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Performing Intracochlear Electrocochleography During Cochlear Implantation

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Corresponding Author:	Stefan Weder Inselspital Universitätsspital Bern Bern, BE SWITZERLAND
Corresponding Author's Institution:	Inselspital Universitätsspital Bern
Corresponding Author E-Mail:	stefan.weder@insel.ch
Order of Authors:	Klaus Schuerch
	Manuel Waser
	Georgios Mantokoudis
	Lukas Anschuetz
	Wilhelm Wimmer
	Marco Caversaccio
	Stefan Weder
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TITLE:

Performing Intracochlear Electrocochleography During Cochlear Implantation

AUTHORS AND AFFILIATIONS:

Klaus Schuerch[1,2], Manuel Waser[1], Georgios Mantokoudis[1], Lukas Anschuetz[1], Wilhelm Wimmer[1,2], Marco Caversaccio[1,2], Stefan Weder[1]

[1]Department of Otorhinolaryngology, Head and Neck Surgery, Inselspital, Bern University Hospital, University of Bern, Switzerland

[2]Hearing Research Laboratory, ARTORG Center for Biomedical Engineering Research, University of Bern, Switzerland

Email addresses of co-authors:

Klaus Schuerch	(klaus.schuerch@artorg.unibe.ch)
Manuel Waser	(Manuel.Waser@insel.ch)
Georgios Mantokoudis	(Georgios.Mantokoudis@insel.ch)
Lukas Anschuetz	(Lukas.Anschuetz@insel.ch)
Wilhelm Wimmer	(wilhelm.wimmer@artorg.unibe.ch)
Marco Caversaccio	(marco.caversaccio@insel.ch)

Corresponding author:

Stefan Weder (stefan.weder@insel.ch)

SUMMARY:

Electrocochleography (ECochG) measures inner ear potentials generated in response to acoustic stimulation. In cochlear implant (CI) candidates, such inner ear potentials can be measured directly with the implant electrodes. In this video, we systematically explain how to perform ECochG recordings during CI surgery.

ABSTRACT:

Electrocochleography (ECochG) measures inner ear potentials generated in response to acoustic stimulation of the ear. These potentials reflect the residual function of the cochlea. In cochlear implant candidates with residual hearing, the implant electrode can directly measure ECochG responses during the implantation process. Various authors have described the ability to monitor the inner ear function by continuous ECochG measurements during the surgery. The measurement of ECochG signals during surgery is not trivial. There are no interpretable signals in up to 20% of cases. For a successful recording, a standardized procedure is recommended to achieve the highest measurement reliability and avoid possible pitfalls. Therefore, seamless collaboration between the CI surgeon and CI technician is key. This video consists of an overview of the system setup and a stepwise procedure of performing intracochlear ECochG measurements during CI surgery. It shows the surgeon's and the CI technician's roles in the process, and how a smooth collaboration between the two is made possible.

INTRODUCTION:

In recent years, the indication for cochlear implants has changed considerably. In the past, the extent of hearing loss in the pure tone audiogram was the primary indication for an implant, whereas today, speech understanding at maximum hearing aid amplification is the decisive factor. This has altered the population of implant candidates. Increasingly, patients who still have natural residual hearing (most commonly in the low-frequency region) receive a CI. Studies have shown that the residual function should be preserved as much as possible during and after surgery. Patients with preserved residual hearing perform better in speech intelligibility tests, have increased spatial awareness, and perceive music more naturally[1,2].

In the past, atraumatic implantation primarily depended on the surgeon's assessment and haptic perception. Intraoperatively measured inner ear potentials (i.e., ECochG) are increasingly gaining interest in monitoring inner ear function[3–6]. They can provide the surgeon with additional information about the functioning of the inner ear during and after surgery. ECochG is a generic term for electrophysiological signals generated by the cochlea in response to acoustic stimulation. There are four different signal components, which can be measured depending on their origin; the cochlear microphonic (CM) is the largest and most stable signal component and is therefore used as a key variable in many studies. The origin of this signal component is predominantly in the outer hair cells. Other signal components are the auditory nerve neurophonic (ANN, an early neural response), the compound action potential (CAP, an early neural response), and the summating potential (a hair cell response).

The course of the ECochG signal during the implantation process provides insights into the state of the inner ear; changes in the intraoperative ECochG signal can be correlated with the postoperative residual function of the inner ear[3,4,7–9]. The measurement of ECochG signals is not trivial. No interpretable signal can be derived in up to 20% of cases[10,11]. On the one hand, there are patient-specific factors (i.e., absence of functioning hair cells) that influence the recordings. On the other hand, numerous technical and operation-specific factors contribute to the success of a measurement. Therefore, residual hearing cannot alone explain the success rate of ECochG. To record data as reliably as possible, a standardized procedure for these measurements is important. This prevents mismeasurements and facilitates the interpretation of intraoperative data.

There is no clear consensus of a required hearing threshold. In our experience, reproducible signals can be obtained in patients with a hearing threshold of up to 100 dB hearing loss (HL). This finding has been confirmed by other authors[12]. Other research groups perform ECochG measurements with a pure tone average (PTA) between 80 and 85 dB or better[3,5,6,8,13,14]. This video shows the system setup and a stepwise procedure of performing successful intracochlear ECochG measurements during CI surgery.

PROTOCOL:

This study was performed in compliance with institutional guidelines (Basec ID 2019-01578). The video shows the recording of ECochG measurements with a MED-EL implant. The required hardware, software, system setup, and intraoperative implementation may vary depending on

the manufacturer. However, the chronological sequence and measurement steps are independent of the brand. If necessary, additional information will be provided for the Advanced Bionics (AB) and Cochlear systems. The description of the theater is given from the surgeon's point of view.

1. Before the surgery

1.1. Indication

1.1.1. Perform ECochG measurements in patients where hearing preservation is the goal.

1.1.2. Stimulate with a 500 Hz pure tone, 30 dB above the hearing threshold with a minimum level of 100 dB HL and a maximum level of 120 dB HL. Ensure the following: an acoustic stimulus of a duration of 8 ms, the measurement window of 10 ms length for recording the ECochG potentials beginning 1 ms after the acoustic stimulus, and the measurement repetition set to 100 iterations.

NOTE: Depending on the preoperative hearing test, other frequencies can also be used (i.e., 250 and 1000 Hz)[8,14]. Stimuli below 1000 Hz are preferred to avoid crossing the corresponding tonotopic intracochlear frequency region (resulting in a non-traumatic drop of the signal amplitude). More recent software versions allow the synchronous real-time measurement of different frequencies[15].

1.2. Clean the patient’s ear canal thoroughly. Check the eardrum.

NOTE: Obstructing ear wax, liquids or debris might affect the sound transmission during ECochG[10]. The eardrum must be intact with no sign of infection.

1.3. Evaluate the preoperative administration of steroids. Use methylprednisolone 125 mg, intravenously administered, 6 h before the start of surgery.

NOTE: Dexamethasone can also be used as part of the standard clinical practice, either the day before or at the induction of anesthesia[16,17].

2. Preparation in the theater

2.1. Check the required hardware and software for ECochG measurements. See **Table 2** for the hardware and software requirements for different manufacturers.

2.2. Have the engineer check the seamless functioning of hard- and software.

NOTE: The following room setup is recommended: the engineer positions him/herself opposite the surgeon. In this way, he/she can monitor the measurement process well and give direct feedback to the surgeon (**Figure 1**).

2.3. Position the patient's head so that the mastoid segment of the facial nerve runs approximately horizontal.

NOTE: The neck is thereby slightly retracted and the upper body in a reverse Trendelenburg position. Furthermore, the neck is slightly tilted away, and the head rotated to the not-operated side to give maximal access to the surgeon.

2.4. Shave the hair in the retro-auricular region (approximately 3 cm).

2.5. Install the facial nerve monitoring.

2.6. Disinfect the surgical site and cover it with sterile drapes.

NOTE: It is important that the auditory canal is included in this step. In addition, it is important that the cover must be as thin as possible in the area of the planned receiver coil position (to avoid connection problems between the transmitting and receiving coil). For this reason, choose thin drapes and place the fluid bag as low as possible (**Figure 2**).

3. Getting started

3.1. Mark the position of the processor, the implant, and the skin incision.

3.2. Inject the local anesthesia (mepivacaine with 1:200,000 epinephrine).

3.3. Check the ear canal and clean traces of disinfectant solution. Check the eardrum.

3.4. Insert the sterile eartip, connected to a sterile sound tube, deep into the external canal.

NOTE: This step is important because displacement of the eartip leads to significant drops in the presented sound pressure[10].

3.5. Place a large swab into the concha of the operated ear and tilt the ear forward. Fix the earlobe (including the eartip, soundtube, and swab) with a transparent adhesive foil.

NOTE: This technique avoids strong buckling of the eartip and sound tube as well as eartip displacement, which can lead to attenuation of the presented signal. Furthermore, irrigation fluid and blood can no longer enter the external auditory canal.

3.6. Before connecting the sound tube to the non-sterile transducer, have the engineer check the functioning of the acoustic output.

3.7. Connect the sound tube to the non-sterile sound transducer handled by the engineer. Cover the non-sterile part with a sterile blanket. Ensure that the sound transmission parts are tension-free.

4. Implant surgery

4.1. Incise the skin up to the temporalis fascia. Make an offset incision (5–10 mm anteriorly) of the periosteum in a lazy S fashion[18]. Dissect the periosteum off the bone and display the bony ear canal and Henle spine for orientation. Check the thickness of the soft tissue above the future receiving coil and thin it out according to the manufacturer's recommendations as needed.

NOTE: The incision should be large enough to show the mastoid plane and accommodate the implant housing in a tight subperiosteal plane under the temporalis muscle.

4.2. Harvest a 5 mm x 5 mm large piece of dermal fat to seal the posterior tympanotomy and 2–3 small pieces (1 mm x 1 mm) of periosteum to seal the entrance point of the electrode into the inner ear later on.

4.3. Place the wound retractors.

NOTE: Ensure that the retractor does not compromise the soft tissue of the auditory canal. This can cause the inserted eartip to dislodge, which leads to attenuation of the presented signal.

4.4. Perform the surgical access to the middle and inner ear.

4.4.1. Drill the mastoid bone with an overhang posteriorly to accommodate the electrode within the mastoid later on. During this step, harvest some bone paté.

4.4.2. Display the lateral skull base cranially and drill out the mastoid bone evenly with the deepest point of dissection above the antrum.

4.4.3. Display the antrum with the lateral semicircular canal.

4.4.4. Thin out the bony ear canal evenly until the short process of the incus is seen.

4.4.5. Drill the bone caudal to the lateral semicircular canal toward the mastoid tip, parallel to the expected facial nerve. Display the nerve and, if possible, the chorda tympani.

4.4.6. Access the middle ear via a posterior tympanotomy. Drill near the buttress between the facial nerve and the chorda until the middle ear space is reached.

4.4.7. Check the position of visible middle ear structures (e.g., the stapedius tendon). Ensure that the ossicular chain remains intact.

4.4.8. Enlarge the posterior tympanotomy caudally until the round window niche is visualized.

4.4.9. Reduce the bony lip of the round window niche until the round window is seen completely.

4.5. Drill an anterior step in the area of the planned implant housing position. Check that the step is of sufficient size with the help of an implant bed indicator. Drill a channel for the electrode.

4.6. Rinse the surgical site thoroughly and perform meticulous hemostasis. Finally, place a 1 cm x 1 cm piece of gelatin sponge in the antrum.

NOTE: In addition to surgical management, it is important that the anesthesiologist monitors blood pressure throughout the procedure (to minimize bleeding; if possible, the systolic blood pressure should be below 100 mg Hg). The gelatin sponge will stop drops of blood or irrigation fluid from running into the middle ear.

4.7. Change gloves and wait for the engineer to pass the non-sterile stimulating coil to the scrub nurse. Instruct the nurse to pack the coil into a sterile sleeve.

5. Insertion and ECochG measurements

NOTE: At this point, the communication between the surgeon and the engineer is crucial.

5.1. Rinse the implant and insert it in the previously created subperiosteal pocket. Ensure a stable implant position against the drilled bony step. Depending on the manufacturer, place the separate reference electrode in an anterior, submuscular pocket. Check that ground and reference electrodes of the implant (on top of the implant, right below the coil) are well covered with soft tissue.

5.2. Place the stimulating coil above the magnet of the receiving coil. Rotate the transmitting coil 180° back and forth to align the MR-compatible magnets. Wait for the engineer to measure the wireless connection (coupling check). When the connection is 100%, fix the transmitting coil with an adhesive foil to ensure that the coils do not displace during implantation.

5.3. Inspect the middle ear again. Ensure that the middle ear space is air-filled. Carefully open the round window membrane. Ensure that the opening is sufficiently large and do not accidentally suction the perilymph.

5.4. Insert the first electrode into the round window. If applicable and depending on the manufacturer, condition the electrode. Now, wait for the engineer to perform an impedance check.

NOTE: Impedance values are manufacturer-specific. As a rough guide, the impedance should be below 10 kΩ.

5.5. Insert the electrode slowly while carefully following hearing preservation techniques[19]. Keep the technician informed of progress (e.g., markers, number of electrodes in the cochlea) during insertion. Also instruct the technician to record and clearly communicate the ECochG potentials, i) if there is a signal (most commonly a CM signal), ii) how the signal evolves, and iii) if there are abrupt signal changes.

5.5.1. With a MED-EL implant, perform the stepwise procedure described previously[7].

5.5.1.1. With the standard software, use condensation polarity with a recording window of 9.6 ms. Set the measurement delay to 1 ms and perform 100 iterations.

5.5.1.2. Insert the electrode slowly and halt the insertion process after every second or third electrode (increase the number of recordings towards the end).

5.5.1.3. Perform an ECochG measurement while holding the electrode array in place. Instruct the engineer to communicate as soon as the measurement is complete. Repeat ECochG until a full insertion is reached.

5.5.2. With AB or Cochlear implants, record ECochG potentials with alternating polarities while the electrode is moved/inserted[8,20]. Communicate visible landmarks to the engineer (e.g., **first implant marker is reached**).

5.6. In case of an amplitude loss of the ECochG signal, retract the electrode slightly and repeat the measurement[21].

5.7. After full insertion, have the engineer continue to record ECochG. Communicate each surgical step (e.g., **sealing of the round window niche**).

5.8. Drape the electrode within the mastoid cavity. Seal the round window with small pieces of the previously harvested fat. Stabilize the electrode within the posterior tympanotomy with a larger piece of fascia or periosteum. Embed the electrode in the bony channel with some bone paté.

5.9. Have the engineer check the integrity of the implant (impedance and electrically evoked compound action potentials). Continue with postinsertion ECochG recordings later.

5.10. Close the wound in layers (periosteal layer, subcutaneous layer, skin).

5.11. Remove the sound tube and eartip; check for possible kinking or dislodgment. Finally, check the eardrum.

REPRESENTATIVE RESULTS:

For ECochG measurements during cochlear implantation, a standardized procedure is important

to achieve the highest possible reproducibility of signals. Here, a setup is proposed wherein the surgeon and the engineer sit opposite each other to facilitate communication (**Figure 1**). When setting up the system, it is important that there is an unimpeded stimulus transmission. For example, the ear canal should be completely cleaned and clear; the eartip must sit deep in the ear canal; the eartip and sound tube are not kinked; the sound tube must run visibly on the sterile cover and be accessible during surgery; the retractor does not impact the ear canal, and thorough hemostasis should be done prior to the insertion process to ensure an air-filled middle ear space. In addition, a stable connection between the transmitting and receiving coils is important to prevent interruptions during the insertion process. Therefore, the sterile drapes should be as thin as possible (**Figure 2**), the skin thickness must be checked at the beginning of the surgery, and the two magnets should be aligned. Furthermore, when starting the ECochG measurement, the implant housing must be covered by soft tissue, and the impedance should be checked before continuing with the insertion.

Using this measurement protocol, we performed measurements with 12 patients (**Table 2**). These patients had a maximum hearing threshold of 100 dB HL at 500 Hz. When calculating the PTA, the mean of the hearing thresholds was taken at 125 Hz, 250 Hz, and 500 Hz. ECochG recordings were performed using an acoustic stimulus at 500 Hz, condensation polarity, and 30 dB above the individual hearing threshold (minimum 100 dB HL, maximum 120 dB HL). The acoustic stimulus had a duration of 8 ms, with a rise/fall time of 2 ms each[22]. In total, 100 recordings were taken in each case. For signal processing, the focus was on cochlear microphonic signals using Python. First, we applied bandpass filtering (Butterworth, 4^{th} order, 100 Hz–3 kHz bandpass) in forward–backward mode. Finally, an ECochG response was considered valid if the signal-to-noise ratio (SNR) was greater than one. SNR was calculated using the ± averaging method[23]. The SNR estimate fluctuates due to the small number of epochs. Therefore, the SNR calculation is repeated 1000 times with random subdivisions to obtain a robust estimate. Example measurements are shown in **Figure 3**: the ECochG signal amplitude increases with its maximum at electrode 9. The mid-peak pattern can be confirmed in the postinsertion measurements (fully inserted electrode). Considering these results, the mid-peak pattern was measured in 8 out of 12 subjects. Others showed an apical-peak (subjects 1, 4, 6) or a start-peak (subject 3)

FIGURE AND TABLE LEGENDS:

Figure 1: Operative room setup. Here, a setup is proposed where the surgeon and the engineer sit opposite each other to facilitate communication.

Figure 2: Draping before the surgery. Care must be taken to ensure that there is a stable connection between the transmitting and receiving coils. (A) Thin, sterile drapes and (B) the fluid bag positioned as low as possible shorten the distance between the two coils. In this way, a good connection to the implant can be achieved. (C) The eartip must sit deep in the ear canal. (D) Using a large swab avoids strong buckling of the eartip and sound tube as well as eartip displacement.

Figure 3: Intraoperative ECochG measurements. ECochG traces during (**A**) and after (**B**) electrode insertion are shown. Please note that the numbering of electrodes for **A** and **B** starts at opposite

ends. (**A**) measures at the electrode tip and counts the number of electrodes inserted into the cochlea. (**B**) indicates the measurement electrodes, starting with the tip electrode as number one. Below (**C**), image taken during the implantation process with six inserted electrodes. Abbreviations: ECochG = electrocochleography; ampl = amplitude; el = electrode.

Table 1: Hardware and software required for ECochG recordings by three different manufacturers. Abbreviation: ECochG = electrocochleography.

Table 2: ECochG recordings during CI surgery in 12 subjects. ECochG recordings during CI surgery in 12 subjects. IOS SNR displays the maximum SNR of the cochlear microphonic signal reached during insertion. IEC shows at how many inserted electrodes this maximum SNR was reached. The final SNR shows the CM amplitude of the fully inserted electrode at the most apical position. Abbreviations: ECochG = electrocochleography; CI = cochlear implant; rw = round window; C = cochleostomy; IEC = inserted electrode contacts; IOS = intraoperative signal; apical = most apical electrode; pre = preoperative; post = postoperative (4 weeks); PT = pure tone threshold; PTA = pure tone average; SNR = signal-to-noise ratio.

DISCUSSION:

ECochG measurements are a promising tool to monitor the inner ear function during implantation. These electrophysiological potentials complement the surgeon's assessment and haptic perception. However, it should be noted that the measurement is not trivial and has many sources of error. To increase the measurement reliability, a standardized procedure is essential. This is key to an accurate interpretation of the signals.

Good communication between the surgeon and the engineer during the entire intervention is particularly important. In addition, the system setup must ensure unimpeded transmission of the acoustic stimulus and good and stable coupling of the transmitting and receiving coil. In a previous paper, we developed a standardized measurement protocol for ECochG recordings during implant surgery[10]. So far, applying this protocol, we have recorded 12 intraoperative measurements receiving MED-EL implants.

If the impedance is low, start the ECochG measurement. If the impedance is high, i) rinse the implant pocket with saline solution, ii) make sure that the ground electrode is well covered by soft tissue, iii) make sure the tip of the electrode is in good contact with perilymph fluid. If the impedance stays high, repeat an impedance measure with the second or third electrode or insert the electrode slightly deeper into the cochlea.

If ECochG signal drops occur during electrode insertion (usually measured by the CM amplitude), preliminary evidence suggests that the surgical response may affect the inner ear function. A randomized study showed that when the CM amplitude decreased by 30% or more (related to the initial maximum amplitude), a slight withdrawal of the electrode resulted in a significant improvement of postoperative residual hearing[21]. However, the definition of a detrimental drop is unclear; another publication reported a CM decrease of 61% (or more) at a slope steepness of 0.2 µV/s (or more) to be significant[9]. A drop in ECochG responses may also be due to other

causes, such as the interaction of different signal generators, passing the 500 Hz range within the cochlea, or contact of the basilar membrane with the electrode array [6,24].

It can be concluded that an increasing number of CI candidates have substantial residual hearing. In this cohort, it is essential to preserve the acoustic component during and after CI surgery. ECochG recordings have the potential to provide objective feedback to the surgeon during the implantation process. However, we are just at the beginning of being able to correlate changes of ECochG recordings to the inner ear function and need to improve our knowledge and understanding of successful hearing preservation. ECochG recordings will thereby play an important role, complemented by other inner ear measurements. The goal will be to have an objectified measurement tool that will allow the preservation of residual inner ear function in most implant recipients.

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DISCLOSURES:

The authors declare that they have no conflicts of interest to declare.

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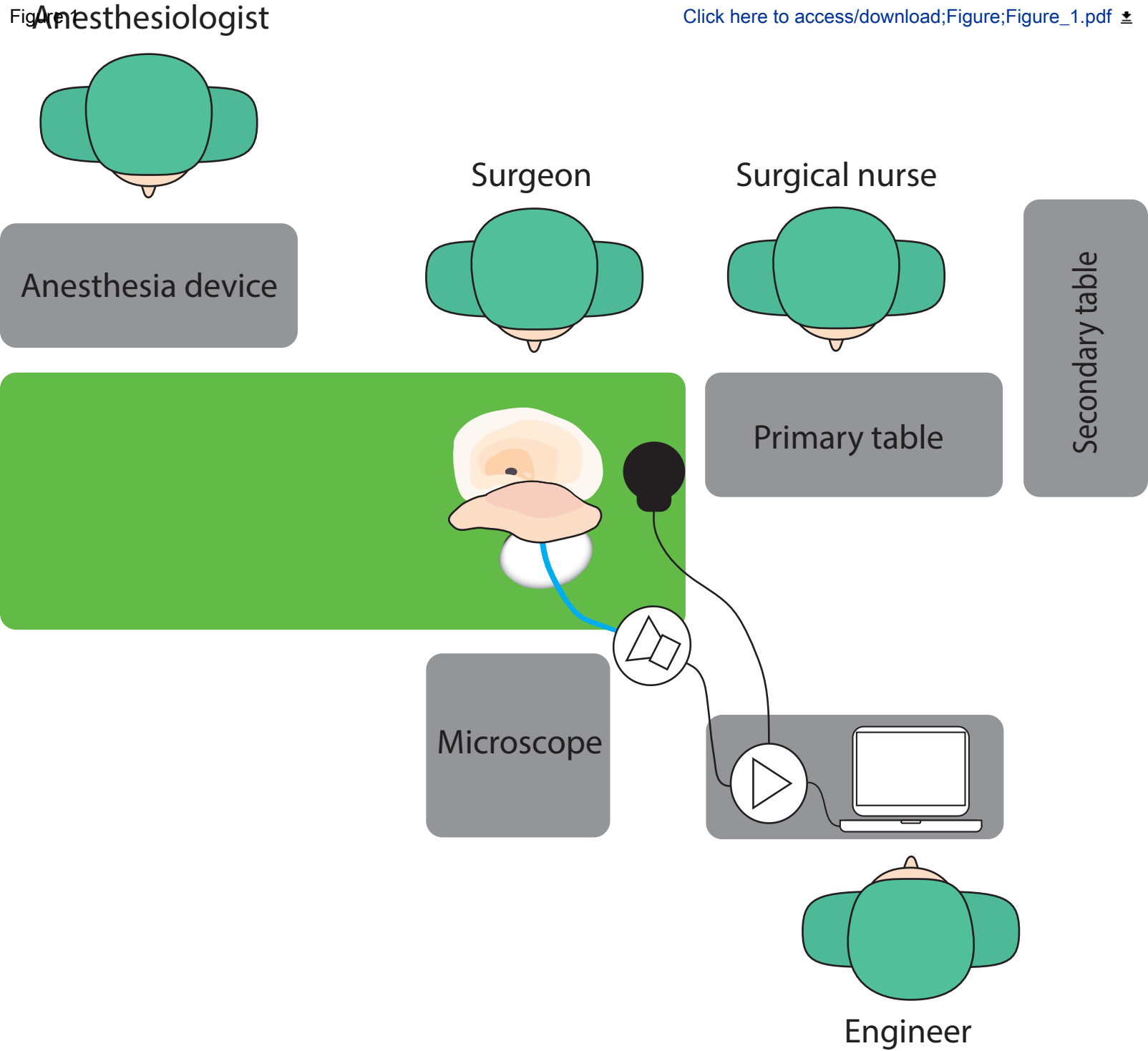


Figure 2

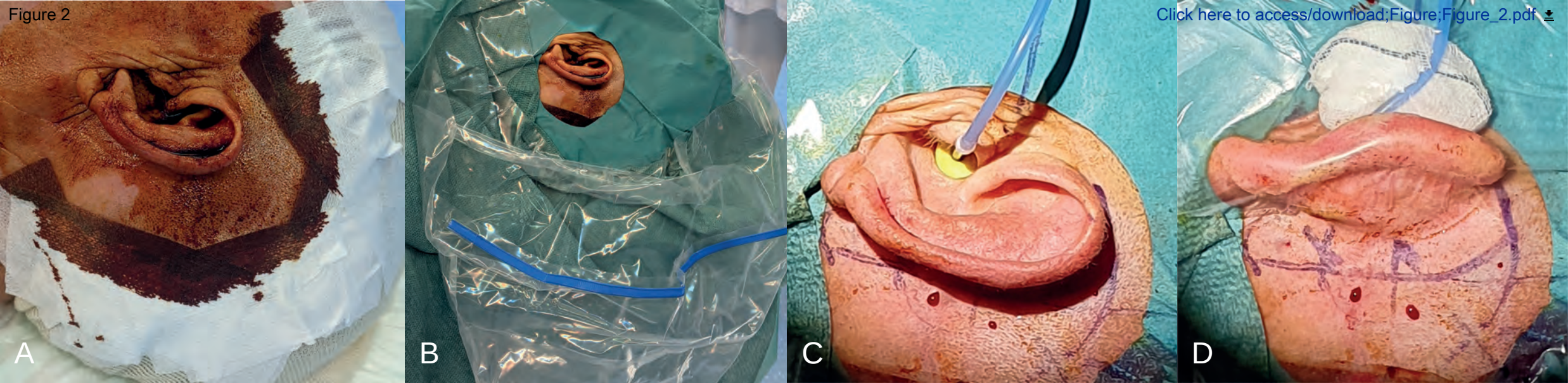
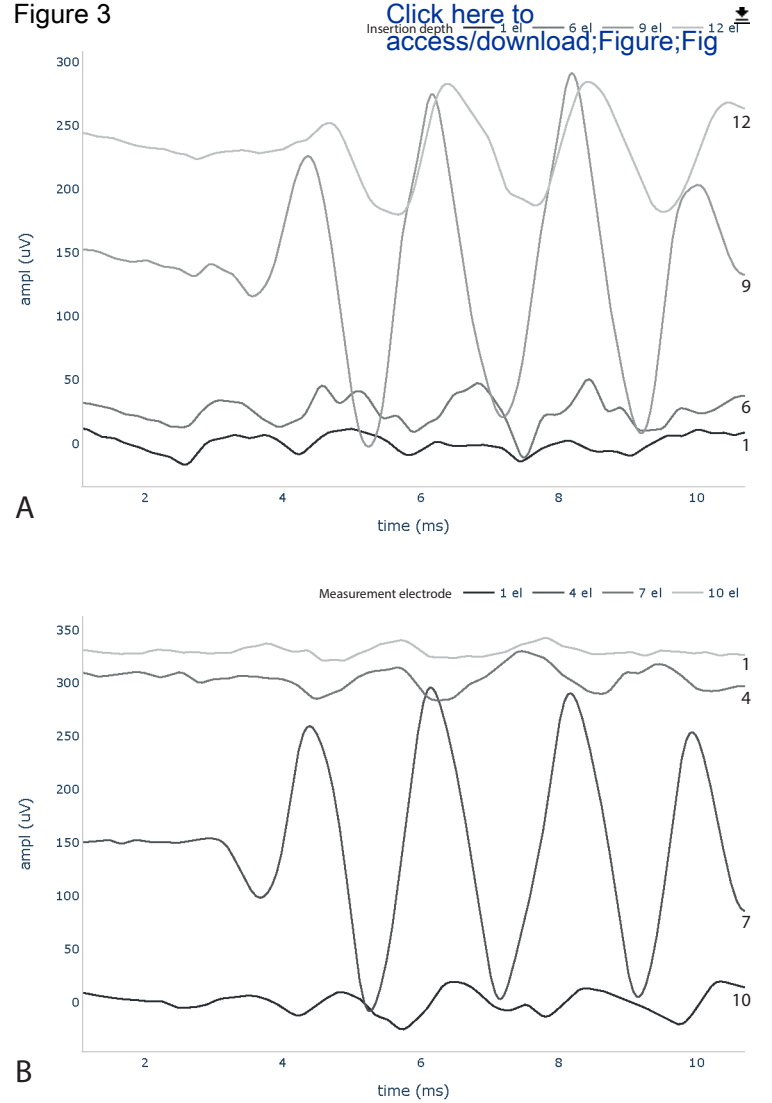


Figure 3



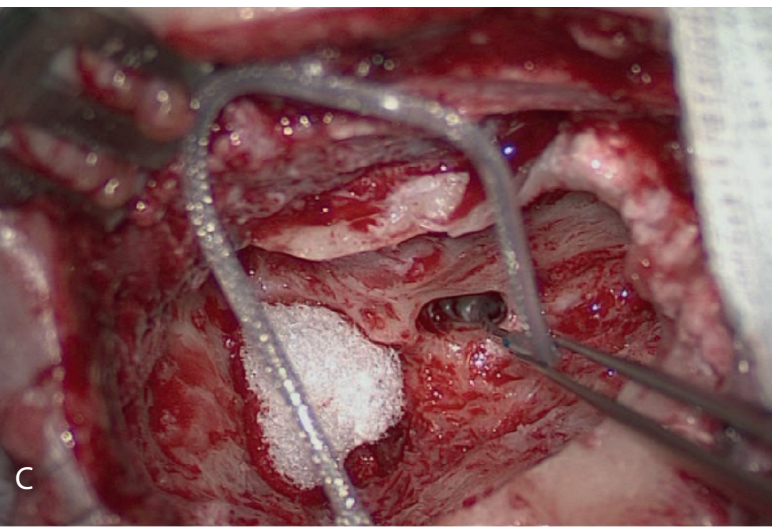


Table 1

	AB	Cochlear	Med-El
Computer	Tablet AIM	Arbitrary	Arbitrary
Software	OMSuite	Cochlear Research Platform	Maestro
Implant interface	Audio processor, coil cable	Audio processor, coil cable	Coil cable
Interface connection	Programming cable	Cochlear Programming Pod, programming cable, USB	MAXInterface, USB
Acoustic stimulation	Transducer AIM	Transducer Cochlear	Arbitrary waveform generator, Transducer Etymotic, trigger cable
Sound tube	Custom	Etymotic	Etymotic
Eartip	Custom	Etymotic	Etymotic

Table 2

Subject	Electrode (inserted ec)	Cochlear access	Pre PT at 500 Hz (dB HL)	Pre PTA (dB HL)	Post PT at 500 Hz (dB HL)	Post PTA (dB HL)
0	Flex 28 (11)	rw	100	80	115	101.7
1	Flex 28 (12)	rw	65	46.7	85	68.3
2	Flex 28 (12)	rw	65	56.7	110	98.3
3	Flex 28 (12)	rw	100	91.7	110	106.7
4	Flex 28 (12)	rw	100	100	125	111.7
5	Flex 24 (11)	c	70	58.3	125	111.7
6	Flex 28 (12)	rw	80	45	110	91.7
7	Flex 28 (12)	rw	55	53.3	125	111.7
8	Flex 28 (12)	rw	70	70	105	80
9	Flex 28 (12)	rw	55	40	105	68.3
10	Flex 28 (11)	rw	65	58.3	100	90
11	Flex 28 (12)	rw	80	78.3	100	85

IOS SNR	IEC	Final SNR
8.68	10	2.32
1.22	12	1.22
2.27	9	0.77
1.35	1	0.95
1.78	12	1.78
3.42	9	0.91
22.9	12	22.9
2.9	6	1.43
2.87	6	1.44
37.8	9	5.3
29.14	9	13.5
3.83	6	1.89

17/09/2021

JoVE63153
"Performing Intra-cochlear Electrocochleography during Cochlear Implantation"

List of our responses to comments on an item-by-item basis

We sincerely thank the editor and the two reviewers for their valuable comments, which helped us to revise and improve the manuscript substantially. Our responses to the comments are given below.

Editorial comments

Please rephrase the Summary to clearly describe the protocol and its applications in complete sentences between 10-50 words: “The present protocol describes. …”. Here the word limit is exceeding.

We reduced the word limit to 40.

Please revise the text to avoid the use of any personal pronouns (e.g., "we", "you", "our" etc.).

We rephrased the manuscript. However, when our personal preference (and not an evidence-based method) was used, we sticked with “we”.

For in-text formatting, corresponding reference numbers should appear as numbered superscripts after the appropriate statement(s).

We changed the format.

Please ensure that the Introduction includes all of the following:

a) A clear statement of the overall goal of this method
b) The rationale behind the development and/or use of this technique
c) The advantages over alternative techniques with applicable references to previous studies
d) A description of the context of the technique in the wider body of literature
e) Information to help readers to determine whether the method is appropriate for their application.

We added the required information in the introduction.

JoVE cannot publish manuscripts containing commercial language. This includes trademark symbols (™), registered symbols (®), and company names before an instrument or reagent. Please remove all commercial language from your manuscript and use generic terms instead. All commercial products should be sufficiently referenced in the Table of Materials (including reagents, instruments, software, etc.). Please sort the Materials Table alphabetically by the name of the material.

We changed the manuscript accordingly.

Please adjust the numbering of the Protocol to follow the JoVE Instructions for Authors. For example, 1 should be followed by 1.1 and then 1.1.1 and 1.1.2 if necessary. Please refrain from using bullets or dashes.

We changed the manuscript accordingly.

The Protocol should contain only action items that direct the reader to do something. Please move the discussion about the protocol to the Discussion.

We changed the manuscript accordingly.

Please ensure that all text in the protocol section is written in the imperative tense as if telling someone how to do the technique (e.g., “Do this,” “Ensure that,” etc.). The actions should be described in the imperative tense in complete sentences wherever possible. Avoid usage of phrases such as “could be,” “should be,” and “would be” throughout the Protocol. Any text that cannot be written in the imperative tense may be added as a “Note.” However, notes should be concise and used sparingly.

We changed the manuscript accordingly.

Please note that your protocol will be used to generate the script for the video and must contain everything that you would like shown in the video. Please ensure you answer the “how” question, i.e., how is the step performed? Alternatively, add references to published material specifying how to perform the protocol action. There should be enough detail in each step to supplement the actions seen in the video so that viewers can easily replicate the protocol.

Please add more details to your protocol steps:

Step 1: Please include the patient inclusion/exclusion criteria.

We included point 1.1.2.

Line 149: Please mention how the anesthetization was carried out. Also, please mention how it is ensured.

Line 151: Please clarify how the dissection was carried out.

We added this information.

Line 155: Please provide additional details regarding how this step is done.

We added this information.

Line 160-172: Please subdivide this step into multiple discrete action steps clearly mentioning how each step is performed.

We subdivided the steps.

Please highlight up to 3 pages of the Protocol (including headings and spacing) that identifies the essential steps of the protocol for the video, i.e., the steps that should be visualized to tell the most cohesive story of the Protocol. Remember that non-highlighted Protocol steps will remain in the manuscript, and therefore will still be available to the reader. Please ensure that the highlighted steps form a cohesive narrative with a logical flow from one highlighted step to

the next. Please highlight complete sentences (not parts of sentences). Please ensure that the highlighted part of the step includes at least one action that is written in imperative tense.

We highlighted the sections accordingly.

Please modify the Result section to include all the observations and conclusions you can derive from the Figures. The Results section should focus on the effectiveness of your technique backed up with data.

We added a paragraph in the result section.

Please include a title and a description of each figure and/or table. All figures and/or tables showing data must include measurement definitions, scale bars, and error bars (if applicable). Please include all the Figure Legends together at the end of the Representative Results in the manuscript text. Each Figure Legend should include a title and a short description of the data presented in the Figure and relevant symbols. The Discussion of the Figures should be placed in the Representative Results. Details of the methodology should not be in the Figure Legends, but rather the Protocol.

We changed the legends accordingly.

As we are a methods journal, please revise the Discussion to explicitly cover the following in detail in 3-6 paragraphs with citations:
a) Critical steps within the protocol
b) Any modifications and troubleshooting of the technique
c) Any limitations of the technique
d) The significance with respect to existing methods
e) Any future applications of the techniques

We adjusted the discussion section.

Reviewer #1

Major concern:

Please describe what approaches the surgeon can take once a drop in response is seen. Also, please describe what is a significant drop in response.

We thank the reviewer for this important point. We added a paragraph (lines 308-314).

Minor concerns:

Line 84 - Stimulating at 1000 Hz complicates the picture as one would expect that the electrode will cross the tonotopic region of the cochlea for 1kHz during the insertion process. New systems now can stimulate at 2 frequencies (both AB and Cochlear).

That is correct. We added this information in lines 96-100.

Line 95 - Out of curiosity, how are you able to get methylprednisolone to patients 6 hrs prior to outpatient surgery?

Patients arrive at our hospital the evening before the procedure. Among other things, this has insurance-related reasons.

Line 204 - To make this protocol universally applicable, maybe conditioning of the electrode should be mentioned which is required for the Cochlear system.

We added the information in line 207-208.

Line 231 - What do you mean by 100 averages? I thought this was a continuous recording. Please clarify.

Thank you for your comment. In fact, we perform 100 epochs and form the average (mean) signal. “100 averages” was a spelling mistake. We changed this in line 262. However, by the time, continuous recordings are not possible with MED-EL implants (instead a step-by-step insertion is done, as described in lines 219-223). To measure 100 epochs and build the average signal, it takes about 30 seconds using a 9.6 ms measurement window.

Line 232 - Python is spelled incorrectly

We corrected accordingly.

Line 235 - Please describe SNR >1 or reference this. I have always seen a different description for significant signals.

Indeed, we use a different technique to calculate the SNR. As we work with raw data, we have all the single epochs available. When calculating the SNR, we work with the so-called +/- *averaging method*[1]. The +/- averaging method has the advantage that all consistent signal components can be eliminated and only the noise remains. We have determined the SNR value of 1 empirically. Hereby, an ECochG response is clearly detectable at an SNR level larger one. We added the method in line 266.

Line 271 - change to need "to" improve

We corrected the wording.

Reviewer #2

Major concerns:

In general, I feel like an overall introduction of ECochG is lacking. It would be helpful to explain in the beginning that ECochG signals are electrophysiological signals generated by the cochlea in response to sound (the sound part is completely missing from your introduction, hence the use of an acoustic stimulus may come as a surprise). Then explain that it consists of different components and introduce these. In the end, you show examples of cochlear microphonic signals but the reader may not know yet which information is represented in ECochG responses, so they do not know what cochlear microphonics are.

We thank the reviewer for this point and included the according information in lines 55-64.

Also, you are describing the measurement protocol for measuring ECochG using software from Med-EL. The procedure varies largely between manufacturers, e.g. you insert the implant in a step-wise manner while for other manufacturers, ECochG is measured continuously during insertion. The duration of the measurement and the flexibility of settings in the software also differs between manufacturers. I would explain the different procedures for measuring ECochG in your introduction, and then mention that your procedure describes ECochG measurements for recipients of Med-EL implants. Are you using a research version of the software or a clinical tool?

We have rewritten the manuscript (lines 78-83, lines 223-230) to include the information for the three common manufacturers (MED-EL, AB, Cochlear). Please also see our new table 1. For MED-EL, to record the data, we used Maestro 8.03 AS, which is a research software.

Line 58, 'Inner ear potentials (i.e. electrocochleography, ECochG) are increasingly measured during the implantation process (real-time measurements, rt) to monitor the inner ear function.' Comment: Later on (line 270), you state that we are only beginning to understand the actual implications of ECochG changes. I therefore think it is too strong to state here that ECochG is increasingly being used to monitor the inner ear function. Atraumatic implantation still mostly depends on the surgeon's judgement and ECochG is currently mostly measured for research purposes.

We rephrased the sentence in lines 55-59.

There are groups that show good results with using ECochG for providing surgical feedback. These could be cited here.

We included references in line 56. Please also consider the new paragraph lines 308-314.

Line 62, 'changes of the ECochG signal are correlated with the residual function of inner ear function'. Comment: To me it is not clear what you mean with this sentence. Intra-OP ECochG changes correlate to pre-operative residual hearing status?

We complemented the sentence, lines 66-67.

Line 64, 'In up to 20% of cases, no interpretable signal can be derived'. Comment: This percentage depends highly in your inclusion criteria for measuring ECochG. I would include a statement like 'despite residual hearing of at least …'. Also, please specify which patient-specific factors you are referring to.

In our experience, the threshold of residual hearing cannot alone explain the success rate of ECochG. Some patients with very good residual hearing have no or only weak signals whereas other patients, who are borderline candidates for ECochG, have strong signals with large amplitudes (also see our revised table 2). Patient-specific factors are mainly the presence or absence of functioning hair cells. We added information to the sentence in line 69-71.

Line 80, 'We perform rt-ECochG measurements in patients where hearing preservation is the goal.' Comment: I would be more specific about the patients in whom hearing preservation is the goal. What are your audiological criteria (e.g. PTA)?

Please consider paragraph 1.1.2.

Line 82, 'Usually, we stimulate with a 500Hz pure tone.'
What are your stimulation settings? How many repetitions, repetition rate, recording window, nr. of averages etc. Here it could be helpful to show which flexibilities your software has and which settings you choose.

Thank you for your questions. We added the configuration settings in lines 101-105.

Line 95-98
Comment: Is point 4 related to ECochG or part of standard clinical practice regardless of whether ECochG is performed? In the prior case, I would state the relevance for measuring ECochG.

It is relevant for both. For ECochG measurements, an unimpeded stimulus transmission is key. Please consider the new paragraph lines 247-260.

Line 106-107
Comment: How did you obtain or sterilize the sterile sound tube and foam eartip. From our experience, this is not trivial.

We sterilized the sound tube and eartip (Etymotic, USA) by gas plasma sterilization.

Line 113-115
Comment: This depends on the setup in the OR and the space requirements. Whether the measurement process can be monitored well also depends on e.g. the placement of screens, which differs between ORs.

This is only a recommendation. In our experience, the communication between engineer and surgeon is crucial. The setup in the OR can have an influence on this. For this reason, we consider the figure to be a helpful illustrative example.

Line 177-178
Comment: Can you explain the relevance when measuring ECochG? I can imagine the anesthesiologist is monitoring many parameters and I am wondering why the blood pressure should be assessed specifically.

To minimize bleeding, if possible, the systolic blood pressure should be below 100mg Hg. We added this information line 188-189.

Line 200
Comment: Which value should the impedance be below to be low enough?

Impedance values are manufacturer-specific. As a rough guide, the impedance should be below 10 kΩ. We added this to the manuscript in line 212-213.

Line 205-209
Comment: why is this step-wise insertion related to the type of implant? In case this is because of the measurement software, I would explain that here and write in your introduction that ECochG can be performed continuously during insertion or in a step-wise manner. Then I would include a rationale for both and include references for both protocols. As the surgeon has to hold the implant still for your protocol, could you mention the duration of one measurement?

Please consider the new subsections 5.5.1. and 5.5.2. We included the requested references. The duration of a step-wise measurement using a MED-EL implant is approximately 30 seconds for each step.

Line 225-236
Comment: I find the results section difficult to interpret in the overall context of your text. I have a few suggestions for improvement:
- 'for signal processing, we focused on cochlear microphonic signals'. Cochlear microphonic signals have not been introduced in your text so far. Maybe a short introduction of the different ECochG signal components in your introduction could help. I would also say you show an example of these signals and why you did so (because they show the best relation to post-OP hearing outcomes?), not that you focused on them for signal processing.

We have revised the introduction section (see comment above) as well as the results section. An example of our recordings is shown in figure 3. As outlined in the introduction, the cochlear microphonic signal is usually employed as it is the most robust signal with (usually) the largest amplitudes.

What is the reason you are post-processing your signals in Python? Bandpass filtering is normally done in the clinical software. Does the Med-EL software not have this option or did you decide to perform additional processing?

No, we obtain raw signals from the device and process the data later on.

You apply bandpass filtering, but you are not mentioning the cutoff frequencies.

Thank you for the question, we added the cut-off frequencies in lines 268-269 (100 Hz / 3 kHz).

Why are you using an SNR of one, do you have a reference of a rationale behind this? I think it is more common to use a higher SNR for considering a measurement as valid. Also, please explain how your SNR is calculated.

We use a different technique to calculate the SNR as we have access to the single epoch recordings. When calculating the SNR, we work with the so-called +/- averaging method[1]. The +/- averaging method has the advantage that all consistent signal components can be eliminated and only the noise remains. We have determined the SNR value of 1 empirically. In our experience, using this SNR, an ECochG response is (visually) clearly detectable.

To me it is not clear why you are using all these Python packages for signal processing, if you are only bandpass filtering your signal. Sklearn is a machine learning package and is not needed for this. Mentioning Python in your manuscript may confuse researchers from a more clinical background who could easily perform ECochG using standard settings, but are not familiar with the use of Python for post-processing. Since you are establishing a standard procedure, I would try to keep it simple. In case these Python scripts are provided together with the clinical software, please mention this.

Implementing the +/- averaging method[1] required us to use these Python packages. Numpy and Scipy are used only for bandpass filtering. Sklearn (sklearn.model_selection.train_test_split) is used only for randomly splitting the individual measurement signals into two groups. We then use these two groups to calculate the SNR. We repeat this process 1000 times and calculate the mean SNR. We repeat the SNR calculation 1000 times as there is a small variance in each SNR which is caused by the small number of epochs (100).

Line 242-244 (Figure 2)
Comment: This figure of the ear could be replaced by a figure in which the earfoam is inserted in the ear canal and the ear is folded forward. This would be more representative of the ECochG setup.

We changed figure 2 accordingly.

Line 246-250 (Figure 3)
Comment: I would replace this figure with some ECochG responses that you measured during insertion, instead of afterwards, as your protocol describes intra-OP monitoring. Then, I would also explain what can be seen in the figure. For example, why does the amplitude change? What should the surgeon do when this happens?

Figure 3a recordings were taken *during* the electrode insertion (at different insertion depths). In figure 3b, ECochG recordings were recorded *after* full insertion from electrode 1, 4, 7, and 10 (counted from the most apical electrode). This study was purely observational. At this stage, we do not give a recommendation what to if a drop occurs. Drops of the ECochG signal may have different causes (e.g. traumatic event during the insertion, passing the 500 Hz region within the cochlea, interaction of two hair cell generators). Please also consider our new section lines 309-115.

Are you sure that the figure shows the cochlear microphonic signal and not just the condensation or rarefaction response? At least in earlier versions of the Med-EL software, cochlear microphonics could not be visualized directly.

Yes, you are right; the standard software only allows the selection of condensation or rarefaction. However, we developed a custom software, which enables to record with alternating stimulation.

Line 248-249, 'Please note that the numbering of electrodes for figure a & b starts at opposite ends.' Comment: Do you mean that for Figure A the apical electrode is EL 1 while for Figure B the basal electrode is EL 1? This does not seem very logical to me.

As outlined above figure 3a shows the insertion depth; figure 3b, displays the electrode position, counted from the most apical one (as suggested by the manufacturer). We added lines 288-290 for better explanation.

Line 252
Comment: Please explain this table. It cannot be interpreted without context. How should we look at the change in PTA with respect to the ECochG amplitude change? Are your post-operative measurements really post-operative or after insertion but in the OR? What should we learn from the SNR - is there much noise in the OR, is it related to the signal amplitude? Cochlear access (RW or cochleostomy) is unrelated to ECochG.

We thank the reviewer for this point and have revised the table.
The new table 2 shows the maximum SNR reached during the electrode insertion and where this maximum was reached. Further, we added the SNR at the peak electrode after full insertion. It should now be clear i) where the maximum amplitude was reached, and ii) if there was a drop of this amplitude when the electrode was fully inserted. This change of the SNR can now be compared to the change of the PTA. Furthermore, as outlined above, it becomes evident, that the measured SNR cannot be correlated to the pre-operative PTA (“the better the acoustic hearing before surgery, the higher the SNR of the ECochG recording”). We mentioned the type of surgical access as this is an important information in regards to hearing preservation. It has been shown that hearing preservation is much more likely in patients with round window access[2].

Minor concerns:

Minor Concerns:
Line 87
Comment: between 80 and 85 dB HL?

We included this information.

References

1. Drongelen, W. van. Chapter 4 - Signal Averaging. in *Signal Processing for Neuroscientists (Second Edition)* (ed. Drongelen, W. van) 59–80 (Academic Press, 2018). doi:10.1016/B978-0-12-810482-8.00004-7.
2. Causon, A., Verschuur, C. & Newman, T. A. A Retrospective Analysis of the Contribution of Reported Factors in Cochlear Implantation on Hearing Preservation Outcomes. *Otol Neurotol* **36**, 1137–1145 (2015).

INSELSPITAL
University Hospital Bern
Department of Ear, Nose and Throat Diseases, Head and Neck Surgery
Prof. Dr. med
Marco Domenico Caversaccio, M.D.
Chairman and Director

PD Dr Lukas Anschuetz
Guest Editor
Journal of Visualized Experiments (JOVE)

Bern, September 28, 2021

Dear Dr Anschuetz

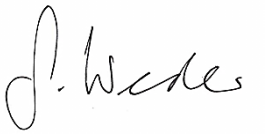
We would like to re-submit our revised manuscript titled "Performing Real-time Electrocochleography during Cochlear Implantation" for consideration as full article/ video in *Journal of Visualized Experiments (JOVE).* We sincerely thank the editor and the two reviewers for their valuable comments, which helped us to improve the manuscript substantially.

We have rewritten our manuscript how ECochG measurements can be performed with all three manufacturers (MED-EL, AB, Cochlear), respectively. We have attached a new Table 1 for this purpose. Furthermore, we have revised our Table 2 according to the comments of the two reviewers.

The present manuscript is not currently under consideration for publication by any other journal nor has it been previously published in whole or in part elsewhere. We attest to the fact that all authors listed on the title page have read the manuscript, attest to the validity and legitimacy of the data and its interpretation, and agree to its submission to *JOVE.*

Please address your correspondence to PD Dr Stefan Weder, Department of Otorhinolaryngology, Head and Neck Surgery, Inselspital, Bern University Hospital, Freiburgstrasse 18, CH-3010 Bern. E-Mail: stefan.weder@insel.ch.

Sincerely yours,



PD Dr Stefan Weder, MD