode array immediately after the drop has occurred. Our current understanding of the intracochlear trajectory of straight, flexible electrodes provides insights into the ways in which these electrodes might disturb cochlear mechanics (Verberne et al. 2017). Lateral wall electrodes tend to ride up the lateral cochlear wall, usually at insertion angles beyond 180 degrees, and contact the basilar membrane. This could explain CM amplitude drop and its prevalence during the last few millimeters of electrode insertion, which coincides with the cochlear location where electrode basilar membrane contact most often occurs (Verberne et al. 2017). This pattern also supports the intervention used in Bester et al. (2021), in which a small withdrawal of the array recovered the amplitude of the CM, hypothesized to occur as the array rides up the lateral wall and contacts the basilar membrane. Partially withdrawing the electrode out of the cochlea would then draw the array inferiorly, releasing the basilar membrane for typical displacement. In other insertions, Verberne found contact between the basilar membrane and the middle of the array, and no contact more apically. This observation provides insights into a potential cause of transient CM amplitude drops; an electrode may touch the basilar membrane temporarily during insertion, reducing CM amplitude when this occurs. Finally, there were CM drops, both permanent and transient, that occurred after full implantation was complete. Review of the surgical videos indicated these typically occurred when the surgeon contacted the electrode array during the fascia placement over the round window or cochleostomy, or when coiling the electrode lead in the mastoid cavity. The approach taken in this study was not sensitive to the exact cause of these postinsertion CM drops.

An important practical observation of this study is that ECochG detection is highly dependent upon preoperative hearing. The substantial number of participants with no detectable ECochG during implantation is partly explained by poor preoperative hearing at the stimulus frequency (84% > 70 dB HL). However, poor neurosensory generator function is just one possible explanation for not recording ECochG. The intraoperative ECochG monitoring protocol used has several possible failure points, primarily associated with maintaining the integrity of the acoustic presentation. These should be kept in mind when considering the participants with good preoperative hearing thresholds (e.g., the outliers

denoted by red crosses in Figure 9, with 20 to 60 dB HL preoperative 500 Hz thresholds), but in whom ECochG was absent during implantation. The foam ear tips used to present the stimuli are seated in the ear canal prior to the general sterile draping of the patient, which may occur at least an hour prior to the cochlear implantation procedure. Between ear tip placement and acoustic presentation, the presentation pathway is underneath sterile drapes, and hidden from view. Inserting the ear tips at a time closer to insertion of the implant array is not always possible due to the surgical approach, which may include folding the external ear over the ear canal, thus limiting access. A small withdrawal of the ear tip from the ear canal, or a small amount of fluid within the canal, substantially reduces the acoustic output, possibly leading to a loss of detectable ECochG. A method to monitor sound levels at the tympanic membrane would solve this issue. An additional consideration was the inverse relationship between high-frequency hearing thresholds and the number of intracochlear electrodes before the CM could be detected on the most apical electrode.

While CM monitoring always began as the tip electrode was inserted into the round window or cochleostomy, in participants with poorer high-frequency hearing the CM remained undetectable until quite late in the electrode insertion process. In some of these cases with poor hearing, the CM was detectable only after insertion of all electrodes to approximately 20 mm. Thus, earlier events which could have been detrimental to hearing would not be detected and could preclude ECochG recording and detection.

The goal of ECochG monitoring is to provide real-time feedback that may guide surgical interventions that save residual hearing. These could include fine tuning the depth of insertion or changing the electrode trajectory to restore or maintain the CM amplitude. The outcomes of this study support this aspiration, but the observational paradigm limits the degree to which our data can inform the success of surgical intervention. Now, in the Bester et al. (2021) study, there is evidence that using fluctuations in CM amplitude to modify the insertion can significantly improve hearing preservation outcomes. In this study, CM fluctuations were used to initiate a surgical intervention to recover CM to within 30% of its maximum amplitude at the end of the insertion, which resulted in a significant improvement in hearing preservation in the intervention group compared with the control. This study used the same CRT measuring system used in the present study, demonstrating the utility of real-time ECochG monitoring for actively preserving residual hearing in cochlear implantation.

## Limitations

The present work had limitations in the protocol and the equipment used. A thorough hearing assessment and postoperative testing regime was required to obtain high quality hearing data; however, this did not always fit into the study sites' existing care protocols. This led to numerous protocol deviations and subsequent loss of data because follow-up visits were missed.

In this study, the equipment used had inherent acoustic presentation limitations. During cochlear implantation, we could present a maximum acoustic output of 110 dB HL at 500 Hz, at a rate slightly over 14 Hz. Given the severity of hearing loss in these participants, a higher stimulation intensity may have led to higher rates of detectable CMs. In addition, most sites place the sound transducer and acoustic tubing under the sterile drapes, as a

result they were inaccessible for the duration of the surgery. Thus, it was impossible for the observer to verify the acoustic presentation level prior to cochlear implantation. A method to verify the sound presentation intensity level at the ear canal would improve the robustness of the procedure and has been successful with other groups (Dalbert et al. 2016).

Finally, the study relied on a derivation of the CM using the difference of two alternating polarity responses and taking the amplitude at the stimulus frequency. While this approach is common in the literature for deriving the CM (Campbell et al. 2016; Dalbert et al. 2020; Sijgers et al. 2021), it likely contains neural contributions that are less location specific and may be more affected by destructive interference than the CM (Forgues et al. 2014). While this approach appears to be effective at predicting hearing preservation, it is important to consider that the complex contributors to the response may obscure the optimal detection of insertion trauma, and this may be a source of improvement in the future.

## CONCLUSION

Constant monitoring of CM amplitude was achieved during intracochlear ECochG in 70% of participants, with monitoring failures usually attributable to poorer preoperative hearing. The participants in whom the CM amplitude dropped by >30% relative to previous levels at any time during the procedure exhibited significantly poorer postoperative residual hearing preservation at 4 to 6 weeks and at 3 months postimplantation. On an average, they lost an additional 14 dB for the low-frequency pure tone average compared to participants with a preserved CM ($p < 0.014$). The median hearing loss in the preserved CM group was less than 15 dB (median LFA hearing shift of 12.6 dB), demonstrating that the majority of these participants had preserved hearing (Skarzynski et al. 2013). Clinically, this resulted in a greater proportion of CI recipients who could use combined electro-acoustic hearing for improved implant outcomes. Continual recording is required to detect CMdrops, as they may be transient. These findings support the use of constant ECochG monitoring from a CI electrode to preserve cochlear function and maintain cochlear health during implantation.

## ACKNOWLEDGEMENTS

We thank all patients participating in the study. A special thank you also to all clinic staff supporting the study at each site. We thank all surgeons who were involved in the study: R. Pennings and Dr. Heutnik from Nijmegen, A. Uziel from Montpellier, F. Fernandez from Buenos Aires, D. Jehannamest and S. Mc Menomey from New York City, R. Kennedy, B. Wei and Andrew McLean from Melbourne, M. Hansen from Iowa; K. Willenborg, R. Salcher, M. Teschner, and N. Prenzler from Hannover. Thank you to clinic staff involved in study subject recruitment, evaluation, and data collection: M. Schüßler, Dr. E. Kludt, and Dr. T. Rocha-Felix in Hannover, P. Y. Chu in Sydney and N. Deep in New York City.

S. O. L. and C. B. reviewed and advised on study protocol proposed by the sponsor. The initial draft version of the article was provided by R. E. and C. B. S. O. L. and C. B. provided significant contributions to the final version of the article. All authors reviewed and approved the final article for submission. Data analysis and graphic representation was performed by C. B. E. M., A. B., T. L., A. B., F. V., M. S., C. B., W. L., F. D., C. B., J. R., B. C., B. G., V. T. were involved in patient counseling and or data collection at their respective clinics. All authors reviewed and approved the final article. K. P., R. E., R. A. drafted the study protocol. R. E. and R. A. provided operational support for the study implementation.

This work was supported Cochlear LTD, Sydney, Australia. A consultant medical writer was engaged by the sponsor to support the final draft version of the article.

K. P., R. E., and R. A. are Cochlear employees. B. G. is a consultant to Cochlear Corporation and EarLens Corporation. F. V. has been granted by the « Fondation pour l'Audition « (RD- 2020-10). Stephen O'Leary

was funded by the National Health and Medical Research Council (Australia), GNT0628679 and GNT1078673. Stephen O'Leary and Christofer Bester's department of Otolaryngology at the University of Melbourne received research grants from Cochlear Ltd. All the other authors have no conflicts of interest to disclose.

## Abbreviations:

| | |
|---|---|
| **AE** | adverse event |
| **ANN** | auditory nerve neurophonic |
| **CM** | cochlear microphonic |
| **CRT** | cochlear response telemetry |
| **ECochG** | electrocochleography |
| **FFT** | fast-fourier transform |
| **FUV1** | follow-up visit 1 |
| **FUV2** | follow-up visit 2 |
| **HL** | hearing level |
| **LFA** | low-frequency average |
| **POV1** | preoperative visit 1 |
| **SAE** | severe adverse events |
| **SP** | summating potential |

## REFERENCES

Adunka OF, Giardina CK, Formeister EJ, Choudhury B, Buchman CA, Fitzpatrick DC (2016). Round window electrocochleography before and after cochlear implant electrode insertion. Laryngoscope, 126, 1193–1200. [PubMed: 26360623]

Bester C, Collins A, Razmovski T, Weder S, Briggs RJ, Wei B, Farah A, Gerard J-M, Mitchell-Innes A, Tykocinski M (2021). Electrocochleography triggered intervention successfully preserves residual hearing during cochlear implantation: Results of a randomised clinical trial. Hear Res, 108353. [PubMed: 34600798]

Campbell L, Kaicer A, Briggs R, O'Leary S (2015). Cochlear response telemetry: Intracochlear electrocochleography via cochlear implant neural response telemetry pilot study results. Otol Neurotol, 36, 399–405. [PubMed: 25473960]

Campbell L, Kaicer A, Sly D, Iseli C, Wei B, Briggs R, O'Leary S (2016). Intraoperative real-time cochlear response telemetry predicts hearing preservation in cochlear implantation. Otol Neurotol, 37, 332–338. [PubMed: 26859542]

Dalbert A, Dalbert A, Pfiffner F, Pfiffner F, R sli C, R sli C, Thoele K, Thoele K, Sim JH, Sim JH, Gerig R, Gerig R, Huber AM, huber AM (2015, Sep 07). Extra- and Intracochlear Electrocochleography in Cochlear Implant Recipients. Audiol Neurotol, 20, 339–348.

Dalbert A, Huber A, Veraguth D, Roosli C, Pfiffner F (2016). Assessment of cochlear trauma during cochlear implantation using electrocochleography and cone beam computed tomography. Otol Neurotol, 37, 446–453. [PubMed: 26945317]

Dalbert A, Rohner P, Roosli C, Veraguth D, Huber A, Pfiffner F (2020). Correlation between electrocochleographic changes during surgery and hearing outcome in cochlear implant recipients:

A case report and systematic review of the literature. Otol Neurotol, 41, 318–326. [PubMed: 31834213]

Dalbert A, Sijgers L, Grosse J, Veraguth D, Roosli C, Huber A, Pfiffner F (2021). Simultaneous intra- and extracochlear electrocochleography during electrode insertion. Ear Hear, 42, 414–424. [PubMed: 32826509]

Dallos P, & Santos-Sacchi J (1983). AC receptor potentials from hair cells in the low-frequency region of the guinea pig cochlea. In Mechanisms of Hearing (pp. 11–16). Monash University Press.

Forgues M, Koehn HA, Dunnon AK, Pulver SH, Buchman CA, Adunka OF, Fitzpatrick DC (2014). Distinguishing hair cell from neural potentials recorded at the round window. J Neurophysiol, 111, 580–593. [PubMed: 24133227]

Gfeller KE, Olszewski C, Turner C, Gantz B, Oleson J (2006). Music perception with cochlear implants and residual hearing. Audiol Neurootol, 11(Suppl 1), 12–15. [PubMed: 17063005]

Giardina CK, Brown KD, Adunka OF, Buchman CA, Hutson KA, Pillsbury HC, Fitzpatrick DC (2019). Intracochlear electrocochleography: Response patterns during cochlear implantation and hearing preservation. Ear Hear, 40, 833–848. [PubMed: 30335669]

Gifford RH, Dorman MF, Skarzynski H, Lorens A, Polak M, Driscoll CL, Roland P, Buchman CA (2013). Cochlear implantation with hearing preservation yields significant benefit for speech recognition in complex listening environments. Ear Hear, 34, 413–425. [PubMed: 23446225]

Golub JS, Won JH, Drennan WR, Worman TD, Rubinstein JT (2012). Spectral and temporal measures in hybrid cochlear implant users: On the mechanism of electroacoustic hearing benefits. Otol Neurotol, 33, 147. [PubMed: 22215451]

Haumann S, Imsiecke M, Bauernfeind G, Büchner A, Helmstaedter V, Lenarz T, Salcher RB (2019). Monitoring of the inner ear function during and after cochlear implant insertion using electrocochleography. Trends Hear, 23, 2331216519833567.

Incerti PV, Ching TY, Cowan R (2013). A systematic review of electric-acoustic stimulation: Device fitting ranges, outcomes, and clinical fitting practices. Trends Amplif, 17, 3–26. [PubMed: 23539259]

Kiefer J, Böhnke F, Adunka O, Arnold W (2006, Nov). Representation of acoustic signals in the human cochlea in presence of a cochlear implant electrode. Hear Res, 221, 36–43. [PubMed: 16962268]

Lenarz T, James C, Cuda D, Fitzgerald O'Connor A, Frachet B, Frijns JH, Klenzner T, Laszig R, Manrique M, Marx M, Merkus P, Mylanus EA, Offeciers E, Pesch J, Ramos-Macias A, Robier A, Sterkers O, Uziel A (2013). European multi-centre study of the Nucleus Hybrid L24 cochlear implant. Int J Audiol, 52, 838–848. [PubMed: 23992489]

Loiselle LH, Dorman MF, Yost WA, Cook SJ, Gifford RH (2016). Using ILD or ITD cues for sound source localization and speech understanding in a complex listening environment by listeners with bilateral and with hearing-preservation cochlear implants. J Speech Lang Hear Res, 59, 810–818. [PubMed: 27411035]

O'Connell BP, Holder JT, Dwyer RT, Gifford RH, Noble JH, Bennett ML, Rivas A, Wanna GB, Haynes DS, Labadie RF (2017). Intra- and postoperative electrocochleography may be predictive of final electrode position and postoperative hearing preservation. Front Neurosci, 11, 291. [PubMed: 28611574]

O'Leary S, Briggs R, Gerard JM, Iseli C, Wei BPC, Tari S, Rousset A, Bester C (2020). Intraoperative observational real-time electrocochleography as a predictor of hearing loss after cochlear implantation: 3 and 12 month outcomes. Otol Neurotol, 41, 1222–1229. [PubMed: 32925842]

Palmer AR, & Russell IJ (1986). Phase-locking in the cochlear nerve of the guinea-pig and its relation to the receptor potential of inner hair-cells. Hear Res, 24, 1–15. [PubMed: 3759671]

Patuzzi RB, Yates GK, Johnstone BM (1989). Changes in cochlear microphonic and neural sensitivity produced by acoustic trauma. Hear Res, 39, 189–202. [PubMed: 2737965]

Rapport F, Bierbaum M, Hughes SE, McMahon C, Lau A, Boisvert I (2019). Barrier and facilitators to cochlear implantation: Qualitative data from Australia and the United Kingdom. British Cochlear Implant Group Meeting 2019,

Roland JT Jr, Gantz BJ, Waltzman SB, Parkinson AJ; Multicenter Clinical Trial Group. (2016). United States multicenter clinical trial of the cochlear nucleus hybrid implant system. Laryngoscope, 126, 175–181. [PubMed: 26152811]

RUBEN RJ, BORDLEY JE, LIEBERMAN AT (1961). Cochlear potentials in man. Laryngoscope, 71, 1141–1164. [PubMed: 14494859]

Sheffield SW, Jahn K, Gifford RH (2015). Preserved acoustic hearing in cochlear implantation improves speech perception. J Am Acad Audiol, 26, 145–154. [PubMed: 25690775]

Sijgers L, Pfiffner F, Grosse J, Dillier N, Koka K, Röösli C, Huber A, Dalbert A (2021). Simultaneous intra- and extracochlear electrocochleography during cochlear implantation to enhance response interpretation. Trends Hear, 25, 2331216521990594.

Skarzynski H, Van de Heyning P, Agrawal S, Arauz S, Atlas M, Baumgartner W, Caversaccio M, De Bodt M, Gavilan J, Godey BJAO-L (2013). Towards a consensus on a hearing preservation classification system. Acta Otolaryngol Suppl 133(sup564), 3–13.

Sosna-Duranowska M, Tacikowska G, Gos E, Krupa A, Skarzynski PH, Skarzynski H (2021). Vestibular function after cochlear implantation in partial deafness treatment. Front Neurol, 12, 722.

Tejani VD, Kim JS, Oleson JJ, Abbas PJ, Brown CJ, Hansen MR, Gantz BJ (2021). Residual hair cell responses in electric-acoustic stimulation cochlear implant users with complete loss of acoustic hearing after implantation. J Assoc Res Otolaryngol, 22, 161–176. [PubMed: 33538936]

Turner CW, Gantz BJ, Vidal C, Behrens A, Henry BA (2004). Speech recognition in noise for cochlear implant listeners: Benefits of residual acoustic hearing. J Acoust Soc Am, 115, 1729–1735. [PubMed: 15101651]

Van Abel KM, Dunn CC, Sladen DP, Oleson JJ, Beatty CW, Neff BA, Driscoll CL (2015). Hearing preservation among patients undergoing cochlear implantation. Otol Neurotol, 36, 416. [PubMed: 25575373]

Verberne J, Risi F, Campbell L, Chambers S, O'Leary S (2017). The effect of scala tympani morphology on basilar membrane contact with a straight electrode array: A human temporal bone study. Otol Neurotol, 38, 47–53. [PubMed: 27755369]

World Medical Association. (2013). World Medical Association Declaration of Helsinki: ethical principles for medical research involving human subjects. Jama, 310, 2191–2194. [PubMed: 24141714]

Weder S, Bester C, Collins A, Shaul C, Briggs RJ, O'Leary S (2020). Toward a better understanding of electrocochleography: Analysis of real-time recordings. Ear Hear, 41, 1560–1567. [PubMed: 33136631]

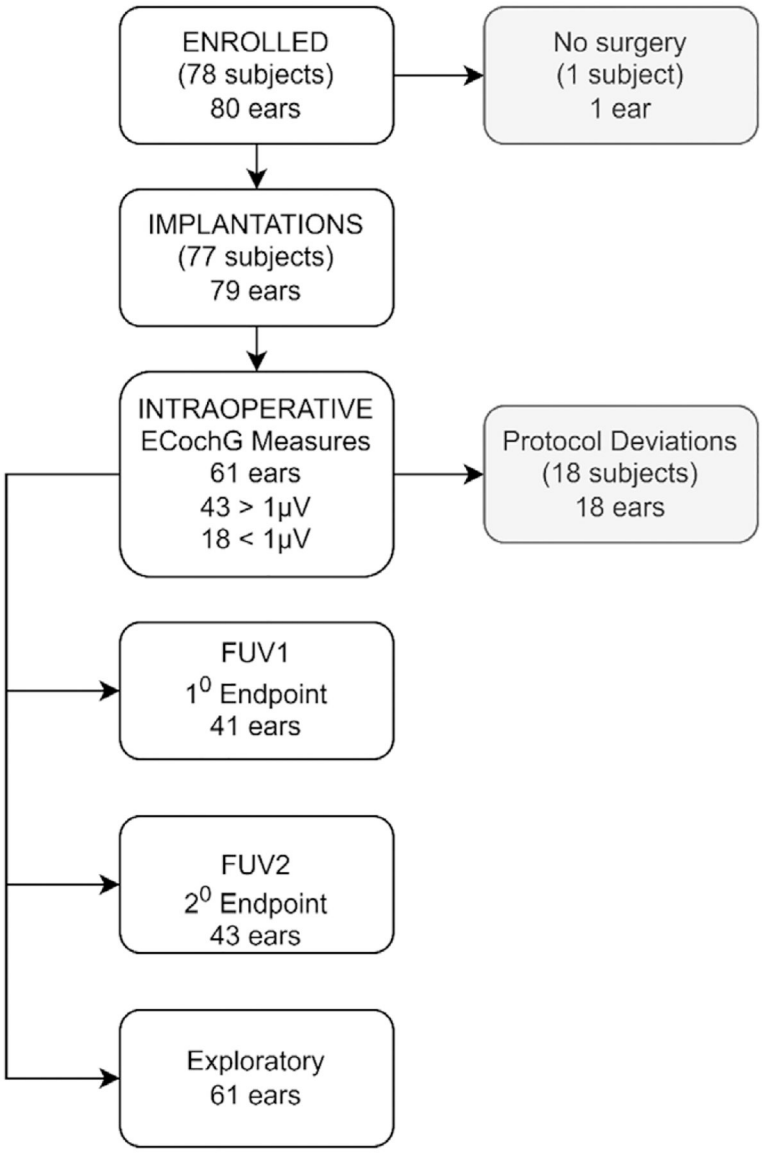


**Fig. 1.**
Participant recruitment and evaluation pathway.

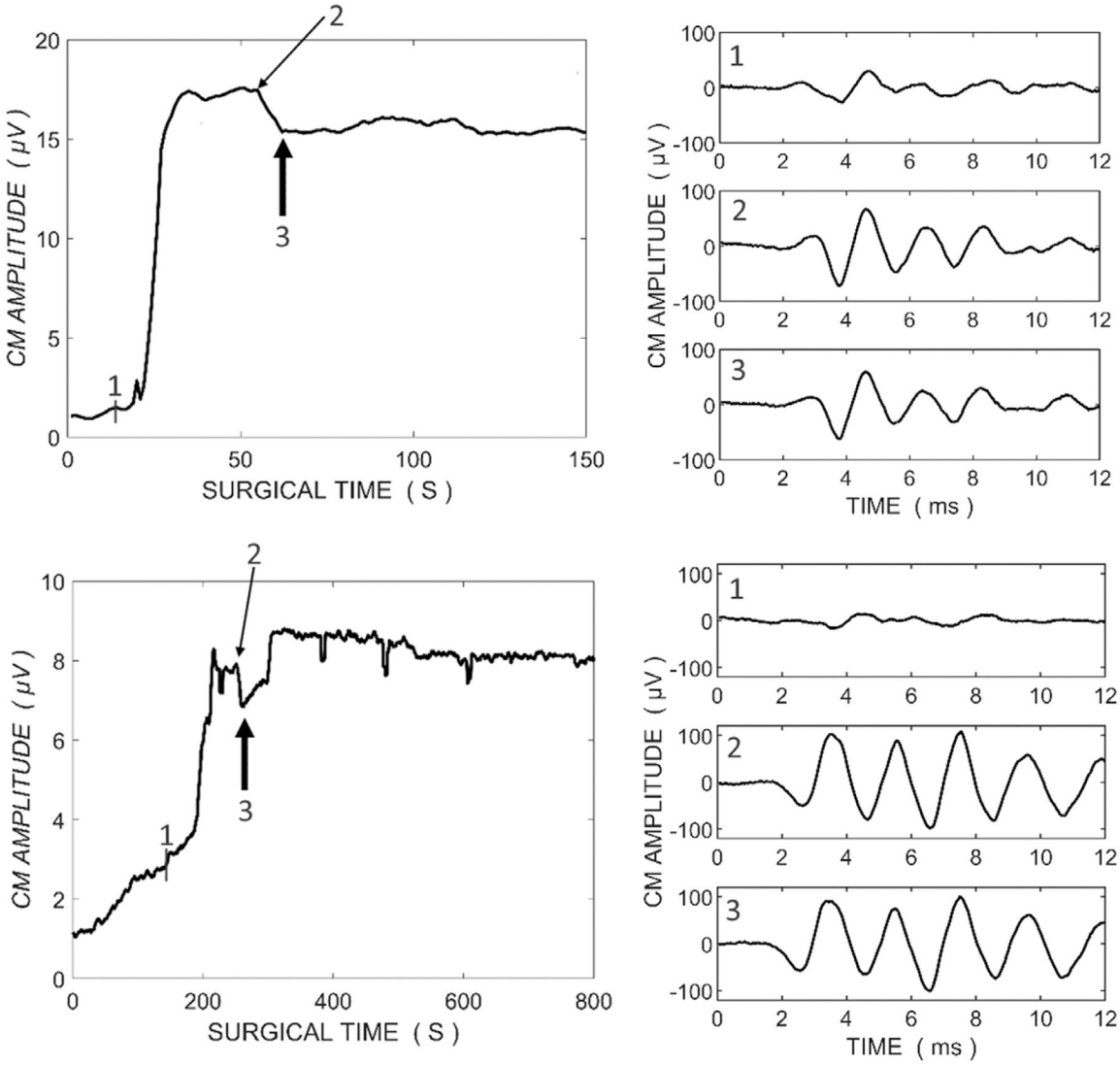


**Fig. 2.**

Left panels, examples of preserved CM in two participants. Small fluctuations <30% maximum amplitude as indicated by the slim arrows were not considered as compromised CM. Upper panel, small drop occurs from 54 to 62 sec, with CM amplitude reduced from 17.5 to 15.4 μV. Lower panel, small drop occurs from 251 to 260 sec, with an amplitude drop from 7.9 to 6.9 μV. Thick arrow represents point of complete insertion. Right panels, waveforms from traces on the left at timepoints shown at 1, 2, and 3. CM indicates cochlear microphonic.

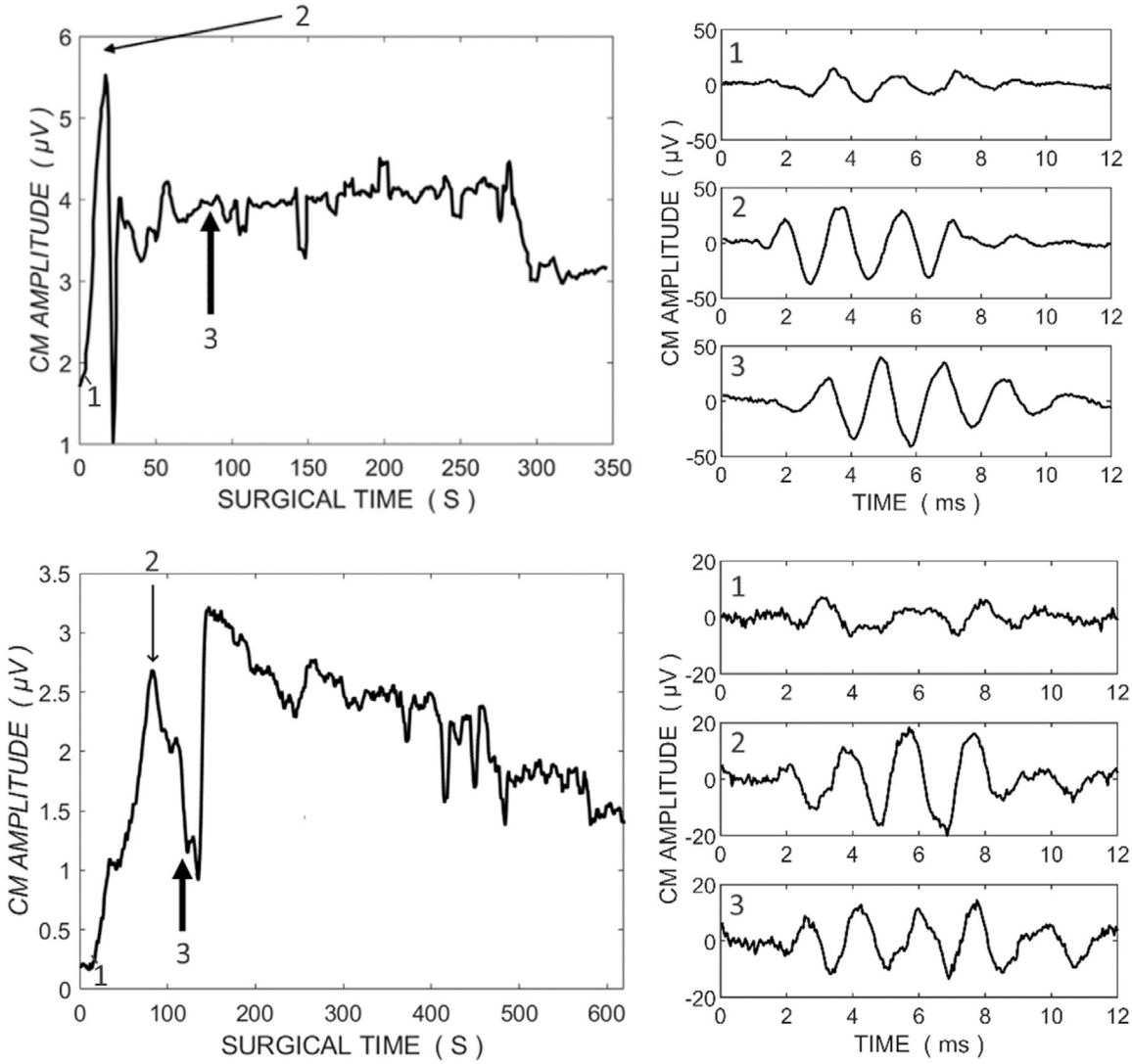


**Fig. 3.**

Left panels, examples of compromised CM in two participants. Large CM drops as indicated by the slim arrows occur often during implantation, as well as when manipulating the electrode after full insertion. Only one drop has been shown with an arrow. Upper panel, CM drop occurs from 17 to 22 sec, with CM amplitude reduced from 5.5 to 1.0 μV. Lower panel, CM drop occurs from 83 to 134 sec, with an amplitude drop from 2.6 to 0.9 μV. Thick arrow represents point of complete insertion. Right panels, waveforms from traces on the left at timepoints shown at 1, 2, and 3. CM indicates cochlear microphonic.

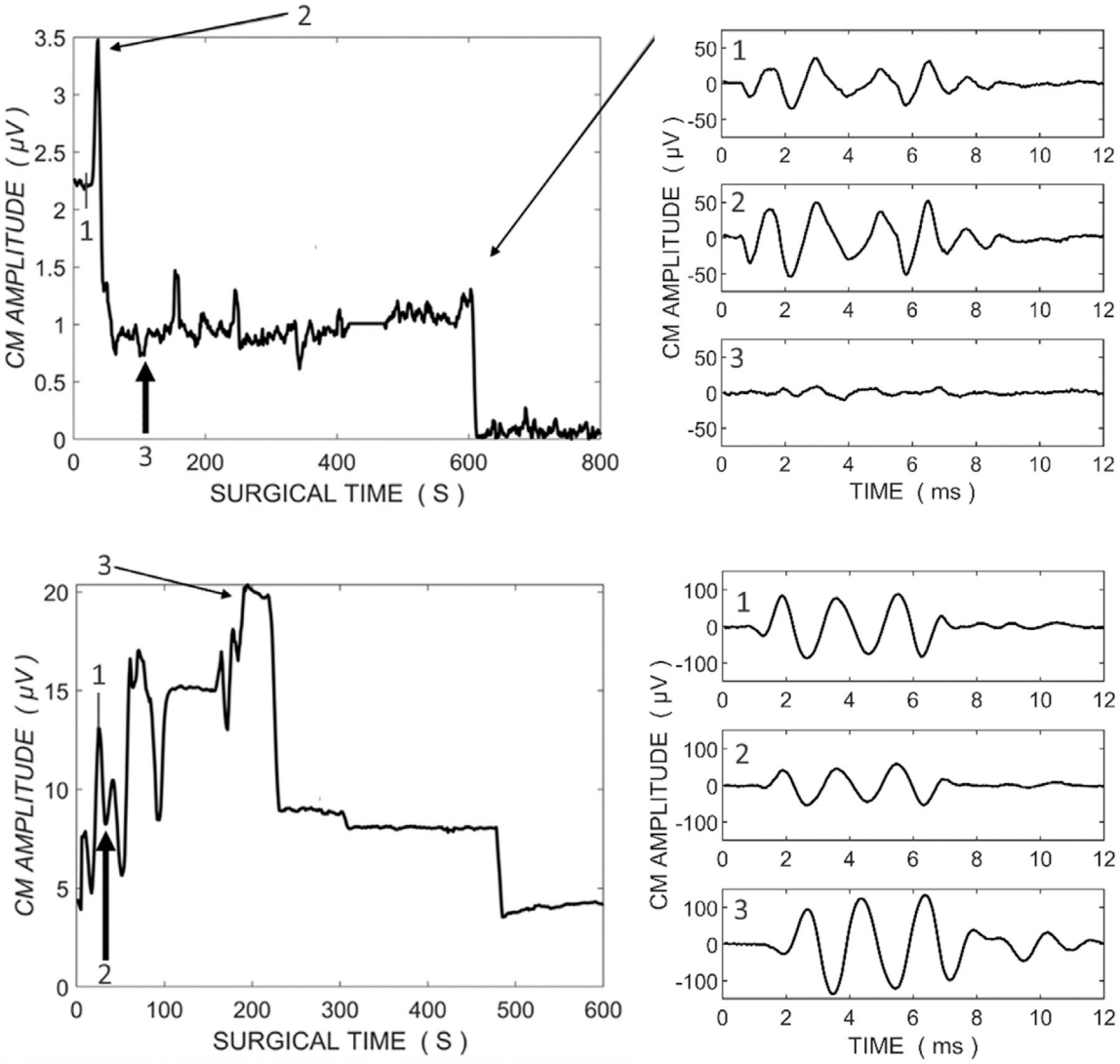


**Fig. 4.**

Left panels, examples of compromised CM in two participants. Any drop >30% maximum amplitude as indicated by the slim arrows immediately classifies the participant as having a compromised CM. Upper panel, CM drop occurs from 37 to 64 sec, with CM amplitude reduced from 3.5 to 0.8 μV. Lower panel, CM drop occurs from 219 to 231 sec, with an amplitude drop from 19.5 to 8.7 μV. Thick arrows represent point of complete insertion. Right panels, waveforms from traces on the left at timepoints shown at 1, 2, and 3. CM indicates cochlear microphonic.

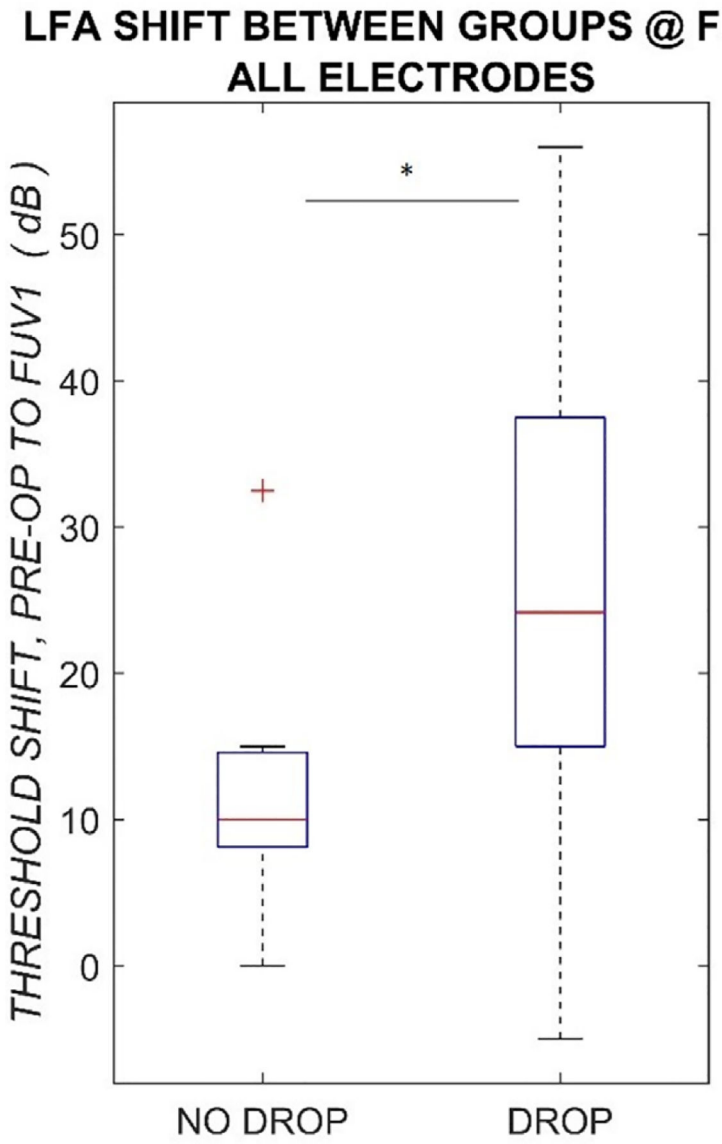


**Fig. 5.**

Pre-op to FUV1 mean threshold deterioration (dB) for the preserved CM (No Drop) (n = 7 ears) and compromised CM (Drop) (n = 34 ears) groups (*$p < 0.05$). Red cross for outliers, automatically calculated as those points exceeding the 75th percentile plus 1.5 times 75th percentile minus the 25th percentile. CM indicates cochlear microphonic; FUV, follow-up visit.

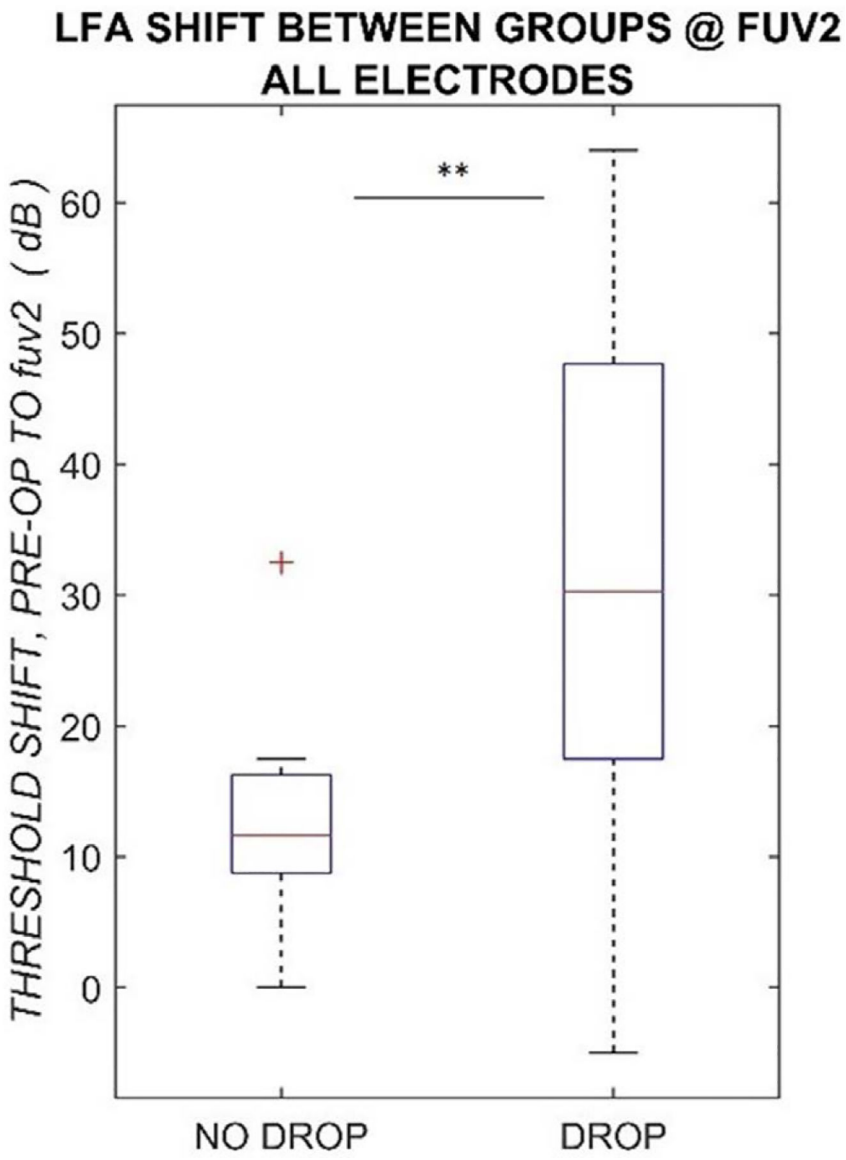


**Fig. 6.**

Pre-op to FUV2 threshold deterioration (dB) for the preserved CM (No Drop, n = 8 ears) and compromised CM (Drop, n = 30 ears) groups (**$p < 0.01$). Red cross for outliers, automatically calculated as those points exceeding the 75th percentile plus 1.5 times 75th percentile minus the 25th percentile. CM indicates cochlear microphonic; FUV, follow-up visit.

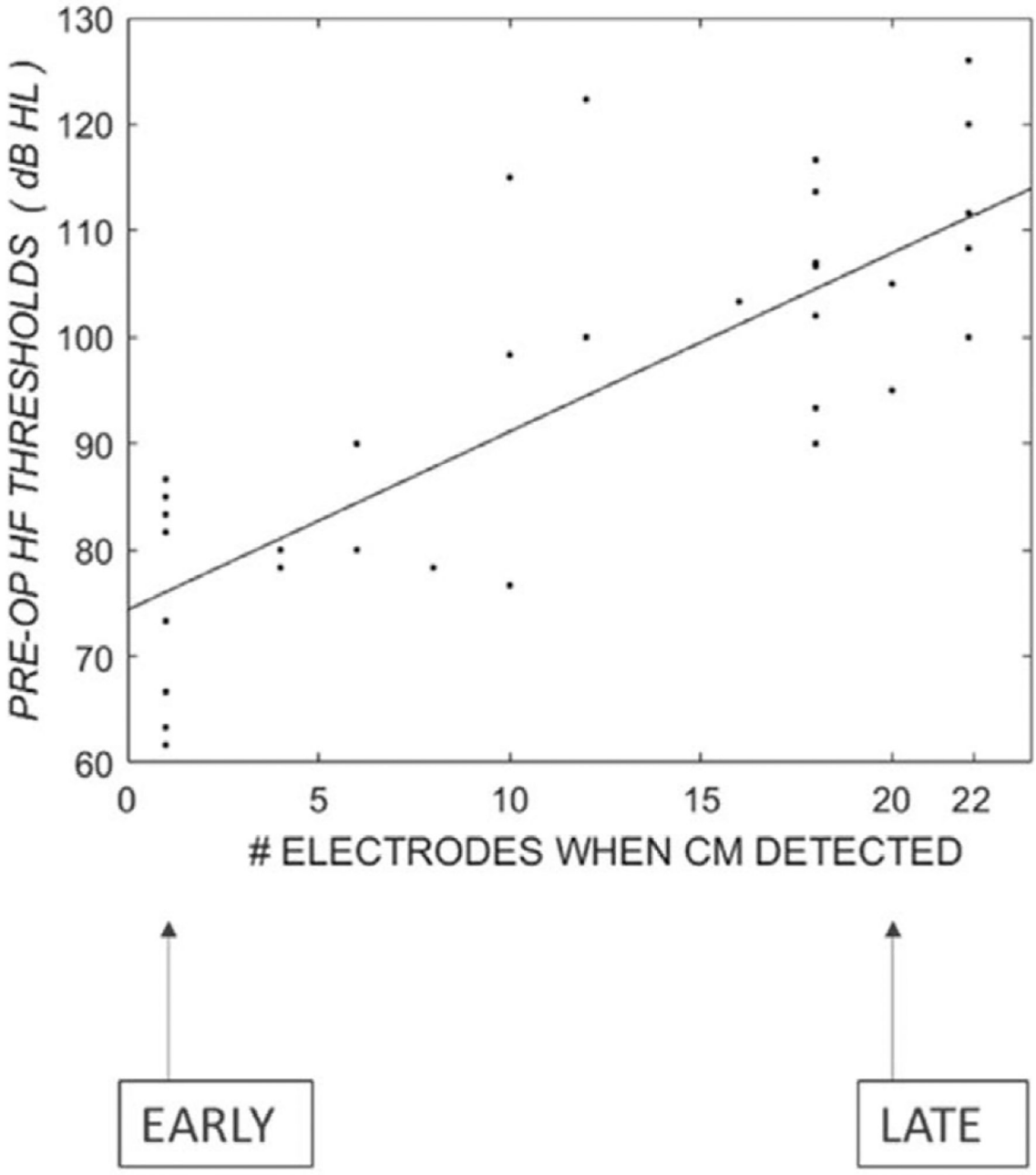


**Fig. 7.**

Relationship between high-frequency thresholds (in dB HL) at POV1 and onset of CM response measured in terms of number of electrodes inserted before a CM was detected. N = 36 ears. CM indicates cochlear microphonic; POV, preoperative visit.

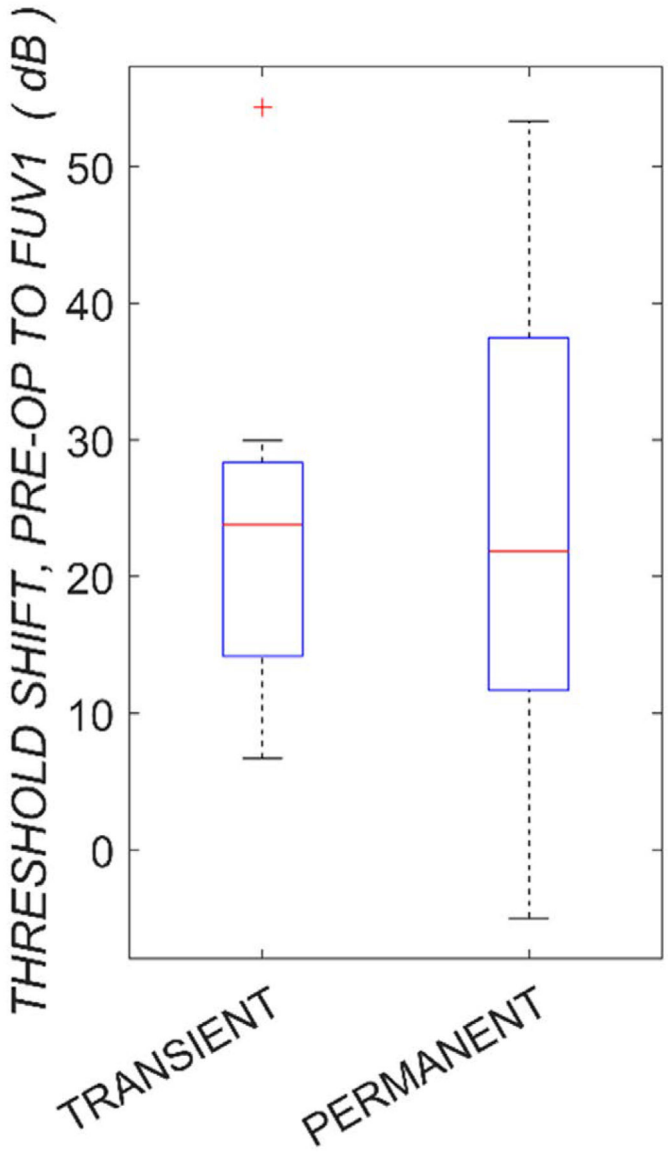


**Fig. 8.**

Low-frequency average hearing loss (dB) at FUV1 for the transient drop (n = 8 ears) and permanent drop CM groups (n = 30 ears). Red cross for outlier. CM indicates cochlear microphonic; FUV, follow-up visit.

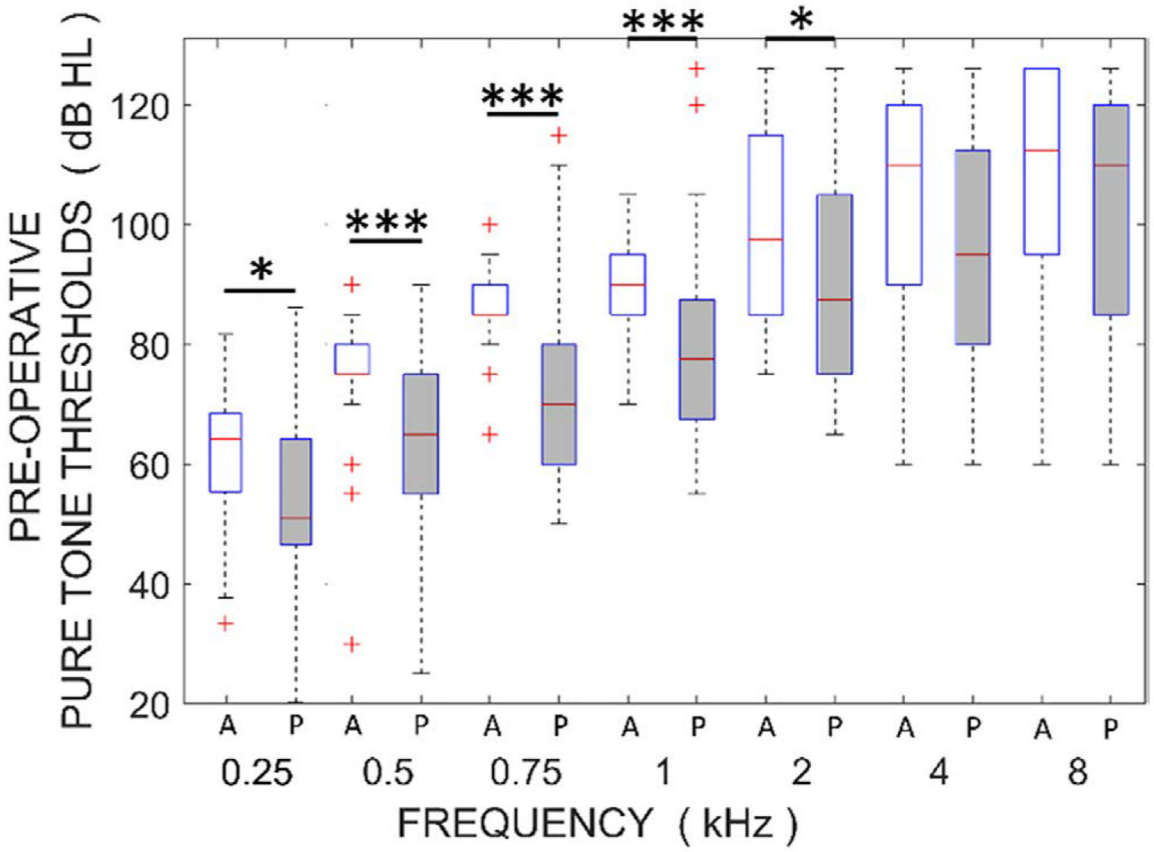


**Fig. 9.**

Preoperative pure tone thresholds (dB HL) grouped according to whether the CM was present (P) or absent (A) at a particular frequency, n = 61 ears. Significantly better mean preoperative thresholds for the CM present group are indicated at 0.25, 0.5, 0.75, 1, and 2 kHz. (* $p < 0.05$), (*** $p < 0.001$). Red cross for outliers, automatically calculated as those points exceeding the 75th percentile plus 1.5 times 75th percentile minus the 25th percentile. CM indicates cochlear microphonic.

**TABLE 1.**

Evaluation schedule

| Procedure | POV1 Preoperative | D0 Surgery | FUV1 4–6 Weeks Postsurgery (±1 week) | FUV2 3-Month Postactivation (±2 weeks) |
|---|---|---|---|---|
| Medical and hearing history | X | | | |
| EcochG | | X | X (either FUV1 or FUV2) | |
| Audiometry and tympanometry | X | | X | X |

D0, day of surgery; EcochG, electrocochleography; FUV, follow-up visit; POV, preoperative visit.

**TABLE 2.**

Study measures and evaluation intervals vs. available datasets for analysis

| Evaluation Interval | POV1 | IOP | IOP | FUV1 | FUV2 | CM Response, N = 61 | | Available Datasets | |
|---|---|---|---|---|---|---|---|---|---|
| **Measures** | **PTA** | **ECochG** | **Z** | **PTA** | **PTA** | **Unclear <1 μV** | **Clear >1 μV** | **Yes** | **No** |
| Endpoints | | | | | | | | | |
| Primary hypotheses | | | | | | | | | |
| FUV1 hearing preservation | X | X | | X | | 18 | 43 | 41 | 2 |
| Secondary hypotheses 1 | | | | | | | | | |
| FUV2 hearing preservation | X | X | | | X | 18 | 43 | 38 | 5 |
| Secondary hypotheses 2 | | | | | | | | | |
| POV1 PTA and onset of cm | X | X | X | | | 18 | 43 | 36 | 7 |
| Exploratory | | | | | | | | | |
| Transient or persistent cm drop and FUV1 | X | X | | X | | 18 | 41 | 34 | 7 |
| POV1 PTA and CM detection | X | X | | | | 18 | 43 | 61 | 0 |

CM, cochlear microphonic; FUV, follow-up visit; IOP, intraoperative; POV, preoperative visit; Z, impedance.

**TABLE 3.**

CM response categorisation and threshold shift (N = 59 ears 57 participants)

| ECochG Response | ≤15 dB HL Threshold Shift; POV1 to FUV1 | > 15dB HL Threshold Shift; POV1 to FUV1 | Total |
|---|---|---|---|
| Preserved CM (no drop) | 6 | 1 | 7 |
| Compromised CM (drop) | 10 | 24 | 34 |
| Unclear CM response | 6 | 12 | 18 |

CM, cochlear microphonic; EcochG, electrocochleography; FUV, follow-up visit; POV, preoperative visit.