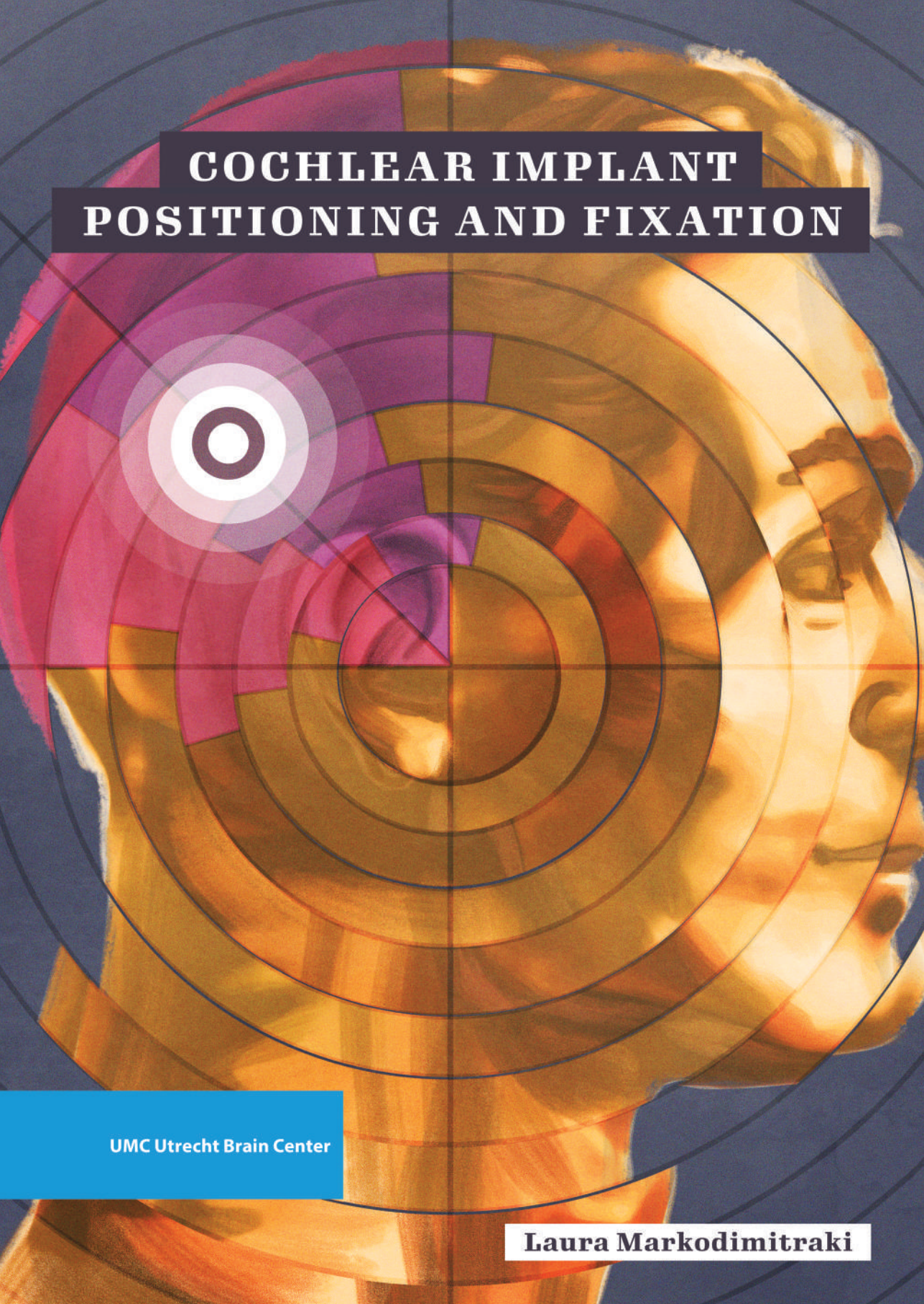
COCHLEAR IMPLANT
POSITIONING AND FIXATION
UMC Utrecht Brain Center
Laura Markodimitraki

Cochlear implant positioning and fixation

Laura Markodimitraki

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Cochlear implant positioning and fixation

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(met een samenvatting in het Nederlands)

Proefschrift

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geboren op 15 mei 1992
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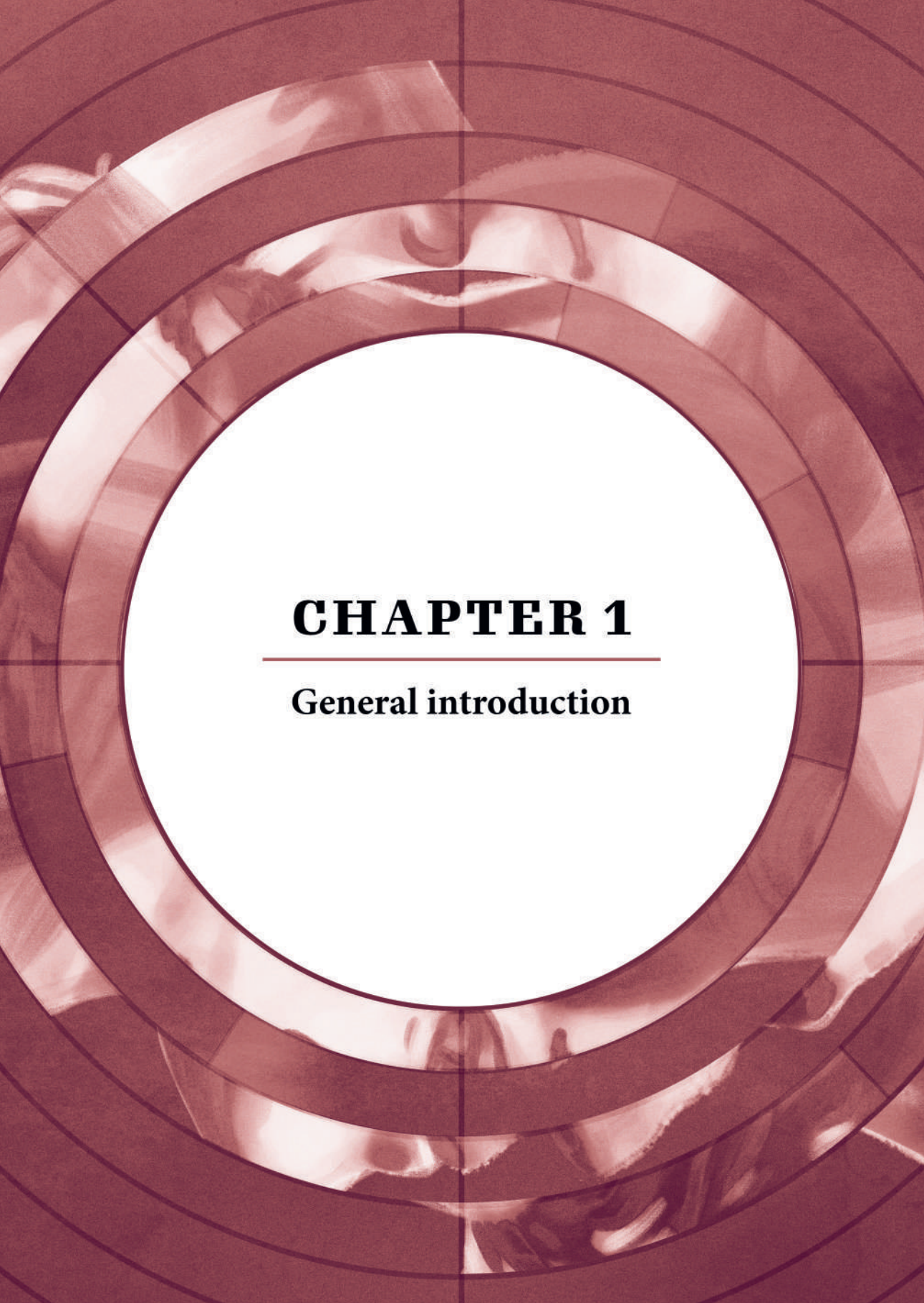

CHAPTER 1

General introduction

Preface

Cochlear implants (CI's) are currently the only effective treatment for auditory rehabilitation for patients with severe to profound sensorineural hearing loss (SNHL) with poor speech perception. Surgical intervention is necessary to implant this medical device, and the techniques used by CI surgeons have undergone modifications over the years, without hard evidence to support one technique over the other. This thesis aims to improve cochlear implant surgery by providing high level evidence for the positioning and fixation of the cochlear implant. To understand the relevance of the research questions answered in this thesis, the first chapter gives an overview of normal anatomy and hearing, followed by a description of the surgical procedure of cochlear implantation. Subsequently, complications of cochlear implant fixation and migration are introduced, and finally methods of assessing migration and impact of wearing a CI are presented.

Anatomy of the ear, normal hearing and hearing loss

The human ear is comprised of the outer, middle and inner part. The outer part consists of the auricle and the external auditory canal, the middle ear including the tympanic membrane and the bony ossicles (malleus, incus, stapes) and the inner ear that consists of the cochlea and the vestibular organ. Sound travels through pressure waves via the external auditory canal to the tympanic membrane. The membrane vibrates in response to the sound pressure waves and passes the vibrations on to the bony ossicles. The tympanic membrane and ossicles conduct the sound mechanically to the oval window of the cochlea. The cochlea is a spiral shaped cavity in the osseous labyrinth and accommodates the membranous labyrinth that contains the organ of Corti. This structure consists of sensory hair cells. Vibrations cause the fluid (perilymph) in the cochlea to move, inducing action potentials by the hair cells thus innervating the afferent nerve fibers which target the brainstem and auditory cortex to perceive sound.

According to the World Health Organisation, over 5% of the world's population (430 million people) suffer from disabling hearing loss worldwide (> 35 decibels loss in the better hearing ear).[1] Hearing loss has a significant negative impact on many aspects of life, both on an individual level and on society as a whole. Severely auditory impaired children either congenital or acquired, have reduced societal chances, and are likely to underperform at school, if they even have the chance to receive schooling. Adults with hearing loss often suffer from unemployment and are at risk for social isolation, depression, and loss of autonomy.[1–3] In elderly people especially, hearing loss significantly decreases quality of life

and increases emotional handicaps.[4] SNHL is the most common type of hearing loss for which to this day there are no approved pharmacological or surgical treatments that reverse the hearing loss and restore normal hearing.[2] SNHL is often caused by a deceased amount of functioning hair cells in the organ of Corti in the cochlea, or an issue with the action potential transition to the brain. Various factors cause SNHL such as aging, overexposure to loud noise, infectious diseases, ototoxic drugs and genetic defects. It is estimated that by 2050 one in every ten people will have disabling hearing loss.

Cochlear implantation

The development of a medical device that bypasses the hair cells and directly stimulates the auditory nerve has been a process of decades. This medical device called a cochlear implant (CI), has undergone tremendous technological improvements since its introduction in 1957.[5] Current cochlear implant models consist of an outer part which is worn behind the ear: a microphone, speech processor and transmitting coil which resides on the scalp, and an internal part which is inserted surgically under the scalp and in the cochlea: a receiver/stimulator (R/S) device and an electrode array (see Figure 1.1). The microphone captures sound waves from the environment, which are then processed and converted into digital codes by the speech processor. This information is sent to the transmitter coil that is attached to the R/S device through a magnet on the scalp. The R/S device then converts the digital code to electrical pulses that are sent to the electrode array inside the cochlea. The auditory nerve is stimulated and the CI user is able to perceive sound.

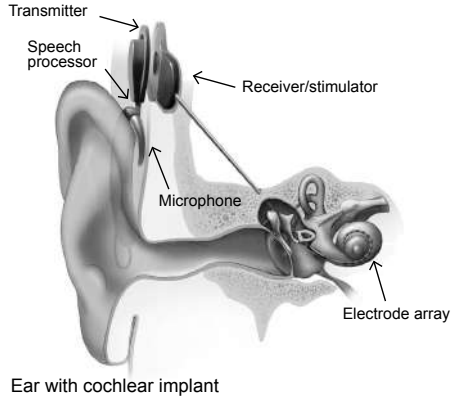

Figure 1.1: Schematic representation of a cochlear implant. The external sound processor converts sound into a sequence of electrical signals that are sent via a transmitter coil to the internal receiver-stimulator. The internal device, which is located under the skin (in a ramp shaped bony well created in the skull), processes the electrical signal and transmits them via the electrode array to the cochlear nerve. Both internal and external devices are equipped with magnets. (Source: NIH/NIDCD)

The surgery to implant the R/S device and electrode array, referred to as cochlear implantation, is regarded as a safe procedure with low complication rates.[6] Patients with severe to profound SNHL are receiving CI's as early as 6 months of age.[7] The following procedure is usually followed to implant the device: a retroauricular incision is made and carried to the level of the fascia temporalis and pericranium. A mastoidectomy and posterior tympanotomy is performed to approach the cochlea through a small opening in the facial recess. An alternative surgical technique for cochlear approach is the suprameatal approach by which the mastoid is bypassed through an oblique tunnel created in the suprameatal region (the suprameatal tunnel) that connects to the lateral groove of the external auditory canal.[8] Other alternative methods are the transcanal approach, canal wall down or Veria approach.[9] The electrode array is inserted in the scala tympani through either the round window or a cochleostomy. The direction and length of the incision, as well as the positioning and fixation of the R/S device on the skull is a matter of preference by the surgeon. The device is usually positioned in the supero-posterior region of the pinna in an angle of 45–60 degrees from the Frankfurter plane with the external auditory meatus as the vertex. The R/S device must be positioned behind the pinna far enough so that there is no physical interaction of the transmitter coil with the speech processor (the behind the ear device), but close enough that the electrode array can be inserted in the cochlea with ease, minimizing the risk of traction on the array. A minimal distance of 1.5 cm between the incision line and the implant must be kept, to minimize the risk of device extrusion or postoperative infection. If a planning of the device position is carried out, it is usually done just prior to incision by drawing on the surgical drapes using the provided templates. The R/S device can be fixated on the skull using various techniques. The main choice is either creating a custom fit tight pocket under the pericranium (minimally invasive technique) or by drilling out a bony well in which the device will reside (the "conventional" or "standard" technique still recommended by CI manufacturers*). CI surgeons can choose to fixate the device with additional bony tie-down non-resorbable sutures, a screw fixation system, meshes (titanium or propylene) or absorbable plates. There is also a CI model with a pin, an attempt to follow a trend towards minimal invasive surgical approach but still using the skull for extra stability.[10,11] A channel, tunnel or bony overhang is made to guide the electrode array to the mastoid cavity and protect it from sharp or blunt trauma. Some surgeons use methylene blue transcutaneous staining locating the well position on the skull and the electrode array channel.[12]

* Cochlear, Advanced Bionics, MED-EL

Complications of R/S device fixation and migration

Positioning and fixation of the R/S device, despite being important though underestimated surgical steps, have received little attention and are carried out by following the directions provided by manufacturers or by applying techniques developed over the years seemingly without hard evidence supporting the results.[10,13] The R/S device is fixated to avoid complications associated with displacement of the device, also known as migration. Positioning the R/S device incorrectly, could lead to device migration. Previous studies have theorized that a faulty angle and wrong placement on the skull of the R/S device can cause this complication. An oblique position and an anterior bony well close to the squamous suture would help avoid R/S migration.[14,15] Additionally, symmetrical placement is an aspect of bilateral cochlear implantation that renders the attention of the CI surgeon. In the Netherlands, bilateral implantation is covered by health insurance only in children.[16] The aesthetic results of symmetrical placement especially in this patient population must not be underestimated.[17]

Conventional fixation methods as described above, are still recommended by manufacturers, however the surgical community is heading away from these invasive methods in favor of soft surgical techniques. There seems to be a need for hard evidence to prove the safety of these methods, demonstrated by the number of studies on this topic.[10–13,18–26] Drilling a bony well and bony holes for the tie-down sutures is not without risks. Intracranial complications that have been described as a result of dural exposure during drilling the bony well or bony tie down suture holes: (delayed) dural tears with cerebrospinal fluid leak,[27–31] acute subdural hematoma,[27,32] epidural hematoma,[33] fatal cerebral infarction,[34] temporal lobe infarction and lateral sinus thrombosis.[35] Although rare, these complications are important and need to be taken into consideration when choosing the surgical technique to apply. Apart from the risks of drilling for fixation of the R/S device, other aspects of the surgery need to be considered which influence the risks of complications. The standard technique usually necessitates a large C-incision and large soft tissue flap to ensure adequate visibility for drilling. These invasive interventions have been associated with complications such as hematoma, seroma, skin flap necrosis and infection.[36,37] Furthermore, drilling a bony well and bony tie down sutures increases operative time, a disadvantage not only because of longer anesthesia but also the cost. A previous study comparing the standard and the minimally invasive technique indeed found that the latter is faster, however there seemed to be more complications.[23] High quality evidence is lacking to validate complication differences.

Complications that have been reported as a direct result of R/S device migration can necessitate revision surgery, are infection,[38] device failure,[6,39–41] electrode migration,[14,42–44] device extrusion,[14,43] and wound complications.[14] R/S device migration rates vary with studies reporting rates of 0.4–1.7% in a general cohort[6,40,44] and comprising 7.0–23.4% of revision surgery cases.[39,40] Maxwell et al reported device migration rates of 20–25% in a general cohort of CI recipients when using an objective method of assessing migration, although the majority of these cases were asymptomatic and not clinically apparent.[25]

Cochlear implant surgery improvements through new technology

In the medical field, and particularly in surgery, technological advancements have made it possible to create detailed planning and use case specific 3-D printed surgical tools to achieve the desired surgical results. High quality imaging enable surgeons in cooperation with 3-D specialists, to go through each step of an operation, improving the surgical results and reducing operation time.[45] In the field of otology, the use of such patient specific tools seems not to be widely used, however there have been successful attempts in implementing 3-D printed intraoperative guides.[46] Intraoperative guides are templates used in a variety of ways for tissue reconstruction, by assisting cutting or drilling. Although acquisition of preoperative imaging (high-resolution computerized tomography scanning) for cochlear implantation is a standard procedure, planning of the operation is usually focusing on anatomical relations between the cochlea, facial nerve and mastoid. The issues of imprecise and arbitrary placement of the R/S device achieved through the current methods, as well as the uncertainty of sufficient skull thickness to drill out a bony well with or without bony tie-down sutures, could be overcome by also using the imaging for preoperative planning.

Impact of cochlear implant on patients

Since the first CI's appeared on the market, manufacturers have invested not only in improving the software, but also the hardware. The inner and outer part of the CI are becoming thinner in profile as well as lighter with each new generation, angled alignment of the magnet coil and anterior part of the implant following the curvature of the skull, the speech processors are more discrete, and some models have an all-in-one design eliminating the need for a behind-the-ear device.[5] Most importantly, speech perception results have increased greatly, thus improving quality of life of CI wearers.[47–49] Although speech results and hearing-related quality of life of CI patients have indeed been the focus of previous

research, the impact of wearing the CI, the factors that influence their wear time and the overall experience of having a CI have rarely been studied or reported in the field. These topics render our attention, as it has been reported that fit and comfort are the second most important factors contributing to non-use of hearing aids.[50] It is unknown to which extend wearing a CI impacts daily activities or sleep, especially if there are discomforts that are caused by the implant. Since CI patients suffer from severe hearing loss, sometimes for years prior to treatment, any increase in speech perception and communication could suppress the inconveniences that accompany wearing a CI.

There are questionnaires known as patient-reported outcome measures (PROMs), that assess CI use, such as the Cochlear Implant Management Skills (CIMS-self) survey, and the Nijmegen Cochlear Implantation Questionnaire (NICQ).[51,52] However, these PROMs evaluate device management and health-related quality of life without assessing the (physical) impact of a CI. There seems to be a need for a validated method to capture the issues caused by wearing a CI, which are of importance from the perspective of patients themselves.

Aims of this thesis

The aims of this thesis are to investigate the different surgical techniques for R/S device fixation, to explore new methods of R/S device positioning, and to develop objective means to assess migration and the impact of wearing a cochlear implant.

Thesis outline and chapter overview

This thesis starts with investigating the surgical techniques currently used by CI surgeons for fixation of the R/S device and electrode array insertion in the cochlea. The differences of these techniques in regards to complications are also appraised. Subsequent chapters explore new methods of objectively assessing migration of the R/S device, skull thickness for optimal positioning and development of tools for precise surgery. These methods are used in a retrospective appraisal of clinical data and temporal bone experiment. Additionally a patient reported outcome measure (PROM) is developed and validated to capture the impact of wearing a CI. Finally a protocol is discussed of a randomized controlled trial of CI recipients that is set up to investigate two different fixation techniques on R/S device migration, complications and patient experience.

In **Chapter 2** we investigated the current practices in surgical techniques used by CI surgeons internationally for positioning and fixation of the internal components of the implant. An online survey was sent out to assess the variability between surgeons and evolution of surgical techniques.

Chapter 3 describes a systematic review that compares the two most used fixation techniques, the bony well versus the tight subperiosteal pocket techniques with or without the use of additional fixation materials such as tie-down sutures or screws. The rates of migration of the internal components of the implant were compared.

In **Chapter 4** we developed and validated a new method of assessing the exact location of the R/S device on the scalp. The inter-rater reliability of this method was tested on healthy volunteers with the use of markers representing the transmitter of a CI. This screening tool could be used in a clinical setting to assess migration of the implant.

Chapter 5 describes the development and validation of a semi-automated algorithm that determines the most optimal position of the R/S device in regards to cortical thickness based on CT imaging. This method makes use of new 3D software and automations to test the feasibility of drilling a bony well in a predetermined region of the skull.

In **Chapter 6** we used the method developed in Chapter 5 by applying it on CT scans of pediatric patients to investigate the feasibility of drilling a bony well in different age groups. We also reviewed the complications and device failures of the pediatric cohort of our tertiary center when using different surgical techniques.

A new surgical tool was developed and validated in **Chapter 7** for accurate placement of the R/S device on the skull. This patient specific and CI model specific guide can be used to determine the position of the R/S device and aid the surgeon in drilling out the bony well in which the implant will reside. Accuracy of CI placement was assessed using Cone Beam CT scans.

In **Chapter 8** we developed and validated a new PROM to evaluate the consciousness of wearing a CI and how this impacts the daily life of patients. This was realized by following the appropriate guidelines with close participation of CI recipients.

Chapter 9 describes a protocol for a randomized controlled clinical trial set up to compare two different fixation techniques, the bony well and the tight subperiosteal pocket technique without any additional fixation materials. The placement of the R/S device and electrode array are assessed with cone beam CT scan postoperatively and during follow up three months and one year post surgery to objectify migration. The method described

in Chapter 4 is applied to determine R/S device placement and is validated to assess R/S device migration. The effects of the different surgical techniques on patient experience are measured using the PROM developed in Chapter 8.

As the final part of this thesis, **Chapter 10** provides a general discussion of the outcomes of the previous chapters in relation to the literature. This chapter also presents clinical implications as well as future perspectives.

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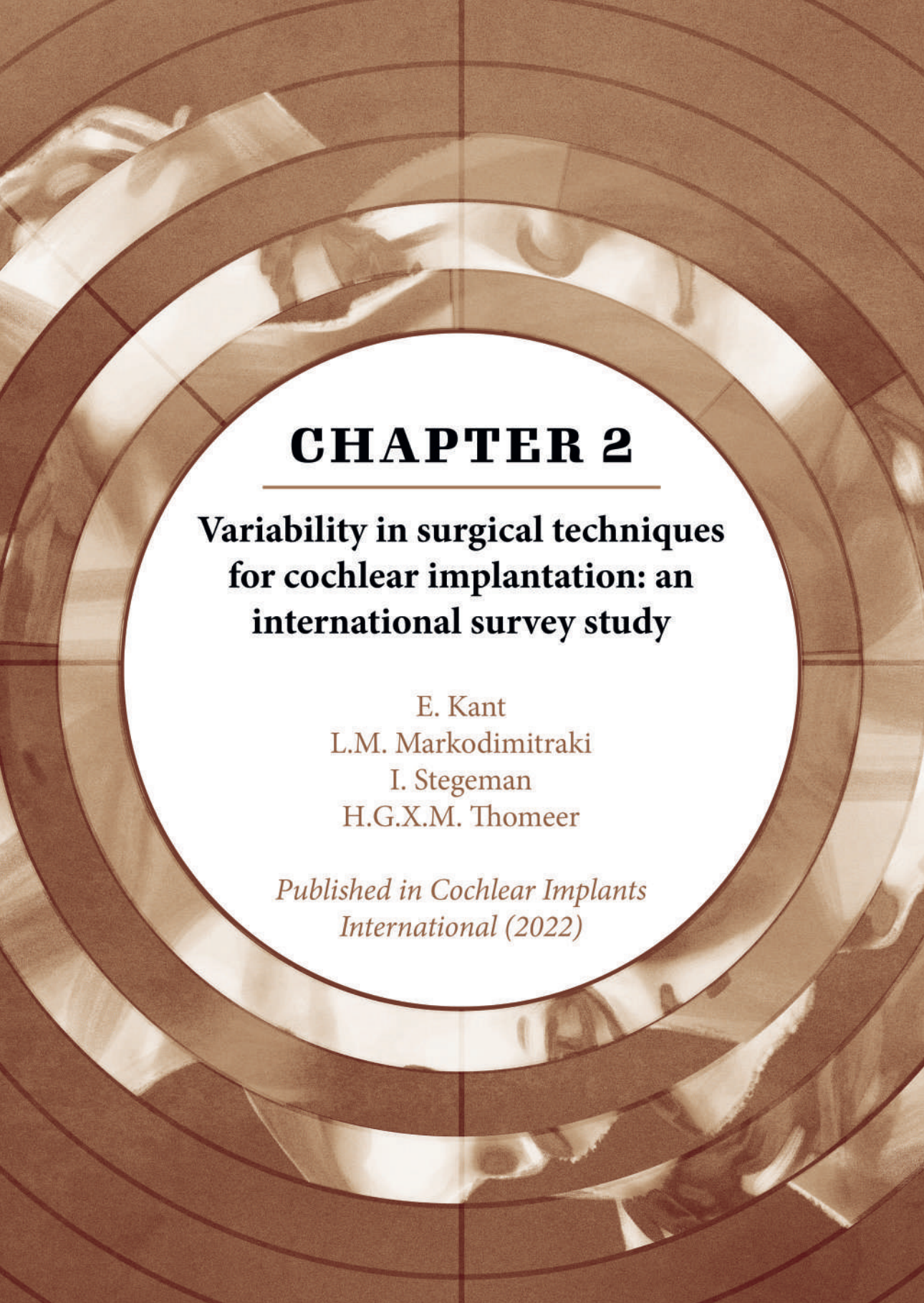

CHAPTER 2

Variability in surgical techniques for cochlear implantation: an international survey study

E. Kant
L.M. Markodimitraki
I. Stegeman
H.G.X.M. Thomeer

Published in Cochlear Implants International (2022)

Abstract

Objective: This study aimed to gain insight into current practices regarding the surgical techniques used for positioning and fixation of internal components of the cochlear implant.

Methods: A questionnaire focused on surgical techniques used for cochlear implantation was distributed among 441 cochlear implant surgeons. Descriptive statistics were reported.

Results: The questionnaire was completed by 59 surgeons working in 13 different countries. The most preferred incision shapes were the S-shape (41%) and the C-shape (36%). The preferred implantation angle for the receiver/stimulator device was either 45° (64%) or 60° (30%), relative to the Frankfurter Horizontal Plane. Most respondents used a drilled bony well with (42%) or without a subperiosteal pocket (31%) to fixate the receiver/stimulator device. All respondents used the facial recess approach. Most used the round window insertion technique to enter the scala tympani (73%). Approximately half of the respondents preferred the lateral wall electrode array, whereas the other half preferred the perimodiolar electrode array. During their career, most (86%) changed their technique towards structure preservation and minimizing trauma.

Conclusion: This study indicates variability in the surgical techniques used to position and fixate the internal components of the cochlear implant. Additionally, surgical preference transits towards structure preservation and minimal invasiveness.

Introduction

The introduction of the cochlear implant in the 1970s was an important development for the treatment of severe to profound sensorineural hearing loss.[1] Deaf patients regained audiological communication abilities. The cochlear implantation surgery has two main goals: adequate positioning and fixation of the receiver/stimulator (R/S) device on the skull and insertion of the electrode array in the scala tympani. In the early days, all cochlear implantations were performed by a large C- or S-shape incision with a skin flap, a drilled bony well to fixate the R/S device on the skull with bony sutures, a mastoidectomy-facial recess approach and cochleostomy to gain access for the electrode array into the scala tympani.

Over time, minimal invasive surgery became of increasing interest. As the indication range for implantation broadened and more patients with residual hearing received a cochlear implant, the preservation of intra-cochlear structures became more important.[2] Modifications in the design of the internal components, e.g. a thinner profile of the internal R/S device, decreased the need for embedding of the device to prevent protrusion and migration. The subperiosteal pocket technique was described to fixate the device without drilling a bony bed.[3] Additionally, the suprameatal approach was introduced to avoid possible facial nerve injury, with no facial recess approach needed, and to preserve the mastoid.[4] Finally, electrode arrays became thinner and electrode insertion directly through the round window became the method of preference.[1,2] Not all these developments proved to be sustainable over time. The suprameatal did not result in lower complication rates, especially regarding facial nerve injury or other post-operative adverse events.[5] The subperiosteal pocket technique harbours potential advantages: less operation,[6] smaller skin incision and reduction of possible complications related to drilling the skull, such as subdural hematoma, cerebrospinal fluid leakage or meningitis.[3,7,8] However high quality evidence regarding the advantages or disadvantages of this minimally invasive technique, such as an increased risk of device migration, is lacking.[6,9–13]

It is useful to be acquainted with the different techniques applied in daily practice. This information can provide insight into the daily practices in the readers own and other regions. Thus, the aim of this study was to assess the current practices in surgical techniques used by surgeons for positioning and fixation of the internal components of the cochlear implant.

Materials and methods

Study design and selection of participants

We performed a cross-sectional study using an online questionnaire. 441 surgeons working in 27 different countries were invited to participate. Their contact information was gathered from the Meniere society, as well as an extensive digital search. Surgeons were included when clinically active in cochlear implant surgery. Residents and surgeons inactive for cochlear implantation surgery for more than 5 years were excluded. The questionnaire was distributed using Castor EDC (version 2019.3) on 30-10-2020 and participants were given five weeks to respond, with two reminders after two and four weeks. All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments. This study is not subject to the Medical Research Involving Human Subjects Act (WMO), therefore it is exempt from review by an accredited medical ethical review committee. Written informed consent was obtained of all participants.

Content of the questionnaire

The survey consisted of six chapters. The first chapter contained questions on respondent demographics and exclusion criteria, e.g. work location, patient population, years of work experience and annual amount of cochlear implantations. In chapters 2–5, surgeons were asked about their preferred surgical techniques and its influencing factors in an anatomically normal patient regarding: the shape of incision, the implant angle of the R/S device, the fixation method for the R/S device, and the insertion approach of the electrode and the electrode array type. Respondents could choose more than one influencing factor for each surgical technique. The sixth chapter contained questions regarding the changes in the surgical technique during the respondents' career. The survey was reviewed prior to its distribution by a researcher, an otologist and an epidemiologist, and was adjusted accordingly.

Data analysis

Only completed surveys were included in the data analysis. Surveys were considered complete when all the multiple-select and single-select questions in chapters 2–6 were answered. Data regarding work location was divided into regions according to the Central Intelligence Agency World Factbook.14 Years of experience and the number of cochlear implantations performed per year were divided into groups to provide an extra overview of its distribution (0–10, 11–20, > 20 years; 0–25, 26–50, 51–75, > 76 implantations;

respectively). Multiple select questions were analysed with multiple response set analyses. Percent of cases were described. Questions regarding possible changes in surgical technique were open answers and optional. Open answers were clustered into several categories, based on the use of same terms or synonyms, when stated by ≥ 2 different surgeons. The most commonly used word was stated. This was done by two researchers independently (EK and LM). Differences were discussed until consensus was reached.

To determine the variation in the surgical techniques used for cochlear implantation, descriptive analyses were used. In case of missing data, the number of missing data was reported per item. Data analysis was performed using SPSS 25.0 for Windows.

Results

Respondent demographics

59 (13.4%) cochlear implant surgeons, working in 13 different countries (Supplemental Digital Content: Work location), answered the survey over a 5-week period. All were included in this study. The median years of work experience was 17 (IQR 10–24). In total, respondents in this study cohort performed 2338 cochlear implantations per year. Most surgeons, n = 45 (76%), performed cochlear implantations in both adults and children. The majority worked in Western Europe, n = 38 (64%), followed by Central Europe, n = 7 (12%), North America, n = 7 (12%), Oceania, n = 4 (7%) and Southern Europe, n = 3 (5%) (Table 2.1).

Surgical technique

The S-shape incision was used by 24 (41%) respondents, whereas 21 (36%) respondents preferred the C-shape incision, and 9 (15%) respondents preferred the linear incision. The majority of the respondents, n = 42 (71%), answered that there were no factors that influence their choice of incision. For the remaining respondents, the influencing factors were the patients' age, n = 7 (12%), the necessity for drilling, n = 7 (12%), the implanted CI-model, n = 5 (8%) and the skin thickness, n = 4 (7%) (Figure 2.1).

For the majority of the respondents the implant angle of 45° relative to the Frankfurter Horizontal Plane was the preferred technique, n = 38 (64%), followed by an implant angle of 60° for 18 (30%) respondents (Table 2.2). Eight of the cochlear implant surgeons (14%) did not use a tool for R/S device positioning. Of the other respondents, 35 (60%) used a silicon implant dummy, 24 (41%) used a steel implant template, 17 (29%) used a processor template, 6 (10%) used a bilateral tool to achieve symmetric placement. More

answers were possible. The most important influencing factors for the position of the R/S device were the distance between the transmitter and the ear, n = 20 (34%), the shape of the skull, n = 18 (31%), the patients' headwear, n = 16 (27%) and the implanted CI-model, n = 16 (27%) (Figure 2.2).

Table 2.1: Demographic data of the respondents

	N	%
Experience cochlear implantation		
0–10 years	15	25
11–20 years	24	41
> 20 years	19	32
Missing	1	2
Median years	16	
Amount of cochlear implantations per year		
0–25	23	39
26–50	26	44
51–75	5	8
> 75	4	7
Missing	1	2
Median amount	30	
Region work location		
Western Europe	38	64
Central Europe	7	12
Southern Europe	3	5
North America	7	12
Oceania	4	7
Patient population		
Adult patients	10	17
Paediatric patients	3	5
Both	45	76
Missing	1	2

N = number of respondents.

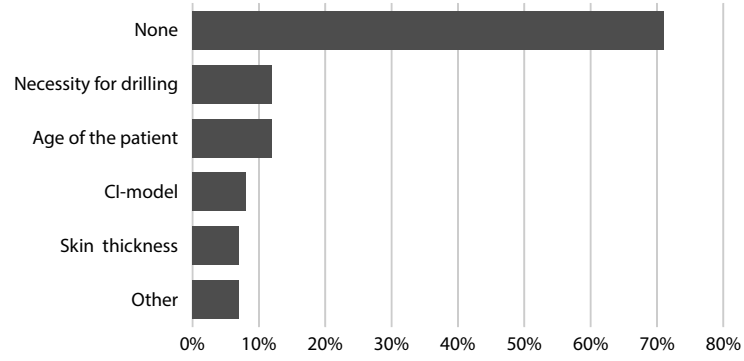

Figure 2.1: Factors influencing type of incision defined by % of respondents (multiple response question). CI = cochlear implant.

Table 2.2: The preferred surgical techniques per region

	All		Western Europe		Central Europe		Southern Europe		North America		Oceania	
	N	%	N	%	N	%	N	%	N	%	N	%
Incision												
C-shape	21	36	13	34	1	14	3	100	4	57	0	0
S-shape	24	41	17	44	4	57	0	0	2	29	1	25
Linear	9	15	4	11	2	29	0	0	1	14	2	50
Other	5	8	4	11	0	0	0	0	0	0	1	25
Position of the R/S device												
Implant angle 0°	1	2	1	3	0	0	0	0	0	0	0	0
Implant angle 45°	38	64	26	68	4	57	1	33	5	71	2	50
Implant angle 60°	18	30	9	23	3	43	2	67	2	29	2	50
Implant angle 90°	1	2	1	3	0	0	0	0	0	0	0	0
Other	1	2	1	3	0	0	0	0	0	0	0	0
Fixation of the R/S device												
Drilled bony well	18	31	11	29	4	57	1	33	2	29	0	0
Drilled bony rim without SPT	1	2	0	0	1	14	0	0	0	0	0	0
Drilled bony rim with SPT	25	42	16	42	2	29	2	67	2	29	3	75
SPT	10	17	7	18	0	0	0	0	2	29	1	25
Other	5	8	4	11	0	0	0	0	1	13	0	0
Positioning and insertion approach of the electrode												
Approach to the middle ear												
Facial recess approach	59	100	38	100	7	100	3	100	7	100	4	100
Suprameatal approach	0	0	0	0	0	0	0	0	0	0	0	0
Transcanal approach	0	0	0	0	0	0	0	0	0	0	0	0
Other	0	0	0	0	0	0	0	0	0	0	0	0
Approach to the scala tympani												
Cochleostomy	3	5	2	5	0	0	1	33	0	0	0	0
Extended RW insertion	13	22	9	24	1	14	0	0	2	29	1	25
RW insertion	43	73	27	71	6	86	2	67	5	71	3	75
Electrode array												
Perimodiolar electrode array	28	48	18	47	4	57	1	33	3	43	2	50
Lateral wall electrode array	31	52	20	53	3	43	2	67	4	57	2	50

N = number of respondents, R/S = receiver/stimulator, SPT = subperiosteal pocket technique, RW = round window.

Three-quarters of the surgeons used a drilled bony well or rim to fixate the internal R/S device on the skull, n = 44 (75%). The remaining used solely a subperiosteal pocket to fixate the R/S device, n = 10 (17%). Of the respondents who drilled for fixation, 18 (31%) performed a drilled well and 26 (44%) a rim (Table 2.2). Additional fixation methods, such as a bony overhang or sutures, were used by 29 (49%) respondents (Table 2.3). If a respondent used intra-cortical tie down sutures, the used materials were both absorbable,

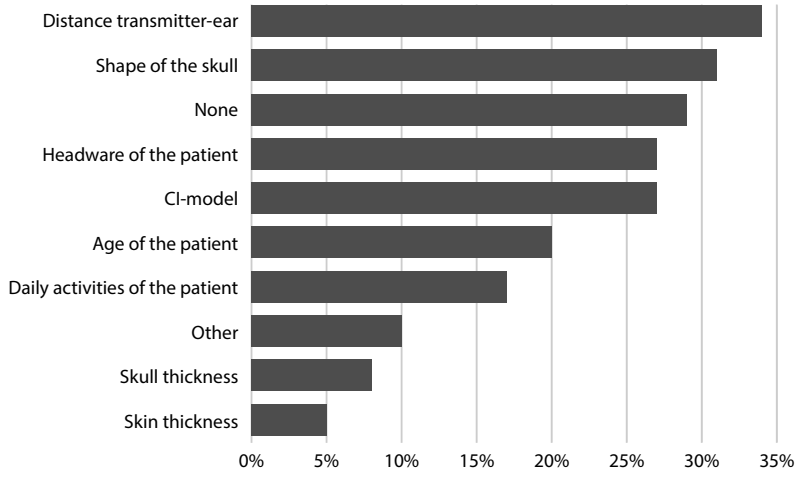

Figure 2.2: Factors influencing the implant angle of the receiver/stimulator device defined by % of respondents (multiple response question). CI = cochlear implant. % of respondents.

Table 2.3: Additional fixation methods for the R/S device

	N	%
None	30	51
Bony overhang	14	24
Bone dust	11	19
Intra-cortical tie down sutures	6	10
Screws	3	5
Tissue glue	3	5
Pins	2	3
Sutures	2	3
Wires	1	2

N = number of respondents, R/S = receiver/stimulator, more options possible.

n = 2 (3%), and non-absorbable, n = 4 (7%). Nineteen (32%) respondents considered the surgical preference and routine of the CI-surgeon as an influencing factor for their choice of fixation technique. Of the other factors, the most important was the CI-model, n = 18 (31%), while 22 (37%) respondents did not consider any factor to be of influence for their choice for the fixation technique of the R/S device (Figure 2.3).

All respondents used the facial recess approach for gaining access to the middle ear. To gain access to the scala tympani, the most preferred method was the round window insertion, n = 43 (73%), followed by the extended round window insertion, n = 13 (22%), and finally the cochleostomy, n = 3 (5%). The preferred electrode array was the lateral wall electrode for 31 (53%) respondents and the perimodiolar electrode array for the remaining 28 (47%) (Table 2.2). The most important other influencing factors regarding the choice of

electrode array were: the presence of residual hearing, n = 42 (71%), congenital aberrant anatomy of the cochlea, n = 40 (68%), otosclerosis of the cochlea or round window, n = 29 (49%), the hearing loss pattern, n = 29 (49%) and a history of infectious processes, n = 25 (42%) (Figure 2.4).

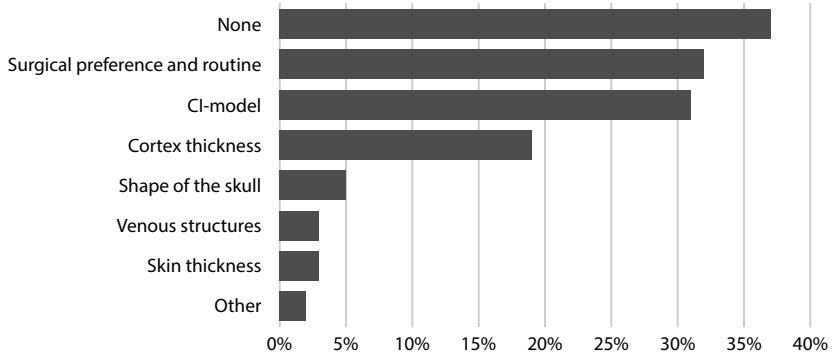

Figure 2.3: Factors influencing the fixation technique for the receiver/stimulator device defined by % of respondents (multiple response question). CI = cochlear implant.

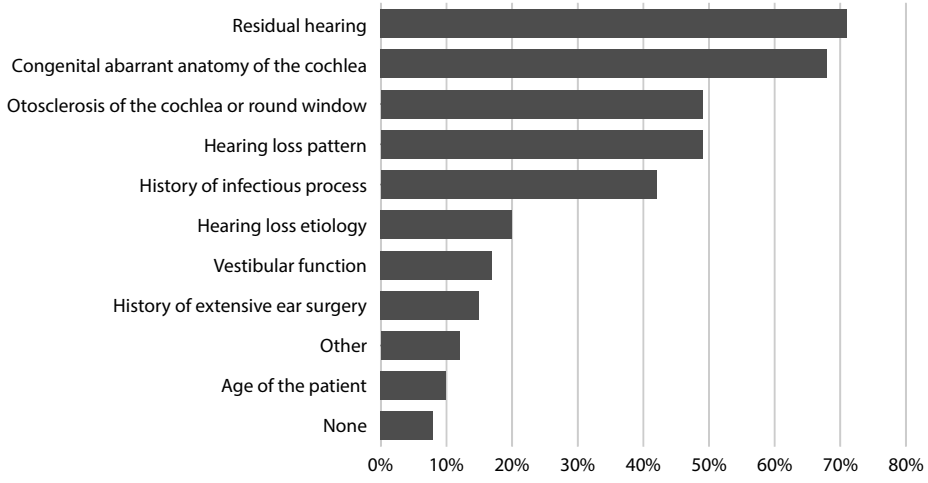

Figure 2.4: Factors influencing the type of favoured electrode defined by % of respondents (multiple response question).

Work region and surgical techniques

The surgical techniques used by all participants were divided per region (Table 2.2). In most regions these numbers were too small to objectify differences by statistics. No major numerical differences were observed between the surgical techniques used in the different regions.

Change in surgical technique over time

Most of the respondents, n = 51 (86%), reported to have changed something in their surgical technique for cochlear implantation during their career. When describing their biggest difference between the current surgical technique and their technique in the past, 14 (27%) respondents mentioned this change focused mainly on prevention of trauma during surgery. The most described changes were the preference for round window insertion, n = 25 (49%) and a smaller incision, n = 18 (35%) (Table 2.4).

Table 2.4: Changes in the surgical technique in the respondents' career

Change towards	N	%
Round window insertion	25	49
Smaller incision	18	35
Soft-surgery or atraumatic surgery	14	27
Subperiosteal pocket	5	10
Less extensive drilling (for implant bed or electrode)	5	10
Slow insertion of electrode array	5	10
Extended round window insertion	4	8
No or less sutures for fixation	3	6
Embedding of the electrode array	2	4
Steeper angle for position of the R/S device	2	4
Intra-operative monitoring	2	4
Facial recess approach	2	4
Change from C- to S-shape incision	2	4
Total respondents with a change in surgical technique	51	100

N = number of respondents, R/S = receiver/stimulator, more options possible.

Discussion

We aimed to assess current practices regarding the surgical techniques used for CI-surgery. This study demonstrated a variability in most of the surgical techniques used in cochlear implantation. The only surgical techniques that all respondents applied unanimously, was the facial recess approach. All other surgical techniques varied between CI surgeons. The C-shape and S-shape were the two most preferred incision shapes. The majority of the respondents preferred the implant angle 45° or 60° to the Frankfurter Horizontal Plane. For the fixation technique, the majority used a drilled bony well or rim. To approach the scala tympani, the greater part preferred the round window insertion. The choice for either one of the electrode array types was approximately equal. Additionally, most of the respondents had made a change in their surgical technique during their career. Their described changes focused in particular on structure preservation or minimal invasive surgery.

We hypothesize that the variation between respondents is caused by different underlying reasons, such as routines of the medical centre and personal preference.

An interesting finding of this study is that surgeons have shifted their focus towards structure preservation and minimal invasiveness. This increased importance of structure preservation is in line with what has previously been reported. A survey distributed in 2007,[15] showed that 16% of the CI-surgeons sometimes performed a round window insertion, whereas their follow-up survey in 2014[16] showed a substantial increase (from 19–69%) of CI-surgeons sometimes using the round window approach. This was comparable to 64% in 2017.[17] There was a further increase towards the round window insertion approach in our data (73%). Additionally, 25 (42%) of our respondents specifically mentioned they changed electrode array insertions in favour of round window insertion. The advantages of aiming for direct round window approach, instead of extended round window or cochleostomy, are possible residual hearing preservation and optimal speech perception outcome.[18]

An optimal electrode array type (lateral wall, perimodiolar, full or partial insertion) has not yet been defined[19,20] and therefore not one specific electrode array is preferred by all respondents. Both were chosen in equivalent numbers, which is comparable to a study published in 2018, in which they found that in cases in which hearing preservation is not a goal, 56% was in favour of the perimodiolar electrode array and 44% in favour of the lateral wall electrode array.[17] In hindsight, we acknowledge a bias in this question as for many surgeons one specific favourite may not exist. This could be explained by both electrode array types having their own advantages. The perfect electrode should provide atraumatic insertion, optimal speech perception outcomes, structure preservation, ascertain full insertion (also in difficult cases, i.e. post-meningitis or otosclerosis), amongst others. However, neither electrode array is optimal on all factors and the choice may differ per situation.[19,20]

All respondents preferred the facial recess approach to gain access to the cochlea. Different alternative techniques have been suggested during the last decades, such as the Veria technique[21] or the suprameatal approach.[4] These were developed to avoid possible facial nerve injury, be less invasive and to shorten operation time. However, these techniques have not been adapted and accepted as default approach, as these did not lead to improved surgical outcomes or superior patient quality of life.[5] An advantage of the facial recess approach is the angle of approach towards the scala tympani. It seems more natural and in line with the cochlear ramp than the angle in the Veria or the suprameatal technique. In both these procedures a cochleostomy is necessary.[4]

A similar tendency towards minimal invasive surgery as seen with the insertion of the electrode array, is seen in this study regarding the fixation of the R/S device. With the decreasing profile and thickness of the R/S device,[22] some CI surgeons perform the subperiosteal tight pocket technique as it might be advantageous to avoid device fixation by cortical bone drilling and embedding. Indeed, we found that, when comparing our results with previous literature, surgeons increasingly use non-drilling techniques or minimal additional fixation methods. A survey-study in 2010,[23] showed that only 3% never drills a well for the R/S device and 18% never secures the internal receiver. In our study, 17% of the respondents did not drill a bony well or rim and 51% did not prefer the use of additional fixation methods. The potential benefits of minimal invasive fixation such as the lower risk of intracranial complications and decreased operative time, make non-drilling techniques more appealing. Interestingly, only anecdotal evidence is available regarding complication rates related to this cortical drilling as well as the subperiosteal tight pocket technique, to fixate the R/S device.[13]

Although we do see that over time, the subperiosteal tight pocket technique is used more frequently, there remains a high diversity in the R/S device fixation techniques used by our respondents. This regards both to the decision to drill or not, as well as additional fixation methods. This variation has also been previously showed in literature, with a review in 2012[24] describing eleven different published fixation techniques. Respondents stated that the CI-model was one of the two most influencing factors for the fixation technique. The different designs of the CI-models, with some having a screw system and the existence of different sizes, thicknesses of the device and different locations of exit of the electrode lead from the R/S device,[22] might contribute to this diversity. Surgical preference and routine of the CI-surgeon was stated as the other most important influencing factor for the preferred fixation technique. There remains uncertainty regarding which fixation methods leads to optimal outcome and lowest risk for complications, such as device migration.[6,9–12] We argue that the preferred fixation technique is defined to a greater extent by routine than evidence.[13]

A limitation of the study that should be addressed is the low response rate of 13%, which could introduce a responder bias and might not be a representative sample of all CI-surgeons. However, the outcomes of this study could provide targets for further research and render CI-surgeons the possibility to compare their individual practices to some of the current preferred and applied methods of cochlear implantation. We recommend randomized controlled trials to compare the surgical techniques to obtain a consensus, supporting one optimal surgical method.

Conclusion

There is a variability in the surgical techniques used to position and fixate the internal components of the cochlear implant in respondents of our survey. Additionally, the descriptive results of this study show the tendency towards structure preservation and minimal invasiveness. Further exploration with a high level evidence research method seems warranted to gain consensus about an optimal method to be used universally.

Acknowledgments

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Disclosure of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplemental Digital Content: Work location

	N
Netherlands	16
France	8
United Kingdom	7
United States of America	6
Belgium	6
Germany	6
Australia	2
Italy	2
New Zealand	2
Portugal	1
Denmark	1
Canada	1
Poland	1
Total	**59**

CHAPTER 3

Cochlear implant fixation techniques: a systematic review of the literature

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R.M. Strijbos
I. Stegeman
H.G.X.M. Thomeer

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Abstract

Objective: Given the lack of consensus on fixation techniques of the cochlear implant (CI), this review aims to create an up to date overview of intra- and postoperative complications, focusing on migration of the internal receiver/stimulator (R/S) device and the electrode array.

Data sources: On June 29th 2020 we conducted a search in PubMed, Embase, Cochrane, Web of Science and CINAHL. Keywords were "Cochlear implant", "complication", "migration" and synonyms.

Study selection: Studies were considered if: 1) the adult study population consisted of ≥ 10 patients, 2) the R/S device was fixated using the bony well or tight subperiosteal pocket technique without bone-anchoring sutures or screws on the implant, and 3) migration of the R/S device or displacement of the electrode array were described as outcomes.

Data extraction: Study characteristics, interventions, follow up, and outcomes were extracted. For critical appraisal, an adapted version of the Newcastle-Ottawa quality assessment scale for cohort studies was used.

Data synthesis: Seven studies were included (n = 430 patients). Migration of the R/S device was reported by three studies. Two studies applying the tight pocket technique, reported migration rates ranging from 9.0–69.2%. One study using the bony bed technique reported migration of 100%, with an average of 2.5 mm. All studies lacked the required standard for comparability, assessment of outcome and follow up.

Conclusions and relevance: There is currently no evidence of a difference between the bony bed- and tight pocket fixation technique, regarding migration of the R/S device or the electrode array, in adult patients.

Introduction

Cochlear implantation has been standard care for patients with severe sensorineural hearing loss for several decades. Surgical techniques are being improved constantly, and manufacturers push the boundaries of technology. This has resulted in low complication rates, better audiological results and improved quality of life of patients. The positive results of cochlear implantation has led to a broadening of indication and age ranges of patients which increase the number of cochlear implant candidates.[1,2] Due to this increase, the number of medical centers performing the surgical procedure has risen, as well as surgeons that are gaining experience in this field.[3,4] Nowadays, cochlear implantation is considered a safe procedure.[5–8] In order to reduce the complication rates even more and to provide less experienced surgeons with clear evidence based overview, further refinements and consensus on safe surgical techniques are needed.[9,10]

An underestimated, though important step of cochlear implantation, is positioning and fixation of the receiver/stimulator (R/S) device, due to the complications that can occur during or after the implant is surgically placed. A high variability between ENT specialists on surgical techniques of fixation has been reported.[11,12] According to the literature, there are currently up to eleven different fixation methods being applied in practice, such as the bony bed technique, with or without bony sutures, screws or mesh, and the tight pocket technique.[11] Possible complications of R/S device positioning and migration are subdural hematoma, cerebrospinal fluid leakage, meningitis, respectively pain, hematoma, behind-the-ear device problems and device failure, all of which can lead to revision surgery.[5,6,13–15] Also, movement of the internal device can lead to malpositioning of the electrode in the cochlea which can have an impact on audiological results. Despite these risks, the position of the device is usually not monitored with objective and validated measurement methods, and migration is often only subjectively reported by the surgeon or patient. Recent studies using objective measures show a higher rate of micro movements of the R/S device than previously reported.[16]

The last systematic review of the literature concerning fixation techniques was published in 2012.[11] After this review, several new studies have been published on this subject. In order to create an up to date clear overview, we performed a systematic review of the literature on the currently two most used fixation techniques,[1] the bony well versus the tight subperiosteal pocket technique, where no screws or tie down sutures are used to fixate the implant. We aim to compare the rate of migration of the internal device and/or the electrode array when fixating the internal device using these fixation techniques.

Methods

Study design

We considered randomized controlled trials (RCTs) and observational studies (retrospective and prospective cohort studies and case series ($n \geq 10$)). We included studies with a minimum study population of 10 adult patients (≥ 18 years old). No restrictions on cochlear implantation criteria or patient comorbidities were applied. Articles were excluded if full text was not available, the study design was unsuitable (e.g. letter to the editor, technical note, case series < 10 cases) or surgical notes were not conclusive or applicable. All authors with available contact information were contacted to retrieve the full text of a paper, and request any additional data clarification if supportive for this research study.

Study outcomes

We included studies that described the following outcomes (either primary or secondary) in their methods section: migration of the R/S device, displacement of the electrode array.

Other intra- and postoperative complications were analyzed for this review, but not used as basis for the inclusion and exclusion of studies.

Participants and interventions

We focused on the rate of migration of the R/S device and the electrode array, in adult patients after unilateral or bilateral cochlear implantation, fixating the R/S device by one of the two following techniques:

- Bony well technique: after exposing the skull bone by elevating the temporalis muscle, a drawn bony bed is drilled out to accommodate the implant.
- Tight pocket technique: the implant is placed under the pericranium in a custom-fit pocket on the skull.

We excluded studies where surgeons fixated the R/S device with bony tie down sutures (around the implant itself), screws, mesh or cement. No restrictions were applied for fitting the electrode lead by making a bony channel.

Search strategy

This review was designed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.[17] We conducted a search of the existing literature by utilizing five different search engines (PubMed, Embase, Cochrane, Web

of Science, CINAHL). The references of the included articles were checked for missing relevant papers. To ensure that all studies on our topic were found, we used a broad search query consisting of synonym terms for 'cochlear implant' and 'complication' (see Supplemental Digital Content 1, which includes the full search query). We included all existing articles published before June 29th 2020; no restrictions or filters were applied. The combined data from all search engines were checked for duplicates. Titles and abstracts and full text screening were performed by two independent authors (LM, RS) based on predefined inclusion and exclusion criteria (see Table 3.1). Any differences were discussed until consensus was reached.

Table 3.1: Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
Cochlear implantation and reporting migration of R/S device and/or electrode array migration	No description of the fixation technique of the R/S device
Adults with unilateral and bilateral cochlear implants	Outcomes not reported in methods
	Animal study
	Review papers containing no primary data
	Unsuitable study design (e.g. letter to the editor, technical note, case study ≤ 10)

Quality assessment

Included studies were critically appraised by two authors (LM, RS), using an adapted version of the Newcastle-Ottawa quality assessment scale for cohort studies (see Table, Supplemental Digital Content 2, which includes all criteria). We adapted the selection category, and defined an exposed cohort as the patient group in whom the cochlear implant is fixated by a new technique. A non-exposed cohort was defined as the patient group in whom the cochlear implant is fixated by the technique already used in that center. Comparability was judged as high risk if only one fixation technique was performed in the study, or if one surgeon only used one fixation technique. Attention was payed to the number of surgeons performing the implantations. Studies were ranked based on the assessment methods of migration. If an objective method was used to determine migration of the internal device or electrode, such as tape measurements or imaging, a high rating of quality was acknowledged. Adequate follow up of patients post implantation was assessed to be ≥ 12 months with a maximum loss to follow up of 10%.

Results

Results of search

The search resulted in 7631 records. After duplicate removal 3981 records remained for further evaluation that included papers, conference abstracts, letters to the editor, reviews, technical notes and case reports with less than 10 adult cases. We removed 3692 records after title- and abstract screening based on relevance, and evaluated the remaining 289 records based on full text. We discarded 275 records due to unsuitable or unclear study designs, unsuitable study population, unclear method description or unsuitable primary/secondary outcomes and/or unavailability of full text (see Table, Supplemental Digital Content 3, for details on the excluded studies).

Fourteen studies were eligible for inclusion in the review. Two studies of the same medical center had overlapping patient cohorts. The study conducted in 2011 was excluded, because this study had the smallest number of participants.[18,19] Six studies were excluded because it was unclear if the study population consisted of the minimum of 10 adult patients.[20–25] Methodological information of one included study 26 was supplemented by a previously published article.[27] The search strategy and reasons for exclusion are given in Figure 3.1.

Included studies

Study design and setting

We included five retrospective reviews[18,26,28–30] and two prospective, non-randomized, observational trials.[31,32] Follow up varied across the retrospective studies from 6 days to 6 years, with only two studies reporting a minimum follow up of 12 months.[26,28] The trial endpoints for the prospective trials were 10–14 weeks[31] and six months[32] postoperatively.

Included studies were published between 2009 and 2019. Six studies were conducted in University hospitals in the USA,[26,29] Germany,[28] Belgium,[30] the Netherlands,[31] and Turkey,[18] and one was set in a specialist ear clinic in Australia.[32]

Population characteristics and sample size

All studies included both pediatric and adult patients, except the study of Dees.[31] Study population characteristics of age and sex were reported on group level for all studies, except Dees[31] who reported these data on participant level. Mean age of the adult study population was reported, or could be calculated from the raw data, for three studies, and ranged from 43.1 to 67.2 years.[18,29,31] The total sample size of adult patients for all

included studies was 430 (range 10 to 120 participants). The retrospective studies included patients through medical records[18,26,28,30] and cochlear implant registry.[29] The prospective trials included exclusively primary implantations.[31,32] One study included patients that met CI conventional criteria without gross cochlear or neural abnormalities.[31] The other prospective trial excluded reimplantations.[32]

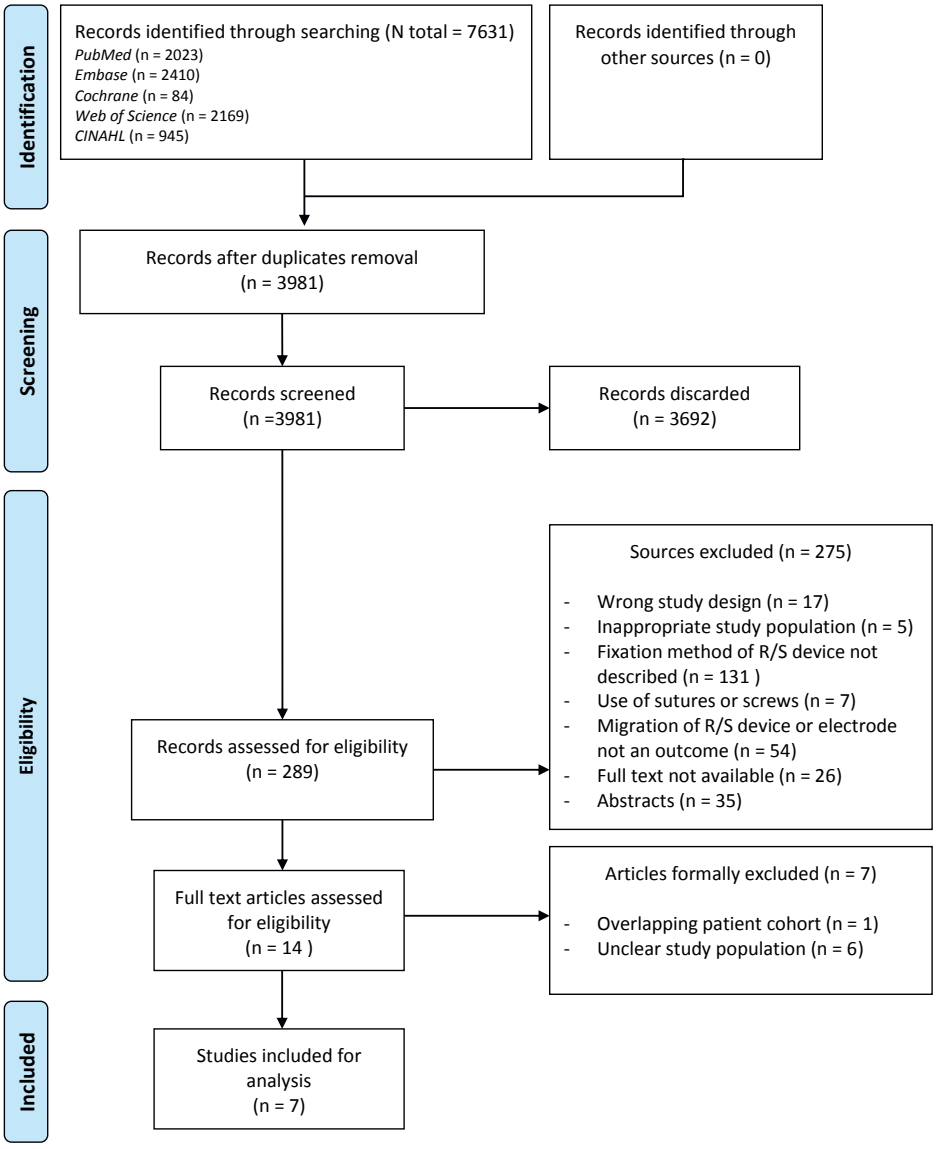

Figure 3.1: PRISMA study flow diagram.

Interventions and comparisons

Three studies[30–32] used exclusively one cochlear implant type: either Advanced Bionics HiFocus Mid-Scala, Cochlear Nucleus 512 implant or Neurelec Digisonic SP. All other studies included more than one type of cochlear implant.[18,26,28,29] The R/S device of the cochlear implant was fixated with a bony bed without additional sutures in two studies.[28,31] Two studies used the tight pocket technique,[18,30] one study used the tight pocket technique with a periosteum to bone suture,[26] one study used the tight pocket technique with periosteum to bone sutures and an electrode bony channel,[29] and one study used the tight pocket technique with bony lead channel without additional bony sutures.[32]

Outcomes

Primary outcomes were intra- and postoperative complications for all studies with a special emphasis on R/S migration in six studies.[18,26,28–30,32] One study reported electrode array migration as primary outcome[31] and R/S device migration was reported as a secondary outcome (Table 3.2). Two studies used external measurements, a ruler, to detect R/S device migration.[29,32] These studies reported different definitions of "true" or clinically relevant migration. In three studies,[18,26,28] R/S migration was detected through clinical observation. Of these studies, only Balkany et al. defined a clinically relevant migration. They considered a migration of the R/S device to be clinically relevant if the anterior edge of the R/S device was noted to be seated right below the wearable sound processor at any time during the study or if the physician noted movement of the R/S in any direction from the original placement site. Dees et al. used CBCT scans to detect electrode array and R/S device migration.[31] Vanlommel et al. did not specify how R/S device migration was defined or detected.[30]

Excluded studies

Details of reasons for exclusion of six studies is shown in the Supplemental Digital Content 4.

Risk of bias included studies

The summary of the critical appraisal is shown in Table 3.3. The items representativeness of the selected cohort, ascertainment of exposure, outcome of interest not present at start were scored as low risk of bias in all studies. One study had a comparison group whose selection was scored as low risk. Comparability was scored as high risk of bias for all studies. Outcome assessment was scored as high risk for four studies,[18,26,28,30] due to a lack of objective assessment methods for the detection of R/S device or electrode array migration. Dees et al.[31] scored low risk on this item because they used CBCT imaging to detect migration

Table 3.2: Characteristics of included studies

Studies	Study design	N	Follow-up	Cochlear implant model	R/S fixation	Primary outcome	Secondary outcome	Measurement of outcome
Balkany et al.[26]	RC	120	12–32(m)	Cochlear MED-EL Advanced Bionics	TP with periosteum to bone suture	Intracranial complications and R/S migration	-	Clinical observation
Dees et al.[31]	PC	14	10–14(w)	Advanced Bionics	BB	Electrode array migration	R/S migration	CBCT scan 3 d and 10–14 w post op
Gekeler et al.[28]	RC	107	12–60(m)	Cochlear (CI24RE) MED-EL Advanced Bionics	BB with channel	Surgical complications with special emphasis on migration	-	Clinical observation
Maxwell et al.[29]	RC	58	6(d)–6(y)	Cochlear MED-EL Advanced Bionics	TP with channel with periosteum to bone suture(s)	R/S migration	-	Ruler
Monksfield et al.[32]	PC	100	6(w)–6(m)	Cochlear (CI500)	TP with channel	R/S migration	-	Ruler
Orhan et al.[18]	RC	21	11–74(m)	Cochlear MED-EL Advanced Bionics Neurelec	TP	Safety of surgical technique and R/S migration	-	Clinical observation
Vanlommel et al. [30]	RC	10	2(m)–7(y)	Neurelec	TP	Surgical complications, R/S migration and hearing results	-	NR

RC: Retrospective cohort study; PC: prospective cohort study; m: months; w: weeks; d: days; R/S: receiver/stimulator device; TP: tight pocket technique; BB: bony bed technique; CBCT: Cone Beam Computed Tomography; NR: not reported.

of the electrode array and the R/S device. Maxwell et al.[29] and Monksfield et al.[32] used an objective measurement method with a ruler, and also scored low risk on this item. Duration of follow up was not sufficient for four studies,[29–32] so these studies scored high risk on this item. Adequacy of follow up was scored as high risk for four studies.[26,28,30,31]

Table 3.3: Critical appraisal using the adapted Newcastle-Ottawa Quality assessment scale

	Selection				Comparability	Outcome		
Study	Representativeness	Selections of comparison group	Ascertainment of exposure	Outcome of interest not present at start	Controls for surgeon	Assessment of outcome	Duration of follow up	Adequacy of follow up
Balkany et al.[26]	+	+	+	+	-	-	+	-
Dees et al.[31]	+	NA	+	+	-	+	-	-
Gekeler et al.[28]	+	NA	+	+	-	-	+	-
Maxwell et al.[29]	+	NA	+	+	-	+	±	+
Monksfield et al.[32]	+	NA	+	+	-	+	-	+
Orhan et al.[18]	+	NA	+	+	-	-	+	+
Vanlommel et al.[30]	+	NA	+	+	-	-	-	-

(+) low risk of bias; (-) high risk of bias; (±) high risk of bias in short-term follow up group, low risk of bias in long-term follow up group; NA: not applicable.

Primary outcome

All studies that used clinical observation to assess the outcome, detected no migration during follow up (see Table 3.4).[18,26,28,30] Balkany et al.[26] and Orhan et al.[18] also reported no other peri- or postoperative complications (Table 3.4). Gekeler et al.[28] reported one case of granulating sterile inflammation, one case of chronic flap infection and protrusion of implant in one case due to reactive bone growth. Dees et al.[31] reported a migration rate of the electrode array of 7% (1/14 patients), where the electrode array migrated > 0.5 mm in the direction of the cochlear duct. Maxwell et al.[29] reported average migration of the R/S device of 3.5 mm (CI 2.2–4.8) for patients with follow up < 1 year, and an average migration of 5.6 mm (CI 1.2–10.1) for patients with follow up ≥ 1 year. Monksfield et al.[32] reported migration of the R/S device of more than > 1 cm after 3 months in nine patients (9% of the adult study population).

Table 3.4: Outcomes table of included studies

			Outcomes		
Studies	R/S fixation	Follow up	R/S migration n/N (%) Mean (CI)	Electrode array migration n/N (%)	Other complications
Balkany et al.[26]	TP with periosteum to bone suture	≥ 12 months	0%	NA	None
Dees et al.[31]	BB	< 12 months	11/11 (100%) 2.5 mm (CI 1.3–3.7)	1/14 (7%)	None reported
Gekeler et al.[28]	BB with channel	≥ 12 months	0	NA	Granulating sterile inflammation; chronic flap infection; protrusion of implant due to reactive bone growth
Maxwell et al.[29]	TP with channel with periosteum to bone sutures	< 12 months	26/45 (57.8%) 3.5 mm (2.2–4.8)	NA	None reported
		≥ 12 months	9/13 (69.2%) 5.6 mm (1.2–10.1)		
Monksfield et al.[32]	TP with channel	< 12 months	9/100 9% (> 1 cm)	NA	None reported
Orhan et al.[18]	TP	≥ 12 months	0	NA	None
Vanlommel et al.[30]	TP	< 12 months	0	NA	Transitory facial nerve palsy; immediate postoperative hematoma; device failure

R/S: receiver/stimulator device; CI: confidence interval of the mean; TP: tight pocket technique; BB: bony bed technique.

Secondary outcome

Dees et al.[31] reported R/S migration as a secondary outcome. R/S migration was detected in all patients in whom the R/S device was visible in two CT scans (n = 11), with an average of 2.5 mm. They reported that migration was clinically irrelevant in all patients.

Discussion

In this systematic review, we investigated two different, frequently applied fixation techniques in the adult population, namely the bony bed and tight subperiosteal pocket technique. Minimal invasive surgery has become more widely used due to a decrease of thickness of the CI devices. Moreover, there are several advantages of a less invasive technique such as a smaller incision, shorter operative time and avoiding the risks that arise from drilling out a bony well and applying bony sutures (dural tears, CSF leaks, subdural hematoma and other intracranial complications).

Our search yielded two prospective and five retrospective trials (n total = 429), none of which directly compared the two techniques. Our results show a small amount of publications reporting variable rates of migration of the receiver stimulator device (0–69%) when using both the bony bed technique and the tight pocket technique with and without additional periosteum to bone suture(s). Interestingly, migration of the receiver package was reported by three out of seven studies,[29,31,32] who used objective measurement methods to detect migration, and reported minimal postoperative R/S device movement that did not lead to associated symptoms, decreased implant functionality or device failure.

The method for detecting migration varied, as did the definition of a clinically relevant migration. Most studies did not provide a definition of migration.[18,26,28,30,31] Maxwell et al.[29] assessed the position of the receiver package by measuring the distance between the closest point of the posterosuperior helical rim, with the rim pressed against the scalp, and a magnetic tool placed over the R/S magnet. They defined true migration as a change of measurements of > 5 mm. Monksfield et al.[32] used two anatomical landmarks, namely the top of the tragus and inferior aspect of the lobule to the center of the external magnet. They defined migration a change in measurements of 10 mm or more. A study by Guldiken et al.[33] that was not included in this review due to their pediatric study population, also evaluated the position of the receiver package by measuring the distance between the lateral canthus, the tragus tip, the mastoid tip and the external magnet. Although these methods provide an objective outcome measure, test-retest variability as well as inter-rater variability, might be taken into account. In a recent publication by our group, a similar measurement

method was tested and validated.[34] According to our results, not all anatomical landmarks are applicable when assessing the position of the R/S device. Measurements from the center of the external magnet to the tragus tip and the lateral canthus, have been proven to be the most reliable.

Electrode migration was assessed only by Dees et al.,[31] that reported electrode array migration of > 0.5 mm in one out of 14 patients, without electrode array extrusion. No information was provided on speech perception performance, electrode impedance values or other audiological or electrophysiological outcomes. Electrode array migration is a complication to consider when choosing the fixation method of the R/S device. Despite this, several studies that have been published on electrode array migration, do not describe the fixation method of the receiver package.[35–39] Rader et al.[39] and Dietz et al.[35] used audiological outcomes such as speech perception performance and radiological methods, to detect electrode array migration and its clinical impact.

Other intra- and postoperative complications were reported in both the tight pocket and bony bed study populations in two studies.[28,30] Gekeler et al.[28] used the bony bed technique and reported surgical site inflammation, flap infection and implant protrusion. Vanlommel et al.[30] applied the tight pocket technique and reported, postoperative hematoma and device failure, amongst others.

Some issues concerning the quality of the included studies, must be discussed. Firstly, a high risk of bias was noted for comparability in all studies. Ideally, more than one surgeon should perform both techniques in order to avoid any confounding bias. Secondly, follow-up was inadequate according to our predefined minimum of 12 months. However, we must consider the evidence of postoperative remodeling of the bone with spontaneous formation of a bony bed that has been noted to take place as early as 5 months postoperatively, when the tight pocket technique is used.[40,41] A fibrous capsule formation around the implant is known to occur as reaction to foreign materials.[23] This also contributes to stabilization of the receiver package. Thirdly, publication bias should always be considered. Nevertheless, the included studies reported both migration and the lack thereof, it therefore seems not to be an issue. Lastly, subjective assessment of outcome could have introduced observer bias. There are currently no validated methods of positioning and fixating the implant at a predefined location on the scalp. Subsequently, only extreme migration could have been detected with absolute certainty. The results of our study support this theory as only minimal movements of the receiver package have been reported when using objective methods. More importantly, our results have shown no clinically significant migration. But, this statement raises the question of the definition of clinical impact of R/S device migration.

Until now postoperative recovery for patients after cochlear implantation has merely focused on hearing outcome and speech intelligibility. However, it might be interesting to investigate the clinical impact or burden of R/S migration from the patient's perspective. Such clinical parameters could include pain, interaction with the behind the ear device, protrusion and/or interaction with eye glasses. In addition, the correlation between fixation of the R/S device and electrode array migration, and subsequently audiological results, has yet to be proven with certainty.

In conclusion, there is currently no evidence of/for a difference between bony bed fixation of the R/S device and the tight pocket technique with or without additional periosteum to bone sutures in adult patients undergoing cochlear implantation, in regards to migration. The included studies in this review lack the required standard of comparability, assessment of outcome and follow up in order to draw conclusions about the differences between the techniques. Future research is needed to compare the two fixation techniques, preferably with a randomized design, on R/S device and electrode array migration, incision length and operation duration, using objective methods to measure the outcome. Of course, the presented data do not cover all types of fixation techniques. For example, Synchrony pins (Med El Corporate®) and screw fixation with Neuro-2 implant (Oticon Medical®) are not mentioned in these data and might be interesting implant types for future investigation. Furthermore, although minimal movements of the R/S device have been found using both techniques, it is questionable whether this has any clinical impact. A shift to patient centered outcome measures could be considered, to investigate the clinical impact or burden of the migration.

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List of Supplemental Content

Supplemental Content 1. Complete search string in Pubmed, Embase, Cochrane Central, Web of Science and CINAHL

PubMed

((((((Cochlear[Title/Abstract]) AND implant*[Title/Abstract])) OR ((cochlear[Title/Abstract]) AND prosthes*[Title/Abstract])) OR (((cochlear[Title/Abstract]) AND prosthesis[Title/Abstract]) AND system[Title/Abstract])) OR ((auditory[Title/Abstract]) AND prosthes*[Title/Abstract])) OR ((cochlear implant[MeSH Terms]) OR cochlear implantation[MeSH Terms])

AND

((((((((((complication*[Title/Abstract]) OR migration[Title/Abstract]) OR displacement [Title/Abstract]) OR dislodgement[Title/Abstract]) OR slipping[Title/Abstract]) OR transposition[Title/Abstract]) OR dislocation[Title/Abstract]) OR shift[Title/Abstract]) OR extraction[Title/Abstract]) OR extrusion[Title/Abstract]) OR movement[Title/Abstract]) OR relocation[Title/Abstract]) OR revision[Title/Abstract]

Embase

cochlear:ti,ab,kw AND implant*:ti,ab,kw OR cochlear:ti,ab,kw AND prosthes*:ti,ab,kw OR cochlear:ti,ab,kw AND prosthesis:ti,ab,kw AND system:ti,ab,kw OR auditory:ti,ab,kw AND rosthes*:ti,ab,kw OR 'cochlea prosthesis'/exp OR 'cochlear implantation'/exp

AND

complication*:ti,ab,kw OR migration:ti,ab,kw OR displacement:ti,ab,kw OR dislodgement:ti,ab,kw OR slipping:ti,ab,kw OR transposition:ti,ab,kw OR dislocation:ti,ab,kw OR shift:ti,ab,kw OR extraction:ti,ab,kw OR extrusion:ti,ab,kw OR movement:ti,ab,kw OR relocation:ti,ab,kw OR revision:ti,ab,kw

Cochrane

(cochlear:ti,ab,kw AND implant*:ti,ab,kw) OR (cochlear:ti,ab,kw AND prosthes*:ti,ab,kw) OR (cochlear:ti,ab,kw AND prosthesis:ti,ab,kw AND system:ti,ab,kw) OR (auditory:ti,ab,kw AND prosthes*:ti,ab,kw) OR 'cochlea prosthesis'/exp OR 'cochlear implantation'/exp OR ‘cochlear implant’/exp

AND

complication*:ti,ab,kw OR migration:ti,ab,kw OR displacement:ti,ab,kw OR dislodgement:ti,ab,kw OR slipping:ti,ab,kw OR transposition:ti,ab,kw OR dislocation:ti,ab,kw OR shift:ti,ab,kw OR extraction:ti,ab,kw OR extrusion:ti,ab,kw OR movement:ti,ab,kw OR relocation:ti,ab,kw OR revision:ti,ab,kw

Web of Science

TOPIC: (auditory) AND TOPIC: (prosthes*) OR TOPIC: (cochlear) AND TOPIC: (prosthesis) AND TOPIC: (system) OR TOPIC: (cochlear) AND TOPIC: (prosthes*) OR TOPIC: (cochlear) AND TOPIC: (implant*)

AND

(complication*) OR TOPIC: (migration) OR TOPIC: (displacement) OR TOPIC: (dislodgement) OR TOPIC: (slipping) OR TOPIC: (transposition) OR TOPIC: (dislocation) OR TOPIC: (movement) OR TOPIC: (relocation) OR TOPIC: (shift) OR TOPIC: (extraction) OR TOPIC: (extrusion) OR TOPIC: (revision)

CINAHL

S1: TI cochlear AND TI implant*

S2: AB cochlear AND AB implant*

S3: TI cochlear AND TI prosthes*

S4: AB cochlear AND AB prosthes*

S5: TI cochlear AND TI prosthesis AND TI system

S6: AB cochlear AND AB prosthesis AND AB system

S7: TI auditory AND TI prosthes*

S8: AB auditory AND AB prosthes*

S9: S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8

S13: (MH "Cochlear Implant")

S14: S9 OR S13

S10: TI complication* OR TI migration OR TI displacement OR TI dislodgement OR TI slipping OR TI transposition OR TI dislocation OR TI movement OR TI relocation OR TI shift OR TI extraction OR TI extrusion

S11: AB complication* OR AB migration OR AB displacement OR AB dislodgement OR AB slipping OR AB transposition OR AB dislocation OR AB movement OR AB relocation OR AB shift OR AB extraction OR AB extrusion

S12: TI revision OR AB revision

S15: S10 OR S11 OR S12

Final search S16: S14 AND S15

Supplemental Content 2. Adapted Newcastle-Ottawa Scale for cohort studies

Categories	Items	Definition of low risk	Definition of high risk
Selection	Representativeness of the exposed cohort. We defined exposure as a patient cohort that undergoes cochlear implantation with a specific R/S device fixation technique.	The exposed cohort was truly or somewhat representative of the average patient group eligible for cochlear implantation in the community	The exposed cohort was a selected group of users or there was no description of the derivation of the cohort
	Selection of the comparison cohort. We defined as a cohort whose R/S device was fixated with a different fixation technique.	The patients are drawn from the same community as the exposed cohort	The non exposed cohort was drawn from a different source or there was no description of the derivation of the non exposed cohort
	Ascertainment of exposure	The data were collected from a secure record (e.g. surgical records) or via record linkage	The data were based on written self reports or there was no description
	Demonstration that outcome of interest was not present at start of study	This item was nog applicable	
Comparability	Comparability of cohorts on the basis of the design or analysis	The cohorts were operated on by the same surgeon	The cohorts were operated on by different surgeons
Outcome	Assessment of outcome	The outcome was assessed by means of an objective method (imaging or otherwise)	The outcome was assessed by self report (by the clinician or patient) or there was no description of the assessment method
	Length of follow up	Follow up was ≥ 12 months.	Follow up was < 12 months
	Adequacy of follow up	There was no loss to follow up or loss to follow up was unlikely to introduce bias (< 10% loss to follow up, or description provided of those lost)	Follow up rate < 10% and no description of those lost or no statement is given on loss to follow up

Supplemental Content 3. Excluded studies during full text assessment

Study design	n = 52
Conference abstract	35
Case report	4
Letter to the editor	1
Not original research	3
Technical note	7
Survey study	2
Study population	**n = 5**
Exclusively pediatric cases	4
Age of study population unclear	1
Methods	**n = 192**
Fixation of the R/S device not described	131
Migration of R/S device or electrode not primary/secondary outcome	54
Use of bony tie-down sutures to secure R/S device	7
Full text not available	**n = 26**
Total	**N = 275**

Supplemental Content 4. Characteristics of excluded studies

Study	Reason for exclusion
Guldiken 2011	Study population: overlapping cohort with included study
Dagkiran 2020	Study population: unclear if the study population consisted of a minimum of 10 adult cases
Jethanamest 2014	Study population: unclear if the study population consisted of a minimum of 10 adult cases
Lavinsky-Wolff 2012	Study population: unclear if the study population consisted of a minimum of 10 adult cases
Pamuk 2018	Study population: unclear if the study population consisted of a minimum of 10 adult cases
Sweeney 2015	Study population: unclear if the study population consisted of a minimum of 10 adult cases
Ulug 2009	Study population: unclear if the study population consisted of a minimum of 10 adult cases

CHAPTER 4

Cochlear implant receiver location and migration: experimental validation pilot study of a clinically applicable screening method

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A.L. Smit
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Abstract

Objectives: Postoperative follow-up after cochlear implantation lacks a reliable screening method to detect cochlear implant receiver device migration. This study aims to validate a clinically applicable method to assess the position and migration of the cochlear implant receiver device.

Study design: Validation study.

Setting: Tertiary university medical centre.

Participants and method: To assess the cochlear implant receiver device location, round markers representing the external magnet were placed on both sides of the head of volunteers. Four independent clinicians took measurements of the distances between reference points on the head and the centre of the marker. The reference points were: the lateral canthus (LC), tragus tip (TT), the mastoid angle (MA) and the mandibular angle (AM).

Main outcome measures: The inter-clinician reliability was determined by calculating the intraclass correlation coefficient (ICC) and confidence interval (CI) with a two-way mixed model and both consistency and absolute agreement types for each distance.

Results: Eight volunteers were included resulting in 16 individual cases. The consistency type ICC's for each reference point were: LC 0.90 (CI = 0.80, 0.96), TT 0.83 (CI = 0.69, 0.93), MA 0.75 (CI = 0.56, 0.89) and AM 0.29 (CI = 0.05, 0.59). The absolute agreement ICC's were: LC 0.87 (CI = 0.73, 0.95), TT 0.83 (CI = 0.68, 0.93), MA 0.68 (CI = 0.42, 0.86) and AM 0.18 (CI = 0.01, 0.46). The inter-clinician reliability was good to excellent for the lateral canthus and tragus tip reference points.

Conclusions: The cochlear receiver device location can be assessed reliably by measuring the distance between the LC, TT and the external magnet. This method can be used to registrate implant receiver location after implantation and detect implant migration postoperatively.

Introduction

Cochlear implantation, first attempted in the 1970's, provides hearing through electrical stimulation for patients with sensorineural hearing loss.[1] Nowadays it is a reliable and safe procedure.[2–4] The advances in technology and the refinement of surgical techniques (even with broadening indication and age range) have led to low complication rates.[1,5] Amongst reported major complications are device failure, infection/wound complications, electrode and device migration, some of which require revision surgery.[5,6]

Electrode migration has been a subject of recent interest resulting in studies exploring the possibilities of imaging for accurate measurement of the electrode position.[7–9] Yet, receiver/stimulator (R/S) device migration is a less explored topic. Recent studies concerning either cochlear implantation complications or fixation techniques, report a R/S migration incidence of 0.0–0.7%.[1,2,10–12] This migration can result in various complaints: pain (e.g. by contact between the behind-the-ear device and the implant), tension headache, interaction with wearing eyeglasses, which can lead to device failure.[2,3,10] Failed fixation can result in R/S device migration and it has been suggested that inappropriate device positioning could negatively impact migration.[2,13,14] Conventionally, the device is positioned roughly in the region supero-posteriorly from the pinna in an angle around 45–60° from the Frankfurt line.[15] In the past years several techniques have been described to fixate the implant. These include drilling a bony bed (with or without a canal directing the electrode array towards the mastoid cavity) and tight sutures to stabilize the implant or a screw fixation system.[16] Recent scientific reports showed that solely a tight subperiostal pocket might be sufficient to position the implant without any further drilling of the bone of the temporal cortex.[10,17] Attempts have been made to establish the safety of certain fixation techniques by reporting complications. However, none of these studies use objective and validated tools to assess the position and possible migration of the R/S device. Additionally, long term follow-up is often missing.

The possible negative consequences and the lack of objective assessment in the literature of device migration underline the need for a validated and robust method to detect R/S device migration. Only a few studies have valuated methods to objectively assess the exact location of the R/S direct postoperatively and during follow up. Two studies have recently introduced a method to evaluate migration of the R/S using different reference points.[18,19] Other studies have used imaging like computed tomography (CT) to determine the position of the R/S device.[13,20] These studies lack methodological and statistical strength to prove reliability of the proposed measurement method.[18,21] Additionally, the proposed techniques are time-consuming, expensive and provide radiation-exposure that might be seen as too

much a burden for cochlear implanted patients without complaints. We opted for a more patient-friendly, inexpensive and practical method. To determine the exact location of the R/S device on the scalp we developed a model to measure the distance between anatomical reference points and the cochlear implant transmitter. With this study we aim to validate this method to assess the position of the cochlear implant R/S device.

Materials and methods

Ethical considerations

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from all participants. The Medical Research Ethics Committee of the University Medical Centre Utrecht (WAG/mb/19/025018) officially declared this study exempt from official approval as the Medical Research Involving Human Subjects Act (WMO) does not apply.

Study design

A pilot study was conducted to design and validate a measuring method to assess the position of the cochlear implant R/S device. For this proof-of-concept study we used healthy volunteers. As the transmitter connects to the R/S device by the internal magnet, the transmitter's centre was used as a reference point to determine the position of the R/S device externally. We measured the distance between certain anatomical reference points and the transmitter. The transmitter magnet was represented by a round adhesive marker placed postero-superiorly of the ear. These markers were placed on both sides of the head of the volunteer directly on the scalp (if the volunteer was bald) or on the hair (which was pulled into a bun) (see Figure 4.1). Placement of the markers was done at random. Four clinicians with variable expertise in the field of cochlear implantation surgery, namely two members of staff, one fellow and one medical student, took the assigned measurements independently. They were given written instructions and carried out the measurements without any additional training. The use of volunteers allowed a high number of raters and sequential measurements under similar conditions using both sides of the head. Either side of each volunteer's head were seen as two individual cases.

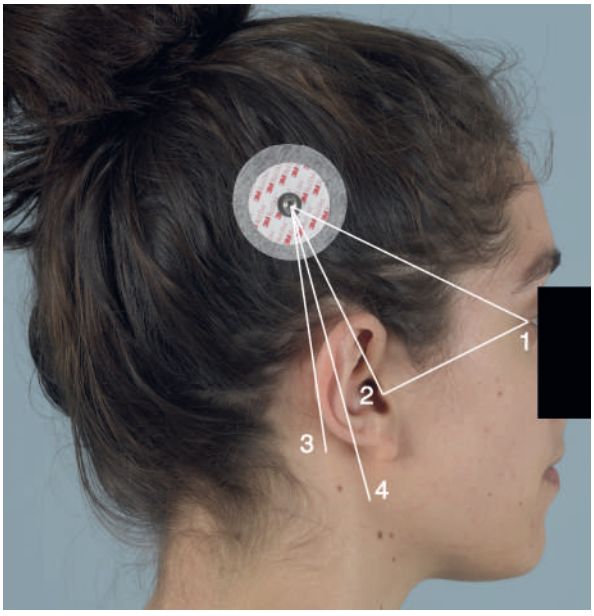

Figure 4.1: An adhesive marker was placed postero-superiorly of the ear. The numbers represent the reference points: 1 = lateral canthus (LC), 2 = the tip of the tragus (TT), 3 = the mastoid angle (MA) and 4 = the mandibular angle (AM). Written consent was obtained from the individual for the use of this image.

Measurement method

The reference points chosen are the lateral canthus (LC), the tip of the tragus (TT), the mastoid angle (MA) and the mandibular angle (AM). Measurements between those points and the centre of the adhesive marker were taken, as well as the distance between the lateral canthus and the tragus tip as a control measurement. A flexible measuring tape was used.

Statistical analysis

Data were analysed using IBM SPSS Statistics for Windows (version 21.0; IBM Corp., Armonk, NY, USA). Measurements between the LC, TT, MA, AM and the marker as well as between the LC and TT were evaluated. We used different reference points due to expected variation of measurement accuracy. To determine reliability between reference points and suitability for clinical practice, intraclass correlation coefficients (ICC) (single measures) with 95% confidence interval (CI) were calculated. This was executed via a two-way mixed model and both consistency and absolute agreement type. We considered ICC values less than 0.4 indicative of poor reliability. Values between 0.4 and 0.75 indicative of moderate reliability, 0.75 and 0.90 indicative of good reliability and ICC values ≥ 0.90 indicative of excellent reliability. These thresholds are based on existing literature. However

the ICC should be interpreted with the sample variability in mind. Therefore we calculate the range of measurement per distance to illustrate the homogeneity of the subjects. Small inter-subject variability results in a depress of the ICC.[22] Means and standard deviation were calculated for each case per distance and for each clinician per distance. This study will be reported according to the guidelines for reporting reliability and agreement and according to the STROBE statement.[23]

Results

A total of nine volunteers were measured by four clinicians on both sides of the head. One volunteer was excluded from the study. The adhesive marker of the excluded volunteer was displaced during the measurements due to the hair bun coming loose before measurements could be completed. This resulted in a total of 16 individual cases (see Supplementary Material). The range of the measurements per distance were as follows: LC to marker 130–169 mm, TT to marker 75–100 mm, MA to marker 65–111 mm, AM to marker 113–158 mm and LC to TT 73–92 mm (Table 4.1). The standard deviation of the mean range calculated for each case per distance was as follows: LC to marker 0.5 to 5.2 mm, TT to marker 1.0 to 6.2 mm, MA to marker 1.6 to 10.2 mm, AM to marker 2.4 to 13.7 mm and LC to TT was 1.3 to 6.2 mm. Furthermore, the standard deviation extracted from all clinicians per distance was between 3.1 and 9.5 mm (Table 4.1).

Table 4.1: Measurements per distance (mm) for all raters and ratios of measurement

	Median (range)				
Raters	LC to magnet	TT to magnet	MA to magnet	AM to magnet	LC to TT
A	147.5 (132–169)	88.5 (76–100)	94.0 (75–110)	134.0 (120–141)	85.0 (80–92)
B	148.0 (132–160)	88.5 (75–100)	93.0 (83–101)	140.0 (130–154)	84.0 (75–89)
C	147.5 (133–163)	89.0 (73–100)	92.5 (80–111)	137.5 (120–158)	85.0 (80–92)
D	145.5 (128–159)	88.0 (70–98)	89.5 (65–108)	126.7 (113–146)	79.5 (73–87)

LC = lateral canthus, TT = tragus tip, MA = mastoid angle, AM = mandibular angle, SD = standard deviation.

The ICC's regarding the various distances calculated with a consistency type and absolute agreement type are found in Table 4.2. The ICC's of LC to marker and TT to marker for both absolute agreement and consistency type are good to excellent. Whereas MA to marker and AM to marker ICC's are moderate to poor.

Table 4.2: Range of measurements per distance (mm) and intra-class correlation coefficient with 95% confidence interval

		Consistency type		Absolute agreement type	
Measured distance	Median (range)	ICC	95% CI	ICC	95% CI
LC to marker	148.0 (130–169)	0.90	[0.80, 0.96]	0.87	[0.76, 0.93]
TT to marker	89.0 (75–100)	0.83	[0.69, 0.93]	0.74	[0.55, 0.88]
MA marker	92.0 (65–111)	0.75	[0.56, 0.89]	0.65	[0.44, 0.83]
AM to marker	135.0 (113–158)	0.29	[0.05, 0.59]	0.26	[0.04, 0.55]
LC to TT	84.5 (73–92)	0.50	[0.25, 0.74]	0.47	[0.24, 0.71]

LC = lateral canthus, TT = tragus tip, MA = mastoid angle, AM = mandibular angle, SD = standard deviation, ICC = intra-class correlation coefficient, CI = confidence interval.

Discussion

As device migration can result in major difficulties for the patient, which in some cases necessitates revision surgery, detection of migration can be of value for the patient. However, simple and validated techniques are missing. With this study, we aimed to validate a method to easily assess the position of R/S device by measuring distances between the magnet of the transmitter and certain anatomical reference points. The ICC's found for the distances LC to marker and TT to marker indicate good to excellent reliability, also considering the 95% confidence interval. By this, the here presented screening method using these distances can be used to determine device position postoperatively. Clinicians should compare the results of the measurements from each outpatient clinic visit in order to detect gradual changes as a possible indication of migration.

In our study the mean of the measurement differences between raters for the distances LC to magnet and TT to magnet were 5.3 mm (SD ± 2.8) and 5.9 mm (SD ± 2.5) respectively (see Supplementary Material). In a previous study by Maxwell et al about R/S migration, measurement differences exceeding 5 mm were proposed as true migration. they reported a migration of the R/S device in 25.9% of the implants within the first 6 months postoperatively ($p = 0.43$).[24] Though, by the lack of using a validated measurement method in the study and without any consensus regarding a clinically relevant R/S device migration no conclusions can be made which cut off values must be met to be defined as 'true migration'.

In recent years, assessment of the precise position of the R/S of the cochlear implant seems to gain momentum as a topic of international interest.[13,18,20] There is need for a validated measurement method that can be integrated in routine outpatient clinical follow up. This method provides clinicians with an objective and easy to use tool to detect migration. In addition to clinical use, this method could provide an objective tool to report reliability

of device fixation techniques and quality of care in the literature. We suspect device migration to be an underreported clinical parameter after cochlear implantation. This can be demonstrated by the study of Lui et al. They reported slight device migration in all included patients when objectively assessing the R/S position and potential migration by using CT scanning (mean ± SD; 2.1 ± 1.4 mm).[13] Although these migrations would not have been detected by our measurement method, it is noteworthy that this objective method detected R/S migration in all included patients.

In this study we did not provide the clinicians with any training before measuring the volunteers. This could lead to differences in measuring technique between clinicians (as seen in Table 4.1), but it did not lower the inter-clinician reliability of the method.

Strengths and limitations

To the best of our knowledge, this is the first validation study of a measurement method for the assessment of the R/S device position that is low-cost, easy to apply, does not expose the patient to radioactive environment and can be used during follow-up in an outpatient setting. Until now there is no validated measurement tool with which comparison of measurements is possible. Additionally, patients sometimes are seen by different clinicians in which inter-rater reliability can influence outcome which is taken in account in the presented study. The measurement method in this study is validated using recommended statistical analysis.[21,22] One limitation of the technique is the need to pull the flexible measurement tape over the pinna, which could influence the accuracy of the measurements. However, the ICC from this measurement from the TT to the marker was satisfactory. A limitation of this study is that we chose to do this pilot study on a small group of healthy individuals, using markers rather than cochlear transmitters to carry out the measurements. The adhesive markers had a clear centre unlike the transmitter magnet. The marker was fixated on the hair rather than the scalp, resulting in unwanted marker mobility. This can be demonstrated by the excluded volunteer. During the measurements of this volunteer it was clear that misplacement of the adhesive marker had taken place due to loosening of the hair. Positional shifts due to hair movement could have occurred also to other volunteers but none was detected at the time of the measurements. However, in a clinical setting the transmitter is attached firmly on the scalp thus eliminating this factor. Finally, this method overcomes the problem of the different processor styles.

Future prospective

The provided measurement method infers future investigation in implanted patients to extrapolate the results in real-life cochlear implant users and relate outcome to fixation techniques. Establishment of a reference standard regarding implant migration assessment is necessary as well as proper postoperative follow-up to detect the device location and potential migration. The relation between implant position and migration and subjective patient experience of this outcome should be part of this investigation.

Conclusion

Measuring distances between the lateral canthus, the tragus tip and the marker as a proxy for the transmitter magnet of a CI, as described in this study, is a reliable method to assess the position of the R/S device. The technique could be implemented during follow-up of cochlear implant patients as an easy to use, radiation-free tool to screen for migration. The next step would be the validation of this method in cochlear implant patients and the relation between migration and subjective quality of life outcome assessment.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Author contributions

LM and AS performed the experiments. LM performed the calculations and wrote the manuscript with input from all authors. LM, IS, AS and HT were involved in the conception and design of the study, provided critical feedback, and helped shape the analysis and final manuscript.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fsurg.2019.00078/full#supplementary-material.

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CHAPTER 5

Cochlear implant positioning: development and validation of an automatic method using computed tomography image analysis

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Submitted to Frontiers in Surgery

Abstract

Aim: The aim of this study was to preoperatively asses the feasibility of drilling a bony recess for the fixation of a cochlear implant in the temporal bone. Even though complications are rare with cochlear implantations, drilling at the site of implantation have resulted in hematoma or cerebrospinal fluid leakage. Mainly in cases with a reduced temporal bone thickness, the risk for complications has increased, such as in paediatric patients.

Methods: An in-house designed semi-automatic algorithm was developed to analyse a 3D model of the skull. The feasibility of drilling the recess was determined by a gradient descent method to search for the thickest part of the temporal bone. Feasibility was determined by the residual bone thickness which was calculated after a simulated drilling of the recess at the thickest position. An initial validation of the algorithm was performed by measuring the accuracy of the algorithm on five 3D models with known thickest locations for the recess. The accuracy was determined by a part comparison between the known position and algorithm provided position.

Results: In four of the five validation models a standard deviation for accuracy below the predetermined cut-off value of 4.2 mm was achieved between the actual thickest position and the position determined by the algorithm. Furthermore, the residual thickness calculated by the algorithm showed a high agreement (max. 0.02 mm difference) with the actual thickness.

Conclusion: With the developed algorithm, a semi-automatic method was created to analyse the temporal bone thickness within a specified region of interest on the skull. Thereby, providing indications for surgical feasibility, potential risks for anatomical structures and impact on procedure time of cochlear implantation. This method could be a valuable research tool to assess feasibility of drilling a recess in patients with thin temporal bones.

Introduction

Born deaf or severely auditory impaired, significantly reduces the societal chances of a child.[1] Therefore, a cochlear implant (CI) is a medical solution which has shown to significantly improve auditory capabilities.[2]

Implantation of the internal component of the CI consists of insertion of the electrode array in the cochlea, and fixation of the receiver/stimulator (R/S) device on the skull. Although there is extensive literature available for the different surgical techniques of electrode array implantation, definitive evidence regarding optimal fixation techniques of the R/S device is lacking.[3] However, migration of the device could lead to surgical complications such as headache, speech processor problems, hematoma, or device failure which can lead to revision surgery.[4–9] Two main methods for fixation are being used today by CI surgeons, namely the bony recess and the subperiosteal pocket technique.[10,11] The mostly used bony fixation technique requires drilling a recess in the temporal bone to embed the R/S device. Usually, a trough, tunnel or overhang is made for protection of the wire. Some CI surgeons use additional sutures or screws to secure the implant. On the other hand, Balkany et al., introduced the more preservative subperiosteal pocket technique in 2009 by which the implant is held in place by the soft tissue of the temporalis muscle and pericranium.[12]

Currently when drilling a bony recess for CI fixation, the location and depth of the recess is chosen perioperatively based on the appropriate distance between transmitter and ear, the shape of the skull, the CI model implanted, and manufacturers guidelines for R/S device placement.[10] However, bone thickness is usually not considered before implantation. The depth of the recess is determined while drilling into the temporal bone during surgery.[10]

Even though, cochlear implantation is a relatively safe procedure with few complications, several cases have presented with hematoma or cerebrospinal fluid leakage after compromising the underlying dura mater, vessels and sigmoid sinus at the site of implantation during drilling.[13–16] Paediatric patients have a higher chance of exposure of the dura mater due to a thinner temporal bone.[17–19] For younger patients it can be questioned whether the temporal bone is thick enough for safe CI placement.

To assess if embedment of the R/S device with sufficient depth according to the guidelines of the manufacturers is possible, preoperative analysis of the temporal bone thickness is needed. Currently, highly accurate and detailed bone segmentations can be calculated from standard computed tomography imaging. These bone segmentations can be used for calculations and measurements in three dimensional space. The results of these three dimensional analysis can provide a preoperative planning to better visualise how to perform

the surgery and which structures are at risk during surgery. The feasibility of the surgery can be tested preoperatively to increase its success. Therefore, the aim of this study was to develop and validate an in-house designed algorithm. This algorithm determines if drilling a bony recess for the fixation of the R/S device is feasible in the temporal bone. This could be used in cases where the thickness of the temporal bone is expected to be inadequate, for example in cases of paediatric cochlear implantation.

Materials and methods

Ethics

All procedures performed in this study involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Written informed consent was obtained from the patient whose computed tomography imaging was used in this study.

Data acquisition

An existing CT scan of a human subject was used (Philips IQon, Netherlands; 236 mA, 120 kV, 0.9 mm slice thickness). Images were stored in DICOM format. Using the segmentation feature in Mimics (version 24.0, Materialise NV, Leuven, Belgium), part of the skull was segmented and reconstructed into a 3D model by thresholding and manual denotation. This 3D model was then imported into 3-Matic (version 16.0, Materialise. Leuven, Belgium). The CI used for this study was the Cochlear CI512, an explanted device from a patient due to hardware failure. Volume data of the CI were acquired by scanning the implant using a 3shape laboratory scanner (3shape, Copenhagen, Denmark). The data was reconstructed into a 3D model.

Thickness analysis

To test the feasibility of drilling a recess in the temporal bone, without exposing the dura mater, an in-house designed algorithm was designed. Input for the algorithm included a 3D model of the CI recess, a 3D model of the skull and the positions of the right and left proximal external auditory canal and the base of the left orbita. These three landmarks were manually denotated on the CT image and used to automatically determine a region of interest (ROI) on the temporal bone within which the recess could be drilled. This ROI was based on expert opinion (senior CI surgeon, HT) and on manufacturer guidelines.

The boundaries of the ROI were defined by several anatomical planes (Figure 5.1). The region proximal of the Frankfurt plane and posterior of the 90-degrees plane locates the R/S device behind the ear. The minimum distance of 20 mm was needed to provide enough space for the mastoidectomy required to insert the electrode array into the cochlea. To limit the size of the incision needed to implant the R/S device, a maximum of 30 mm was selected.

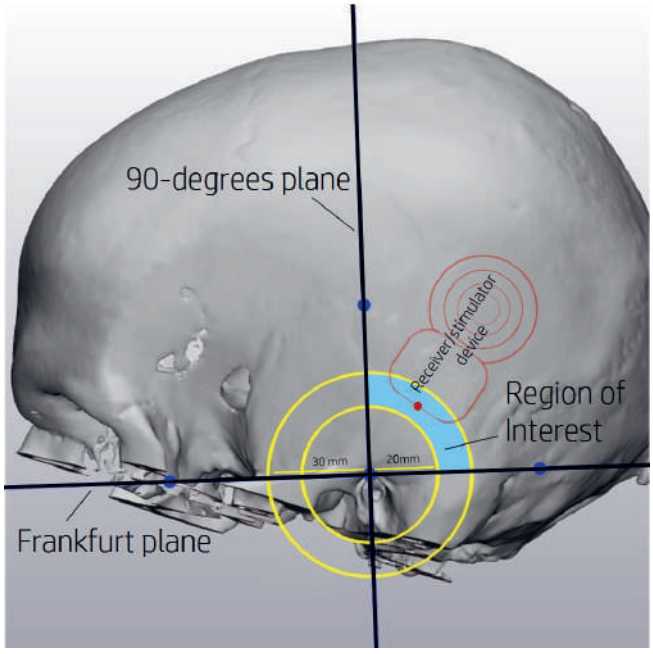

Figure 5.1: Region of Interest (ROI) defined proximal of the Frankfurt plane and posterior of the 90-degrees plane. A minimum distance of 20 mm and a maximum of 30 mm from the external auditory canal further defines the ROI. An example position of the R/S device is depicted by the red outline.

The feasibility was determined by a systematic search performed by the algorithm. This process was performed in two steps. Firstly, a suitable position for the recess was searched iteratively within the ROI, each iteration searching for a thicker position (Step 1 of Figure 5.2). Secondly, the feasibility of drilling the recess on the final location was determined (Step 2 of Figure 5.2).

The iterative search within the ROI was performed by a gradient descent method which selects for each iteration a new position based on the direction and intensity of the gradient of the previous iteration. The gradient descent algorithm used a learning rate of 0.7, a step size of 0.8 mm and had a limit of 30 iterations to achieve an optimal location.

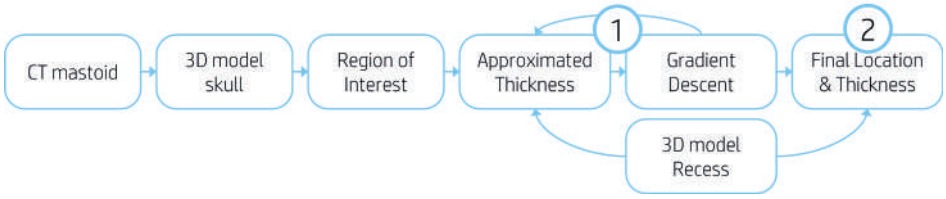

Figure 5.2: Flow chart of algorithm processes. 1) Iterative search for thicker position. 2) Recess feasibility calculation.

To minimise chance of protrusions by the recess, while limiting the computational power needed for the algorithm, six reference points based on the size of the R/S device model were used to perform thickness measurements (Figure 5.3). Furthermore, the recess has an increasing depth. To incorporate this gradient, thickness weights were added to each reference point based on the recess depth.

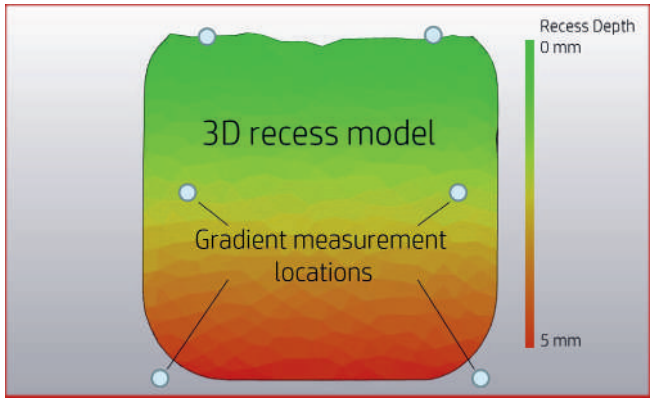

Figure 5.3: Locations of six reference points in relation to the recess. Colouring representing recess depth related to the original skull surface.

The locations of the recess within the ROI were defined by a length and angle (Figure 5.4). The length is a distance measurement between the external auditory canal and the deepest side of the recess. The angle is measured between the Frankfurt plane and the line created for the length measurement.

Feasibility of drilling the recess was calculated at the final location determined by the gradient descent method (Figure 5.5). The residual thickness after recess placement was calculated with a resolution of 2x2 mm. If no residual thickness of the skull at any position within the recess was measured, the drilling of a bony recess on the skull was defined as unfeasible.

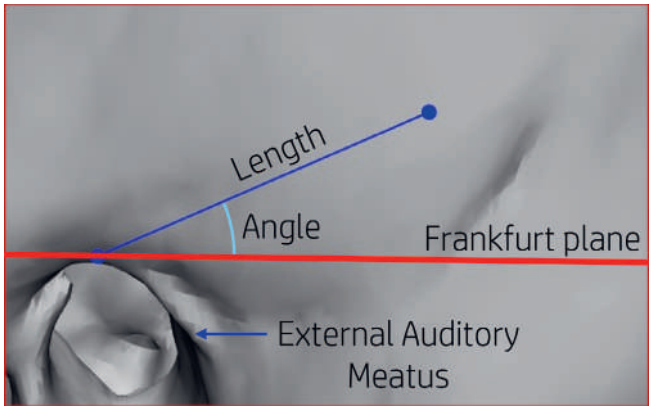

Figure 5.4: Positions on the skull are defined by a length and angle measured from the proximal point of the external auditory canal in relation to the Frankfurt plane.

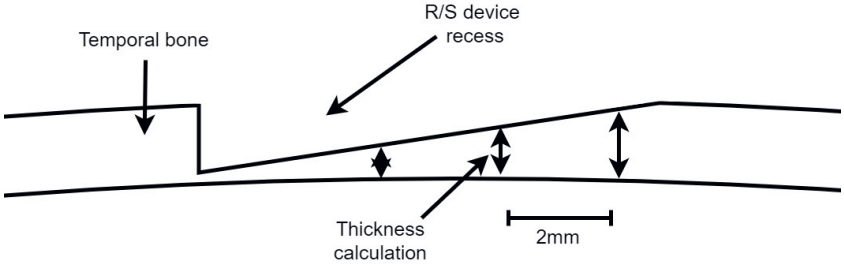

Figure 5.5: Calculation of R/S device recess feasibility by measuring the thickness of the temporal bone after virtual placement of the recess.

Validation analysis

To validate the developed algorithm, two validations were performed. First, three 3D spherical models were designed with an insufficient thickness for the recess. The models had a wall thickness of 4.0 mm, 4.5 mm and 4.8 mm respectively. This was done to determine the accuracy of the thickness measurement and to assess if the algorithm would correct identify models with insufficient bone thickness.

Secondly, 3D models of the skull with a known optimal location for embedment of the R/S device were designed to assess the algorithms ability to identify this area with sufficient bone thickness. The contour of the R/S device was placed within the ROI of the skull and was used to create a local offset. The optimal location for each model was chosen such that different scenarios needed to be solved by the algorithm. These included positions at extreme locations in the ROI. A total of five models from one patient were analysed using the algorithm.

The accuracy between the planned location and the location that was found by the algorithm was calculated by two methods. First a part comparison analysis was performed, resulting in the standard deviation (std) between the two parts. Second the overlapping volume between the planned and algorithmically determined locations was calculated. These calculations were performed by the 3-Matic software (version 16.0, Materialise. Leuven, Belgium).

The optimal locations designed for the 3D models used a 3 mm larger R/S device contour. Therefore, the R/S device could translate 3 mm in the x- and y-direction within the optimal location. Based on the Pythagorean theorem, a standard deviation of 4.2 mm or less was considered to be a valid outcome in which the algorithm provided accurate results. The overlapping volume was calculated by dividing the colliding volume with the total volume of the device and multiplying it with 100%.

Results

The three models with insufficient thickness were correctly identified by the algorithm. The mean thickness measured by the algorithm were 4.02 mm, 4.52 mm and 4.82 mm for the 4.0 mm, 4.5 mm and 4.8 mm models respectively. All with a standard deviation of 0.01 mm.

The standard deviations of the second validation analysis ranged from 0.70 to 5.40 mm in the five models (Table 5.1). For model 1, 3, 4 and 5 standard deviation of less than 4.2 mm was achieved. Model 2 did not achieve a standard deviation below the cut-off value. Overlap volumes of model 4 and 5 exceeded 80%. Model 2 performed worst with a standard deviation of 5.40 and an overlap volume of only 36%. Model 5 performed the best with a standard deviation of only 0.78 and an overlap volume of 87%.

Table 5.1: Results from part comparison analysis and volume overlap for every model

Model	Std (mm)	Overlap volume (%)
1	2.20	65.12
2	5.40	35.75
3	1.85	69.94
4	1.25	82.45
5	0.78	87.00

Discussion

In this study we aimed to develop and validate a proof of concept of an algorithm to determine if a recess of the R/S device of a cochlear implant is feasible in the temporal bone ROI. The designed algorithm uses preoperative CT scan imaging and 3D medical software, and is designed to be used by clinicians for research and clinical purposes. Validation of the algorithm was performed to test the two steps of the algorithm. We first tested the ability of the algorithm to measure bone thickness accurately and detect insufficient bone thickness. Then we assessed if the optimal thickness location could be detected by the algorithm. Five different 3D models with optimal thickness locations were created based on CT imaging of one patient to validate the model. The five created models had sufficient thickness for safe R/S placement during surgery, as described by the algorithm. The algorithm poorly determined the optimal location for model 2. While, the optimal locations for models 1, 3, 4 and 5 were determined moderately to good by the algorithm.

3D Preoperative analysis of the temporal bone thickness to determine the feasibility of a R/S device recess has been performed before.[17,18] However, standard locations for the recess were used to determine the feasibility, not accounting for differences in anatomy of individuals. The aim of these studies were to calculate a general chance for recess feasibility instead of the personalised analysis provided by the described algorithm. This study was designed to accommodate the needs of the clinician by providing an easy to use, adaptable preoperative analysis method that incorporates operational parameters. Subsequently, the developed algorithm provides more insight in the location of the recess and thereby the relationship with surrounding anatomical structures. The preoperative analysis could provide indications for surgical feasibility, potential risks for anatomical structures and impact on procedure time. In paediatric patients, a higher risk of adverse operational events exists due to their thinner temporal bones. Prior knowledge on the feasibility of the R/S device recess could reduce the risks of the CI implantation for these paediatric patients. The described algorithm is a first step in providing a detailed analysis of the temporal bone thickness and surgical feasibility for cochlear implantation.

The methodology used for the algorithm provides high flexibility for calculation of applicability. The recess model can easily be changed to fit alternative parameters of the ROI, the CI model used, and the recess dimensions. Although the algorithm was designed for thickness feasibility measurement of a R/S device recess, it could also be used for any implantable device requiring a bony recess such as a subcutaneous bone conduction device. Furthermore, the time required to perform the analysis is minimal thanks to the limited manual input needed, providing physicians readily available results.

Limitations of this application include the added time and availability of the software needed to perform the analysis. The developed algorithm takes approximately 10 minutes to apply, however the use of the software applications do require some basic training. Furthermore, the models designed for the validation of the algorithm were derived from a single patient. A reason why future clinical implementation studies will be required. These models retained most of the natural organic features of the skull, thereby potentially introducing confounders. Lastly, the sample size of the used validation models was small. Further validation is needed on a larger scale and optimization of the workflow is necessary, before it can be used in clinic. The robustness of the current gradient descent algorithm can be improved by addition of a stochastic component. Nevertheless, the proposed algorithm is a proof of concept for the use of automatic thickness measurements in cochlear implantation. Plentiful possibilities exist for further development and optimisation of the algorithm.

With the developed algorithm a semi-automatic method has been created to analyse the temporal bone thickness within a specified ROI. The algorithm provides an easy and flexible way to determine if a recess for the R/S device of a cochlear implant can be made. This method could be a valuable tool to assess feasibility of drilling in patients with thin temporal bones for research purposes. For clinical purposes further validation and optimization is needed.

Tools

Mimics (RRID:SCR_012153)

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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CHAPTER 6

Retrospective cohort study analyzing temporal bone cortical thickness and perioperative complication rate, in pediatric cochlear implantation

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Abstract

Hypothesis: We aim to assess the feasibility of drilling a bony recess adequate for cochlear implant (CI) receiver/stimulator (R/S) device embedment, in pediatric patients of different age groups, without exposing the dura matter. We also aim to review our pediatric cohort that received a CI in our center, reporting the occurred complications and device failure rates using different surgical techniques for the cochlear approach and fixation of the implant.

Background: Cochlear implant fixation in pediatric patients by drilling out a bony recess to lower the profile and accommodate the implant, can be challenging due to the thin cranial bone. The dura matter can be exposed or damaged leading to possible major complications and surgical revision. A minimally invasive fixation method such as the subperiosteal tight pocket technique could avoid such risks, however cochlear implant migration could be an issue.

Methods: In this study we identified and evaluated two different pediatric groups: a randomly selected sample of pediatric patients and our pediatric CI cohort. To assess the feasibility of drilling a bony recess, we identified all pediatric patients that underwent a computed tomography (CT) scan of the skull in our center in 2021, regardless of the indication for the scan. We evaluated 96 pediatric patients (192 ears). The feasibility of drilling a bony recess was assessed, using an in-house designed algorithm in Materialise Python API, by digitally removing a ramp shaped bony recess and determining whether or not the residual skull was intact. In order to review the (peri)operative complication rate of cochlear implant surgery in our center we retrospectively identified all pediatric patients that received a CI in our tertiary center between 1996 and 2021. Patients were categorized into groups based on the surgical techniques used for cochlear approach and fixation of the R/S device. The occurrence of complications (major and minor) as well as device failure was determined.

Results: The randomly selected patient group, in which we assessed the feasibility of drilling a bony recess, showed that in 153 ears (79.7%) it was not feasible to create a bony recess without exposing the dura matter. In young children aged 0–4 years, drilling a bony recess was not feasible in almost all patients (n = 69, 98.6%). Mean minimum bone thickness of the location determined by the algorithm, in different age groups, varied from 1.84 mm in the 0–4 years, to 3.31 mm in the 15–17 years age group.

Our pediatric CI cohort included 344 cochlear implants in 230 patients with a mean age of 3 years and 7 months ± 4.1 years at time of surgery. Most implants were placed using the mastoidectomy with posterior tympanotomy (MPTA) approach technique (n = 256, 74.4%) and fixated with the bony recess fixation technique with or without bony tie-down sutures (n = 293, 85.1%). Major complications occurred in all surgical techniques groups, however the suprameatal approach (SMA) was used more often in the major complications subgroup compared to the general cohort (n = 17, 58.6% versus n = 85, 24.7% respectively). This was also the case for the patients operated with the subperiosteal tight pocket technique, although device related complications occurred in both the bony recess and the tight pocket groups.

Conclusion: According to the results of this study, drilling a bony recess for fixation of the cochlear implant without exposing the dura matter is nearly impossible for children aged zero to four years and very difficult in children aged five to nine years. The SMA approach and the tight subperiosteal technique led to more major complications in our cohort, although there was no difference between the device failure subgroups.

Introduction

For infants and children with severe to profound sensorineural hearing loss, either congenital or acquired, cochlear implantation has become standard care. Literature shows that implantation in pediatric patients at early age is beneficial for auditory development, and minimizes language delays that result from hearing loss.[1,2] Bilateral cochlear implantation (binaural stimulation) in children provides even more benefits, leads to increased audiophysiological stimulation of the auditory cortex at an early age, and is therefore the mainstay of treatment in children that meet implantation criteria in Dutch healthcare.[3,4]

Cochlear implantation surgery has been proven to be a safe procedure, with low complication rates. Revision surgery rates vary between 4.6% and 8.7%, and are mostly due to device failure as a result of which re-implantation is necessary.[5–8] Complications that are not due to device failure, such as migration or protrusion of the receiver/stimulator (R/S) device, wound infection with implant extrusion or electrode misplacement or migration can also occur.[5,9–12] The complication rate reported in the literature varies greatly between studies with reported rates of 0.6% to 30.9%.[9,11–14] Due to broadening of the indication criteria and expected improved functional outcome after bilateral cochlear implantation, more children are receiving a CI and at a younger age.[3,15]

Recent publications stress the importance of recognizing the challenges associated with operating on young children in order to prevent complications.[2,16] The standard surgical technique for cochlear implantation in our center is the mastoidectomy with posterior tympanotomy approach (MPTA). The alternative suprameatal approach (SMA) has also been used, although Bruijnzeel et al.[14] reported a higher (infectious) complication rate when using this technique. It would be informative to update and assess these data with a prolonged follow up. Another important step in the surgical procedure is the positioning and fixation of the R/S device which can be achieved by several surgical techniques. The most used bony recess technique, requires drilling a recess in the temporal bone in which the implant will reside. Usually a canal, tunnel or overhang is made for protection of the electrode array. Some CI surgeons use additional sutures, screws or wires to secure the implant. The less invasive subperiosteal pocket technique uses the soft tissue of the pericranium-temporalis muscle to fixate the implant.[17] Both techniques of CI fixation have been used in our academic medical center over the years since the start of pediatric cochlear implantation in 1996. However, our experience is that drilling a bony recess to accommodate the implant is not always feasible in young children due to insufficient skull thickness. Cochlear implant manufacturers advise a bony recess depth of at least 1.0–3.0 mm for sufficient fixation of the device, depending on the implant model.[18–20] In order to

lower the profile of the housing, an even deeper recess is required. This is challenging in infants, with their immature skull thickness. Furthermore, the dimensions of a cochlear implant demand a bony recess with a width of at least 30 mm to house the case. The curvature and irregularity of the temporal bone make embedment of a flat surface such as a CI challenging. Additionally, attempting drilling a bony recess without preoperative imaging data or planning to measure thickness, introduces possible risks to the patient. However, these attempts of drilling would be redundant if we knew that drilling a bony recess under a certain age is not feasible or necessary.

Previous studies describe an adaptation of the fixation technique where (partial) exposure of the dura is necessary and a bony island is left in the center to function as resistant and protective layer.[21–23] These studies demonstrate the difficulty of drilling in young infants and the risks involved. Possible complications associated with drilling are dural tears with subsequent cerebrospinal fluid leakage as a direct result of drilling close to the dura.[10,21,24] Other complications that have been reported (but occur very rarely) and associated with the bony recess technique are late onset hematomas, epi-/subdural hematoma, tentorial herniation, and cerebral infarction, as well as meningitis.[24–29]

Therefore, in this study we aim to assess the feasibility of drilling a bony recess adequate for CI embedment in different age groups. We also aim to review the pediatric cohort implanted in our institution, reporting the occurred complications, revision and device failure rate occurring with different surgical techniques.

Materials and methods

This mono-center, retrospective study was conducted at the University Medical Centre (UMC) Utrecht The Netherlands, in compliance with the principles of the Declaration of Helsinki. This study was exempt from approval of an ethics committee under Dutch law. Exemption was granted by the local ethical committee (Institutional Review Board of the UMC Utrecht) (METC protocol 22/560). All data was pseudonymized, thus exempt from acquiring informed consent. In this study we identified and evaluated two different pediatric groups. The first group consisted of a randomly selected sample of pediatric patients, to assess the feasibility of drilling a bony recess. The second group consisted of our pediatric CI cohort, to assess the occurrence of complications and outcome.

Feasibility of drilling a bony recess

To assess the feasibility of drilling a bony recess, we identified all pediatric patients that underwent a computed tomography (CT) scan of the skull in our center in 2021. The indications for the scans were not considered. The pseudonymized CT scans were identified via the appropriate radiologic code, made available for research. Imaging data analysis was realized using CT scans of 96 pediatric patients. These scans included the temporal bone bilaterally. Each ear was seen as an individual case, resulting in 192 cases (ears). The information of the temporal bone thickness was analyzed as follows. Scans were imported into the software program Mimics (version 24.0, Materialise NV, Leuven, Belgium) for segmentation of the scan. A 3D model of the skull was exported in Materialise 3-matic (version 16.0, Materialise. Leuven, Belgium). To determine if it was feasible to drill out a bony recess, an in-house developed and validated script was used to automate the analysis. The automation was done using Python scripting and the Materialise Python API. The analysis was performed based on the following steps (Figure 6.1). Firstly, not each location on the temporal bone is suitable for placement of the R/S device. Therefore a region on each skull was determined in which the feasibility analysis took place, defined as the region of interest (ROI). The boundaries of this region were the following: the Frankfurter Horizontal plane, a perpendicular plane originating from the external auditory canal (EAC), a minimum radius of 20 mm from the EAC and a maximum radius of 30 mm from the EAC (Figure 6.2). Secondly, a systematic search must be performed within the ROI to identify the location in which the cortical thickness would be sufficient to implant the CI. This was realized using a gradient descent algorithm that approximates the gradient of the skull thickness determined by the size and location of the bony recess. Thirdly, a 3D model of the bony recess was used to subtract digitally from the ROI (Figure 6.3). This 3D model was ramped shaped, based on the dimensions of the Cochlear CI512 model. A thickness of 5.0 mm at the anterior edge of the bony recess was used. Feasibility of drilling a bony recess was determined based on the remaining skull thickness after digital removal of the bony recess. The remaining skull had to be intact. Skull thickness descriptive data were calculated for the specific area where the bony recess was digitally made, before and after the removal of the bone. The intactness of the skull after digital removal determined the feasibility of drilling a bony recess. If the dura matter was exposed, the analysis was labeled as not feasible.

Cochlear implant cohort outcomes

In order to review the (peri)operative complication rate of cochlear implant surgery in our center, we conducted a retrospective chart review. Pediatric patients who underwent primary cochlear implant surgery in our center between January 1, 1996 and December

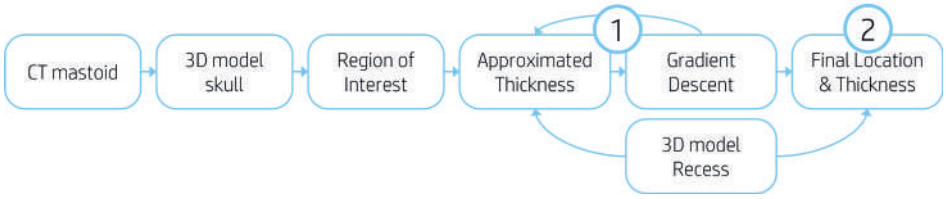

Figure 6.1: Flowchart of CT scan analysis.

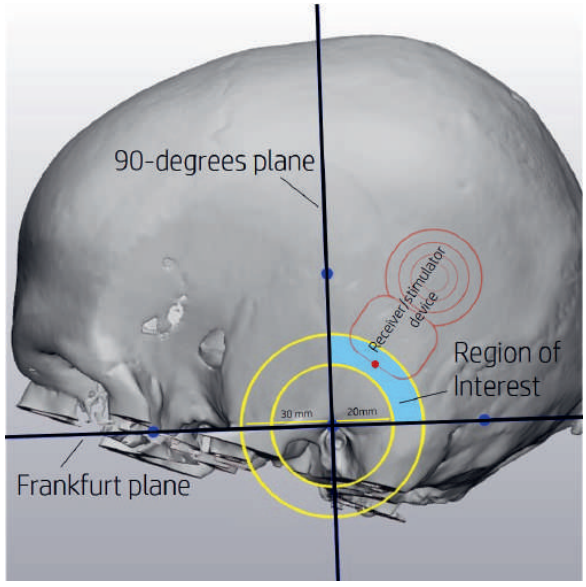

Figure 6.2: Boundaries of the region of interest: the Frankfurter Horizontal plane, a perpendicular plane originating from the external auditory canal (EAC), a minimum radius of 20 mm from the EAC and a maximum radius of 30 mm from the EAC.

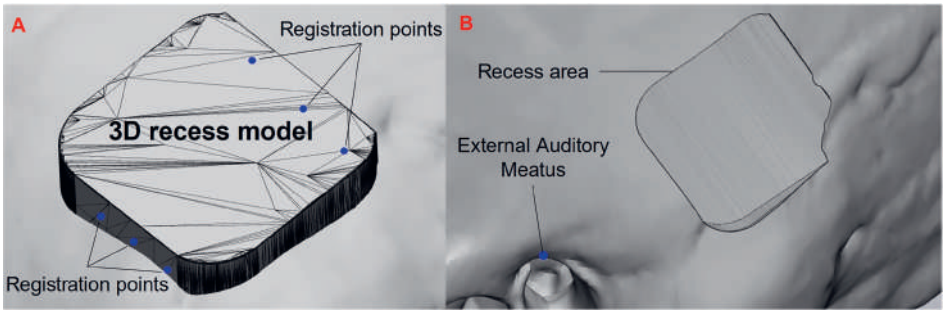

Figure 6.3: 3D recess model and recess area. **Image 6.3A** depicts a 3D recess model already in place on the skull after systematic research for best placement based on the gradient descent algorithm. The six registration points are used for thickness measurements. The recess is ramped shaped, therefore we added thickness weights to each reference point based on the recess depth. **Image 6.3B:** an example of a temporal bone after digital removal of the bony recess. The remainder of the skull is intact. In this example the algorithm determined drilling of a bony well as feasible.

31, 2021 were identified. These patients were identified from the electronic patient dossier with the code of the surgical procedure. All patients that were younger than 18 years of age at the time of implantation were included. Patients were excluded if the postoperative follow up was less than 12 months. Each operated ear was considered an individual case. Clinical data were reviewed to collect demographic records, the date of the first implant, the surgical techniques used for cochlear approach and fixation of the CI, the type of CI, complications and device failures. In our cohort both the mastoidectomy with posterior tympanotomy approach (MPTA) and the suprameatal approach (SMA) techniques were used for cochlear implantation. For the fixation of the R/S device the applied surgical techniques include drilling a bony recess with or without tie-down sutures, and the minimally invasive subperiosteal tight pocket technique. Complications were classified into major and minor depending on the degree of management, according to the proposal of Hansen et al.[30] A complication was considered as major if it was significant medical problem (e.g. meningitis), additional major surgery was required (e.g. cholesteatoma surgery or reimplantation due to a patient-related problem), explanation of the device was performed for any reason other than device-related failure, in case of any degree of permanent disability (e.g. facial nerve paralysis). Complications were considered as minor in the following cases: leading to extended hospitalization or treatment on an outpatient basis, settling spontaneously or by conservative medical treatment, managed by a minor surgical procedure (e.g. simple haematoma aspiration by syringe). Depending on the time of presentation, complications were labeled as peri- and postoperative. Perioperative complications include complications occurring during and up to 24 hours after surgery. Pre-existing conditions were not classified as a complication if encountered postoperatively. Cases in which revision surgery took place, causative mechanisms for revision such as device failure and the time between operation and revision were reported. Device failure was classified into hard or soft failure using the standardized criteria described in the 2005 in the Cochlear Implant Soft Failures Consensus Development Conference Statement.[31] This report follows the STROBE guidelines for cohort studies.

Results

Feasibility of drilling a bony recess

The randomly selected patient group, in which we assessed the feasibility of drilling a bony recess, yielded the following the results. Most ears analyzed were from male patients (n = 118, 61.5%). The largest age group was zero to four years of age (n = 70, 36.5%) (Table 6.1). In the majority of the analyzed ears, it was not feasible to drill a bony recess (n =

153, 79.7%), meaning that the remaining skull after digital removal of the bony recess was not intact in these cases. This was especially frequent in the zero to four age group (n = 69, 98.6%). We found that the minimum bone thickness in all cases in this age group was below 3 mm (Figure 6.4). As expected, the number of cases in which it was feasible to drill a bony recess increased per age group (Table 6.2).

Cochlear implant cohort outcomes

The retrospective data review of our pediatric CI cohort resulted in 383 implanted ears, 39 were excluded due to lack of information (n = 4), follow up of < 12 months (n = 32), three

Table 6.1: Feasibility of drilling a bony recess analysis results

Ears scanned (n = 192)	N	%
Gender		
Male	118	61.5%
Female	74	38.5%
Age groups		
0 to 4 years	70	36.5%
5 to 9 years	44	22.9%
10 to 14 years	52	27.1%
15 to 17 years	26	13.5%
Feasibility of drilling a bony well		
Not feasible	153	79.7%
Feasible	39	20.3%

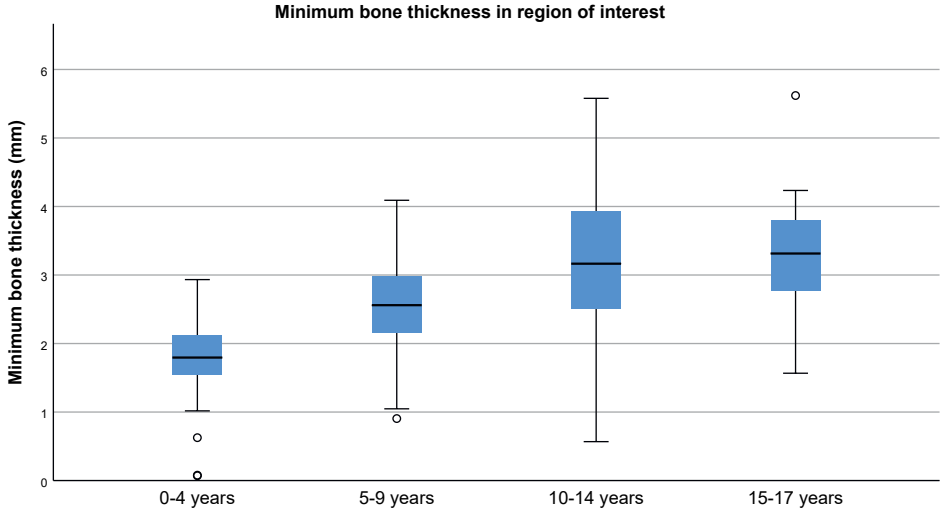

Figure 6.4: Minimum bone thickness per age group at the temporal bone location determined by the algorithm as most suitable for implantation.

cases were operated in a different medical center. A total of 344 ears of 230 patients were included in our study (Table 6.3). Ages ranged from 4 months in a child with SNHL after meningitis, to 18 years and 6 months, with a mean age of 3 years and 7 months at time of surgery. The majority of the cases (N = 229, 66.6%) were bilaterally implanted, of which 132 cases (57.6%) simultaneously. One patient was included as bilaterally implanted, but the first operation took place elsewhere. The unilateral implants were placed in 73 right and 42 left ears. Most CI's implanted were Cochlear Nucleus® devices (89.2%) followed by Med-el® (6.4%) and Advanced Bionics® (4.1%). Median follow up time was 8 years and 8 months.

Table 6.2: Feasibility of drilling a bony recess analysis per age group

Ears scanned (n = 192)	0–4 years	5–9 years	10–14 years	15–17 years
Feasibility of drilling a bony well n (%)				
Not feasible	69 (98.6%)	38 (86.4%)	35 (67.3%)	11 (42.3%)
Feasible	1 (1.4%)	6 (13.6%)	17 (32.7%)	15 (57.7%)
Minimum bone thickness (mm)				
Mean (SD)	1.84 (0.57)	2.58 (0.78)	3.10 (1.03)	3.31 (0.77)
Min	0.07	0.91	0.57	1.57
Max	2.93	4.09	5.58	5.62

Table 6.3: Demographics and clinical characteristics of cochlear implant cohort

Implants placed (n = 344)	n	%
Bilateral	229	66.6%
Bilateral sequential	97	28.2%
Bilateral simultaneous	132	38.4%
Unilateral	115	33.4%
Placement		
Right ear	73	21.2%
Left ear	42	12.2%
Indication for operation		
Congenital	185	53.8%
Meningitis	58	16.9%
Genetic condition	55	16.0%
Cytomegalovirus infection	22	6.4%
Other	20	5.8%
Missing	4	1.2%
Brand of implant		
Cochlear	307	89.2%
Med-el	23	6.7%
Advanced bionics	14	4.1%
Time of Implant Follow-up Median (range; SD)	8 y and 8 m	12 m – 25.7y; 6 y

Y = years; m= months.

Major complications

The patient records revealed 29 major complications in 29 implanted ears (26 patients); yielding a complication rate of 8.4% per implanted ear (Table 6.4 and Table 6.5). Two bilaterally implanted patients had a major complication on each of their implants. One unilaterally implanted patient underwent revision surgery twice due to an incorrect electrode position, replacing the implant both times. Almost all complications were postoperative (N = 28, 96.6%) (Table 6.5). The most frequent major complication was infection at the operation site or the implant itself (N = 6, 20.7%), followed by electrode array migration (N = 5, 17.2%) and non-iatrogenic trauma (N = 5, 17.2%) (Table 6.5).

Table 6.4: Complications and device failure characteristics per implanted ear

	Total implants n (%)	Major complication n (%)	Minor complication n (%)	Device failure n (%)
Implants placed	344 (100%)	29 (8.4%)	166 (48.3%)	16 (4.7%)
Mean age at implantation (range; SD)	3y and 7m (4m – 18.5y; 4.1y)			
Mean time to complication or failure (range; SD)*		3y and 1m (1m – 14y; 4.1y)	2 y and 5 m (0.3m – 14.7y; 3.5y)	3 y and 8 m (2m – 12.6y; 3.2y)
Brand of implant				
Cochlear	307 (89.2%)	27 (93.1%)	146 (88.0%)	10 (62.5%)
Med-el	23 (6.7%)	1 (3.4%)	11 (6.6%)	3 (18.8%)
Advanced Bionics	14 (4.1%)	1 (3.4%)	9 (5.4%)	3 (18.8%)
Cochlea approach				
MPTA	256 (74.4%)	12 (41.4%)	127 (76.5%)	12 (75.0%)
SMA	85 (24.7%)	17 (58.6%)	37 (22.3%)	4 (25.0%)
Missing	3 (0.9%)		2 (1.2%)	
Fixation technique				
Bony well (with bony canal or tunnel)	283 (82.2%)	19 (65.4%)	136 (82.0%)	12 (75.0%)
Tight pocket	39 (11.3%)	7 (24.1%)	13 (7.8%)	3 (18.8%)
Bony well with bony sutures	10 (2.9%)	2 (6.9%)	9 (5.4%)	1 (6.3%)
Unknown/missing	12 (3.5%)	1 (3.4%)	8 (4.8%)	
User or non-user				
User	316 (91.9%)	22 (75.9%)	150 (90.4%)	14 (87.5%)
Non-user	26 (7.6%)	7 (24.1%)	16 (9.6%)	2 (12.5%)
Missing	2 (0.6%)			

Y = years; m = months.
* Time to major or minor complication were calculated per implant in years only for the postoperative complications. Perioperative were not taken into account.

Table 6.5: Major complications characteristics

	Major complications n (%)
Time to complication	
Perioperative	1 (3.4%)
Postoperative	28 (96.6%)
Perioperative complications	
Tip foldover	1 (3.4%)
Postoperative complications	
Infection of operation site or implant site	6 (20.7%)
Electrode array migration	5 (17.2%)
Non-iatrogenic trauma	5 (17.2%)
Electrode array issue	3 (10.4%)
R/S migration	2 (6.9%)
Pain at operation site or implant site	2 (6.9%)
Facial nerve paralysis	1 (3.4%)
Mastoiditis	1 (3.4%)
Magnet related issues	1 (3.4%)
Facial nerve stimulation	1 (3.4%)
Cholesteatoma	1 (3.4%)
Treatment of complications	
Revision surgery	18 (62.1%)
Explantation	9 (31%)
Minor surgical procedure	1 (3.4%)
Hospitalization for treatment	1 (3.4%)
Total	29 (100%)

The majority of cases with major complications were operated with the SMA surgical technique (N = 17, 58.6%). The tight pocket technique was used more frequently (N = 7, 24.1%) in the major complications subgroup than the general cohort (N = 39, 11.3%). All cases operated with the tight pocket technique, were also operated with the SMA technique. Most major complications required revision surgery (N = 18, 62.1%); nine cases had to be explanted (31%). In five cases, the patients did not receive a new implant after explantation. One of these five patients was bilaterally implanted and had major complications in both ears, permanent facial nerve paralysis and infection of the implant. This patient deceased due to a pre-existing neurological condition. One bilaterally implanted patient became a non-user of the left ear due to magnet problems (the magnet falling off the head) despite conservative and invasive attempts to elevate the issue.

Table 6.6: Minor complications characteristics per complication

	Minor complications n (%)
Time to complication	
Perioperative	52 (22.9%)
Postoperative	175 (77.1%)
Perioperative complications	
Dural exposure or tear	13 (5.7%)
Exposure of facial nerve during operation	9 (4.0%)
Chorda tympani manipulation or sacrifice	8 (3.5%)
Partial insertion of the electrode array	6 (2.6%)
Other iatrogenic defect during surgery	5 (2.2%)
Incus resection during surgery	5 (2.2%)
CSF leak or gusher	4 (1.8%)
Hematoma	1 (0.4%)
Other	1 (0.4%)
Postoperative complications	
(Recurrent) otitis media acuta	51 (22.5%)
Infection of operation site or implant site	16 (7.0%)
Other	18 (8.0%)
Otitis media with effusion	12 (5.3%)
Otorrhea	9 (4.0%)
Otitis externa	8 (3.5%)
Hematoma	7 (3.1%)
Mastoiditis	7 (3.1%)
Pain at operation site or implant site	6 (2.6%)
Magnet related issues	6 (2.6%)
Pain at the site of the R/S device	5 (2.2%)
Dizziness	5 (2.2%)
Non-iatrogenic trauma	4 (1.8%)
Facial oedema	4 (1.8%)
R/S migration	3 (1.3%)
Facial nerve stimulation	3 (1.3%)
R/S device issues	2 (0.9%)
Facial nerve weakness	2 (0.9%)
Meningitis	2 (0.9%)
Headache	2 (0.9%)
Pain n.o.s.	2 (0.9%)
Pain on stimulation	1 (0.4%)
Treatment of complication	
Oral or topical treatment	87 (38.3%)
Conservative treatment	56 (24.7%)
Wait and see	38 (16.7%)
Minor surgical procedure	25 (11%)
Hospitalization for treatment	20 (8.8%)
Missing	1 (0.4%)
Total	227

Minor complications

We reported 227 minor complications in 166 implants (132 patients), yielding a complication rate of 48.3% per implant (Table 6.6). The majority of ears (114/166) was bilaterally implanted. Of those ears, 34 patients had minor complications in both ears, 46 patients had a complication only in one ear. The most frequent of the 52 (22.9%) perioperative complications, was dural exposure or tear (N = 13, 5.7%), followed by exposure of the facial nerve during operation (N = 9, 4.0%) and chorda tympani manipulation or sacrifice (N = 8, 3.5%). Otitis media acuta was the most frequent postoperative complication (N = 51, 22.5%), followed by infection of operation site or implant (N = 16, 7.0%) and otitis media with effusion (N = 12, 5.3%). Two of the three patients that presented with R/S device migration, had been operated using the tight pocket fixation technique.

Device failures

Device failure occurred in 16 cases (4.7%), of which 14 (4.1%) were hard failures and 2 were soft failures (0.6%). Most hard failures (9/14) had no identifiable cause, in three cases the implant was defective due to trauma. In one case of electrode array migration and one case of implant infection, the devices were found to be defective after explantation. In two cases of soft failure, one case was due to unbearable pain at the implant site due to which the implant was explanted, and one case suffered from facial nerve weakness. For the latter the integrity testing was inconclusive. Most device failures were of the brand Cochlear (n = 10, 62.5%). Two cases became non-users after re-implantation, one case was due to disappointing audiological results, the other case was due to persistent pain symptoms. The latter case was explanted a year and 8 months after re-implantation.

Discussion

The analysis of CT data of 192 ears of pediatric patients aged 0 to 17 years, showed that in the majority of the cases (79.7%, n = 153) it was not feasible to drill a bony recess deep enough to lower the profile of the housing. The temporal bone thickness has been studied previously for the safety of implanting various bone-anchoring devices. In most cases a thickness of at least 3 mm was found in patients of five years and older. Below the age of five, several patients had a thickness of less than 3 mm. However, these studies used either a fixed location on the skull where the measurement took place[32,33] or searched randomly within the segmented temporal bone.[34] In our study, the search for an optimal location was systematic and the ROI was defined based on surgical practices for cochlear implantation. Our analysis of the most optimal location in the ROI showed that the mean minimum

bone thickness for the age group 0–4 years was 1.84 mm with a range of 0.07 mm to 2.93 mm (Table 6.2). These data confirm the difficulty and even impossibility in this age group, of drilling a bony recess that complies with the advised dimensions of CI manufacturers. This is due not only to the depth of the recess but also the surface area that needs to be drilled out in order to accommodate the implant housing. This surface area is larger for the current R/S devices than previous generations.[28] The curvature of the skull and irregularity of the surface increase the probability of exposing the dura mater.

In the retrospective review of our pediatric cohort data we included 230 patient records (344 ears) operated between 1996 and 2021 with a follow up of at least 12 months. The records showed a complication rate of 61.1% with 8.1% (n = 29) major and 48.3% (n = 227) minor complications. Device failure occurred in 16 implants (4.7%). The tight pocket technique was more frequently applied in the major complication group (24.1%, n = 7) than in the general cohort (11.3%, n = 39). The most frequent major complication was infection of the operation site or implant site (20.7%, n = 6), followed by electrode array migration and non-iatrogenic trauma occurring in both fixation groups. Also no apparent difference was found in the fixation subgroups regarding device failure.

Previous studies on CI implantation in infants and small children have advised a limited bony recess due to the thin cranial bone.[11,35] To avoid risks such as dura exposure, especially in very young children, alternative fixation techniques have been introduced. In 2009 Balkany et al.[28] first reported the minimally invasive subperiosteal tight pocket technique. Variations of this technique have since been applied in pediatric and adult cohorts reporting a low major complication rate of 0–5.2%.[11,35–37] Jethanamest et al.[38] reported no device migration or any complications related to device migration using the subperiosteal tight pocket technique. Some surgeons prefer to create a shallow recess to fixate the implant.[11,35] Our clinical data on the complication rates of the different fixation techniques were inconclusive. Although the tight pocket technique was used more frequently is the major complications subgroup than the general cohort, there was no apparent difference in the rate of R/S device related issues between fixation technique groups, such as R/S device migration, infection of the implant or electrode array migration or extrusion. Furthermore, all tight pocket cases in the major complications subgroup were also operated with the SMA technique. The sample size of the tight pocket subgroup was too small to perform a statistical significance analysis. A previous review on R/S device complications in adults reported no evidence of a difference for the different fixation techniques.[39] To fill this knowledge gap we are doing more research on R/S device related complications by directly comparing the two fixation techniques (bony recess versus tight pocket) in a prospective, randomized controlled study design.[40]

The differences found in our retrospective study regarding the cochlear approach subgroups, were noteworthy. The most frequently used technique was the MPTA technique (74.4%, n = 256) (Table 6.4). However, in the major complications group, the most frequently applied surgical technique was the SMA technique (58.6%, n = 17), contrary to the general cohort. These findings are in line with an older study that included part of our cohort.[14] The minor complication rate has increased over the years which could be explained by the increase of children operated under 12 months age. We included 102 children (29.7%) operated under the age of 12 months, versus 17.7% (n = 33) that were included previously. The high number of young children could also explain the high rate of minor complications in our cohort of 48.3% (n = 166), compared to the literature, that reports rates of 1.8–16%.[10,11,41–43] Infectious (minor) complications such as acute otitis media and mastoiditis are known to occur more frequently in children under the age of 12 months, and comprised 30.9% (n = 86) of the minor complications in our cohort.[44,45] The higher rate could also be due to a difference in classification of complications, or potential bias such as information bias or selection bias.

This study is also at risk of beforementioned biases due to the retrospective design. Retrospective chart reviews have limitations, as is the case in our study. Clinical data could be missed due to the lack of a standardized reporting method, introducing reporting bias. There could be variability in identification of complications. Moreover, the majority of CI's implanted in our study were of the brand Cochlear (n = 307, 89.2%) and most were of the CI400 series or older. The older CI models have different dimensions (thicker profile) making the comparison of R/S device related complications between subgroups difficult. Limitations are also introduced by the use of an in-house designed algorithm. However the effect of this limitation is minimized, thanks to the validation of the used algorithm. It should be noted that the algorithm searched the most optimal location within a predetermined ROI, based on expert opinion which could vary depending on the CI surgeon.

Conclusion

Our results showed a higher number of major complications in the SMA technique subgroup versus the MPTA group. Due to the retrospective design of the study and the subsequent biases, as well as the small sample sizes, we are unable to give a clinical recommendation for the safest technique for cochlear approach. The results concerning the fixation techniques for the R/S device were inconclusive, but there is reason to question the current practices in pediatric patients of drilling out a bony recess, especially in the 0–4 years age group. There is currently no evidence of a difference of the two surgical

techniques regarding R/S migration and electrode array migration in adults.[39] Further research is needed to validate complication differences in light of patients experiences.[46] These outcomes are investigated in our ongoing randomized controlled trial, the results of which will be published in a peer-reviewed journal.[40]

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Declaration of competing interest
None

Author contributions
Conceptualization: all authors. Data curation: LM, JD, HT. Formal analysis: LM. Methodology: all authors. Project administration: LM, JD. Visualization: LM. Writing–original draft: LM. Writing–review & editing: JD, IS, HT.

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CHAPTER 7

Cochlear implant positioning and fixation using 3D-printed patient specific surgical guides; a cadaveric study

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Abstract

Hypothesis: To develop and validate the optimal design and evaluate accuracy of individualized 3D-printed surgical guides for cochlear implantation.

Background: Positioning and fixation of the cochlear implant (CI) are commonly performed free hand. Applications of 3-dimensional (3D) technology now allow us to make patient specific, bone supported surgical guides, to aid CI surgeons with precise placement and drilling out the bony well which accommodates the receiver/stimulator device of the CI.

Methods: Cone beam CT (CBCT) scans were acquired from temporal bones in 9 cadaveric heads (18 ears), followed by virtual planning of the CI position. Surgical, bone-supported drilling guides were designed to conduct a minimally invasive procedure and were 3D-printed. Fixation screws were used to keep the guide in place in predetermined bone areas. Specimens were implanted with 3 different CI models. After implantation, CBCT scans of the implanted specimens were performed. Accuracy of CI placement was assessed by comparing the 3D models of the planned and implanted CI's by calculating the translational and rotational deviations.

Results: Median translational deviations of placement in the X- and Y-axis were within the predetermined clinically relevant deviation range (< 3 mm per axis); median translational deviation in the Z-axis was 3.41 mm. Median rotational deviations of placement for X-, Y- and Z-rotation were 5.50°, 4.58° and 3.71°, respectively.

Conclusion: This study resulted in the first 3D-printed, patient- and CI- model specific surgical guide for positioning during cochlear implantation. The next step for the development and evaluation of this surgical guide will be to evaluate the method in clinical practice.

Introduction

Cochlear implantation has been an accepted treatment for patients with severe-to-profound sensorineural hearing loss for several decades.[1] Nowadays, it is regarded as a safe procedure with low complication rates, and surgical techniques are continuously improving to achieve better audiological results.[2] Placement and fixation of the cochlear implant (CI) is an underestimated step during the cochlear implantation procedure. The internal part of the cochlear implant, also known as the receiver/stimulator (R/S) device, is designed to reside in close proximity to the pinna, without any interference with the external processor. During cochlear implantation the CI surgeon positions the R/S device under the temporalis muscle by either drilling out a part of the skull cortex (a bony well) with or without suture retaining holes, or by creating a subperiosteal pocket which holds the device in place. CI manufacturers provide information about the optimal distance from the pinna and the angle relative to the ear canal/pinna. Templates are provided by the manufacturers to draw the outlines of the external and internal parts on the surgical drapes to aid in positioning the implant. However, these templates provide an estimate at best of where the implant will reside.[3] The drawings on the surgical drapes are often arbitrary, imprecise and during the operative procedure it is difficult to match the external drawing to the skull surface. Some surgeons additionally apply a percutaneous marker (small diamond burr or methylene blue stain) through the skin on the bone, thereby locating more exactly the position of the definitive implant position on the temporal cortex during surgery.[4,5] In case of bilateral implantation, achieving symmetrical placement is challenging as well. Interindividual variability of cortical thickness of the temporal bone between patients, can also be a factor of influence when drilling out a bony well.[6] We believe some of these issues can be solved by using patient-specific, bone-supported, surgical guides.

Intraoperative guides are templates used in a variety of ways for tissue reconstruction, by assisting cutting or drilling. In health care, and surgery specifically, the concept of patient-specific surgical guides is far from new, and it is being applied in everyday medical practice.[7] In the field of otology, 3D-printed guides have already successfully been used for hearing implant surgery.[8] Until now, R/S device placement and drilling is usually performed free hand. The goal of the surgical guide is to aid the CI surgeons with precise placement and drilling procedure of the bony well, which accommodates the R/S device. This study aims to develop and validate a patient specific, bone supported surgical guide.

Materials and methods

Specimens

For this feasibility study, we used fresh frozen human cadaveric heads that were obtained through the Human Body Donation program of the University of Utrecht (https://www.umcutrecht.nl/nl/meedoen-aan-wetenschappelijk-onderzoek). From these persons written informed consent was obtained during life that allowed the use of their entire bodies for educational and research purposes. The possibility for body donation is part of the Dutch law on dead bodies. As no living human subjects were involved, this work was exempt from review by the Institutional Review Board of the UMC Utrecht. The specimens had to have an intact temporal and parietal bone and retroauricular skin. A power analysis was conducted to calculate sample size. We estimated a translational difference of 3.0 mm to be clinically relevant, based on expert opinion, with a standard deviation of 2.0 mm. With an alpha of 0.05 and a power of 85%, we needed to include 17 ears. Rotational deviations above 5° in the sagittal plane were deemed clinically relevant.

Planning and guide design

Specimens underwent Cone Beam CT scans (VGi evo, NewTom, Cefla C.S., Italy) with a 24 x 19 cm field of view (FoV), and 0.3 mm slice thickness. Images were stored in DICOM format. Using the segmentation feature in iPlan (Brainlab, Munich, Germany), the skull was segmented and reconstructed into a 3D model. This 3D model was then imported into 3-matic version 14.0 medical design software (Materialise). The CI's used for this study were Cochlear CI512, Oticon Neuro Zti and MedEl SONATA TI(100). The CI's from Cochlear and MedEl were used models, acquired after revision or explantation surgery due to device failure or patient dissatisfaction with speech recognition results. The CI from Oticon Medical was provided by the manufacturer for research purposes. Volume data of the CI's were acquired by scanning the implants using a 3shape laboratory scanner (3shape, Copenhagen, Denmark). The data was reconstructed into 3D models.

The planning of the implantation was conducted by the following steps. First two virtual planes were created on the 3D model of the skull, namely the Frankfurt Horizontal plane that connects the inferior margins of the orbits and the superior margin of the external auditory canal (EAC), and a 45° plane relative to the Frankfurter Horizontal plane, originating from the EAC (Figure 7.1a). Next, the CI was aligned to the 45° plane with a distance of 2.5 cm from the EAC. During the positioning of the CI the curvature of the skull was taken into account. The position for the Cochlear and MedEl models was determined so that the anterior part of the implant (receiver/stimulator) would be embedded whilst

allowing the posterior part (magnet with coil) to rest on the skull. The Oticon implant was embedded in the skull in its entirety. In order to achieve symmetrical placement, the 3D model of the cochlear implant was duplicated and mirrored to the contralateral side over the sagittal plane as defined by the Frankfurt Horizontal plane. With the implants in place, the drilling guides were designed. The skull surface of the mastoid bone and the supramastoid crest were used as contact areas and were defined (Figure 7.1b and 7.1c). After each implantation the surgical guide was reviewed based on the feasibility and the deviation results. The surface contact area was extended or reduced accordingly to optimize the design. Screw holes were created to stabilize the guide on the area of the mastoid bone. All guides were produced using a medical certified photopolymer resin (Model 2.0, Next-Den, Soesterberg, The Netherlands) using selective laser sintering 3D printing.

Surgical workflow

Implantations were carried out by a clinical research physician (LM) who had undergone surgical training prior to start of the study. One implantation was carried out by a senior CI surgeon (HT). Fixation of the CI's using the drilling guides was carried out as follows. A retroauricular Lazy-S incision of approximately 8–9 cm was made. The bony surface was exposed to fit the designated location on the temporal bone. The periosteum was

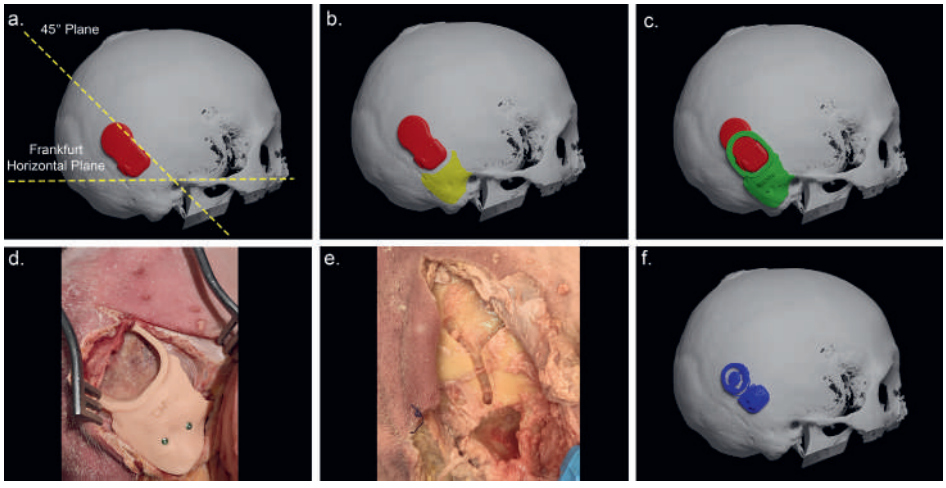

Figure 7.1: Planning, guide design and surgical procedure using the 3D-printed guide on a cadaveric head. (a) The 3D model of the cochlear implant (CI, shown in red) aligned with a 45° plane relative to the Frankfurter Horizontal plane, originating from the external auditory canal (EAC). (b) The skull surface of the mastoid bone and the suprameatal crest used as contact areas (marked yellow on the skull). (c) Surgical guide depicted in green. (d) The surgical guide in place on a cadaveric head. (e) Surgical guide removed with a clear view of the drilled cortical recess. (f) Segmented 3D model of the implanted CI based on the postoperative CBCT scan (shown in blue).

elevated to place the drilling guide. The guide was secured to the bone with two screws (Figure 7.1d). A cortical recess was drilled out (Figure 7.1e), with a bony overhang if bone thickness was adequate. The surgical guide was then removed and the fit of the bony bed was tested by means of a silicone dummy. When the optimal fit was achieved, the cochlear implant was placed in the bony bed and the periosteum was closed, in order to perform the post implantation scan. Each side of a specimen was implanted and scanned sequentially, in order to assess the depth of the bony bed without scattering created by the implant.

Analysis

After implantation, a CBCT scan was carried out using the same settings as mentioned above. The DICOM images were imported into iPlan and image fusion with the preoperative scan was achieved by first performing manual alignment followed by automated registration based on voxel based matching. Image fusion was visually verified by the researcher. The implanted CI was segmented and exported as a 3D model (Figure 7.1f). The image fusion step ensured that the pre-implantation 3D models of the CI's and the post-implantation 3D models of the CI's were in the same coordinate system.

In order to compare the accuracy of the CI placement between the specimens we assessed the pre-implantation 3D models to the post-implantation 3D models per case. The 3D models of the CI's were placed in the same coordinate system. This alignment of the CI's between specimens, was achieved by performing the following three steps in 3DMedX (v1.2.11.1, 3D Lab Radboudumc, Nijmegen). First, the 3D models of the CI's were manually placed at the origin of the coordinate system and aligned to the principal axis of this coordinate system, referred to as the centered CI (Figure 7.2a). Secondly, the 3D model of the planned CI (pre-op) was registered toward the centered CI of the respective CI model, using rigid surface based matching (Figure 7.2b). This registration was based on the Iterative Closest Point (ICP) algorithm.[9] An important note is that the 3D models of the centered CI and planned CI were identical, removing the potential of a registration error. Thirdly, the transformation matrix determined by the ICP registration in the previous step was also applied to the 3D model of the implanted CI, extracted from the postoperative CBCT scan (Figure 7.2b). This placed the implanted CI in the same relative position to the planned for accurate comparison. In order to enable the direct comparison of the left and right implanted CI, the 3D models from the CI's implanted on the left side of the head were mirrored in the sagittal plane before performing the previous three steps.

Finally, the accuracy of the CI placement was determined by performing a second ICP registration from the planned CI, now located at the center of the coordinate system, to the

registered 3D model of the implanted CI. The translation (mm) and rotation, expressed as the roll, pitch, and yaw, were derived from the transformation matrix as determined by the second ICP registration. The transformation matrix was converted to the Euler angles using the YXZ sequence. A perfect CI placement would result in a 0 mm translation and 0° rotation along all axis.

Since the combination of a translation and rotation can be difficult to interpret, the accuracy of the CI placement was also expressed as the translation between the center of the magnet of the planned CI and the implanted CI. The center of the magnet only needed to be determined once for each model of CI used in this study, removing a potential observer error of selecting the center of the magnet separately for each cadaver.

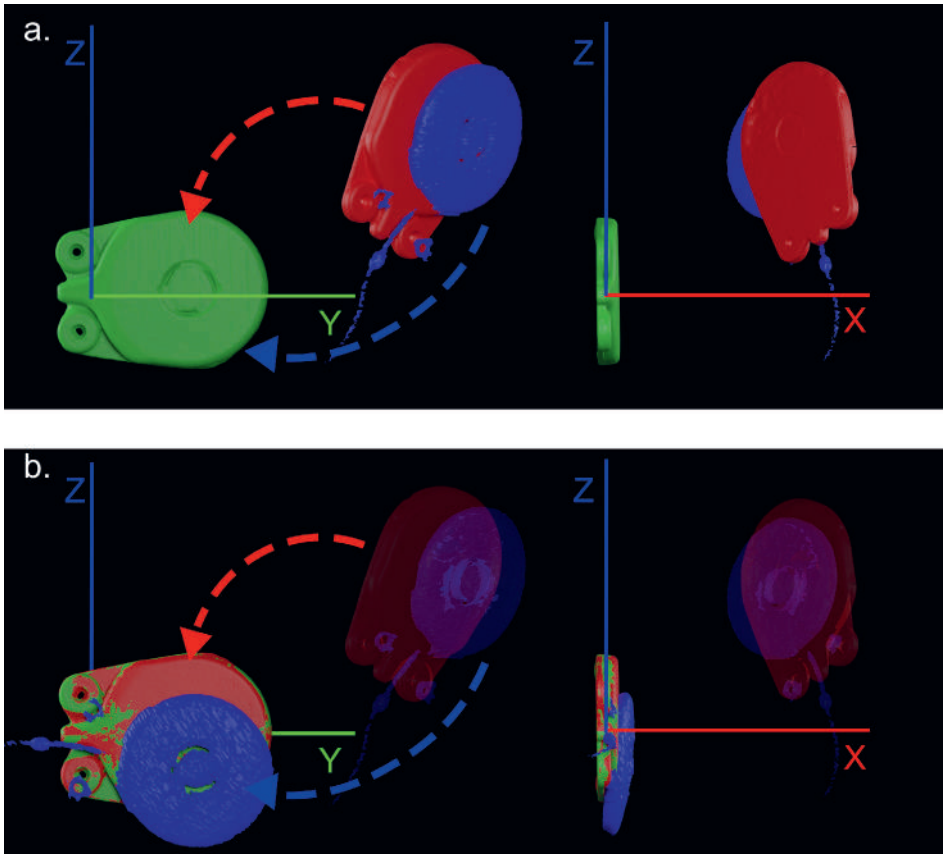

Figure 7.2: Analysis steps of the alignment of cochlear implants to eliminate errors due to skull size and planning variability. The X, Y, and Z axis are marked red, green, and blue, respectively. (a) Depiction of the manually placed cochlear implant (CI) at the origin of the coordinate system (0,0,0) (green color); the 3D model of the planned CI (red color); the 3D model of the implanted CI (blue color). (b) Registration of the planned CI (red color) towards the centered CI model (green color) using rigid surface matching.

Statistical analysis

Data were analyzed using IBM SPSS Statistics for Windows (version 25.0; IBM Corp., Armonk, NY, USA). Translational and rotational deviations between the planned CI and the implanted CI were analyzed using descriptive statistics. In order to prevent the effect of positive and negative values cancelling each other out, we used the absolute numbers for the statistical analysis. Each ear was analyzed as an individual case. Since we expect the outcome of the study to be not dependent on the characteristic of the specimen, we did not apply adjustment for the correlation between the two ears. This study will be reported according to the guidelines the STROBE statement.

Results

We implanted and analyzed 9 specimens and 18 ears in total. Specimen 8 was implanted by HT, all other specimens were implanted by LM. Due to outliers, in particular subject 1, 2 and 8, the data were not normally distributed. An overview of the absolute translational and rotational deviations between the planned CI and implanted CI are shown in Table 7.1. Translational deviation of placement under the 3.0 mm threshold, was achieved in the X- and the Y- axis (median deviation of 1.59 mm with IQR 0.95 and 2.34 mm with IQR 3.84 respectively). Translational deviation was highest in the Z-axis (median deviation of 3.41 mm with IQR 4.55) with also the largest range of deviation. Rotational deviation of placement ranged from 1.53 to 23.73 degrees on the X-axis, 0.10 to 19.55 degrees on the Y-axis and 0.22 to 11.07 degrees on the Z-axis. Specimens number 1 (left side) and 8 (both sides) had Z translational deviations of more than 10 mm (Figure 7.3a). These cases also had large rotational deviations in the X- and Y-axis (Figure 7.3b).

Table 7.1: Absolute translational and rotational deviations between the planned cochlear implant (CI) and the implanted CI calculated with the Iterative Closest Point (ICP) algorithm

	Translational deviations (millimeters)			Rotational deviations (degrees)		
	X-translation	Y-translation	Z-translation	Pitch	Roll	Yaw
Median	1.59	2.34	3.41	5.50	4.58	3.71
IQR	0.95	3.84	4.55	8.90	6.26	4.25
Mean ± SD	1.65 ± 0.73	3.84 ± 3.68	4.93 ± 4.95	8.02 ± 6.37	6.20 ± 5.55	4.14 ± 3.20
95% CI	1.28–2.01	2.01–5.67	2.47–7.39	4.85–11.18	3.43–8.96	2.55–5.73
Min	0.67	0.25	0.32	1.53	0.10	0.22
Max	3.48	14.33	20.30	23.73	19.55	11.07

IQR: interquartile range; SD: standard deviation; CI: confidence interval; Pitch: X-rotation; Roll: Y-rotation; Yaw: Z-rotation.

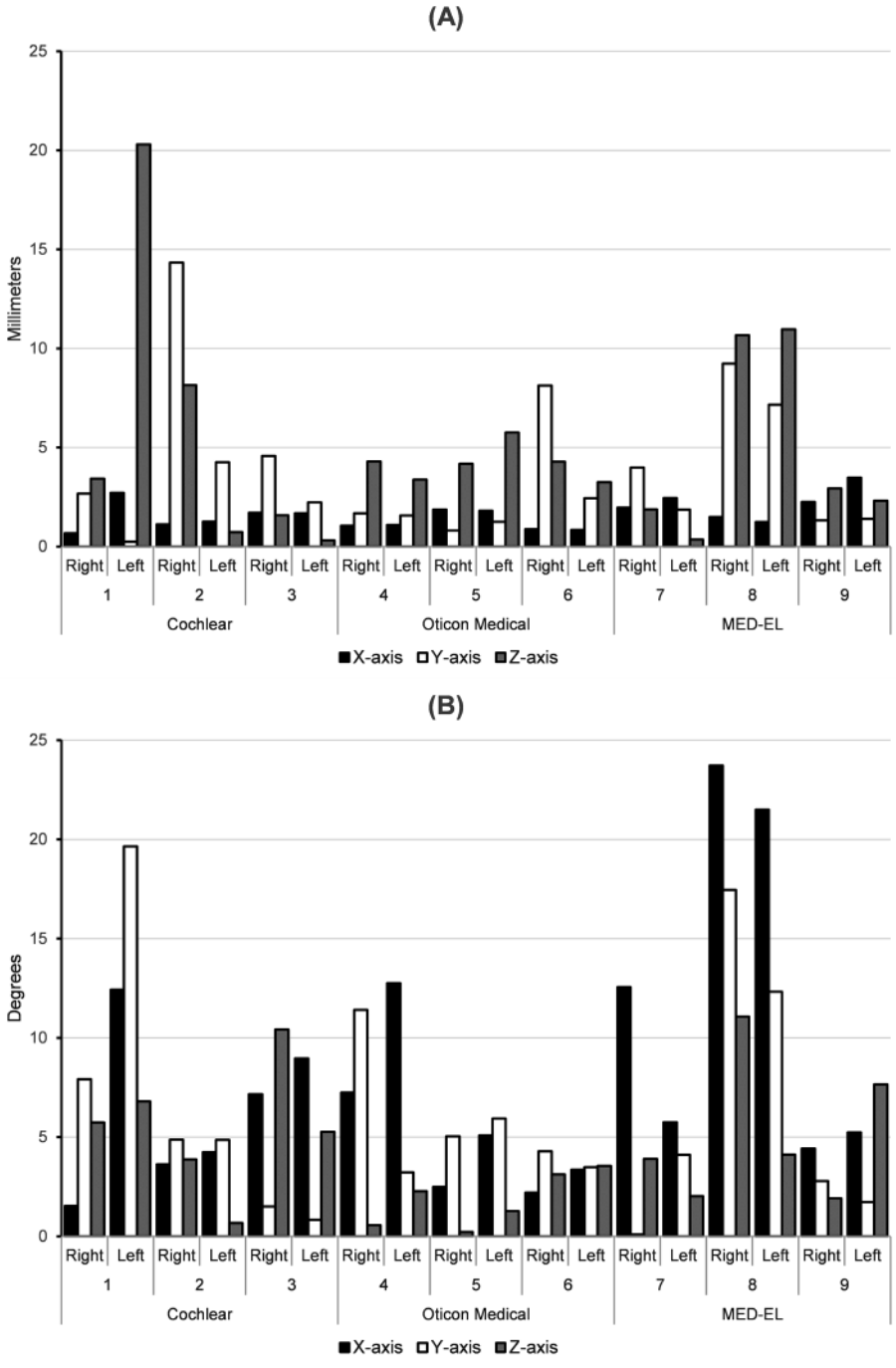

Figure 7.3: Translational and rotational deviations (absolute values) per case between the planned CI and implanted CI, expressed in millimeters and degrees. (a) Translational deviations (absolute values) in millimeters per axis, per case; (b) Rotational deviations (absolute values) in degrees per axis, per case; Horizontal numbers represent the specimens.

Analysis of the translational deviations between the planned CI and implanted CI calculated for the center of the magnet from each CI, also resulted in median deviations under the 3 mm threshold in the X- and Y-axis respectively (Table 7.2 for the absolute translational displacement and Figure 7.4 for the true translation per case). The median translational deviations in the Z-axis was 4.94 mm with IQR 5.42 mm.

Table 7.2: Absolute translational deviations (in mm) between the planned cochlear implant (CI) and the implanted CI calculated of the center of the magnet for each CI type with the landmark based analysis

	X-translation	Y-translation	Z-translation
Median	1.92	2.13	4.94
IQR	2.47	3.26	5.42
Mean ± SD	2.46 ± 1.95	3.17 ± 3.34	7.43 ± 7.92
95% CI	1.49–3.43	1.51–4.83	3.49–11.37
Min	0.24	0.43	0.55
Max	7.20	13.85	26.05

IQR: interquartile range; SD: standard deviation; CI: confidence interval.

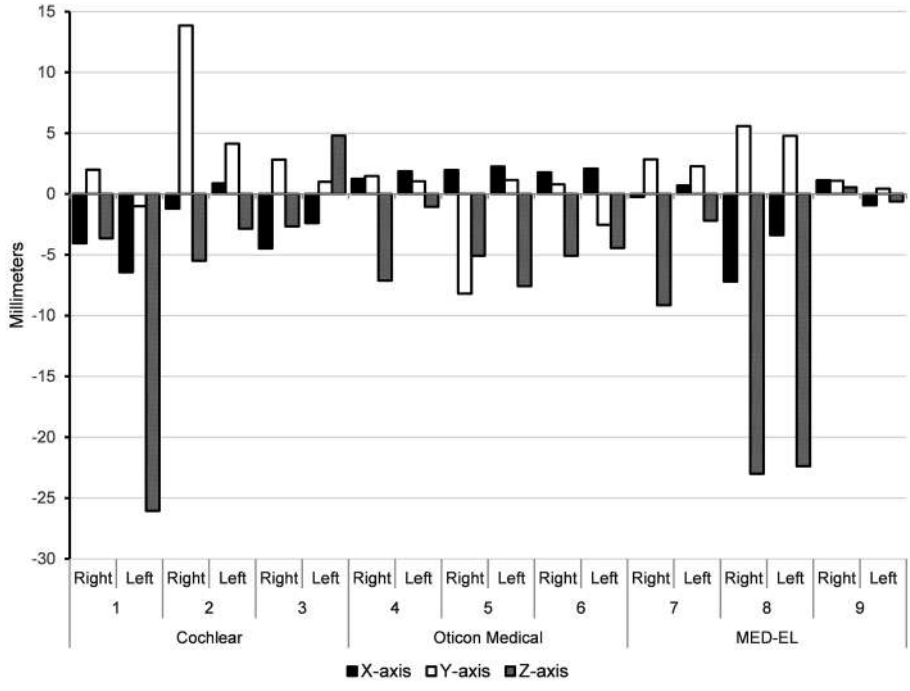

Figure 7.4: Translation deviations (true values) of the center of the magnet for each CI type, between the planned CI and the post-op CI per case expressed in millimeters. Displacement of the center of the magnet between the planned CI and the post-op CI (true values); Horizontal numbers represent the specimens.

Discussion

In this cadaveric study, we developed a preoperative planning workflow for the positioning and fixation of CI's, and designed a 3D-printed, patient- and CI model-specific surgical guide. The feasibility of using a 3D-printed guide for drilling of the R/S device bony bed was evaluated in conditions as close to reality as possible. To optimize use of the surgical guide screws were added that hold the guide in place, to accommodate the surgeon during the drilling procedure. By staying within 2.5 cm distance from the bony ear canal (which is a stable and reliable landmark visible during preoperative planning on the CBCT), and using the mastoid as well as the external meatus rim and suprameatal crest as landmarks for the surgical guide, more exact positioning on the skull was achieved. The analysis of the planned and implanted CI showed that the median deviations of the X-, and Y-translation were within the predetermined clinically relevant threshold of 3 mm for both landmarks (Table 7.1 and 7.2). Rotational deviations varied between the directions with the Z-rotation having the smallest and X-rotations having the largest deviations (Figure 7.4).

3D printing is increasingly utilized in otolaryngology in all facets of surgery, from planning to execution.[10,11] Operative templates in craniofacial and head and neck surgery are mostly used for intraoperative cutting of bony tissues, such as reconstruction of mandibular bony defects.[11] Virtual planning and 3D-printed templates for drilling are less common in otological surgery, although there is increasing interest in applying these techniques in clinical practice. For instance, a method for accurate placement of a bone conduction hearing device has been developed which has shown promising results and has already been used in clinic.[12–15] Another example of surgical templates for drilling, is a study by Vijbergen et al. that used skin-supported guides for bone anchored auricular prostheses.[16] Our study utilized the same principles, applying similar methods in regards to workflow and execution, and faced the same challenges. This study is feasible with any validated software and 3D printers approved for medical use. Furthermore, the preoperative planning and designing of the surgical guide can be realized with different imaging techniques including computed tomography and magnetic resonance imaging.[17]

This surgical guide is an easy-to-use tool for CI surgeons when drilling a bony bed and optimizes accuracy in regards to positioning on the skull. Moreover, no rough estimates are necessary beforehand when surgically planning the positioning. The template provides the exact location on the skull during surgery. Especially during bilateral cochlear implantation (simultaneous or sequential), it might be a valuable addition to the existing surgical instruments. Symmetrical placement is one of the main aspects visible from outside, regarded as important by these infants' parents, based on our experience. The time invested preop-

eratively to plan and produce the surgical guide could benefit the surgical procedure by reducing its duration. Furthermore, the process of preoperative planning and production can be automated, making this surgical tool suitable for use in clinic. With the data of this study we cannot conclude if this surgical tool is financially beneficial. This would have to be examined in future clinical studies to weigh the potential reduction of operation time against the costs of production and sterilization.

A challenge we faced during this study was finding the balance between optimizing the surgical guides' accuracy, while also maintaining the low level of invasiveness that is exercised in clinical practice. A study by Caiti et al. that tested the accuracy of guide positioning on the radius, reported that the accuracy of bone supported surgical guides can vary depending on the location of the bone contact area as well as the size of the surgical guide. They found that extended guides, that is to say guides that covered a larger area of the cortical bone, resulted in a higher placement accuracy.[18] The first designs of our surgical guide had a small contact area and also did not include the mastoid bone. We found that using both the external meatus rim and the mastoid bone as contact areas for the surgical guide gave the best results. These conditions were met by seven cases. The median difference of translation for these cases was under the preset threshold of 3 mm deviation for all translational directions, although the difference with the cases that did not meet these conditions was not statistically significant. The greatest translational improvement using these contact areas was seen in the Z-axis, which was also found by Caiti et al. in their experimental study.[18] Therefore we will use these contact areas when implementing this surgical tool for clinical use. Our results also show a high translational deviation in the Y-axis in these specimens, suggesting a tendency to place the implant more posteriorly. Finally, the translational analysis of the center of the magnet is an easy to interpret analysis of the accuracy which could also be applied in clinic using a flexible tape measure method, validated by our group.[19] Based on the results from this study the largest median deviation would be expected in the Z-axis.

Another point of interest is the apparent learning curve in using the surgical guide. The results of the implantation (only one) executed by HT showed considerable deviation from the planning (Figure 7.3). This learning curve is to be expected when using a new surgical tool, and this is in line with previous publications of surgical drilling guides.[12,20] We recommend applying this technique on phantoms such as temporal bones before applying it in vivo.

An important factor that influences accuracy of placement is drilling direction. The surgical tool developed in this study guides the external outline of the bony bed, but it does not guide the direction of the drilling, nor the depth of the bony bed. Due to the

fact that the posterior side of the CI (in cases of MedEl, Advanced Bionics and Cochlear, the magnet is situated posteriorly) is not embedded in the skull, the depth of the bony bed is only related to the anterior side of the implant and available cortex thickness. The electrode lead exit also influences the antero-inferior aspect and shape of the bed. Despite these factors influencing the procedure, the translational deviation results of X-translation were satisfactory and evenly distributed between the different implantees, thus we do not expect problems when implementing this method in clinical practice. In this study we used simple guide designs, tested the templates under conditions as close to reality as possible and adhered to a pragmatic accuracy threshold. Satisfactory results were not achieved within the preset limits in all specimens, which is to be expected in a feasibility and pilot study. We identified the potential problems using this tool such as the surgical learning curve as well as the importance of the implant-bone surface contact area, and adapted the design while maintaining a minimally invasive approach. One additional detail is the shape of the retroauricular incision. This should be as minimal invasive as possible (taking into account: scar, pain sensation, esthetics, postoperative morbidity, possible skin related complications) though provide enough space and exposition for adequately drilling a bony well. Therefore in this study a S-shaped "à minima" cut (Lazy S) is applied. It might be discussed whether a C-shaped incision could be opted for (a viable alternative frequently adopted by CI surgeons), however in our experience it does provide insufficient exposure in that region whilst in the same time enough visibility for mastoidectomy and posterior tympanotomy. The optimal skin incision should therefore be included as an objective during future research on this challenging and underestimated topic.

Conclusion

In this study we developed and tested the first 3D-printed, (patient- and CI model) specific drilling guide. The surgical guide performed well in translational accuracy, and showed more heterogeneity in rotational accuracy. We therefore consider the surgical guide developed in this feasibility study helpful and confirm its potential to increase positioning accuracy in unilateral and bilateral cochlear implantations. The next step for the development and evaluation of this surgical guide will be to evaluate the method in clinical practice.

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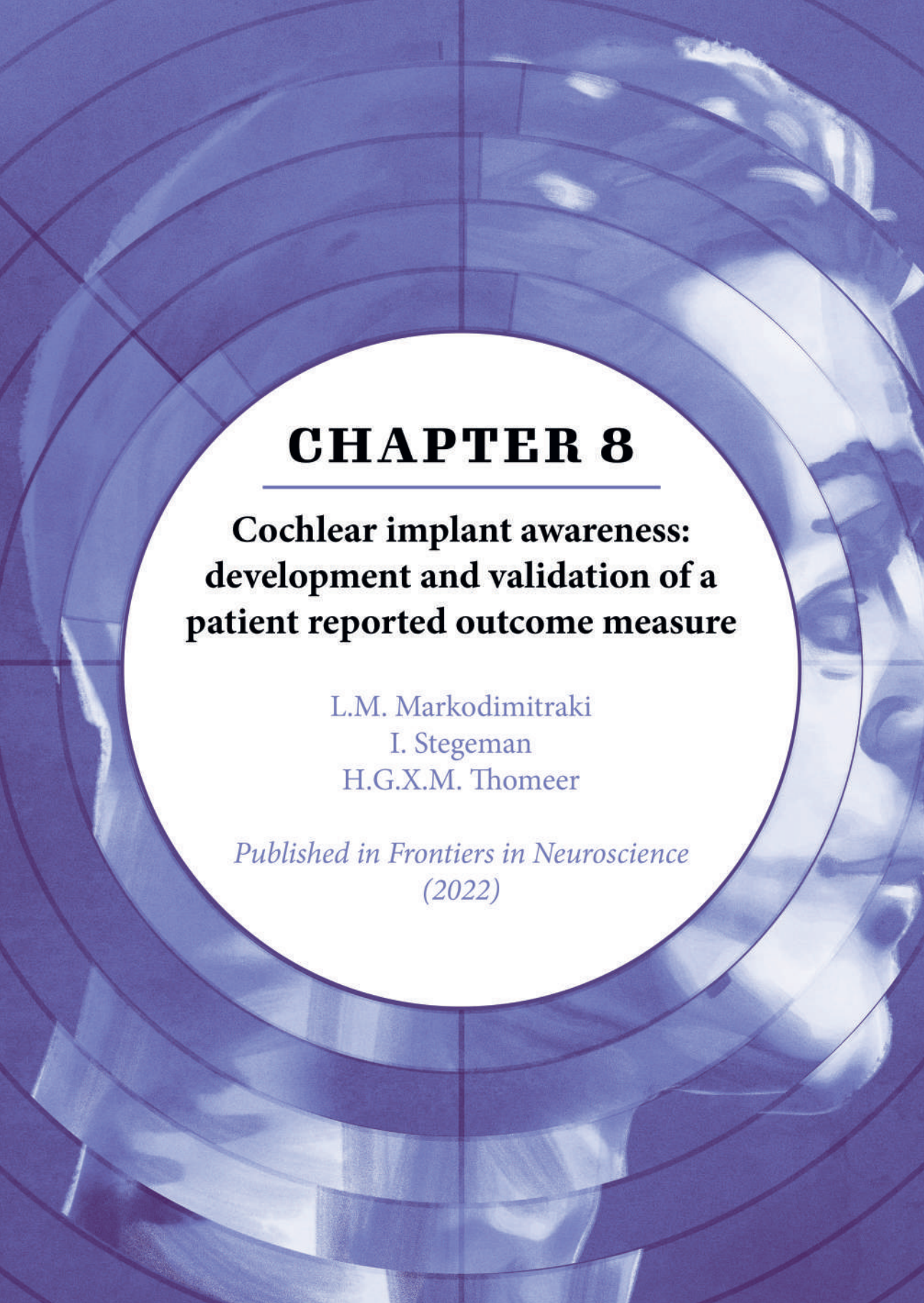

CHAPTER 8

Cochlear implant awareness: development and validation of a patient reported outcome measure

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Abstract

Background: Surgical success of cochlear implantation is usually measured through speech perception and quality of life questionnaires. Although these questionnaires cover a broad spectrum of domains, they do not evaluate the consciousness of wearing a cochlear implant (CI) and how this impacts the daily life of patients. To evaluate this concept we aimed to develop and validate a standardized patient reported outcome measure (PROM) for use in cochlear implant users.

Methods: Development and evaluation of the COchlear iMPlant AwareneSS (COMPASS) questionnaire was realized following the COSMIN guidelines in three phases: (1) item generation, (2) qualitative pilot study to ensure relevance, comprehensiveness, comprehensibility and face validity, and (3) quantitative survey study for the assessment of reliability (test-retest) with 54 participants.

Results: Nine domains of CI awareness were identified through literature research and interviews with experts and patients. These resulted in the formulation of 18 items which were tested with a pilot study, after which 3 items were deleted. The final 15-item COMPASS questionnaire proved to have good validity and satisfactory reliability. The intraclass correlation coefficient calculated for items with continuous variables ranged from 0.66 to 0.89 with seven out of eight items scoring above the acceptable level of 0.7. The Cohen's kappa calculated for items with nominal variables ranged from -0.4 to 0.78 with 11 (sub)items out of 15 scoring above fair to good agreement. Measurement error analysis for items with continuous variables showed a mean difference of -2.18 to 0.22. The calculated 95% limits of agreement for these items revealed no statistically significant difference between the two administered questionnaires. For items with nominal variables, the percentages of agreement calculated, ranged between 0% and 95%, and 83.3% and 96.6% for positive and negative agreement, respectively.

Conclusion: The COMPASS questionnaire is a valid and reliable PROM for evaluating the cochlear implant awareness, and it can be easily used in routine clinical practice.

Introduction

Cochlear implants (CI's) are currently the only effective treatment for auditory rehabilitation for patients with severe-to-profound bilateral sensorineural hearing loss with poor speech perception. Since the introduction of this medical device in the 1970's, great advancements have been made regarding the functionality and hardware design. The internal part of the implant, the receiver/stimulator (R/S) device that resides under the skin behind the pinna of the ear, has undergone technological improvements resulting in thinner implants with smaller footprints.[1] Comfort of the external parts of the CI use has increased over the years with more discrete designs and lighter speech processors that allow patients to wear their implant throughout the day. Most importantly, the speech perception results have increased greatly, improving quality of life of patients with hearing loss.[2–4]

Despite the wealth of knowledge and research regarding speech perception results and health-related quality of life of CI recipients, little is known about the CI-experience and -awareness by patients. We define awareness of having a cochlear implant as "the state of mind or situation in which the patient is physically conscious he or she is wearing a cochlear implant and how this consciousness impacts their daily life". There are patient-reported outcome measures (PROMs) assessing CI use such as the Cochlear Implant Management Skills (CIMS-self) survey and the Nijmegen Cochlear Implantation Questionnaire (NICQ).[5,6] The CIMS-self focuses on device management exclusively, and the NICQ assesses health-related quality-of-life by how sound and speech perception limits a CI-recipient in their daily life. However, these PROMs do not evaluate the (physical) impact of a CI, thus they may fail to capture cochlear implant awareness topics in daily life that are of importance from patient perspective. To our knowledge, no CI-specific PROM has been developed yet that included patients in item development, following the standards of the Patient Reported Outcomes Measurement Information System (PROMIS) or the COnsensus-based Standards for the selection of health Measurement Instruments (COSMIN).[2]

CI awareness could be important for speech recognition results and quality of life of CI recipients. Studies have shown that wear time of the CI affects speech recognition outcomes in pediatric and adult patients.[7,8] In addition, previous research on hearing aids has shown that fit and comfort are the second most important factors contributing to non-use of hearing aids.[9] Specifically, the satisfaction of patients with comfort of use, burden during daily activities, sleep disturbances related to location of the implant in relation to the preferred sleeping position, pain, or other discomfort caused by the implant are all contributing factors to reduced wear time. Moreover, there might be an underestimation of the

prevalence of above mentioned problems in CI recipients, especially when a significant increase in hearing and communication is achieved using the CI. The benefits of the CI could suppress the concomitant inconvenience that accompanies wearing the processor.

In order to assess the physical awareness of the cochlear implant, we aimed to develop and validate a patient reported outcome measure (PROM) questionnaire.

Materials and methods

This development and validation study was conducted between December 2019 and April 2021 at the University Medical Center (UMC) Utrecht, in compliance with the principles of the Declaration of Helsinki. This study was exempt from approval of an ethics committee under Dutch law. Exemption was granted by the local ethical committee (Institutional Review Board of the UMC Utrecht) (METC protocol 19-722/C). A three-stage procedure for development and validation of the patient reported outcome measure (PROM) was conducted, in accordance with the COSMIN guidelines (see Figure 8.1).[10] Participants were recruited at the time of routine control at the CI center UMC Utrecht, and through an open e-mail invitation to patients registered in the CI database of the UMC Utrecht sent by their attending physician. Written informed consent was obtained from all participants.

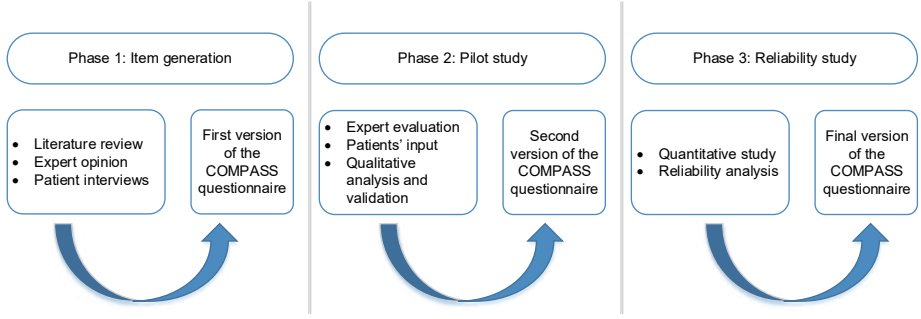

Figure 8.1: The three phase procedure for development and validation of the COMPASS questionnaire.

Construction of the concept

We aimed to develop the COchlear iMPlant AwareneSS (COMPASS) questionnaire to assess the awareness of having a cochlear implant as previously defined. The PROM development group consisted of a otorhinolaryngologist, an epidemiologist and a junior researcher. This questionnaire was designed for adult, Dutch speaking, CI recipients. The instrument was developed to be used as a self-administered evaluation tool, in daily clinical practice, for clinical studies, and for comparison within patients over time (possible evolution

of awareness). The questionnaire was designed to detect issues in different categories, specifically concerning the external parts of the CI (speech processor and transmitter) and the internal part (the receiver/stimulator device). In order to assess CI awareness, different domains were identified. It is important to distinguish the situation of awareness and how burdensome the awareness is. Therefore, the questionnaire should consist of multiple choice items as well as scale items to measure the burden. With the results of the questionnaire, health care professionals should be able to identify problems that can be solved by adapting the hardware or by counseling.

Phase 1: Item generation

Qualitative data were obtained by a literature review, a series of interviews with seven specialists in cochlear implantation care, including an otorhinolaryngologist, speech therapists and audiologists, and individual interviews with a sample (n = 7) of CI recipients were conducted, to identify and select relevant aspects of CI awareness. Included patients were adult CI recipients that were using their implant for at least one year prior to inclusion in order to have adequate experience with everyday use of their implant to contribute to data collection. The semi-structured interviews of approximately one hour each were recorded and were conducted by a trained investigator (LM) using an interview guide (see Supplementary Material). The recorded interviews were then transcripted verbatim. Content analysis was performed independently by two researchers (LM and IS), by coding the transcripts and then grouping the codes into thematic categories. Data collection was continued until saturation was reached. The emerging domains as well as the pertinence of the findings were discussed within the research group until consensus was reached. The questionnaire is based on a formative model, the indicators (items) define the value of CI awareness (the construct measured).

Phase 2: Pilot study (Cognitive Debriefing Test)

A pilot study was conducted to assess the content validity of the questionnaire, the comprehensibility and comprehensiveness. The above mentioned experts in the field of cochlear implantation evaluated the content, wording, format, answer options and intelligibility. Changes were made appropriately. The evaluated questionnaire was administered to ten adult CI patients that were using their implant for at least 3 months prior to inclusion in order to have adequate experience with everyday use of their implant to contribute to data validation. Participants filled out the questionnaire while "thinking aloud", followed by a semi-structured interview with open-ended questions (see Supplementary Material) that were audio-recorded. This interview was conducted to capture information

on the participant's understanding of the instructions, the intended meaning and clinical relevance of each item, the response options, patient's opinion regarding the questionnaire and missing concepts. The time required to fill out the questionnaire was also recorded. Adjustments were made to the questionnaire based on these interviews.

Phase 3: Reliability study

A quantitative study was conducted to assess the reliability of the final version of the COMPASS questionnaire. The questionnaire was administered twice to 54 adult CI patients, thereby meeting the COSMIN criteria of participants necessary for quantitative validation.[10] These CI patients were using the CI for at least 3 months prior to inclusion in order to have adequate experience with everyday use of their implant to contribute to data validation. Two weeks after the participants filled out and returned the questionnaire, they were send and filled out the same questionnaire again. The questionnaire was distributed on paper or digitally through Castor EDC (version 1.6, Ciwit B.V., Amsterdam, the Netherlands), an electronic data capture platform, depending on the patients' preferences.

Data analysis

Data was analyzed using IBM SPSS Statistics for Windows (version 26.0.0.1; IBM Corp., Armonk, NY, USA). Reliability (test-retest) was calculated using the interclass correlation coefficient (ICC) for continuous scores and Cohen's Kappa with standard error and 95% confidence interval for nominal scores. We used the two-way random effect model with interaction for the absolute agreement between single scores to calculate the ICC with 95% confidence interval. This model was chosen because time is a relevant factor for the test-retest assessment, and because the results will be generalized beyond the study points. Also the participants are assumed to be stable for the construct of interest across the two time points.[11] Values > 0.70 are generally considered as good.[12] However, the ICC should be interpreted with the sample variability in mind. Therefore, we calculate the range of scores per item to illustrate the homogeneity of the subjects. Small inter-subject variability results in a depress of the ICC.[13] To interpret the values of kappa we used the criteria by Fleiss et al.: values < 0.40 represent poor agreement, 0.41–0.75 fair to good and ≥ 0.75 represent excellent agreement.[14]

Measurement error, the systematic and random error of an individual patient's score that is not attributed to true changes in the construct to be measured, was assessed by Bland-Altman plots with the 95% limits of agreement for continuous scores, and the positive and negative percentage agreement for nominal scores.

Scoring the COMPASS

The final version of the COMPASS questionnaire consisted of 15 items. These were divided into two subdomains: external and internal device domains. The external device (speech processor and transmitter) domain and the internal device (receiver/stimulator) domain consisted of seven and eight items, respectively. Items were either multiple choice or visual analogue scale questions. Each item had a maximum score of 5, with a total maximum score of 75. A higher COMPASS score represented a higher awareness level.

Results

Phase 1: Item generation

Domains of awareness that were identified through literature search were bulging of the implant under the skin, discomfort or pain caused by the implant and sleep disturbances related to the implant. Domains identified through expert interviews were pain caused by the speech processor and transmitter, problems with wearing glasses, satisfaction with the position of the transmitter on the head, and interference of the external implant with daily activities and with wearing head covers (such as helmets). These domains were all mentioned by patients during the interviews in addition to problems with the transmitter coil (magnet falling off or being too strong). These domains of awareness were included in the first draft of the questionnaire. The domains most frequently mentioned were pain caused by the speech processor and/or magnet (mentioned by five out of seven participants), fear or discomfort caused by the external implant falling off the ear, and feeling a bulge where the internal implant resides under the skin (both mentioned by four participants). In order to measure these domains, 18 items were formulated. These items assessed the presence of the domains contributing to awareness and the burden that it created for the patient. Eight dichotomous (yes/no) items assessed the presence of domains; one multiple choice item assessed the ideal position of the transmitter according to the patient; seven visual analogue scale (VAS) items assessed the burden of these domains and two VAS item assessed pain caused by the external parts of the CI and in the area of operation.

Phase 2: Pilot study (Cognitive Debriefing Test)

A pilot study was conducted with 10 CI patients (see Table 8.1 for characteristics of the participants). The mean time to complete the questionnaire was 5 minutes and 21 seconds (range 3:10–9:40). Based on the results of the item analysis and the cognitive debriefing test small revisions to the questionnaire items and response options to ensure comprehensibility

and comprehensiveness. Four items measuring interference of the CI with daily activities that overlapped and two items measuring interference of the CI with wearing glasses were fused into two items, one multiple choice item including all activities that the CI could pose troubles with wearing glasses, and one visual analogue scale item measuring burden experienced by these problems. Two items assessing satisfaction with the position of the CI were removed that were deemed not specific for identifying the underlying issue that causes CI awareness. Thus the scoring results of these items would not be helpful for the clinician using this PROM. Two items assessing sleep disturbance caused by the implant were split into four items to increase specificity of the domain by assessing change of sleep position and awareness of the implant while lying on the operated side of the head. Lastly, one item was added to include more complaints other than pain, as suggested by the CI patients. Thus, the number of items was reduced to 15 (see Table 8.2 and Supplementary Material Figure S8.1). Additionally, the lay-out of the paper questionnaire was adapted based on the suggestions of the CI patients.

Phase 3: Reliability study

We included 54 participants in the reliability study. A total of 52 participants (96.3%) filled out and returned both questionnaires. The unilaterally implanted study group had a wide age range (18–82 years) with an average age of 65 years (see Table 8.1 for demographics of the reliability study participants). Most of the population was male (67.3%). On average, the participants had been using the CI for 30 months (range 3–234 months).

Table 8.1: Characteristics of study participants per study phase

Characteristics	Phase 1 n = 7	Phase 2 n = 10	Phase 3 n = 52
Age, mean (SD) [range]	68.6 (7.3) [62–80]	60.7 (14.3) [31–76]	65 (12.9) [18–82]
Sex, No. (%)			
Male	3 (42.9)	6 (60.0)	35 (67.3)
Female	4 (57.1)	4 (40.0)	17 (32.7)
CI model, No. (%)			
Cochlear	4 (57.1)	4 (40.0)	25 (48.1)
Advanced Bionics	2 (28.6)	3 (30.0)	6 (11.5)
MED-EL	1 (14.3)	2 (20.0)	18 (34.6)
Oticon Medical	0	1 (10.0)	3 (5.8)
Operation side			
Right	5 (71.4)	3 (30.0)	26 (50.0)
Left	1 (14.3)	4 (40.0)	26 (50.0)
Bilateral	1 (14.3)	3 (30.0)	0
CI use (months), mean (SD) [range]	100 (88.0) [13–253]	56.9 (74.7) [3–220]	30 (44.1) [3–234]

Table 8.2: COMPASS questionnaire items, answer options and scoring calculations (not original lay-out)

Disclaimer:
This is a translation of the original Dutch questionnaire for the purpose of this paper only. Please refrain from using in the English language without validation.

Instructions:
With this questionnaire we aim to assess how much your life is affected in the last month by having a cochlear implant. Mark the answer that best resembles your situation, or click and hold the bar to move on the scale. Filling out the questionnaire will take approximately 10 minutes.

No	Items	Answer options	Scoring calculation
1.	When I wear headgear (hat/cap/ helmet/head scarf), I have to remove the transmitter (magnet).	o Yes o No (go to question 3) o Not applicable for me. I never wear head gear. (go to question 3)	Yes: 5 points No/Not applicable: 0 points
2.	If yes, how bothersome do you find having to remove the transmitter?	Not bothersome ——— Extremely bothersome	Visual analogue scale: 0–10 *Calculation:* score / 2 = maximum 5 points
3.	The transmitter (magnet) sometimes falls off my head.	o Yes o No (go to question 5)	Yes: 5 points No: 0 points
4.	If yes, how bothersome do you find that the transmitter (magnet) sometimes falls from your head?	Not bothersome ——— Extremely bothersome	Visual analogue scale: 0–10 *Calculation:* score / 2 = maximum 5 points
5.	The speech processor and transmitter (magnet) have inhibited me in the following activities: *(more than one option can be chosen)*	o Work o Sport o Transport (e.g. bicycling or driving) o Social activities o Wearing glasses (regular glasses/reading glasses/sunglasses) o None of the above (go to question 7)	Each multiple choice item: 1 point None of the above: 0 points *Calculation:* Maximum 5 points

Table 8.2 continues on next page.

Table 8.2: *Continued*

No	Items	Answer options	Scoring calculation
6.	If yes, how bothersome do you find that the speech processor and transmitter (magnet) inhibits you?	Not bothersome ——— Extremely bothersome	Visual analogue scale: 0–10 *Calculation:* score / 2 = maximum 5 points
7.	When lying with my head on the operated side, I feel the cochlear implant under the skin.	o Yes o No (go to question 9)	Yes: 5 points No: 0 points
8.	How bothersome do you find that you feel the cochlear implant under the skin when lying on it?	Not bothersome ——— Extremely bothersome	Visual analogue scale: 0–10 *Calculation:* score / 2 = maximum 5 points
9.	I adjusted my sleeping position after the implantation because I want to avoid lying with my head on the operated side.	o Yes o No (go to question 11)	Yes: 5 points No: 0 points
10.	If yes, how bothersome do you find adjusting your sleeping position.	Not bothersome ——— Extremely bothersome	Visual analogue scale: 0–10 *Calculation:* score / 2 = maximum 5 points
11.	I feel a protrusion where the cochlear implant resides under the skin.	o Yes o No (go to question 13)	Yes: 5 points No: 0 points

12.	If yes, how bothersome do you find feeling a protrusion where the cochlear implant resides under the skin?	Not bothersome |——————————————————|	Extremely bothersome	Visual analogue scale: 0–10 *Calculation:* score / 2 = maximum 5 points
13.	How much pain have you had due to wearing the speech processor and the transmitter (magnet)?	No pain |——————————————————|	Unbearable pain	Visual analogue scale: 0–10 *Calculation:* score / 2 = maximum 5 points
14.	I have had the following symptoms in the area of the operation. (more than one option can be chosen)	o Pain o Numbness o Itchiness o None o Other: _____		Each multiple choice item: 1.25 points None: 0 points *Calculation:* Maximum 5 points
15.	*Fill out this question if you answered "Pain" in question 14. If not you can skip this question.* How much pain have you had in the area op operation.	No pain |——————————————————|	Unbearable pain	Visual analogue scale: 0–10 *Calculation:* score / 2 = maximum 5 points
				Total score: maximum 75

Table 8.3: Reliability and measurement error analysis for visual analogue scale items (continuous data)

No	Items	Sample size	Reliability analysis		Mean difference (SD)	95% Limits of agreement	
			ICC	95% CI		Lower limit	Upper limit
2	Impact of taking off transmitter	17	0.73	0.24–0.9	0.15 (3.40)	-6.51	6.82
4	Impact of falling of transmitter	30	0.66	0.28–0.84	0.13 (3.50)	-6.73	6.99
6	Impact of speech processor and transmitter inhibiting activities	30	0.86	0.7–0.93	0.22 (2.08)	-3.85	4.29
8	Impact of feeling the cochlear implant under the skin	16	0.79	0.41–0.93	-0.72 (2.61)	-5.83	4.39
10	Impact of adjustment sleep position	5	0.84	-0.87–0.98	-2.18 (2.58)	-7.24	2.88
12	Impact of feeling the protrusion	41	0.88	0.78–0.94	-0.17 (1.34)	-2.79	2.46
13	Pain due to wearing the speech processor and the transmitter	52	0.89	0.81–0.94	-0.20 (0.97)	-2.10	1.70
15	Amount of pain in the operation area	8	0.83	0.1–0.97	0.26 (1.59)	-2.86	3.38

Items are numbered in accordance with the COMPASS questionnaire.

Regarding the reliability analysis, the ICC, which represent reproducibility for the visual analogue scale items, ranged from 0.66 to 0.89 with only one item not meeting the acceptable level of 0.7, namely the item assessing the impact of the transmitter falling off the ear (see Table 8.3 for all ICC values with 95% confidence intervals). The Cohen's kappa that was calculated for nominal items ranged from -0.4 to 0.78, with six (sub)items out of 15 scoring above fair to good agreement and five (sub)items scoring excellent agreement. The two multiple choice items (number five and fifteen), contained the four subitems that had poor agreement kappa values, with one subitem on inhibition of work due to the speech processor and transmitter scoring a negative value of -0.40 implying that there was no effective agreement between the two questionnaires on this item (see Table 8.4 for all Cohen's kappa values with standard error and 95% confidence intervals).

The mean difference for items of continuous variables was -2.18 to 0.22. The 95% limits of agreement (LoA) revealed no statistically significant difference between the two administered questionnaires in all continuous variables (zero is included in each interval) (see Table 8.3). We observed higher mean differences with wider 95% LoA for items with smaller sample sizes (see Supplementary Figure S8.2 for Bland-Altman plots). Percentages of agreement ranges between 0% and 95%, and 83.3% and 96.6% for positive and negative agreement, respectively. The positive agreement percentage showed the widest range, with the multiple choice items number three and eight scoring the lowest values (see Table 8.4).

Discussion

The purpose of the study was to develop and validate a PROM to assess CI awareness, thus the state of mind or situation in which the patient is physically conscious he or she is wearing a cochlear implant and how this consciousness impacts their daily life. The COMPASS questionnaire was developed following the COSMIN guidelines[10] for development of PROMs and was based on expert opinion and patient interviews, pilot tested with a cognitive interview study, and validated by administrating it to a population of CI recipients. We tested the content validity (comprehensibility, comprehensiveness and relevance), and reliability of the questionnaire. The COMPASS questionnaire consists of 15 items and showed fair to excellent test-retest reliability for almost all items and measurement error analysis revealed no systematic or random errors of the score per patient. The lowest reliability and positive agreement scores were calculated for the activities impeded by the speech processor and transmitter; in particular work, transport and social activities. This could suggest that any restrictions caused by the external part of the CI during these particular activities, varies over time, even in the short test-retest time period of two weeks.

Table 8.4: Reliability and measurement error analysis for checkbox and multiple choice items (nominal data)

No	Items		Cohen's kappa	Standard error	95% CI	Agreement (%)	
						Positive	Negative
1	Taking off transmitter to wear headgear		0.7	0.09	0.53–0.88	82.8	90.9
3	Transmitter falls of head		0.73	0.09	0.55–0.91	87.3	85.7
5	Speech processor and transmitter inhibiting activities:	i. Work	-0.40	0.02	-0.44– -0.36	0	96.0
		ii. Sports	0.51	0.16	0.19–0.82	58.8	92.0
		iii. Transport	0.24	0.23	-0.22–0.69	28.6	94.8
		iv. Social activities	0.19	0.21	-0.22–0.60	25.0	93.8
		v. Glasses	0.63	0.12	0.39–0.86	73.3	89.2
		vi. None of the above	0.62	0.11	0.40–0.83	81.5	80.0
7	Feeling the cochlear implant under the skin while lying on it		0.76	0.10	0.57–0.96	82.8	93.3
9	Adjustment of sleep position		0.78	0.15	0.49–1.07	80.0	97.9
11	Feeling the protrusion of the cochlear implant		0.78	0.10	0.58–0.99	95.0	83.3
14	Symptoms in the area of operation	i. Pain	0.77	0.13	0.51–1.02	80.0	96.6
		ii. Numbness	0.77	0.13	0.51–1.02	62.5	96.6
		iii. Itchiness	0.56	0.16	0.24–0.87	87.9	93.2
		iv. None	0.67	0.11	0.46–0.88	61.5	94.5

Items are numbered in accordance with the COMPASS questionnaire.

We believe that prospective assessment of CI awareness using a PROM, can provide more accurate information on any existing problems. We know that hearing aid issues such as discomfort and handling problems, are common amongst users of these medical devices, one study reporting a prevalence of 98%.[9,15] However some patients might experience problems with their hearing aids, though do not report them to their clinician.[16] One study on cochlear implant recipient issues, reported that the majority of patients included in the study (89.8%), had at least one CI device handling problem.[5] Previous studies using patient reported outcome measures also found a high prevalence of other adverse events, such as change of taste. Mikkelsen et al. and Lloyd et al. reported changes of taste after surgery in 16.9% and 45% of CI patients, respectively.[17,18] The COMPASS questionnaire could be used by clinicians to assess issues caused by the external and internal components of the CI that contribute to awareness of the cochlear implant. These issues could be solved by counselling or arranging accessories such as an adjustment of magnet power. Moreover, the location of the implant in relation to the ear pinna might be adjusted likewise (cap wearing interferes with superior implant positioning).

The questionnaire fills in the gap and responds to the needs of the implantees that experience negative effects of the presence of the subperiosteal implant. Cochlear implants have undergone tremendous developments in the last decades regarding shape, hardware volume and intrinsic technical refinements. The different manufacturers produce R/S device aspects that are quite divers. One of the interesting developments is the significant reduction in implant volume, that might decrease implant protrusion visible at the level of the skin. Moreover, this might prevent the surgeon to drill a bony well in the temporal cortex as beforehand with the older implant the gold standard has been to drill a well, to tackle this issue. To our knowledge, there is little evidence thus far available regarding the influence of implant volumes reduction or the effects of drilling or not drilling a bony well, on CI awareness of a patient and implant related complaints. Our developed questionnaire meets these goals. Items assessing burden by issues caused by the internal device such as protrusion of the skin, sleep disturbances due to the implant or problems with headgear, could be rectifiable post-implantation by revision surgery (and re-positioning the implant) however it might be advisable to perform the implantation correctly during primary implantation. Therefore the COMPASS questionnaire could be used in clinic to assess the impact of different surgical methods for positioning and fixation of the R/S device on CI awareness.

A limitation of this study is the study population sample used for development and validation of the questionnaire, which was recruited from a single center. This could introduce selection bias, however participants were operated by several CI surgeons with different

surgical techniques. Also, assessment of the criterion validity of the COMPASS questionnaire could not be executed. After extensive literature research, we were unable to find validated outcome measures assessing CI use as defined in this study. Furthermore, despite our hypothesis that there are indeed differences of CI awareness between groups, it was impossible to execute this validation step. We expect that patients operated with different fixation techniques of the R/S device will differ in CI awareness. However, in our center we only use one fixation technique (the bony bed technique), and thus we couldn't compare these groups. Lastly, all four CI device brands were represented in the study population, and patients included in the study had sufficient experience with using the CI to contribute to the study.

In conclusion, the COMPASS questionnaire has good reliability and validity. Combining this PROM with clinical findings may assist in the routine follow up of patients with CI. Furthermore, it can be used as an endpoint in a clinical study, to evaluate different surgical techniques and its effect on awareness.

Conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Authors contributions

All authors contributed equally to draft and revised the manuscript and approved the final submission.

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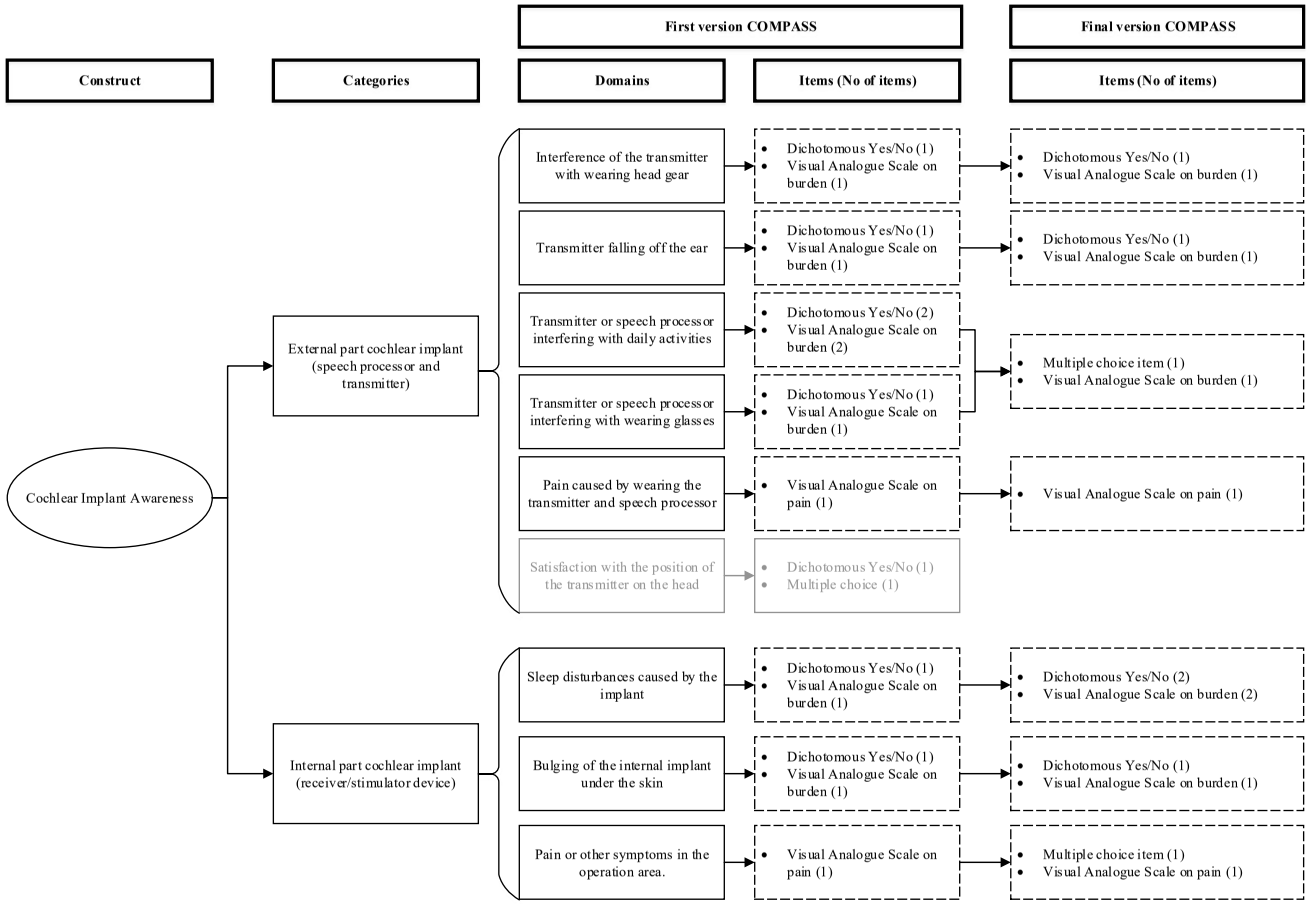
Supplementary material

Interview probe for Phase 1 interviews: Item generation

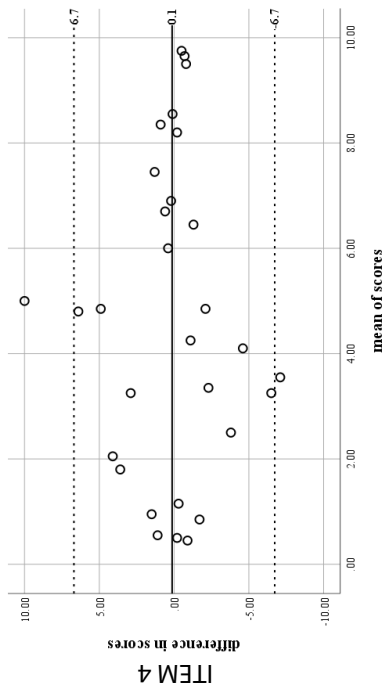
- Have you had or do you currently have any issues with the use of the cochlear implant?
- Does wearing the cochlear implant cause you any (physical) problems?
- Are you aware of your cochlear implant while using it? If so, in which situations are you aware of it?
- Are there aspects of the hardware of the implant that you would change if that were possible?
- What information were you given during the preoperative consultation about how the implant looks like and how you operate it?
- Were there any aspects about the use of the implant that you would have wanted more information on?
- Are you satisfied with the position of the implant on your head?
- Does the internal part of the implant protrude from the skin? If so, does this bother you?

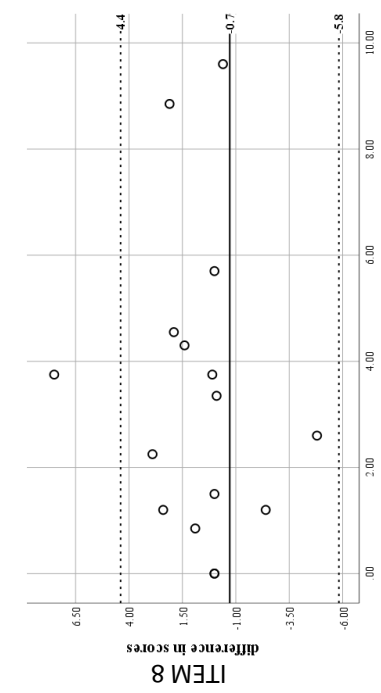
Interview probe for Phase 2 interviews: Pilot study (Cognitive Debriefing Test)

- Could you describe what this questionnaire is about?
- Were the questions clear for you? If not, which questions were unclear and why?
- Did you understand the instructions for filling out the questionnaire?
- Do you feel there were any topics or aspects of wearing a cochlear implant that were missed by the questionnaire?
- What did you think of the way the questions are posed and the answer options?
- (optional in case of a hesitation in filling out a specific question) Could you explain what question (…) is about?
- Do you have any suggestions to improve the questionnaire?



Supplementary Figure S8.1: COMPASS questionnaire domains and items per version.


ITEM 4
difference in scores
mean of scores
-6.7
0.1
-6.7


ITEM 8
difference in scores
mean of scores
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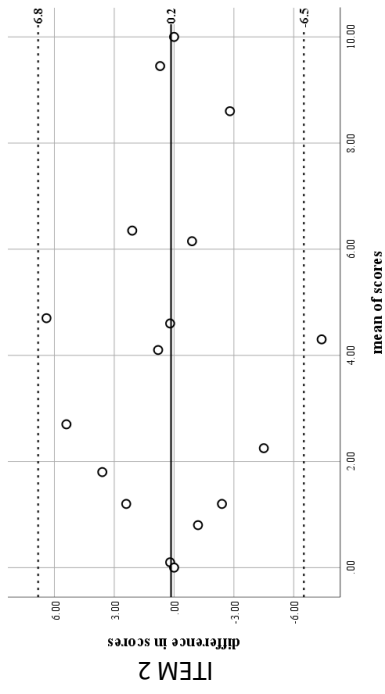
-0.7
-5.8


ITEM 2
difference in scores
mean of scores
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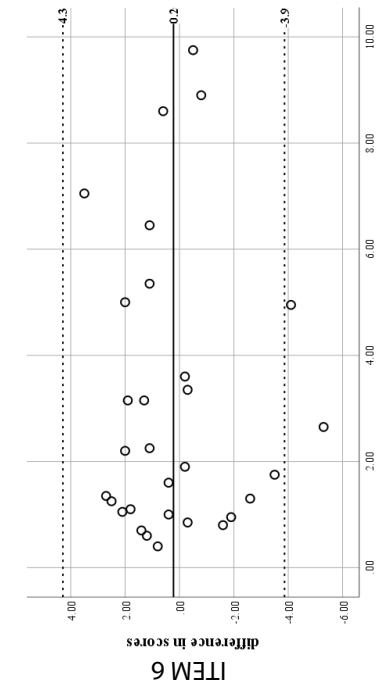
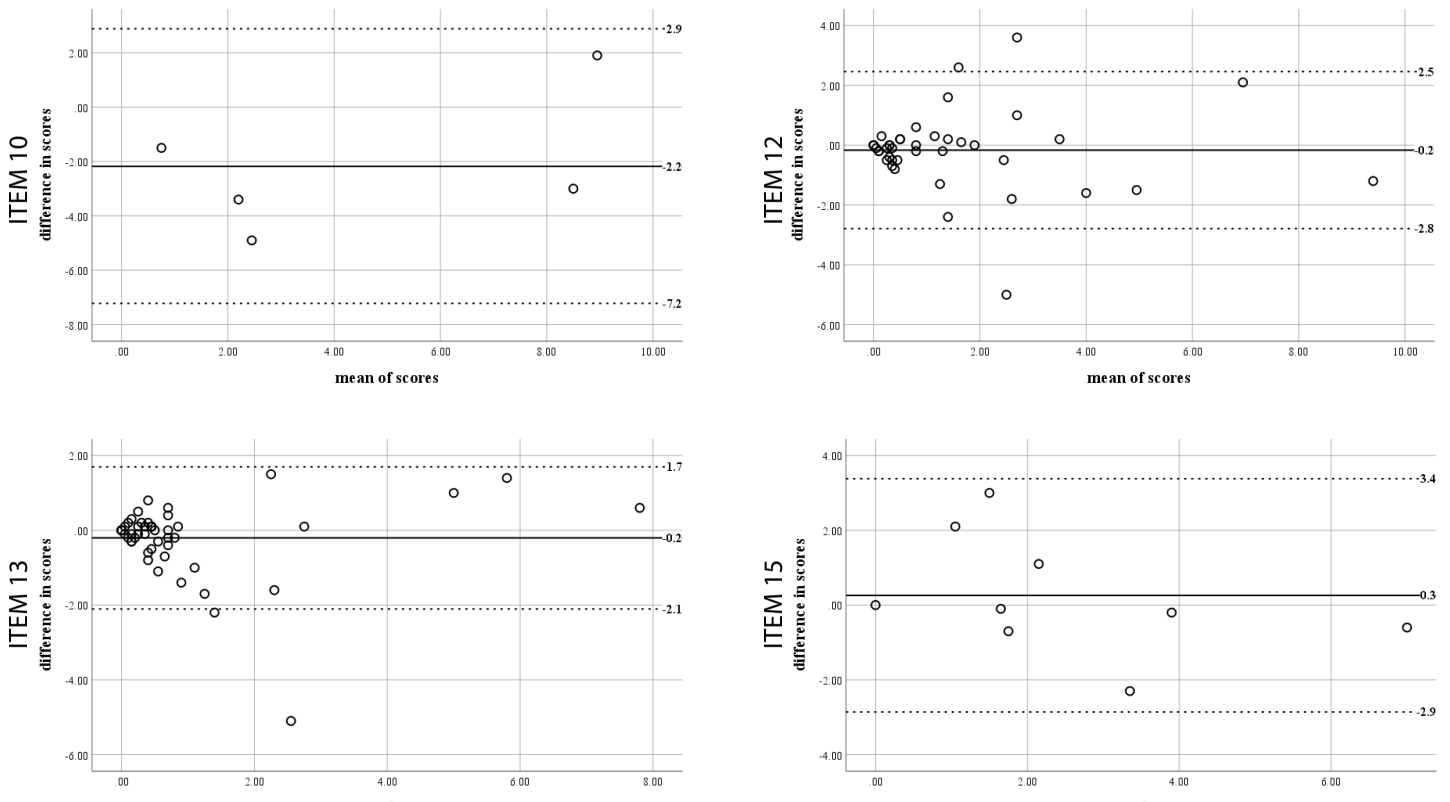
0.2
-6.5


ITEM 6
difference in scores
mean of scores
-4.3
0.2
-3.9



Supplementary Figure S8.2: Bland-Altman plot for the test-retest reliability. The plot illustrates the agreement between test and retest of the questionnaire and identifies possible outliers. Each sample is represented on the graph by conveying the mean value of the 2 assessments (x-axis) and the difference between the 2 assessments (y-axis). The mean difference was the estimated bias, and the standard deviation (SD) of the differences measured the fluctuations around this mean (outliers being above 1.96 SD diff). Reference lines shows mean difference between time 1 and time 2 (solid line), and 95% limits of agreement for the mean difference (broken lines).

CHAPTER 9

A mono-center, patient-blinded, randomized, parallel-group, non-inferiority study to compare cochlear implant receiver/stimulator device fixation techniques (COMFIT) with and without drilling in adults eligible for primary cochlear implantation

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Abstract

Background: During the cochlear implantation procedure, the receiver/stimulator (R/S) part of the implant is fixated to prevent postoperative device migration, which could have an adverse effect on the position of the electrode array in the cochlea. We aim to compare the migration rates of two fixation techniques, the bony recess versus the subperiosteal tight pocket without bony sutures.

Methods and analysis: This single-blind randomized controlled trial will recruit a total of 112 primary cochlear implantation adult patients, eligible for implantation according to the current standard of practice. Randomization will be performed by an electronic data capture system Castor EDC, with participants block randomized to either bony recess or standard subperiosteal tight pocket in a 1:1 ratio, stratified by age. The primary outcome of this study is the R/S device migration rate; secondary outcomes include patient-experienced burden using the validated COMPASS questionnaire, electrode migration rate, electrode impedance values, speech perception scores, correlation between R/S migration, electrode array migration and patient complaints, assessment of complication rates, and validation of an implant position measurement method. Data will be collected at baseline, one week, four weeks, eight weeks, three months and 12 months after surgery. All data analyses will be conducted according to the intention-to-treat principle.

Discussion: Cochlear implantation by means of creating a tight subperiosteal pocket without drilling a bony seat is a minimally invasive fixation technique with many advantages. However, the safety of this technique has not yet been proven with certainty. This is the first randomized controlled trial that directly compares the minimally invasive technique with the conventional method of drilling a bony seat.

Trial registration: Netherlands Trial Register NL9698. Registered 31 august 2021.

Background and rationale

Cochlear implants (CI's) provide hearing through direct electrical stimulation of the auditory nerve in patients with sensorineural hearing loss, and have become standard care for adult and pediatric patients with severe to profound bilateral hearing loss. Cochlear implantation surgery requires careful planning and execution. The correct electrode array positioning in the cochlea is crucial for optimal functionality of the device. This array is connected to the body of the implant, known as the receiver/stimulator (R/S) device. During cochlear implantation, the R/S device is placed and fixated on the skull. It should be placed close to the pinna, without possible interference of the microphone in the behind-the-ear device laying (partially) on top of the R/S device.

The standard fixation technique of the R/S device, which is recommended by the surgeon's guide that are supplied with the respective implants, consists of drilling out a part of the bony cortex of the skull (a bony recess), as well as non-absorbable suture retaining holes.[1] The bony recess technique lowers the profile of the R/S device in relation to the skull surface and holds it in place with non-absorbable sutures to the bone. Although rare, complications that are due to drilling of the bony recess can have serious consequences. Depending on the extent of drilling and the cortex thickness of the patient, the dura mater is sometimes exposed.[2,3] Several studies report on dural tears with subsequent cerebrospinal fluid leakage as a direct result of extensive cortical drilling.[4–6] Other complications that have been reported (but occur very rarely) and associated with this technique are late onset hematomas, epi-/subdural hematoma, tentorial herniation, and cerebral infarction, as well as meningitis.[5,7–11] To avoid such risks, in recent years ENT surgeons have adopted less invasive techniques.[1–3,10,12–20] Additionally, later CI models have a lower profile and a flatter bottom. However, the lowering of the profile is a trade-off for a larger footprint which results in a larger bony recess thus a larger area of the skull is drilled out.

Complications that can occur as a result of failed fixation of the R/S is a shift/migration of the internal components of the implant: the R/S device itself and the electrode array.[16,21] Migration of the R/S device can lead to pain/headache, behind-the-ear device problems, hematoma or device failure and in some cases necessitating revision surgery.[19,22–26] It can also have an effect on the position of the electrode array in the cochlea. Electrode migration or extrusion is one of the most common indications for revision surgery.[23–25] This complication can cause poor performance, pain, vertigo, tinnitus, and facial nerve stimulation, but can also present without complaints.[27] Increase of impedance values has also been described as a result of electrode array migration.[28] The rate of reported electrode migration varies in the literature and seems to occur more than previously thought.[27,29]

A minimally invasive technique that does not require drilling out a bony recess, known as the subperiosteal tight pocket technique, was first described by Balkany et al. in 2009.[10] This technique uses the anatomical boundaries of the pericranium to create a tight subperiosteal pocket in which the R/S device is inserted. Apart from the advantage of not having to drill out a bony recess, thus eliminating the risk of complications associated with the bony recess, the subperiosteal tight pocket technique also has the advantage of a smaller incision and shorter operating time.[16] Creating the subperiosteal pocket might also require less manipulation and straining of the temporalis muscle (compared to the mentioned bony recess technique), thereby reducing postoperative pain or tissue related complaints even more.

Since the publication of the study by Balkany et al. in 2009, many ENT specialists are applying the tight subperiosteal technique.[1,2,12–14,16–18,20,30–33] However, since the R/S device is not fixated in a bony recess or by sutures, migration of the device is a point of concern due to the complications that can occur. To evaluate the difference in migration rates between the fixation technique currently used in our center (the bony recess technique), and the intervention technique (subperiosteal tight pocket technique), we conducted a literature review.[34] The results were inconclusive due to a lack of high quality studies from a methodological point of view. Thus, there is no quality evidence to support the superiority of either technique. Therefore in the COMFIT trial we aim to compare the subperiosteal tight pocket technique with the bony recess technique, for fixation of the R/S device of the cochlear implant.

Objectives

The primary objective of our study is to compare the migration rates of the two fixation techniques (bony recess vs. subperiosteal tight pocket) by analyzing 3D reconstructions of the R/S device, acquired by Cone Beam Computed Tomography (CBCT) scans at baseline and baseline and at 3 and 12 months post-surgery. Secondary objectives are to investigate the difference between the two fixation techniques in patient-experienced burden using the validated COMPASS questionnaire, electrode array migration rate, and electrode impedance values. Other secondary objectives are to investigate the association of electrode impedance values with R/S device and electrode migration, and whether complaints of performance drop, vertigo, tinnitus, headache or nonauditory stimulation are associated with electrode array migration and R/S device migration. We will also compare the complication rate of these surgical techniques, for major and minor complications. Finally, we will validate the measurement method technique with flexible tape measure for the assessment of migration of the R/S device.[35]

Trial design

This is a single-blind, non-inferiority randomized controlled trial, with two study arms (Figure 9.1). Patients will be randomly allocated into equally sized groups: group A and group B (allocation ratio 1:1). Patients in group A will be operated with the bony recess technique, patients in group B will be operated with the subperiosteal tight pocket technique. Inclusion in the study will have no consequence for the model or brand chosen by the patient, as is currently standard practice.

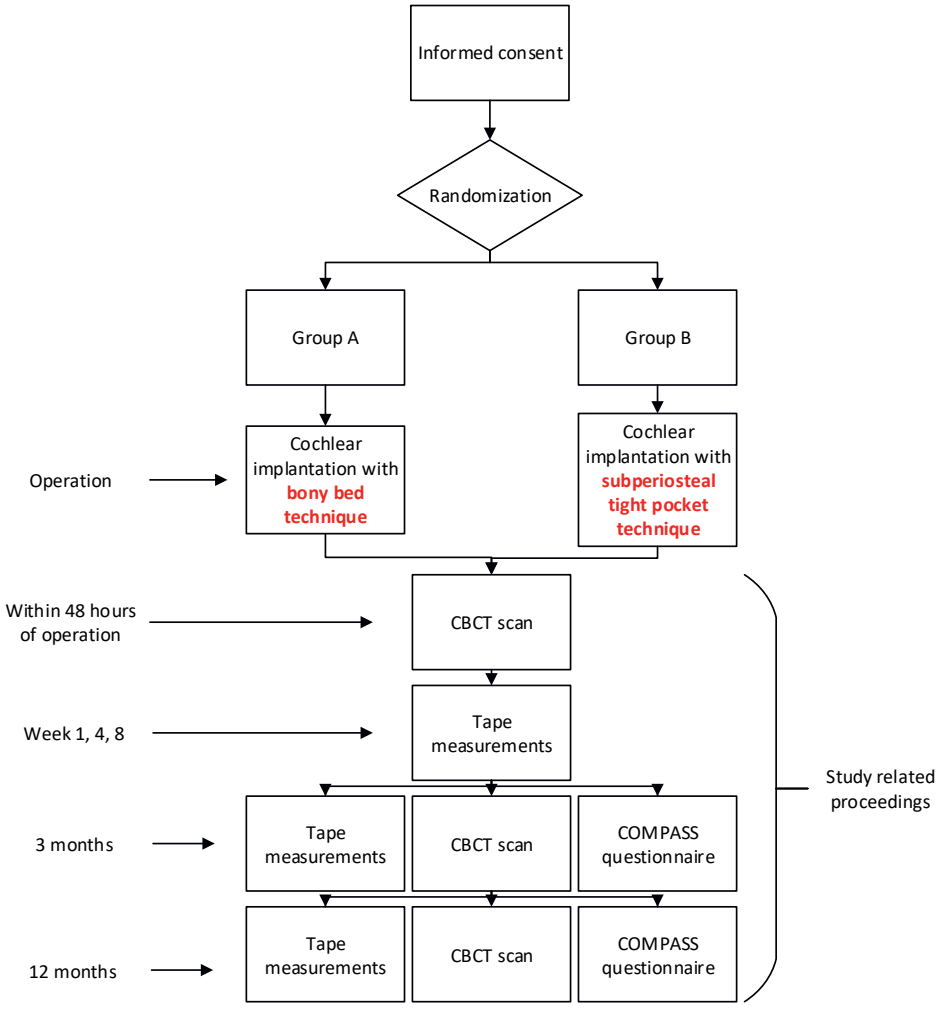

Figure 9.1: Flowchart of the study. CBCT: Cone Beam CT scan; COMPASS questionnaire: patient reported outcome measure on cochlear implant awareness; Patients will be randomized in two groups according to a variable, weighted block randomization module subgroups with stratification for age (18–50 years, and > 50 years).

Materials: participants, interventions and outcomes

Study setting

This is a monocenter study performed in a tertiary referral clinic in the Netherlands, the University Medical Center (UMC) Utrecht.

Eligibility criteria

The study population consists of adult patients (> 18 years old) that are approved for cochlear implantation according to standard care criteria. Patients will initially undergo a series of diagnostic tests to assess eligibility for cochlear implantation. These are: a CT-scan, a pure tone audiogram/speech test, psychological evaluation, and a consultation by the audiologist and ENT specialist. The Cochlear Implant Team of the UMC Utrecht will assess the work-up results and assess eligibility for cochlear implantation, according to the current clinically applied criteria.

All cochlear implant models will be included in this study. The choice for the cochlear implant model lies with the patient and the CI team of the UMC Utrecht and will not be affected by taking part in this trial. In order to be eligible to participate in this study, a participant must have provided written informed consent authorization before participating in the study. They also must have Dutch written language proficiency and be physically able to undergo a CBCT scan.

A potential participant who is a revision or re-implantation candidate, is unable to understand or sign informed consent or is pregnant during the trial, will be excluded from participation in this study.

Interventions: description

The standard surgical procedures for cochlear implantation will be followed. A retro-auricular S-shaped incision will be made to expose the mastoid. The electrode array will be inserted via a posterior tympanotomy and round window implantation by soft-surgery techniques. The R/S device will be fixated according to the group the patient is allocated to. The bony recess technique will be used in group A; a bony recess will be drilled at an angle of 30 to 60 degrees relative from the Frankfurt Horizontal plane. The provided silicone dummy will be used to ensure the depth and dimensions of the recess are sufficient. No tie down sutures will be used. Patients allocated to group B will be operated using the subperiosteal tight pocket technique as described by Balkany et al.[10]

Interventions: modifications

Modifying the allocated intervention would require a revision surgery where the cochlear implant would be removed. Revision surgery is potentially harmful for the patient therefore it will only be performed in rare cases such as device failure, wound infection, or persisting pain.

Interventions: adherence

The measurements scans will be performed on the same days as the regular follow up visits of the medical rehabilitation programme.

Interventions: concomitant care

Not applicable, this study does not alter the regular care pathway.

Outcomes

At intake, demographic data will be extracted from the electronic patient database: age, gender, if the deafness is pre- or postlingual and electronic address. The following outcomes will be assessed at the baseline visit and follow-up visits at 1, 4 and 8 weeks and at 3 and 12 months postoperatively (Figure 9.2). All measurements will be performed by the research team following the same protocol procedures.

Primary outcome measure

The main outcome of this study is R/S device migration and will be calculated by analyzing 3D reconstructions of the R/S device, acquired by Cone Beam CT (CBCT) scans at baseline and during follow up and at 12 months. We consider migration either translational or rotational above 1.0 mm or 1° as clinically relevant. Any migration under these cut-offs are considered within the measurement error margin of the analysis (0.3 mm or degrees). These calculations will be carried out by using 3DMedX® (v1.2.24.1, 3D Lab Radboudumc, Nijmegen). R/S positions will be superimposed, compared and analyzed based on the Iterative Closest Point (ICP) algorithm.[36] The 3D reconstructions of the R/S device at baseline and 12 months will be compared to calculate the primary outcome measure.

Secondary outcome measures

Electrode migration

Electrode array migration is defined as a displacement of the basal electrode outside the cochlea of ≥ 1 mm (i.e. approx. 1 contact spacing). To compare the electrode array

COMFIT TRIAL	STUDY PERIOD								
	Enrollment	Allocation	Post-allocation						Close out
Timepoint	$-t_1$	0	t_1	t_2	t_3	t_4	t_5	t_6	
ENROLMENT									
Eligibility screen									
Informed consent									
Allocation									
Surgery									
Activation of Cochlear Implant									
INTERVENTIONS									
Group A, (BR)			←	—	—	—	—	→	
Group B (TP)			←	—	—	—	—	→	
ASSESSMENTS									
Baseline variables									
Primary outcome: *R/S migration (CBCT scan)*									
Secondary outcomes:									
Electrode array migration (CBCT scan)									
CI Awareness (COMPASS)									
Speech perception									
Tape measurements									

Figure 9.2: Schedule of enrolment, interventions, and assessments adapted from the Standard Protocol Items: Recommendations for Interventional Trials (SPIRIT).
$-t_1$: 2 weeks before surgery
t_1 : within 48 hours of cochlear implantation
t_2 : 1 week post-surgery
t_3 : 4 weeks post-surgery
t_4 : 8 weeks post-surgery
t_5 : 3 months post-surgery
t_6 : 12 months post-surgery

migration rate between the two surgical techniques we will analyse the acquired CBCT scan images following a previously validated method.[29,37] Electrodes, situated at the level of the round window, will be categorized as extracochlear, since electrodes at this position do not provide adequate stimulation or accurate pitch perception so that they mostly have to be removed from the stimulation map.

Electrode impedance values

Electrode impedance values will be measured by the patient's audiologist at 1, 3 and 12 months after operation for all eletrodes. This is according with regular care. Electrode impedance values measured in kOhm (a measure of the resistance to current flow) in common ground stimulation. Values above 20–30 kOhms will be considered abnormally high. Additionally, an increase of impedance values ≥ 75% from the averaged baseline after 1 month of activation will be considered a significant increase.[29,38]

Speech perception

Three months and 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. Each list contains 11 words with a total of 33 phonemes. This is according with regular care. The speech tests can be quantified with a simple correct percentage score in bimodal solution if the patient has a hearing aid in the contralateral ear.

Complications

Incidence and degree of complications according to the following categories:

- Device failure, which is classified into hard or soft failure using standardized criteria described in the 2005 Cochlear Implant Soft Failures Consensus Development Conference Statement.[39]
  - Major and minor complications according to the proposal of Hansen et al. 2010.[40]
  - Major: a significant medical problem (e.g. meningitis), additional major surgery (e.g. cholesteatoma surgery or reimplantation due to a patient-related problem), explantation of the device for any reason other than device-related failure, any degree of permanent disability (e.g. facial nerve paralysis)
- Minor: complications leading to extended hospitalization or treatment on an outpatient basis, complications settling spontaneously or by conservative medical treatment, complications managed by a minor surgical procedure (e.g. simple haematoma aspiration by syringe).

Questionnaire

The questionnaire used in this study is the validated COchlear iMPlant AwareneSS (COMPASS) survey that assesses patient-experienced burden by wearing the CI in their day-to-day activities.[41] It contains 15 items, multiple choice as well as visual analogue scale items. Each item had a maximum score of 5, with a total maximum score of 75. A higher COMPASS score represents a higher awareness level. This questionnaire was developed in Utrecht and validated for use in the Dutch language. The questionnaire will be sent at 3 and 12 months post operatively, by email through the data capture system Castor EDC to the study participants. If a patient does not wish to fill out the questionnaire online, it will be sent by post.

Validation of measurement method

The measurement technique to determine the position of the R/S device using a flexible tape measure, previously validated,[35] will be compared to the results of migration measured by the CBCT scans. Validation of a measurement technique with flexible tape measure to detect migration. Repeated measurements will be done and results will be compared to the results of migration measured by the CBCT scans.

Participant timeline

All patients will undergo a high resolution CBCT within 48 hours after surgery, to assess the R/S device and electrode array position. Patients will undergo two more CBCT scans at 3 months and 12 months postoperatively. The R/S device position will also be assessed with a validated external measurement method after 1, 4, and 8 weeks, and at 3 and 12 months postoperatively by a researcher or by the patients' audiologist or speech therapist.[35] Patients will fill in a questionnaire after 3 and 12 months postoperatively. See Figure 9.1 for an overview.

Sample size

This sample size calculation was based on the primary outcome, R/S migration after 12 months. Due to limited quality evidence on the migration rate for both techniques, an estimation of the migration rates cannot be based on literature, therefore we base our assumptions on clinical expertise.[34,42,43] We consider a migration under 1.0 mm or 1° to be clinically irrelevant. Migration under these cut-off points is within the measurement error margin of the measurement technique of the CBCT scan analysis. A sample size of 51 per study arm reaches 80% power ($\beta = 0.8$) and a significance level (α) of 0.05 with a non-inferiority margin of 1.0 mm. Standard deviation are estimated at 2.0 mm based on

the database of Maxwell et al.[43] In order to cover for possible loss to follow up estimated at a maximum of 10%, we will include 56 patients per study arm.

Recruitment

Patient recruitment started in October 2021 we anticipate recruiting approximately 60 patients per year, thus recruitment should be completed in 2 years. Patients are recruited from the outpatient Otorhinolaryngology department at the University Medical Center Utrecht. Eligible patients will be informed about the study by their treating physician. These patients have already been approved for cochlear implant surgery by the CI team. The investigator provides the patient with an information letter and informed consent form, which is signed by both the investigator and the patient before the surgery. Patients consent to the use of their data for the research purposes outlined in this protocol which includes publication of the results once the trial has been completed. Patients will not receive compensation for participation in the trial.

Randomization and blinding

Patients will be randomly assigned to one of the two study groups with 56 patients allocated in each group. Randomization takes place in the UMC Utrecht endorsed electronic data capture system Castor EDC. (https://www.castoredc.com/). After given informed consent, patients will be randomized with an allocation ratio of 1:1 and variable block sizes, with stratification for age (18–50 years, > 50 years). Stratification is applied in both study groups. This is a single blind study, meaning that only participants are blinded for the treatment allocation. The randomization will be done before surgery and patients will not be informed about the allocation. The research team is not blinded. The outcome data will be blindly analyzed. Blinding of the data will be performed by the electronic Case Report Form system used (see section 'Data collection plan'). In the event that a revision surgery is necessary for removal or repositioning of the CI, unblinding is permitted. A member of the research team will inform the subject of the allocation.

Methods: data collection, management and analysis

Data collection plan

After given informed consent, the patient will receive a unique identifier, after which members of the research team will extract all necessary clinical parameters 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.). The assessors are specialized in the field of otology and are therefore trained to interpret the results of the various outcome measures (CBCT scans, speech performance tests, impedance values). Participant retention will be promoted by efficient schedule strategies, namely inviting participants for the follow up appointments on the same days as the clinical rehabilitation consults. The study participants will receive a separate invitation for each follow up appointment, shortly before.

Data management

Data handling and protection is conducted according to the ISO 27001 compliant processes and ICH-GCP and applicable regulations. Confidentiality will be maintained at all times and participant information will not be disclosed to third parties. After given informed consent, the patient will receive a unique identifier. All generated (meta)data will be stored in a secure research folder structure for access control. Only researchers directly involved in the study and the monitor of the study are allowed to access the key-linking table to enable patient re-identification. The paper data files and informed consents will be stored in a locked cabin in a locked room. Only research members directly involved in this study and the monitor of the study will get access to all of the collected research data. When required, authorized personnel of the study can access the pseudonymized source data for intermediate analysis or business intelligence reports.

Statistical analysis

To assess whether continuous variables are normally distributed, histograms and Q-Q plots will be computed. Continues data will be expressed as mean ± standard deviation (SD) when normally distributed, and as median ± interquartile range (IQR) when skewed. Number of cases and percentages will be presented as categorical variables. A p-value < 0.05 is considered statistically significant. All analyses will be conducted according to the intention-to-treat principle.

Statistical analysis primary objective

The main outcome is R/S device migration calculated by analysing 3D reconstructions of the R/S device, acquired by CBCT scans at baseline and during follow up. Migration will be reported in millimetres and angle degrees (continuous variables) between the intervention group and the control group at baseline, 3 and 12 months after implantation. Differences between the intervention and control group will be calculated using the unpaired t-test or the Mann Whitney U test.

Statistical analysis secondary objectives

COMPASS questionnaire scores between intervention and control at 3 and 12 months after cochlear implantation will be calculated using the unpaired t-test (or the Mann-Whitney u test).

For statistical analysis of electrode migration data will be compared in number of cases and percentages. To calculate any association between electrode migration of ≥ 1 mm and R/S device migration, and between electrode migration and a decrease in speech performance tests, Pearsons correlation test or a Spearman rank correlation test will be performed. Electrode impedance values will be compared between the groups with the unpaired t-test (or the Mann-Whitney u test). CVC word score tests (with and without noise) will be compared between the groups with the unpaired t-test. Within group comparisons will be calculated with differences of mean values. A clinically relevant speech performance decrease is a speech performance test score decrease of ≥ 7% when scoring between 30 and 80%, and ≥ 5% when the patients scores < 30% or > 80% on the speech performance test, a definition based on clinical experts. Incidence and degree of complications will be reported by means of frequencies.

Participants who withdraw from the study prematurely will be considered as lost and will be replaced. Reasons for withdrawal or premature termination will be documented. Potential missing data will be handled using multiple imputation. Complete cases analyses will be performed as a sensitivity analysis. All analyses will be performed on an intention-to-treat basis.

Oversight and monitoring

Composition of the coordinating center and trial steering committee

- Dr. H.G.X.M. Thomeer (principal investigator) and dr. L.M. Markodimitraki (research physician)

- Design and conduct of the COMFIT trial
- Preparation of protocol and revisions
- Preparation of case report forms
- Organizing steering committee meetings
- Identification of potential recruits
- Taking informed consent
- Supervising the trial
- Bi-weekly meetings
- Members of Trial management committee

Trial management committee

- (see title page for members)
- Agreement of final protocol
- Reviewing conduct and progress of study and if necessary agreeing changes to the protocol
- Advice on management matters

Monthly meetings data management

Trial quality will be monitored independently by a local monitor (UMC Utrecht) once a year. The local monitor will check 10% of signed ICs, inclusion and exclusion criteria, source data and serious adverse events (SAE). From the first three participants, the inclusion and exclusion criteria will also be checked. The study does not have a public involvement group.

Harms

The investigator will submit a summary of the progress of the trial to the accredited MREC once a year. Information will be provided on the date of inclusion of the first participant, numbers of participants included and numbers of participants that have completed the trial, serious adverse events (SAEs)/serious adverse reactions, other problems and amendments.

Ethics and dissemination

The results (positive or negative) of this study will be disclosed unreservedly. Data and results of research are owned by the investigators. The results of research will be submitted for publication to peer-reviewed scientific journals. Disputes on the interpretation of the results may not lead to an unnecessary delay in publication. None of the parties concerned has a right of veto. In addition, trial results will be communicated via symposia and relevant

conferences on otology and cochlear implantation. Results will be summarized for the general public and interested trial participants and shared on the sponsor's website.

The sponsor 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.

Discussion

Cochlear implantation by means of creating a tight subperiosteal pocket without drilling a bony seat is a minimally invasive fixation technique with many advantages. However, the safety of this technique has not yet been proven with certainty. The objective of this study is the comparison of two broadly used surgical techniques for the fixation of the receiver/stimulator device during cochlear implantation, with and without drilling. This is the first randomized controlled trial that directly compares the minimally invasive technique with the conventional method of drilling a bony seat. Multiple outcomes will be assessed, using objective measures for the assessment of R/S device and electrode array migration, speech performance and patient experience. A limitation of this trial is the monocentre design, which may affect recruitment rate and external validity.

Trials status

Protocol version 2, 20-01-2022. The trial is currently in recruitment phase. The first patient was recruited on 27 October 2021. Thirteen of 112 patients were included in the study on 11 May 2022. Approximate date of trial completion: 27-10-2023.

List of abbreviations

3D: three-dimensional
AE: Adverse Event
CBCT: Cone Beam computed tomography
CI: Cochlear implant
COMPASS: Cochlear implant awareness questionnaire
CVC: Consonant-vowel nucleus-consonant, Dutch speech perception test
ENT: ear, nose and throat

IC: informed consent
ICP: Iterative Closest Point
IRB: Institutional Review Board
MERC: Medical research ethics committee (MREC); in Dutch: medisch ethische toetsing commissie (METC)
R/S: receiver/stimulator device
WMO: Medical Research Involving Human Participants Act; in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen

Declarations

Ethics approval and consent to participate

The study will be conducted according to the principles of the Declaration of Helsinki (version 2013, Fortaleza) and in accordance with the Medical Research Involving Human Subjects Act (WMO). The research protocol was approved by the Institutional Review Board (IRB) of the UMC Utrecht Medical Research Ethics Committee (MREC) Utrecht (NL76872.041.21, version 3, August 2021). Amendments are changes made to the research after a favorable opinion by the accredited MREC has been given. All amendments will be notified to the MERC that gave a favorable opinion. Written informed consent will be obtained from all participants.

Consent for publication

See the informed consent form (supplementary materials).

Availability of data and materials

Only research members directly involved in this study and the monitor of the study will get access to all of the collected research data. Any data required to support the protocol can be supplied on request.

Competing interests

The authors declare that they have no competing interests.

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Part of cost involved of this study is indirectly funded by Oticon Medical as a non-restrictive research grant (grant number N/A). Oticon Medical did not and will—by a research contract—not have influence on the data collection, analysis, data interpretation and publication.

Authors' contributions
All named authors adhere to the authorship guidelines of Trials. LM, IS and HT conceived the study, and wrote the project application for funding and all authors contributed to the development of the study protocol. LM, TH and EB designed data analysis methods. All authors contributed to the drafting of the manuscript or revising it critically for important intellectual content. All authors read and approved the final manuscript.

Availability of data and materials
Data sharing including the participant dataset, full protocol and statistical codes, will be considered upon reasonable request.

Acknowledgements
Not applicable

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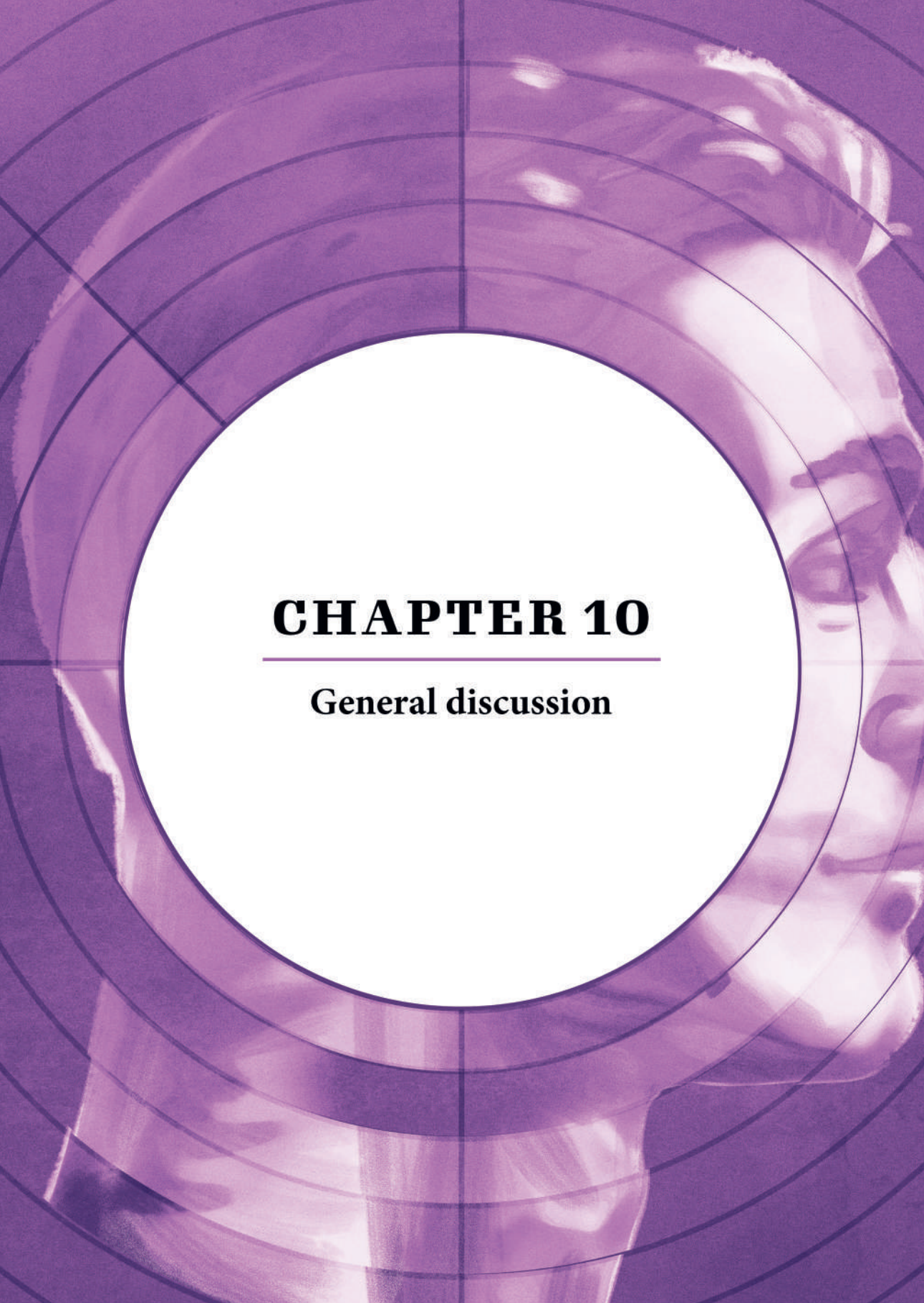

CHAPTER 10

General discussion

The aims of this thesis were threefold. First, we aimed to investigate the different surgical techniques used for R/S device fixation to prevent complications associated with drilling and migration of the implant. Second, we explored new methods of R/S device positioning through development of a semi-automated algorithm and a patient specific 3D-printed surgical guide. Third, we aimed to develop objective means to assess migration and the impact of wearing a cochlear implant. This chapter provides a summary of the main findings, a general discussion of the outcomes of the chapters of this thesis, presents clinical implications and provides suggestions for future perspectives.

Summary of main findings

Hearing loss is one of the world's most prevalent conditions worldwide causing a significant social and economic burden.[1,2] Cochlear implantation is standard care for patients with significant hearing impairment, and consistent use of a cochlear implant (CI) can greatly increase quality of life.[3–5] Thanks to improvements in CI design, surgical techniques and programming strategies, the indication and age range has broadened increasing the number of CI candidates.[6] However, there is currently no consensus among CI surgeons, on the safety of surgical techniques for CI positioning and fixation. There seems to be a great variability between surgeons on the techniques used during cochlear implantation. To assess the current practices in cochlear implantation surgery, we conducted an international survey study by sending an online questionnaire to CI surgeons, described in **chapter 2**. Fifty-nine participants working in 13 different countries were included, with most respondents operating on both adults and children. For all surgical techniques except the cochlear approach, we demonstrated high levels of variability. The majority of respondents used the bony well or bony rim technique for fixation of the implant with or without additional fixation materials. The preferred approach to the scala tympani was the round window insertion over cochleostomy or extended round window. There was no clear preference of electrode array type, perimodiolar or lateral wall. Most participants indicated that during their career, they had steered towards structure preservation or minimal invasive surgery. It was unclear what caused the variations between individual surgeons.

In **chapter 3** we compared the rate of migration of the internal device components (both R/S device and electrode array) when fixating the CI using the two most used fixation techniques, the bony well and the tight subperiosteal technique in a systematic review. Seven studies were included, none of which directly compared the two techniques. All three studies that used objective means to report migration of the R/S device, detected rates varying from 9–100% when using either the bony well technique or the tight pocket

technique with and without additional fixation materials. All other studies that used clinical observation as an outcome measure, reported no migration of the internal device. We concluded that there is no evidence of a difference between the two fixation techniques in adult patients regarding migration rates. Further research is needed to compare the two fixation technique, preferably with a randomized design, using objective outcome measures.

The observed difference between reported migration rates depending on the outcome measure used led us to believe there is need for an objective, easy to use method to assess R/S device position and migration. This method was developed in **chapter 4**, where we concluded that the R/S device location can be assessed reliably by measuring the distance between the lateral canthus, the tragus tip and the external magnet with a flexible tape measure. In order to use this method to reliably assess migration of the implant, further validation is needed.

In **chapter 5** we aimed to develop and validate a semi-automated algorithm that determines the most optimal position of the R/S device in regards to cortical thickness based on CT imaging. The algorithm determines if drilling a bony well of predetermined dimensions is feasible in a patient, determined by the residual thickness after virtually creating the bony well on a 3D model of the patient's skull. We concluded that the algorithm is not capable of consistently detecting the thickest location within the region of interest, however it is reliable in determining the feasibility of drilling.

This method was applied in **chapter 6** where we retrospectively assessed clinical data of 192 ears of children to investigate the feasibility of drilling a bony well adequate for CI embedment in different age groups. For 79.7% of the included ears, it was not possible to drill a bony well without reaching the dura mater. For most children aged zero to nine years, creating a bony well that adheres to the standards of most manufacturers is sometimes difficult and often impossible. In this chapter we also retrospectively investigated our clinical cohort of pediatric CI patients to report complication and device failure rates using different fixation techniques: bony well with or without additional fixation strategies and the minimally invasive tight subperiosteal pocket. We included 230 patient records (344 ears) and found a complication rate of 8.1% for major complications and 48.3% for minor complications. There was no apparent difference between fixation groups in the rate of R/S device related issues, such as R/S device migration, infection of the implant or electrode array migration or extrusion. We need more research to conclusively determine the safety the minimally invasive technique.

In **chapter 7** we developed a new patient specific, 3-D printed surgical tool that can be used for accurate placement of the R/S device on the skull. Accuracy of placement using

this guide was assessed using Cone Beam CT scans. Nine post mortem heads (18 ears) were implanted using the bone-supported drilling guides. The guides performed well in translational accuracy but showed more heterogeneity in rotational accuracy. We therefore concluded that although this guide has the potential to be a helpful tool in clinic, it needs further development to increase accuracy and should be tested before it can be incorporated in clinical practice.

The experience and the impact of having a CI on patients, in relation to the surgical techniques used during implantation, has not yet been studied. In **chapter 8** we explored the patients point of view by developing and validating the COMPASS questionnaire, a patient reported outcome measure that captures CI awareness. This PROM can be used by clinicians and researchers to assess and tackle issues that influence CI comfort, wear time and satisfaction. It can also be used as an endpoint in a clinical study, to evaluate different surgical techniques and their effect on awareness.

In **chapter 9** we described the study protocol of an ongoing randomized controlled trial designed to compare COchlear iMplant R/S device FIxation Techniques (COMFIT) with and without drilling. With this study we aim to fill the knowledge gap on CI fixation techniques and provide high quality evidence regarding differences in migration rates of the internal components of the CI, as well as surgical-, audiological- and patient reported outcomes. Future results will be made available and accessible in a peer-reviewed journal after completion of the trial.

To drill or not to drill

The basic steps of cochlear implant surgery involve creating a pathway to the cochlea for insertion of the electrode array in the scala tympani, and fixating the R/S device on the skull. Previous studies have demonstrated the large variety of surgical techniques that are applied to achieve these steps.[6–8] In **chapter 2** we investigated the current landscape of cochlear implantation and confirmed the high variability of chosen surgical methods.

In this thesis we found that work location seems to be associated with choice of applied surgical technique for fixation of the R/S device. In **chapter 2** we included mostly European CI surgeons, of whom n = 34 (75.5%) (57.6% of all respondents) drill a bony well with or without additional fixation materials. A similar study carried out with an all North American study population reported that the majority (n = 50, 65%) of the respondents use a variation of the tight subperiosteal pocket technique. Considering the lack of high quality evidence supporting one fixation technique over the other, as demonstrated in

chapter 3, it is surprising to see such clear differences. It would be interesting to know why surgeons choose one technique over the other.

In the past, drilling a bony well was necessary to lower the profile of the implant to avoid skin tension over the implant and thus avoid risk of extrusion, but also to improve comfort for the patient. To avoid complications related to migration of the implant, surgeons also use bony tie down sutures. Other fixation materials are also used such as bone dust, screws, tissue glue, wires and pins. These methods are still used today as demonstrated in **chapter 2**. However, evolution of the cochlear implant designs has resulted in thinner implants with larger surface areas. Lowering the profile of these implants therefore seems a redundant surgical step. These technological developments logically have led to the shift towards minimally invasive surgery. The advantages of the tight pocket technique consist of a low risk of soft tissue complications due to the small incision and minimal tissue manipulation, the shorter operational time thus lower costs, and the elimination of the risks associated with drilling. However, the lack of high quality evidence on complication rates found in **chapter 3**, raises the question of the safety of the soft surgery techniques.

Skull thickness is a factor that should be considered, especially in small children. In **chapter 6** we found that it is almost impossible to drill a bony well in children zero to four years of age without exposing the dura mater. The tight subperiosteal pocket technique eliminates the risks associated with drilling a bony well and bony tie down sutures, and would therefore be the appropriate technique to use in this age group. We also found no clear difference in complications and device failures between surgical technique subgroups, even though the sample size was not large enough to test statistical significance.

Chapter 3 demonstrates the large differences in the literature, regarding reported migration rates of the R/S device and electrode array. Studies that used clinical observation to assess migration of the internal components detected no migration during follow up. Subjective assessment of the outcome could have introduced observer bias, therefore it is likely that only extreme cases of migration could have been detected with certainty. The studies that did use objective methods of assessing migration, utilized different definitions of migration and the migration rates differed greatly. However it was interesting to note that small movements of the internal components of the CI occurred much more frequently than previously reported. True migration rates could therefore be higher than initially thought, and investigating the clinical impact of small movements that could result in impedance abnormalities and non-auditory sensations.[9] The correlation between fixation of the R/S device and electrode array migration, and subsequently audiological results, has yet to be proven with certainty.

When it comes to highly specialized surgeries such as cochlear implantation, it is difficult to acquire data of adequate volume and quality, to definitively prove the superiority of a surgical technique. Furthermore, surgery is a craft specialty that relies on practice to perfect skill and is a profession with cultural barriers that prevent the adoption of evidence-based medicine (EBM). Many surgeons recognize the value of EBM but prefer to use the practices learned through experience.[10]

Usefulness of modern technologies

In **chapter 5, 6 and 7** we explored new methods of CI surgery planning, positioning and fixation by using virtual surgical planning coupled with computer-aided design, automations and 3-D printing. 3-D Technology is already being used in medical care for a broad range of applications such as virtual, augmented and mixed reality, tailor made implants and guides, artificial intelligence and machine learning.[11–16] In the field of otolaryngology there are numerous applications and future directions using 3-D technology for educational purposes such as surgical training and patient counselling, as well as customized surgical planning, implantable prosthetics, surgical templates and guides.[16–18]

The high resolution of data derived from CT and MRI scans have made it possible for surgeons to acquire 3-D models created by the planning software quickly and accurately, to visualize and trial different surgical approaches. The models aid surgeons to visualize anatomy, practice surgical techniques, reduce guesswork and anticipate errors. This has proven to increase accuracy, efficiency and reduce operative time, thus improving surgical results and lowering costs.[17,19,20]

In this thesis we used 3-D medical image processing software to create a semi-automated method for feasibility testing, described in **chapter 5**, as well as a patient specific, 3-D printed surgical guide described in **chapter 7**. Creating a custom-made surgical guide for the most optimal position on the temporal bone in regards to cortical bone thickness, could easily be achieved if these methods would be combined. It could aid CI surgeons to avoid complications such as dura exposure and increase accuracy of placement. In addition it could reduce the duration of the surgical procedure by eliminating the position planning and providing guidance during drilling. This method could also be applied for other implantable medical otologic devices such as the bone conduction implant tranducer.

The technologies described in this thesis present new and exciting opportunities by introducing new treatments and providing patient tailored solutions. However, medical 3-D technology is a specialized field, necessitating the purchase of (often expensive) computer-aided

design software, 3-D printers and the knowledge to not only apply the many applications that these technologies can provide, but also to navigate the newly introduced regulations. The current European law, known as the Medical Device Regulation (MDR), mandates that before medical devices can be utilized in clinical settings, they must be adequately supported by documentation.[21] These regulations, paired with the production costs of many of the aforementioned applications, can intimidate clinicians and discourage the adoption of novel approaches. Furthermore, large-scale studies are needed to confirm the cost and clinical effectiveness of these applications.[22,23] In the case of our developed 3-D printed guide we need to ask the question: is being more accurate at drilling a bony well also clinically relevant? Based on the results of **chapter 6**, we conclude that patient specific surgical guides could be of added value for patients with thin skulls, in whom accuracy is needed to avoid complications due to dura exposure. Nevertheless, further research is needed to investigate whether the benefits of this innovation outweigh the increased cost of the intervention.

Patient centered care

When it comes to hearing aids, wear time greatly influences the clinical benefit acquired.[24] Consistent use of the CI on a daily basis has been associated with increased speech perception scores and speech production scores.[25–27] Studies on hearing aid users, found that discomfort and lack of knowledge on how to put them in correctly are major reasons for not wearing their hearing aids.[28] Additionally, a recent study on hearing aid use, found that hearing aid users report lower levels of hearing aid benefit and satisfaction with their hearing aid, when experiencing a greater number of device-related problems.[24] In a cochlear implant recipient study they reported that 89.8% of the participants had at least one CI device handling problem.[29] Another study found that one of the reasons given for shorter daily CI use were accidental detachments of the CIs external transmission coil.[30] Furthermore, some patients are reluctant to ask for the help of their clinicians, despite experiencing problems with their hearing aids for different reasons, such as regarding problems as not rectifiable and less perceived difficulties with hearing and communication in everyday life. There were also emotional barriers reported that prevented patients from seeking help such as emotions of shame, embarrassment and being a burden to the clinic. Bennett et al showed that there is a disparity between patients and clinicians on the role of the latter in the rehabilitation process. It seems that the current attitudes of clinicians make the patient dependent on them, instead of helping self-sufficiently in problem solving. There seems to be a blind spot for clinicians when it comes to their patients' lives outside of the clinic.[31] These examples demonstrate the importance of CI device related problems which are currently evaluated by clinicians without the use of objective tools.

Until recently, the focus of quality of life research in CI users has centered around hearing outcomes and their impact on the daily life of patients.[32] Little is known about the CI (physical) impact on daily life. In **chapter 8** we developed a patient reported outcome measure (PROM), the COMPASS questionnaire, to assess CI awareness. We defined this as "the state of mind or situation in which the patient is physically conscious he or she is wearing a cochlear implant and how this consciousness impacts their daily life". The concepts that this PROM addresses were derived from CI experts, both clinicians and patients themselves. This self-administered questionnaire can aid clinicians to capture and tackle issues that could influence CI wear time, comfort and satisfaction with the implant. However, not all issues addressed by the COMPASS are easily solvable. These include the burden experienced by CI recipients from feeling the implant under the skin, sleep adjustments due to the implant, and R/S device position. It is unknown whether different surgical techniques of R/S device positioning and fixation, have an impact on these issues. Further research is needed, therefore we chose the COMPASS as a secondary outcome in the randomized controlled trial described in **chapter 9** to assess differences in CI awareness between groups operated with different surgical techniques. The perspective of patients and the impact of CI awareness on their daily lives should be an important factor for the CI surgeons when choosing the surgical technique.

Concluding remarks

Surgical techniques used for positioning and fixation of the internal R/S device of the cochlear implant vary greatly among CI surgeons. The conventional fixation method of drilling a bony well comes with risks, and the alternative minimally invasive technique has many advantages. However, high quality evidence is lacking to prove the non-inferiority of this technique compared to the conventional method. Migration of the R/S device and electrode array seem to occur more often than we thought, although the clinical impact of these complications is unclear. We have developed new tools for the planning and execution of cochlear implant positioning and fixation, utilizing 3-D planning software and 3-D printing that can be further developed for more precise surgery in appropriate patient groups. This thesis also contributes to a more patient centered approach in cochlear implantation. The presented protocol in this thesis for the ongoing randomized controlled trial will hopefully provide enough evidence to conclusively determine the safety of the minimally invasive fixation technique and the impact of cochlear implantation techniques on CI awareness.

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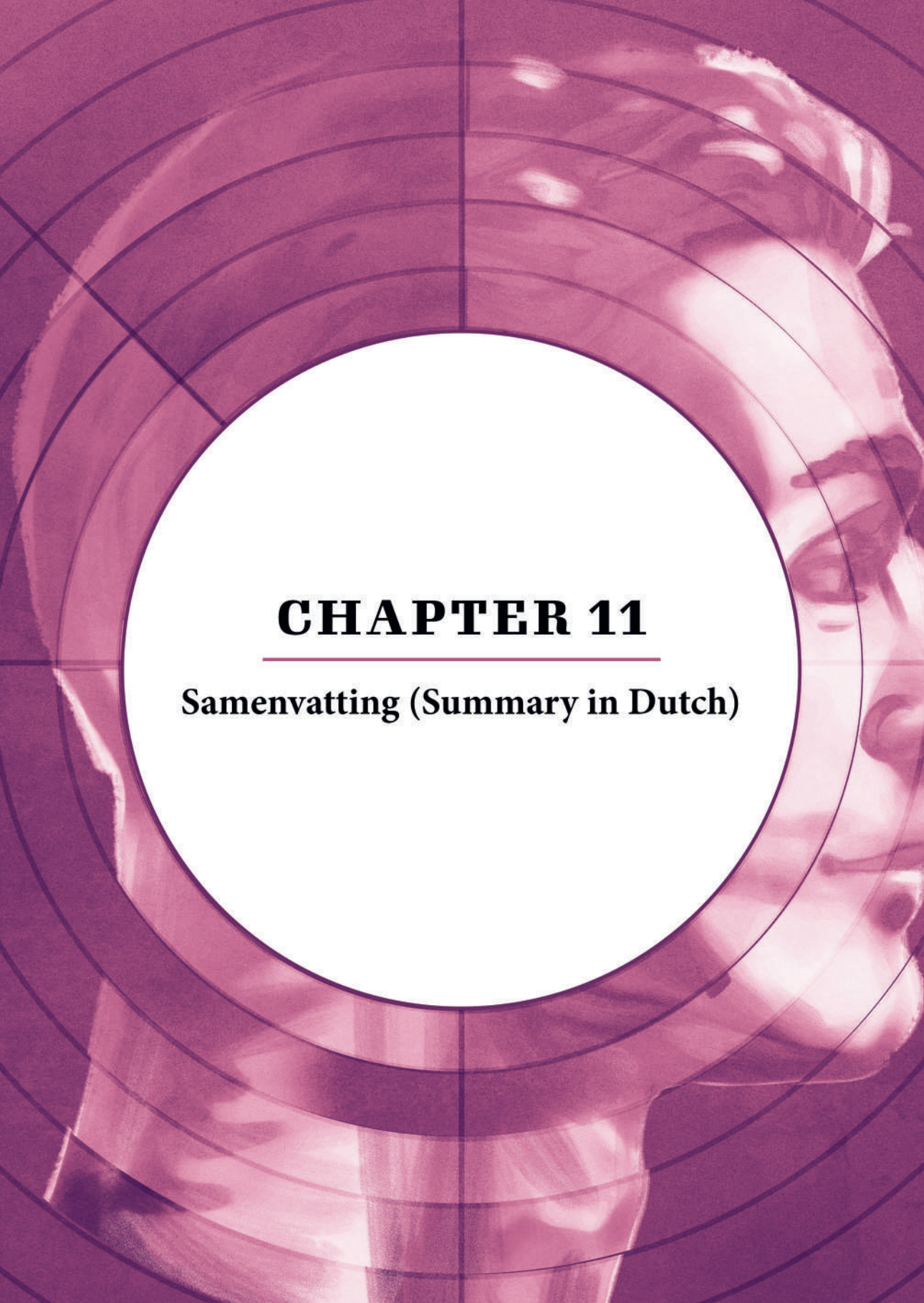

CHAPTER 11

Samenvatting (Summary in Dutch)

Nederlandse samenvatting

Gehoorverlies is één van de meest voorkomende aandoeningen ter wereld. Bijna een half miljard mensen wereldwijd lijdt aan invaliderend gehoorverlies en dit aantal zal naar verwachting de komende jaren stijgen. Deze aandoening heeft negatieve gevolgen voor zowel het individu, als voor de gehele samenleving. Mensen met ernstig gehoorverlies hebben een verminderde kwaliteit van leven, risico op sociaal isolement, depressie en verlies van autonomie. Perceptief gehoorverlies is de meest voorkomende vorm van gehoorverlies, wat vaak veroorzaakt wordt door het verlies van haarcellen in het slakkenhuis. Dit kan verschillende oorzaken hebben, zoals een geluidstrauma, infectieziektes, ototoxische medicatie of genetische afwijkingen.

Hoortoestellen zijn vaak een goed hulpmiddel om het gehoor (deels) te herstellen. Wanneer het gehoorverlies zodanig ernstig is dat hoortoestellen niet voldoende zijn, kan een cochleair implantaat (CI) uitkomst bieden. Het geluid wordt door een processor omgezet naar elektrische signalen en afgegeven aan een elektrode in het slakkenhuis. Het CI neemt de functie van de beschadigde zenuwcellen over, en stimuleert direct de gehoorzenuw. Het implantaat bestaat uit een uitwendig en een inwendig (geïmplanteerd) deel. Het uitwendige gedeelte bestaat uit de microfoon en spraakprocessor die achter het oor gedragen worden, en een zendspoel die via een magneet verbonden is aan het inwendige deel. Deze bestaat uit de magneet met de ontvangspoel en de elektrode. De magneet met de ontvangspoel wordt onder de huid in het bot achter het oor geplaatst. Er wordt een uitsparing geboord voor de ontvangstspoel om het CI in te bedden om het vast te zetten (fixeren) en het profiel te verlagen. Soms worden er ook hechtingen of andere materialen gebruikt om het CI te fixeren.

De operatie die nodig is om het CI te plaatsen, cochleaire implantatie genoemd, is een veilige ingreep met weinig complicaties. De operatietechnieken die gebruikt worden om het implantaat te fixeren onder de huid en in het slakkenhuis te plaatsen verschillen per centrum en per CI chirurg. De technologie van CI's maakt voortdurend stappen naar kleinere, dunnere implantaten en lichtere spraakprocessoren voor meer comfort tijdens het dragen. Steeds meer operateurs gebruiken daarom minimaal invasieve chirurgie, er is echter geen consensus onder CI chirurgen over de veiligheid van de nieuwere technieken. Hoewel de minimaal invasieve techniek veel voordelen biedt zoals een kleinere incisie, kortere operatietijd en geen risico op intracraniële complicaties, lijkt er onvoldoende wetenschappelijk bewijs te zijn om deze technieken veilig te kunnen gebruiken. Verkeerde positionering en onvoldoende fixatie van de ontvangstspoel met magneet kan leiden tot verschuiving van het implantaat, ook wel migratie genoemd. Complicaties ten gevolge

van ontvangstspoelmigratie zijn infectie, defect implantaat, elektrodemigratie, extrusie van het implantaat en wondproblemen. Als de ontvangstspoel tegen de spraakprocessor komt kan dat leiden tot fysieke klachten zoals (hoofd)pijn, maar er kunnen ook softwareproblemen worden veroorzaakt. Deze complicaties kunnen leiden tot revisiechirurgie met een grote belasting voor de patiënt tot gevolg. De incidentie van ontvangstspoelmigratie die gerapporteerd wordt in de literatuur loopt uiteen van 0,4 tot 25%, afhankelijk van de gebruikte methode om migratie vast te stellen. Bovendien is er nooit onderzocht hoeveel last patiënten hebben van het dragen van het CI en of deze last geassocieerd is met de gebruikte operatietechniek.

In dit proefschrift hebben we de chirurgische technieken onderzocht die gebruikt worden tijdens cochleaire implantatie om de ontvangstpoel te fixeren, waarbij we specifiek hebben gekeken naar de complicaties die te maken hebben met het boren van een benige uitsparing en migratie van de ontvangstpoel onder de huid. We hebben nieuwe methoden ontworpen om de ontvangstspoel te positioneren, waarbij we gebruik hebben gemaakt van 3-D software en 3-D printen. Als laatste hebben we getracht objectieve middelen te ontwikkelen om migratie van de ontvangstspoel vast te stellen en de impact van het dragen van een CI bij patiënten in kaart te brengen.

Om de variabiliteit tussen CI operateurs in kaart te brengen, hebben we in **hoofdstuk 2** een vragenlijstonderzoek verricht. Negenenvijftig otologen uit dertien verschillende landen, met name uit Europa, hebben een vragenlijst ingevuld over de operatietechnieken die zij gebruiken voor cochleaire implantatie. De resultaten laten zien dat er een hoge mate van variabiliteit bestaat tussen chirurgen voor bijna alle operatietechnieken. CI operateurs gaven aan dat zij gedurende hun carrière de toegepaste operatietechnieken hebben aangepast om minder invasief te kunnen opereren. Het was onduidelijk wat de oorzaak is van de hoge variabiliteit.

Hoofdstuk 3 beschrijft een systematische review waarin we de mate van migratie van de inwendige componenten van het CI (de ontvangstspoel en elektrode) vergelijken tussen de twee meest gebruikte fixatietechnieken. Deze zijn de benige uitsparing en de minimaal invasieve techniek. Onze resultaten laten wederom een grote spreiding zien van gerapporteerde migratie voor allebei de technieken door studies van lage wetenschappelijke kwaliteit. Er werd een duidelijk verschil in de gerapporteerde mate van migratie gezien tussen de studies, afhankelijk van de uitkomstmaat die gebruikt werd om migratie vast te stellen. De conclusie van dit hoofdstuk is dan ook dat er geen bewijs is voor een verschil tussen de technieken, en dat er meer onderzoek nodig is om de technieken direct te kunnen vergelijken met objectieve uitkomstmaten.

De gevonden verschillen in gerapporteerde migratie in de literatuur afhankelijk van de uitkomstmaat vormden de aanleiding voor de opzet van een pilotstudie in **hoofdstuk 4**. In deze studie hebben we getracht een methode te ontwikkelen die gebruikt kan worden om de positie van het implantaat (en de eventuele migratie daarvan) objectief en betrouwbaar vast te stellen. Het betreft een meetmethode met een meetlint die in dit onderzoek gevalideerd is voor het vaststellen van de positie van het implantaat. De positie van de ontvangstspoel wordt gemeten met behulp van de externe magneet. Er is verder onderzoek nodig om de sensitiviteit van deze meetmethode te valideren voor het vaststellen van migratie.

Het boren van een benige uitsparing kan uitdagend zijn, met name bij patiënten met een dunne schedel zoals bij kinderen. In **hoofdstuk 5** beschrijven we een door ons ontwikkelde en gevalideerde methode die gebruikt maakt van 3-D software om de mogelijkheid op het boren van een uitsparing pre-operatief te testen. Een semi-geautomatiseerd algoritme bepaalt de meest optimale positie voor de ontvangstspoel op de schedel, afhankelijk van de schedeldikte op basis van een CT scan. Het algoritme stelt vast of het boren van een uitsparing van bepaalde afmetingen mogelijk is in een patiënt door de restdikte van de schedel te meten na het virtueel creëren van de benige uitsparing op een 3D model van de schedel van de patiënt. Onze conclusie is dat het algoritme niet in staat is om consequent de optimale diktelocatie aan te wijzen, maar wel betrouwbaar is in het bepalen van de mogelijkheid om te boren.

Deze methode hebben we toegepast in **hoofdstuk 6** waarbij we CT scans van kinderen in verschillende leeftijdscategorieën hebben geanalyseerd op de mogelijkheid om een benig bed te boren. In 79,7% van de geïncludeerde oren was het niet mogelijk om een benige uitsparing te maken zonder de onderliggende dura mater bloot te leggen. Voor bijna alle kinderen van nul tot negen jaar was het niet mogelijk om een benige uitsparing te maken met de aangewezen afmetingen van de meeste CI fabrikanten. Ook hebben we retrospectief klinische data van ons pediatrisch CI cohort geanalyseerd om het aantal complicaties en het optreden van implantaatfalen bij de verschillende fixatiemethoden te onderzoeken. We hebben geen duidelijke verschillen gevonden tussen de fixatiesubgroepen wat betreft implantaat-gerelateerde complicaties (zoals ontvangstspoelmigratie, infectie van het implantaat, elektrodenmigratie of extrusie). Concluderend lijkt het boren van een benige uitsparing met voldoende diepte bij jonge kinderen tussen de nul en negen jaar onmogelijk, maar de zin of onzin van een ondiepe uitsparing kan met deze studie niet worden vastgesteld. Er is meer onderzoek nodig om dit uit te zoeken.

In **hoofdstuk 7** hebben we een patiëntspecifieke, 3-D geprinte boormal ontwikkeld en gevalideerd, die gebruikt kan worden voor nauwkeurige plaatsing van de ontvangstspoel

op de schedel. Deze studie is verricht op humaan stoffelijk overschot materiaal. We hebben CI's geïmplanteerd in achttien rotsbeenderen met behulp van de ontwikkelde boormallen. De resultaten lieten zien dat deze nieuwe chirurgische instrumenten potentie hebben om positionering van de ontvangstspoel nauwkeuriger te maken, maar dat er verdere ontwikkeling nodig is alvorens deze gebruikt kunnen worden in de kliniek.

De last die patiënten ervaren door het dragen van een CI is onderzocht in **hoofdstuk 8**. In deze studie hebben we de ervaringen van patiënten gebruikt om de COMPASS vragenlijst te ontwikkelen en te valideren. Deze vragenlijst is een patiënt-gerapporteerde uitkomstmaat die CI awareness vastlegt. Met awareness bedoelen we de situatie waarin de patiënt zich bewust is van het dragen van een cochleair implantaat, en hoe deze bewustwording zijn of haar dagelijks leven beïnvloedt. Deze vragenlijst kan gebruikt worden in de kliniek om problemen in beeld te brengen en te verhelpen die van invloed kunnen zijn op het draagcomfort, de draagtijd en de tevredenheid. De COMPASS vragenlijst kan ook gebruikt worden als uitkomstmaat in het kader van wetenschappelijk onderzoek, om bijvoorbeeld verschillen in patiënt-gerapporteerde uitkomsten tussen operatietechnieken in kaart te brengen.

Hoofdstuk 9 beschrijft het onderzoeksprotocol van een lopend gerandomiseerd onderzoek (de COMFIT studie), waarin de twee fixatietechnieken van de ontvangstspoel, boren en niet boren, met elkaar worden vergeleken op verschillende vlakken. Met dit onderzoek trachten wij het kennishiaat te dichten over zowel de verschillen in migratie van de ontvangstspoel als chirurgische, audiologische en patiënt-gerapporteerde uitkomstmaten. De resultaten van deze studie zullen te zijner tijd beschikbaar worden gesteld in een open access wetenschappelijk tijdschrift.

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About the author

Curriculum vitae

Laura Maria Markodimitraki was born on the 15th of May 1992 in Heraklion, Crete in Greece. She completed her primary and secondary education there, graduating cum laude from the 8th Lyceum of Heraklion. After graduation, she moved to the Netherlands to follow her dream of becoming a medical doctor. In 2010 she enrolled at the Utrecht University Medical School, graduating in 2018. During her final year she focused on otorhinolaryngology and developed an interest in research. Her research internship at the Ear-, Nose- and Throat department of the UMC Utrecht, under the supervision of dr. Thomeer, was the stepping stone to her future PhD career.

After obtaining her medical degree she gained valuable clinical experience by working as a physician (ANIOS) at the Emergency department, as well as the Cardiology department at the Beatrix Hospital (Gorinchem). In 2019 she started working as a PhD student at the ENT department of the UMC Utrecht. During this time she also followed the research educational program "Clinical and Experimental Neuroscience" at the Graduate School of Life Sciences at Utrecht University.

In March 2023 she started her residency in Family Medicine (Huisartsgeneeskunde) at Utrecht University of and is currently working in a general practice in Moergestel.

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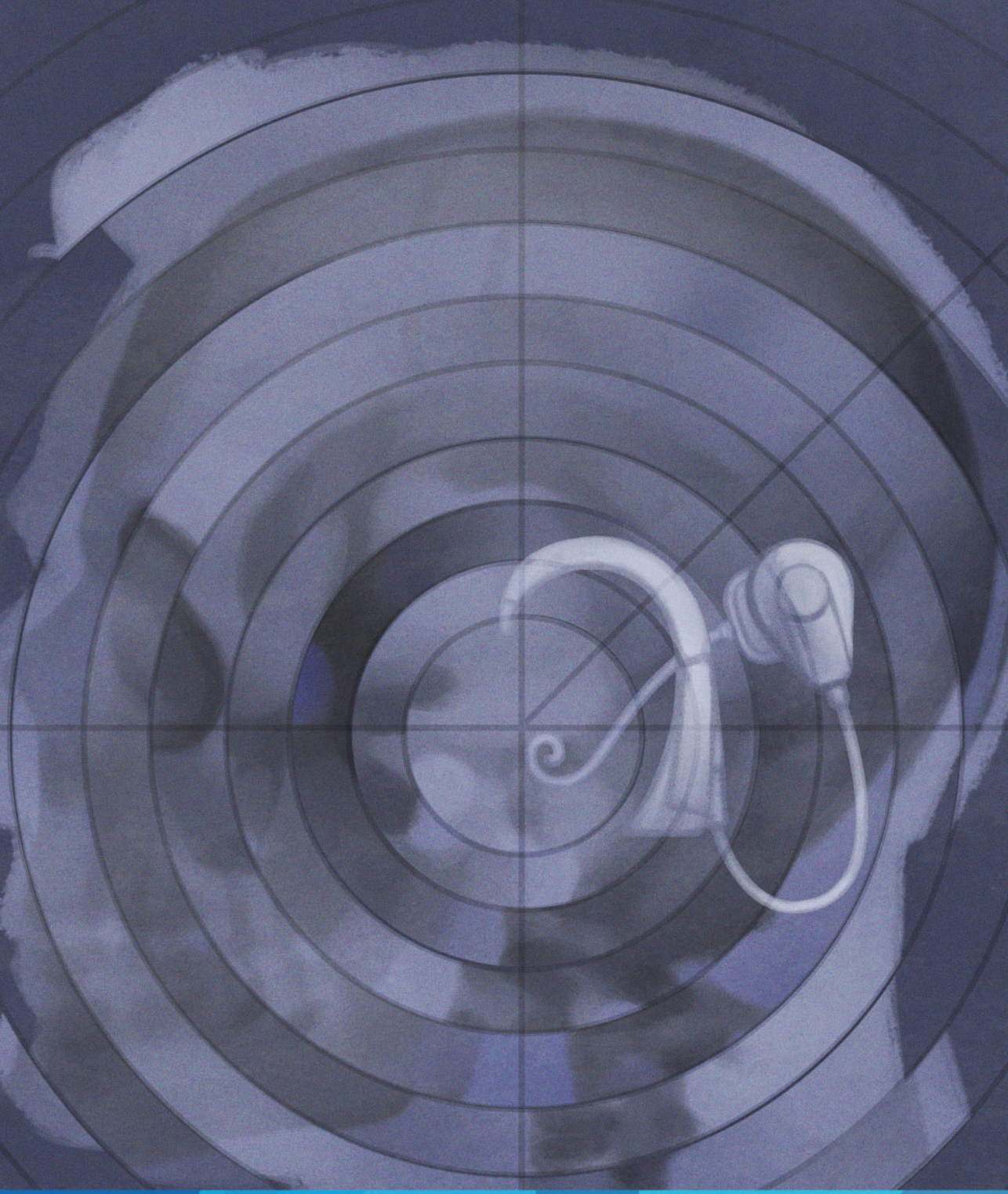

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