Hearing preservation in cochlear implantation surgery (February 2025)

PROTOCOL TITLE Hearing preservation in cochlear implantation surgery

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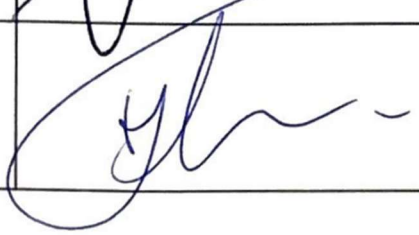
Principal Investigator: ***Dr. Thomeer, otologist UMC Utrecht***		**17-02-2025**

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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

ABR	**ABR form, General Assessment and Registration form, is the application form that is required for submission to the accredited Ethics Committee (In Dutch, ABR = Algemene Beoordeling en Registratie**
AE	**Adverse Event**
CB-CT	**Cone beam computed tomography**
CCMO	**Central Committee on Research Involving Human Subjects; in Dutch: Centrale Commissie Mensgebonden Onderzoek**
CI	**Cochlear implant**
CO	**Cochleostomy approach**
CV	**Curriculum Vitae**
CVC	**Consonant-Vowel-Consonant, dutch speech perception test**
eCAP	**Evoked compound action potential**
ECochG	**Intracochlear electrocochleography**
EU	**European Union**
GCP	**Good Clinical Practice**
IC	**Informed Consent**
LW	**Lateral wall electrode array**
METC	**Medical research ethics committee (MREC); in Dutch: medisch ethische toetsing commissie (METC)**
MPT	**Mastoidectomy-posterior tympanotomy**
PTA	**Pure tone audiometry**
PM	**Perimodiolar electrode array**
RW	**Round window approach**
(S)AE	**(Serious) Adverse Event**
Sponsor	**The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party.**
SRT	**Speech Reception Threshold**
SNHL	**Sensorineural hearing loss**
Wbp	**Personal Data Protection Act (in Dutch: Wet Bescherming Persoonsgevens)**
WMO	**Medical Research Involving Human Subjects Act (in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen**

SUMMARY

Rationale: In order to preserve the residual hearing in patients with sensorineural hearing loss (SNHL) receiving a cochlear implant (CI), the insertion trauma to the delicate and microscopic structures of the cochlea needs to be minimized. The surgical procedure starts with the conventional mastoidectomy-posterior tympanotomy (MPT) approach to the middle ear, and is followed by accessing the cochlea, with either a cochleostomy (CO) or via the round window (RW). Both techniques have their benefits and disadvantages. Another aspect is the design of the electrode array. There are fundamentally two different designs: a 'straight' lateral wall lying electrode array (LW), or a 'pre-curved' perimodiolar cochlear lying electrode array (PM). Interestingly, until now, the best surgical approach and type of implant is unknown. Our hypothesis is that the combination of a RW approach and a LW lying electrode array minimizes insertion trauma, leading to better hearing outcome for SNHL patients.

Objective: Comparison of hearing preservation and outcome of two fundamentally different cochlear implants designs (LW or PM) and the two most used surgical approaches (RW or CO). Secondly, asses the structure preservation (i.e., scalar position) of each combination of electrode design/surgical approach. Thirdly, find objective electrophysiological measures for insertion trauma.

Study population: A total of 48 patients with severe SNHL, age ≥ 18 years, who meet the in/exclusion criteria used for cochlear implantation.

Study design: Randomized controlled single-blind trial consisting of four groups: 1: RW and LW, 2: CO and LW, 3: RW and PM and 4: CO and PM.

Intervention: Randomization to one of the four groups.

Main study parameters/endpoints: Primary outcome: Pre- and postoperative hearing thresholds of (low frequency) pure tone audiometry (LF-PTA), secondary outcomes: scalar position of the electrode array, ECochG measures and speech perception score.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Cochlear implantation by way of a cochleostomy or round window approach, using different electrode array types, is the standard medical care for patients with severe bilateral hearing loss, as it is a relative simple and low-risk procedure that greatly benefits the patients. Cone-beam CT (CB-CT) imaging postoperatively leads to exposure of low-dose radiation (effective dose: 0.18 mSv), and is therefore considered to be of low-risk.

1. INTRODUCTION AND RATIONALE

In people with severe hearing loss or deafness, hearing can be (partially) restored with a cochlear implant (CI). A cochlear implant bypasses the hair cells and directly stimulates via electrical impulses the auditory nerve, allowing patients with non-functioning hair cells to hear again. Cochlear implantation for severely hearing impaired patients has become a standard and accepted treatment throughout the years in high income countries. A tremendous development in auditory perception with a CI has been achieved since first implantations in the 1980s, from only sound detection to speech understanding (Eshraghi et al., 2012). However, speech understanding is not yet optimal, especially in difficult situations where background noise is present. Several studies have shown that preserving residual hearing can lead to better hearing outcomes, especially in noisy environments (Skarzynski et al., 2014; Gifford et al., 2013; Buechner et al., 2008; Gfeller et al., 2006). In order to preserve residual hearing, insertion trauma to the delicate structures of the cochlea needs to be minimized, by making the surgical implantation procedure as minimally invasive as possible. Therefore, we consider the various possible surgical approaches. The surgical procedure commonly starts with the conventional mastoidectomy-posterior tympanotomy (MPT) approach to the middle ear, and is followed by accessing the cochlea, with either a cochleostomy (CO) or via the round window (RW). Several papers including systematic reviews comparing CO and RW approaches in literature, concluded that evidence lacks to show preference for one or the other approach with respect to hearing preservation (Havenith et al., 2013, Wanna et al., 2014, Wanna et al., 2015, Fan et al., 2018, Snels et al., 2019). Both techniques of accessing the cochlea have their pros and cons (e.g. cochleostomy leads to better angle of insertion, while RW approach ensures correct localization of the implant and leaving the integrity of the anatomical structures intact). One may also argue a preference for a certain approach based on individual cochlear structures. Several studies have clearly shown that each human cochlea has a different micro-anatomy in parallel with one's unique fingerprint (Avci et al., 2017, Escude et al., 2006, Rask-Andersen et al., 2011).

Another aspect relevant for minimizing insertion trauma, is the design of the electrode array. There are two fundamentally different designs: a 'straight' lateral wall lying electrode array (LW), or a 'pre-curved' perimodiolar lying electrode array (PM). No evidence has been provided that one design outperforms the other in terms of hearing outcome and structure preservation (Wanna et al., 2014, Snels et al., 2019, Holden et al., 2013). On the one hand, lateral wall positioning might be the best way to preserve the microscopical structures (spiral/osseous ligament, basilar membrane, lateral wall, see **fig. 1**); on the other hand, perimodiolar positioning might provide better hearing outcome (which is the ultimate objective for deaf

patients with a CI), as the electrodes are situated close to the spiral ganglion cells to be stimulated. Also, the perimodiolar electrode might not touch the lateral wall if inserted correctly, leading to preservation of the microanatomy of the intracochlear structures. Speech performances scores were better for the LW group, also if the scalar translocations were accounted for in the PM group (O'Connell 2016). While other studies report better outcomes for speech performance for the PM group (Holden et al., 2013, Wanna et al., 2014). The majority of the studies, however, show no difference between both groups (van der Jagt et al., 2016, van der Marel et al., 2015, Fabie et al., 2018, Moran et al., 2019, Doshi et al., 2015). However, all these studies had a high risk of bias. In addition, they did not differentiate between the surgical approaches, which induces a major confounding factor.

It is unclear which surgical approach and electrode design is most suited to achieve minimal insertion trauma, and thereby preserving the residual hearing in cochlear implantation surgery. Therefore, it is not surprising that worldwide both type of approaches and electrode designs are used.

Considering the surgical approach and electrode array design, it is important to note that during insertion no reliable feedback is provided, regarding the array tip position in relation to the intracochlear structures. After inserting the tip of the electrode array in the round window perforation or cochleostomy, only tactile feedback is available, which might not be sufficient to know whether the implant is correctly inserted. Correct insertion, for both cochleostomy and round window approach, ensures that the implant is in the scala tympani of the cochlea. If during insertion, the CI translocates to the scala vestibuli or scala media, the basilar membrane with the organ of Corti (the actual hearing receptor organ) is damaged (see **fig. 1**). Scalar translocation negatively influences the final hearing outcome and hearing preservation for CI patients (Holden et al., 2013, Shaul et al., 2018).

One of the possibilities to view the intracochlear structures and thereby asses the scalar location of the CI (thus providing postoperative feedback), is by applying imaging techniques after surgery such as cone beam computed tomography (CB-CT) (see **fig. 2**), which has been proven to be suitable in detecting the scalar position of the electrode array (Zou et al., 2015, Saeed et al., 2014, Mosnier et al., 2017). Another possibility to detect insertion trauma is the intraoperative, intracochlear electrocochleography (ECochG) which measures responses of residual functioning hair cells to acoustic tone stimuli. During insertion, ECochG measures can be used to assess insertion trauma, providing feedback of the insertion (Choudhury et al., 2012, Dalbert et al., 2015b, Giardina et al., 2019, Fontenot et al., 2019).

Our first aim is to compare the hearing preservation in CI recipients with different combinations of surgical approach (CO and RW) and type of cochlear implant (LW and PM). Secondly, we want to investigate these treatment options by assessing the cone beam CT images postoperatively. Thirdly, we want to find ECochG outcome measures that reflect best the extent of insertion trauma by comparing these measures to the CT images and hearing test scores.

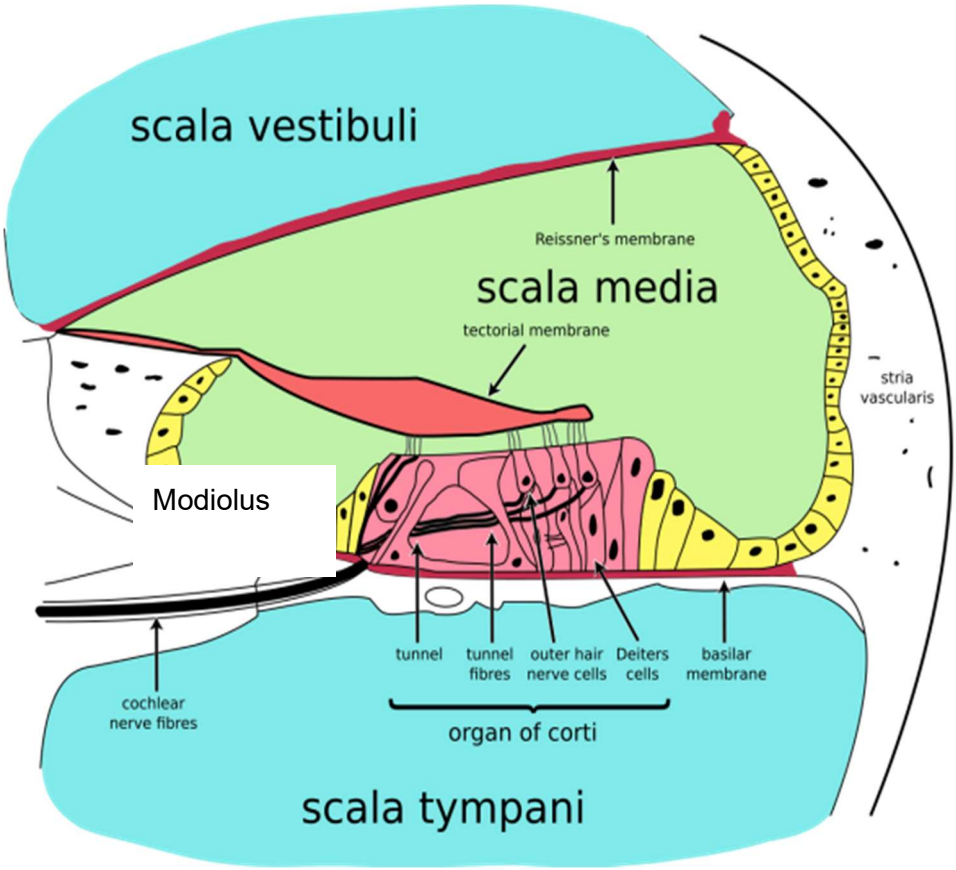


Figure 1: This is a schematic coronal plane of a cochlear duct. The cochlea consist of several compartments: scala vestibuli, scala media and scala tympani. The CI should reside in the scala tympani, herein laterally and medially for the LW and PM electrode array respectively. Translocation of the CI from scala tympani to the scala media or scala vestibuli (from downward to upward) damages vital structures like the basilar membrane with the organ of Corti or stria vascularis.

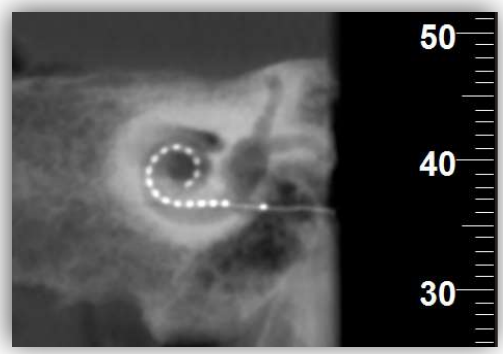


Figure 2: Cone beam CT scan. 'Cochlear view': position of the CI (the white dotted radiopaque curled line) can be easily assessed. The 16 electrodes of the CI are reflected by the white dots.

2. OBJECTIVES

Primary Objective:

To compare hearing preservation percentage after cochlear implantation between two surgical approaches (CO, RW) and two electrode array designs (LW, PM).

Secondary Objective(s):

- To determine the relationship of scalar position of the electrode array and hearing preservation (i.e. residual acoustic hearing).
- To determine the relationship of scalar position of the electrode array and hearing performance after one year with CI.
- To assess residual hearing over time after implantation.
- To find which ECochG measures can be used best for assessment of insertion trauma.
- To determine the relationship between ECochG measures and residual hearing and speech perception postoperatively.
- To determine the relationship between ECochG measures and scalar position of the electrode array.

3. STUDY DESIGN

The study design is illustrated in **figure 3:**

This study concerns a single-blind mono-center randomized controlled, with 18 year and older severely or profoundly hearing-impaired patients who are eligible for a cochlear implant. Every candidate for cochlear implantation needs to have severe hearing loss bilaterally, should not have contraindications for surgery and should be able to follow an intensive medical rehabilitation program. The study will be performed at the department of Otorhinolaryngology in the University Medical Center Utrecht, and will run till 01-01-2027.

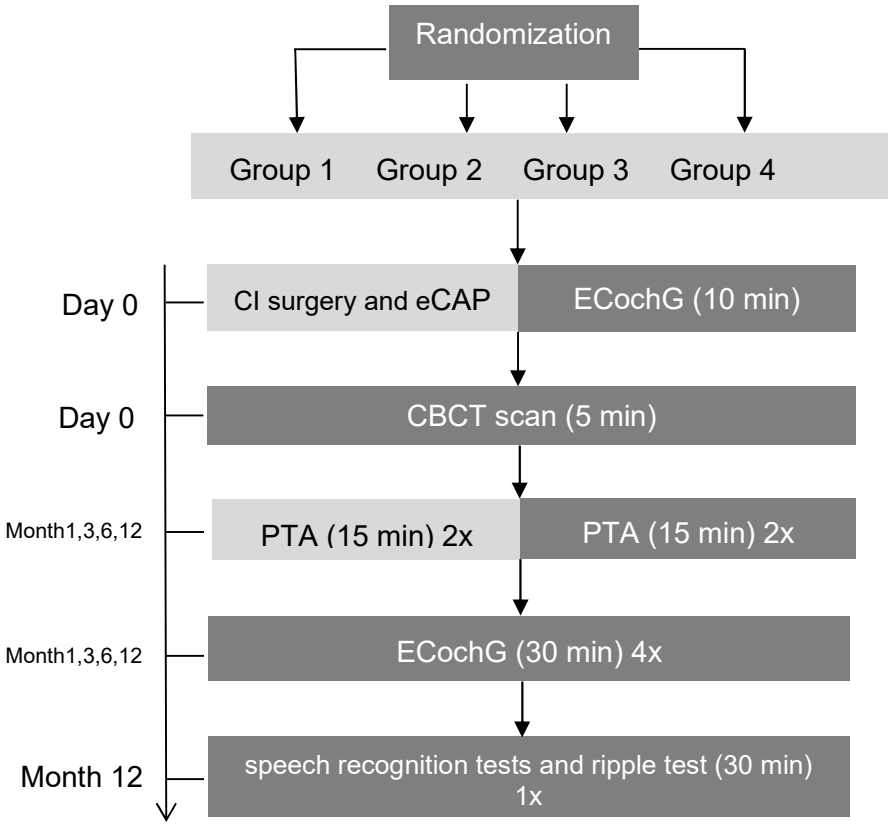
All participants will undergo the usual standard medical care of work-up before cochlear implantation. The work-up includes a pure tone audiogram (PTA), a speech audiogram, a preoperative CT, and interviews with speech therapist, audiologist, ENT surgeon and social worker. In a multidisciplinary meeting, the Cochlear implantation team of the UMC Utrecht will assess all results and decides whether a patient is suited for a cochlear implant.

Eligible cochlear implant candidates will then for this study be randomized to group 1 (RW + LW), 2 (CO + LW), 3 (RW + PM) or group 4 (CO + PM).

Study procedures:

For all patients, during implantation, the standard measurements for eCAP and electrode impedances and the experimental measurements of ECochG will be performed,. Postoperatively, a cone beam CT scan will be made to assess the scalar position of the CI. After activation of the CI, which is usually around three to four weeks postoperatively, the ECochG measurements will be repeated. For this study, we add two extra pure tone audiograms at 6 /12 months, resulting in a total of 4 audiograms (at one three, six and 12 months). Pure tone audiometry is without CI, which will allow us to determine the residual acoustic hearing capability of the patients. At 12 months, a conventional speech perception test with consonant-vowel-consonant (CVC) word score with/without noise will be performed. The speech perception test is with CI and determines the maximal electrical hearing capability of the patients. Finally, at 12 months, we will add a spectral ripple test, allowing us to measure hearing performance independent of cognitive and linguistic skills (Drennan et al., 2014).

Study Design



Light grey: Standard medical care
Dark grey: Extra for study

Figure 3. Flow chart study procedures. PTA: pure tone audiometry, CB-CT: conebeam CT, ECochG: Intracochlear electrocochleography, eCAP: Evoked compound action potential, CI: cochlear implant.

4. STUDY POPULATION

4.1 Population (base)

Subjects eligible for participation in the study are:
Patients with severe to profound bilateral hearing loss (thresholds >70 dB HL for 2-8 kHz) who were diagnosed and counselled by the Cochlear Implantation team of the UMC Utrecht, and willing to participate in this study.

4.2 Inclusion criteria

- 18 years of age or older
- normal function of middle ear (i.e. no acute middle ear infections)
- dutch language proficiency
- choice for Advanced Bionics implant

4.3 Exclusion criteria

- prior otologic surgery in the implanted ear (excluding tympanostomy tube placement)
- inner ear malformation present in the ear to be implanted (i.e. ossification, Mondini malformation)
- retrocochlear pathology present in the auditory system to be implanted
- neurocognitive disorders
- sudden deafness

4.4 Sample size calculation

Hearing preservation is the main outcome variable (see further 5.1). Based on literature (Manjaly et al., 2018; Rader et al., 2018; Sierra et al., 2019) we expect a large range of hearing preservation for each group, from 0 (no preservation, i.e., loss of all hearing) to 100 (full preservation, hearing stable), and occasionally above (improved hearing). The three studies showed means of 56, 74, and 53, respectively and witin-group standard deviations, $\sigma_{W,}$ of 37, 19 and 37. Weighing the larger studies more (Manjaly, Sierra) we estimate σ_W = 35group means of 50 with clinically interesting differences of 40 between best and worst group means. This yields a variance between groups of 400, i.e., $\sigma_B = \sqrt{400} = 20$ (σ_B: standard deviation between groups). Thus, effect size $\sigma_B / \sigma_W = 0.57$. Using a group size of 12 yields a robust power of 0.9. We used G*power (version 3.1.9) to calculate the power based on effect size and sample size with a one-way ANOVA test, with fixed effects.

5. METHODS

5.1 Study parameters/endpoints

5.1.1 Main study parameter/endpoint

Hearing preservation is the main outcome, which will be expressed in percentage. Hearing preservation is calculated by the following formula: HP= 1 - (PTA post – PTA pre) / (PTA max – PTA pre). See section 5.3.

5.1.2 Secondary study parameters/endpoints

Scalar position of the electrode array (scala tympani or scala vestibuli assessed by CB-CT), ECochG (among others amplitude in µV), and speech perception test with/without noise in CVC words correct score (in percentage).

5.2 Randomisation, blinding and treatment allocation

Patients will be randomly allocated to one of four groups. Block randomization will take place electronically by the study management system researchtool. The Julius Center will handle this randomization procedure. All groups carry the same equal weight. They will stratify the groups for age, with two subgroups, 18-50 years and > 50 years. This study is single-blind, meaning that only participants are blinded for the treatment allocation. However, research assistants will be blinded for the treatment.

5.3 Study procedures

For this study there are procedures before, during or after the cochlear implantation surgery, or pre, intra and post-operatively respectively.

Preoperatively (standard medical care): Before randomization, each participant will undertake the normal standard preoperative work-up: a CT scan, a pure tone audiogram/speech test and interviews with ENT specialist and audiologist.

Intraoperatively: all participants will undergo, according to the group they are allocated to, either a CO or RW insertion approach and receive either the PM or the LW electrode array. During and right after cochlear insertion, ECochG potentials will be recorded to study possible insertion trauma. The surgical procedures are standard medical care.

Postoperatively: all patients will receive a cone beam CT scan, to assess the scalar localization of the electrode. Upon activation of the CI, around 3-4 weeks after surgery, the first postoperative PTA/ECochG will be measured. In the following months, the PTA/ECochG is

repeated at 3, 6 and 12 months after surgery. At one year after surgery, the clinical ripple test and the standard CVC word tests with and without noise will be performed to study the eventual hearing outcome for each group. See **study design diagram** for an overview.

1. Hearing preservation

Preoperative pure tone audiometry is already a standard test to assess the eligibility for a cochlear implant for severe hearing impaired patients. With postoperative pure tone audiometry (without CI) we can calculate the hearing preservation by the following equation:

HP= 1 - (PTA post – PTA pre) / (PTA max – PTA pre)

In this equation, HP is Hearing preservation, PTApre is the average pure-tone (unaided) hearing threshold of 125, 250 and 500 Hz measured preoperatively, PTApost is the same average pure-tone hearing threshold measured postoperatively, and PTA max is the maximum sound intensity generated by a standard audiometer (usually between 90-120 dB HL) (Skarzynska et al., 2018).

2. Scalar positioning of the electrode array

We will use the cone beam CT scanner to postoperatively assess the scalar location of the electrode array for all four groups. The CB-CT has been proven to be the best imaging modality for assessing the scalar location postoperatively, as it has low radiation artefacts (caused by the metal parts of the cochlear implant) and high spatial resolution needed to image the cochlea and its internal parts. In addition, it has relatively low radiation exposure, is less likely to trigger claustrophobic reactions and requires shorter scanning durations compared to traditional CT scanners (Li, 2013, Nardi et al., 2018, Casselman et al., 2013).

We will assess CI translocation by making multiplanar midmodiolar reconstructions of the cone beam CT images, which is validated by numerous papers (Mosnier et al., 2017, Zou et al., 2015, Saeed et al., 2014). These multiplanar reconstructions will allow us to systematically indicate for every stimulation point of the cochlear implant the exact scalar position (i.e. scala tympani or scala vestibuli). The main researcher and an experienced otologist will analyse the CT scans blindly for each patient.

3. ECochG

'Electrocochleography' (ECochG) is a method for recording the electrical potentials of the cochlea. The ECochG is composed of several components: the compound action potential (CAP), cochlear microphonics (CM) and the summating potential (SP). In essence, the CAP is generated by the auditory nerve activity, the CM and SP are generated by the hair cells of the

organ of Corti. The CM is an AC response following the tone, and the SP is a DC response. Outcome measures include the CM amplitude and the total ECochG amplitude. Potentially, the difference in the amplitude of the total ECochG response after and before insertion might contain information about insertion trauma, i.e. damage to the basilar membrane, stria vascularis or other structures.
We will use the most apical contact point of the electrode array to measure these outcomes. The acoustic pure tones and click stimuli will be delivered via the insert earphone. This will be coupled to the measurement equipment that is provided with the CI by the manufacturer. The amplifier in the implant will be used for amplification of the response.

4. *Speech perception scores*

One year after cochlear implantation, a conventional speech perception test with/without noise test will be performed with CVC words from the 'Nederlandse Vereniging voor Audiologie' (NVA) word-list. The speech tests can be quantified with a simple correct percentage score. Also, the clinical ripple test, which uses tones instead of words, can be used to complement speech perception scores (Drennan et al., 2014).

5.4 Withdrawal of individual subjects

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The investigator can decide to withdraw a subject from the study for urgent medical reasons.

5.5 Replacement of individual subjects after withdrawal

Subjects who withdraw from the study or who terminate the recording session prematurely will be considered as lost and will be replaced. Reasons for withdrawal or premature termination will be documented. We expect a withdrawal rate of subjects of no more than 10% (since N=48, this is 5). The number of replacements will be limited to two persons per subgroup.

5.6 Follow-up of subjects withdrawn from treatment

Subjects who withdraw from the study or who terminate the recording session prematurely, in the absence of any adverse event, will not be followed.

5.7 Premature termination of the study

Serious adverse events are not expected, but in case they do occur, the research group can decide to premature terminate the study.

6. SAFETY REPORTING

6.1 Section 10 WMO event

In accordance to section 10, subsection 4, of the WMO, the sponsor will suspend the study if there is sufficient ground that continuation of the study will jeopardize subject health or safety. The sponsor will notify the accredited METC without undue delay of a temporary halt including the reason for such an action. The study will be suspended pending a further positive decision by the accredited METC. The investigator will take care that all subjects are kept informed.

6.2 Adverse and serious adverse events

Adverse events are defined as any undesirable experience occurring to a subject during the study, whether or not considered related to the surgery or audiological follow-up. Up to three days after the last test, all adverse events reported spontaneously by the subject or observed by the investigator or his staff will be recorded.

A serious adverse event is any untoward medical occurrence or effect that at any dose:

- results in death;
- is life threatening (at the time of the event);
- requires hospitalisation or prolongation of existing patients' hospitalisation;
- results in persistent or significant disability or incapacity;
    - is a congenital anomaly or birth defect; or
    - any other important medical event that did not result in any of the outcomes listed above due to medical or surgical intervention but could have been based upon appropriate judgement by the investigator.

An elective hospital admission will not be considered as a serious adverse event

All SAEs will be reported through the web portal *ToetsingOnline* to the accredited METC that approved the protocol, within 15 days after the sponsor has first knowledge of the serious adverse reactions.

SAEs that result in death or are life threatening should be reported expedited. The expedited reporting will occur not later than 7 days after the responsible investigator has first knowledge of the adverse reaction. This is for a preliminary report with another 8 days for completion of the report.

6.3 Follow-up of adverse events

All adverse events will be followed until they have abated, or until a stable situation has been reached. Depending on the event, follow up may require additional tests or medical procedures as indicated, and/or referral to the general physician or a medical specialist.

7. STATISTICAL ANALYSIS

7.1 Descriptive statistics

We will use an ANOVA test to compare the primary outcome measure hearing preservation (see 5.3) between the four groups. We will do the same for the CVC word score tests (with and without noise) between the groups.

Fisher's exact test of independence will be used to compare the electrode location within the scala tympani (correct location after insertion) between CO or RW approach, and between PM or LW electrode insertion.

We will also use multiple regression analysis to identify independent predictors of hearing preservation. Among the factors to examine are insertion depth and cochlear volume.

We will use a Pearson correlation test to examine the correlations between the ECochG responses and hearing preservation at the various time points (during and after cochlear implantation)..

8. ETHICAL CONSIDERATIONS

8.1 Regulation statement

The study will be conducted according to the principles of the 64th WMA General Assembly in Fortaleza (Brazil, October 2013), and in accordance with the Medical Research Involving Human Subjects Act (WMO).

8.2 Recruitment and consent

Subjects will be recruited by their ENT-physician or audiologist during visits to the outpatient clinic. Additional verbal and written information about the study will be provided to all subjects by an investigator. An investigator will also give the informed consent form. There will be ample opportunity (at least 1 week) for the subjects to consider participation and discuss their questions with one of the investigators before the subjects may decide to sign the informed consent form in order to participate. Participation in the study is entirely voluntary. If a subject wants to participate, two extra appointments will be added to the standard visitation scheme.

If a patient does not want to participate, contact with the investigator will be terminated.

8.3 Benefits and risks assessment, group relatedness

Cochlear implantation is widely used in the Netherlands and worldwide, as it is a relative simple and low-risk procedure that greatly benefits severe hearing impaired patients.

There is extra radiation exposure as the subjects will undergo postoperatively a cone beam CT scan. The total equivalent dose in microsievert is around 0.18 mSv for our protocol, as calculated by the department of radiation in our Hospital. (Casselman et al., 2013, Li, 2013, Nardi et al., 2018), which is a fraction of a conventional multi-slice CT (which is standard medical care for the pre-operative work-up). To compare the cone beam CT equivalent dose to another example: normal atmospheric radiation is around 2.5 mSv /year.

The extra ECochG measurements and tone/speech tests are not considered to be of any risk for the participants.

8.4 Compensation for injury

The sponsor/investigator has a liability insurance which is in accordance with article 7 of the WMO.

The sponsor (also) has an insurance which is in accordance with the legal requirements in the Netherlands (Article 7 WMO). This insurance provides cover for damage to research subjects through injury or death caused by the study.
The insurance applies to the damage that becomes apparent during the study or within 4 years after the end of the study.

8.5 Incentives (if applicable)

All participants will receive compensation for travel expenses made: €0.19 per kilometer travelling distance for study related visits to the outpatient clinic for the 6 and 12 months session after CI surgery. The subjects will be compensated for travel expenses made, irrespective of whether the test sessions are planned on the same day as routine follow-up visits or if participation is prematurely stopped.

9. ADMINISTRATIVE ASPECTS AND PUBLICATION

9.1 Handling and storage of data and documents

For this prospective study, only eligible patients according to upper mentioned criteria (see paragraph 4.3 and 4.4) will be asked by their treating physician to participate during their pre-operative consultation. Direct identifiable—personal data from these patients will be recorded in an Excel file and stored in a designated secure research folder on the UMC Utrecht network drive. This is for an overview of which patients are asked to participate. The original signed informed consent forms will be kept in a binder in a locked closet in a locked room at the ENT department of the division Surgical Specialties.

Members of the research team will extract all necessary clinical parameters, such as results of the audiograms, from the electronic health records (EHRs, HiX) into an electronic Case Report Form (eCRF) the UMCU endorsed system Castor EDC. Castor EDC is a browser-based, metadata-driven EDC software solution and workflow methodology for building and managing online databases. The eCRF contains data items as specified in this research protocol. Modification of the eCRF will be made only if deemed necessary and in accordance with an amendment to the research protocol. Access to the eCRF is password protected and specific roles are assigned (e.g. study coordinator, investigator, monitor, etc.). Radiographic preoperative CT scans from PACS are made available for research via our Research Imaging Architecture (RIA). Postoperative CBCT scans will be stored anonymously in the designated secure research folder on the UMC Utrecht network drive. Source data of the electrophysiological measurements will be stored in a computer database SPSS file with the patient's study number as key to all records.

All data will be handled confidentially and research data will be coded by using a unique patient identification number. The key to the code will be safeguarded by the investigators. All data will be stored on the research network disc of my division in a secured research folder structure. Only the team of investigators will have access to the database files. To be able to reproduce the study finding and to help future users to understand and reuse the data all changes made to the raw data and all steps taken in the analysis will be documented in text document. The database files will be kept for 15 years after the study has ended. More details can be found in the Data Management Plan (https://dmponline.dcc.ac.uk/plans/168138).

9.2 Monitoring

The monitoring will be minimal since the risks are qualified as negligible, and the monitoring will be executed by Julius Clinical. The procedure for monitoring is described in a monitoring plan (file K6).

9.3 Amendments

Amendments are changes made to the research after a favourable opinion by the accredited METC has been given. All amendments will be notified to the METC that gave a favourable opinion.

9.4 Annual progress report

The sponsor/investigator will submit a summary of the progress of the trial to the accredited METC once a year. Information will be provided on the date of inclusion of the first subject, numbers of subjects included and numbers of subjects that have completed the trial, serious adverse events/ serious adverse reactions, other problems, and amendments.

9.5 End of study report

The investigator will notify the accredited METC of the end of the study within a period of 8 weeks. The end of the study is defined as the last patient's final visit.
In case the study is ended prematurely, the investigator will notify the accredited METC, including the reasons for the premature termination.
Within one year after the end of the study, the investigator/sponsor will submit a final study report with the results of the study, including any publications/abstracts of the study, to the accredited METC.

9.6 Public disclosure and publication policy

The data from this study will be used for publication in peer-reviewed international journals. It will be part of a thesis on minimal invasive cochlear implantation surgery.

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