UNRAVELING THE IMPLANTED COCHLEA

Radiological Evaluation of Cochlear Morphology and Electrode Position in CI patients

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Voor mijn moeder

Voor Michiel en Ravel

CONTENTS

Chapter One

General Introduction

GENERAL INTRODUCTION

Disabling hearing loss affects 360 million people (328 million adults and 32 million children), which accounts for 5% of the world's population [World Health Organization, 2013]. Hearing loss is a reduced sensitivity to normally audible sounds. To compensate for hearing losses up to 60 dB, conventional hearing aids offer rehabilitating options in most people hindered in their communication. A conventional hearing aid uses amplification of sounds (air conduction) to improve hearing or transduces sounds via vibration onto the temporal bone (bone conduction). However, when severe to profound sensorineural hearing loss (SNHL) exists, hair cells are largely damaged and no longer capable of transforming fluid vibrations into electrical pulses on the auditory nerve. In these patients, conventional hearing aids will not restore hearing capabilities sufficiently to allow communication and participation in many daily social activities. The solution for these individuals may be a cochlear implant.

A cochlear implant (CI) bypasses the hair cells and the whole preceding normal route of sound conduction. The electrode array of the implant directly converts sounds into electrical pulses, which stimulate the auditory nerve fibers beyond the hair cells (Figure 1). Thus, functional hair cells are no longer required for the CI to function, while they are essential in normal hearing or with conventional hearing aids.

During cochlear implantation, the electrode array is positioned inside the cochlea and an internal receiver is placed in the temporal bone under the skin behind the ear. The array consists of several electrode contacts, all of which are programmed to stimulate a different frequency. The stimulation of different frequencies by the separate contacts is designed to mimic the normal tonotopic organization of the cochlea [Baskent and Shannon, 2005]. This tonotopic organization is often described as a frequency-to-place map meaning that any perceived frequency is location-dependent. The frequency depends on the location along the basilar membrane of the cochlea, where the electrical signal is generated and detected by the auditory nerve fibers of the modiolus [Stakhovskaya et al., 2007]. This location-dependent organization, with high frequencies detected at the beginning of the cochlear spiral (basally), and low frequencies detected further inside (apically) also extends into the auditory cortex [Greenwood, 1990]. Based on this concept, the cochlear implant software uses a standard frequency map for all implanted patients, with the possibility of individual adjustments in terms of selecting stimulation strategies and defining stimulation levels.

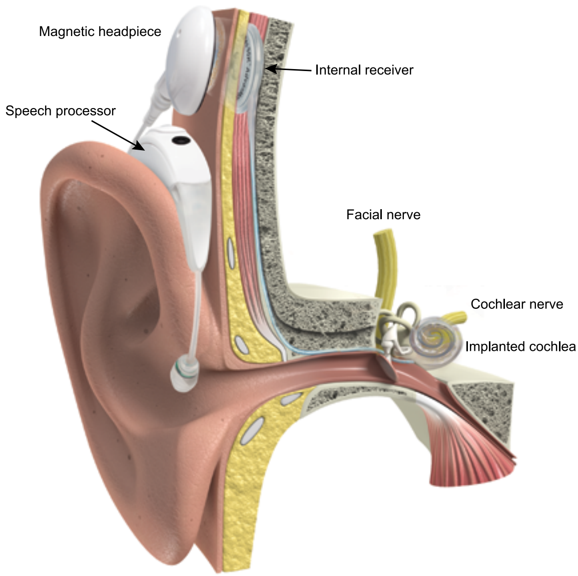

Figure 1. Illustration of a cochlear implant and its electrode inside the cochlea (Image courtesy of Advanced Bionics)

Nowadays, more than 320 thousand people have received a cochlear implant in one or both ears. However, various estimates indicate that as many as 25 million persons worldwide could benefit from a cochlear implant (stated by Blake Wilson in his acceptance remarks upon receiving the Lasker award) [Rubenstein Communications Inc., 2013]. The implant restores hearing which enables most adults to take part in everyday life again. In our center, CI-users reach an average speech perception score of 79% (SD:16) phonemes correct and 60% (SD:22) words correct on the Dutch Society of Audiology CVC monosyllable word test [Smoorenburg, 1992] (average score of 308 postlingual implantees 1 year after implantation at 65dB SPL in quiet surrounding) (unpublished Leiden University Medical Center (LUMC) results as of January 1st, 2015). Many CI-users are able to use the phone. And children can, as a result of early cochlear implantation, develop and improve oral speech and language. Some of them almost reach a normal age-appropriate level [Niparko et al., 2010].

Consequently, a large part of these CI-using children is able to attend mainstream schools. To obtain such compelling results, a multidisciplinary CI team is essential during the whole process of cochlear implantation, starting with candidate selection, to preparation and execution of the surgery, until the rehabilitation phase and after care. This team consists of otologic surgeons, radiologists, scientists, speech and language therapists, psychologists and audiologists. All members of this team have their value during the process.
Unfortunately, the population of cochlear implantees still shows large variability in outcomes which makes predicting individual post-implantation speech perception scores prior to the surgery very difficult, if not, impossible. Various functional aspects of the cochlear implant can still be improved and are the current topics of research, such as music appreciation (especially melody recognition is difficult compared to rhythm) [Kohlberg et al., 2014], speech discrimination in noise [Schumann et al., 2015], tonal language perception (many Asian languages) [Li et al., 2014], and detecting prosodic information (enabling understanding the emotional status of the speaker) [Hopyan et al., 2015]. The performance and perceived quality of life with an implant may be upgraded by implementing new innovating techniques, like speech coding strategies using spanning, phantom stimulation and current steering [Snel-Bongers, 2013], applying noise reduction algorithms and directional microphones, improving connectivity with blue tooth, and changing electrode array designs.
Worldwide, three manufacturers dominate the market with their cochlear implant systems; MED-EL, Cochlear and Advanced Bionics. The available devices differ in many ways; the electrode arrays vary in length (18-31mm), number of electrode contacts (12-22 contacts), and configuration of the array (straight or pre-curved). All of these aspects influence electrode position inside the cochlea. Yet, none of these devices really show clear superior performance compared to the others. This could be explained by the fact that besides device-related factors, other factors like surgical techniques and patient-specific factors, influence performance outcomes of CI-users.
To obtain more insights in the relation between electrode position, surgical techniques and patient-specific factors and how they, all together, influence performance outcomes, it is important to apply standardized imaging analysis techniques. This rationale formed the basis for initiating one of the main research projects in the Leiden University Medical Center on 'imaging in the field of cochlear implantation'. The publications of Verbist et al. [2010a;2010b] formulated consensus on the subject and a method for evaluation of cochlear anatomy and cochlear implant position with computed tomography CT for many CI centers in and outside the Netherlands.

Since the past years, the role of CT and magnetic resonance imaging (MRI) in the field of cochlear implantation has been transformed from preoperative candidacy evaluation of anatomy and postoperative confirmation of electrode position to individualized implant selection, detailed electrode-contact evaluation, methods for visualizing trauma to the delicate intracochlear structures, and possible device failure investigation [Verbist, 2010]. Current studies are also evaluating the quality of new imaging modalities such as cone beam computed tomography (CBCT) [Ruivo et al., 2009], flat-panel computed tomography [Arweiler-Harbeck et al., 2012] and digital volume tomography (DVT) [Aschendorff, 2011] compared to the conventional multi-slice computed tomography (MSCT).
This thesis aims to explore the capabilities and limitations of MSCT during the preoperative and postoperative trajectory of cochlear implantation. Several clinical applications of the postoperative CT are illustrated by studying how electrode position influences performance with the CI. In addition, a goal is to study how imaging can navigate the implantation procedure. This introductory chapter continues with a short overview of the past and present of the cochlear implant. Then, the function of a cochlear implant and the cochlea itself is shortly explained. To explain the role of imaging within the cochlear implant trajectory, the standardized imaging and reconstructive evaluation techniques used in the LUMC are illustrated to provide insights in the methods used for this research. This chapter is completed by some recent insights provided by previous research about this topic, followed by a short outline of this thesis.

The Past and Present of Cochlear Implantation

The use of electrical stimulation of the inner ear was developed by the two Frenchmen, Charles Eyries and André Djourno, an ENT surgeon and an engineer. They were the first scientific couple who reported on transcutaneous implantation of a deafened patient in 1957 with a single channel implant on the auditory nerve [Djourno A. et al., 1957]. This ground breaking report appeared more than sixteen decades after Volta described in 1800 that he experienced 'une recousse dans la tête' ('a boom within the head') when performing a dangerous technique of placing a 50 Volt electrode in his own ear to evoke auditory sensations [Volta A., 1800]. The patient implanted by Djourno was able to hear sounds, though unable to understand speech. However after a reimplantation due to a broken lead, the new implant did enable the patient to distinguish different sounds after endless practicing and helped with his daily functioning for some months. The scientific duo separated after this first candidate

as a result of irreconcilable differences in their vision about collaborating with the industry to improve the implant.
Fortunately, the inspired American ENT surgeon of the House Ear institute in Los Angeles, William F. House, picked up the pace in 1972 and developed a cochlear implant [House W.F. and Urban J., 1973], which was approved by the American Food and Drug Administration (FDA) for clinical use in 1979. Even though the outcomes with the single channel cochlear implant were somewhat disappointing during the first years, the innovation proceeded and the invention transformed into a multi-channel implant in the mid-eighties, the predecessor of the current CI nowadays. Since then, time has proven this device would lead to a revolutionary new therapy for the deaf and severely hard-of-hearing individuals. That this device transformed the lives of about 320 thousands of people was confirmed in 2013 when three scientists that developed the cochlear implant, Graeme M. Clark, Ingeborg Hochmair and Blake S. Wilson, were awarded with the Lasker~DeBakey Clinical Medical Research Award [Strauss, 2013]. The Lasker Foundation stated that their work has, for the first time, substantially restored a human sense with a medical intervention.
In the Netherlands, cochlear implantation is reimbursed by the basic health insurance for both adults and children since 2000 and the surgery is performed in 8 University Medical Centers. In 2012 the health insurance coverage of cochlear implantation for children was further expanded by the CVZ (College of health insurances in Netherlands)[van Eijndhoven et al., 2012]. It was decided to approve bilateral implantation when performed in prelingually deaf children (younger than five years old) as it had been concluded that studies performed between 2009 and 2012 on the effectiveness of bilateral implantation in that population supplied enough evidence of beneficial outcomes in terms of better speech perception in noise, spoken language development and sound localization acuity [Boons et al., 2012]. This is in line with the consensus statement by the European Bilateral Pediatric Cochlear Implant Forum [Ramsden et al., 2012]. As of January 1st, 2015, a total of 5953 cochlear implantations have been performed in the Netherlands, consisting of 4098 adults and 1855 children. A bilateral cochlear implantation was performed in 437 persons, of which 75 were adult and 362 children [OPCI, 2015].
Currently in the Netherlands, cochlear implantation is considered if the level of hearing loss is above 70-90 dB and speech perception is below 50% (phonemes correct on the Dutch Society of Audiology CVC monosyllable word test) [Smoorenburg, 1992]. These criteria are subject to continuous change and may be extended as new insights arise and show beneficial prospects

for an increasing group of patients with severe sensorineural hearing loss. Importantly, each individual case will first be evaluated carefully by the multidisciplinary CI team. Obtaining preoperative imaging is part of this evaluation process.

Temporal Bone Imaging and Multiplanar Reconstructions

The availability of imaging is crucial to accurately assess and control the position of the electrode. In the LUMC, temporal bone anatomy is evaluated preoperatively, by MRI and CT, guiding the surgeon to choose the surgical approach, implantation technique, and most appropriate electrode type. CT is performed to evaluate the middle ear and bony cochlear structures, while MRI provides detailed information about the status of the labyrinth and the retrocochlear structures. A combination of these imaging modalities is necessary to identify abnormalities, such as a cochlear malformation, nerve hypoplasia or aplasia or cochlear ossification.

Cochlear implants are a relative contra indication for MRI because of the risk of displacement and demagnetization of the internal implant magnet. Moreover the presence of the implant will lead to image degradation due to metal-induced artifacts. A 1.5 Tesla (T) MRI is claimed to be compatible with several cochlear implant devices for imaging without removal of the internal magnet [Crane et al., 2010]. However, a serious complication of magnet dislocation leading to revision surgery has been reported when performing a 1.5 T MRI despite the compression head bandage [Hassepass et al., 2014]. Only the Synchrony device of MED-EL is approved by the FDA for use with 3.0 T MRI systems, without surgical removal of the device's internal magnet [MED-EL, 2015]. Mostly, either a conventional X-ray or a CT is obtained postoperatively to check electrode position. Many implant centers use X-ray to confirm intracochlear position as it has the advantage of a low radiation dose. On the other hand, despite the higher radiation exposure, CT provides much more detail than simply confirmation of an intracochlear position by showing individual contacts and their position in relation to the modiolus, as shown in Figure 2. Moreover, insertion depth can be defined clearly with CT and even some indications about scala tympani or scala vestibuli position can be derived from these images.

CT scanning in the Leiden Cochlear Implant Program

Since 2000 preoperative and postoperative CT scans are obtained of all cochlear implant candidates. This resulted in a large cochlear implant imaging database. In this thesis we analyzed the radiological data of all patients implanted between 2000 and 2012 with normal

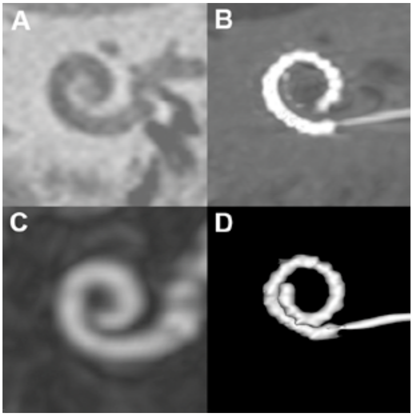

Figure 2.
A= MPR of pre-implantation CT of the cochlea, B= MPR of post-implantation CT with the HiFocus 1J electrode of Advanced Bionics inside the cochlea, C= MIP of heavily T2-weighted MR images of the cochlea, D= volume render segmentation of the HiFocus 1J electrode.

anatomy who received a CII Hifocus 1 or HiRes90k HiFocus1J electrode of Advanced Bionics (Valencia, CA). Figure 3 shows how serial multi-planar reconstructions (MPRs) of the CT images are obtained with planes parallel to the basal turn of the cochlea.

Upon these CT images two coordinate systems are superimposed. The first coordinate system applied is a three dimensional one which was agreed upon by an international panel of researchers from various fields, including surgeons, audiologists, radiologists and histologist, and representatives of the three main cochlear implant manufacturers [Verbist et al., 2010b]. The basis of this 'consensus coordinate system' is formed by the two-dimensional Cochlear View as described by Xu and Cohen to be used on plain X-rays [Xu et al., 2000]. The third dimension consists of a z-axis through the center of the modiolus with its origin at the helicotrema. In the two-dimensional plane the axes are formed by a line connecting the center of the round window (0-reference) with the center of the modiolus (the red line in Figure 3) in combination with a perpendicular line (the blue line). Applying this coordinate system results in measurements defined by a rotational angle (with the center of the round window as 0-reference angle) and a distance to the modiolus (the purple line: angle and distance to the center of all axes). The second coordinate system is called 'the Leiden coordinate system'. This coordinate system is supplemented by two extra axes in the two-dimensional plane, as described by Verbist et al [2010a]. It provides the other two axes; a line connecting the center of the modiolus to the most lateral point of the horizontal semicircular canal (the black line in Figure 3) combined with a perpendicular line (the orange line). The extension to the original coordinate system is useful for the assessment of postoperative MPRs, especially, since it eliminates the need for fusion between pre- and postoperative images. In addition, during cochlear implantation the horizontal semicircular canal remains stable, while in case of an (extended) round window approach for insertion the round window might be drilled out, and its configuration changes due to the surgery which makes the round window a poor

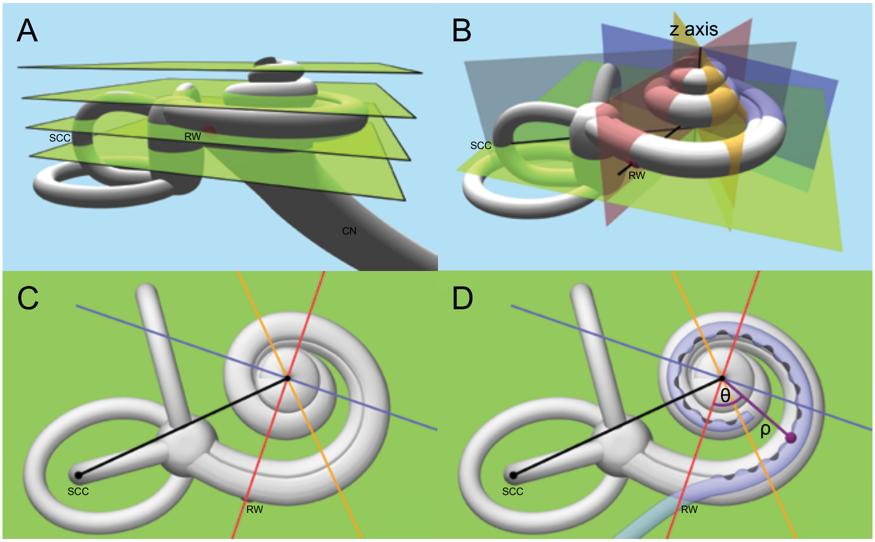

Figure 3. Schematic illustrations showing application of the two coordinate systems within the cochleovestibular system. A=serial MPRs of the CT with planes parallel to the basal turn of the cochlea, showing the round window (RW), horizontal semicircular canal (SCC) and cochlear nerve (CN), B=two coordinate systems are superimposed upon the MPRs with the z-axis through the center of the modiolus (first 'consensus coordinate system': red and blue planes, second 'Leiden coordinate system': gray and orange planes), C=Measurement axes of both coordinate systems before cochlear implantation measuring cochlear dimensions, D=Measurement axes of both coordinate systems after cochlear implantation measuring electrode position and its proximity to the modiolus. The purple line represents the angular (θ) and linear (ρ) measurement of each electrode contact to define its position.

landmark on the postoperative scan. The robustness of this procedure was demonstrated in a previous study showing intraclass correlation coefficients (ICC) between 0.74 and 1 for both angular (ICC 0.74-1; SD<5 degrees) and linear measurements (ICC 0.77-1; SD<0.5 mm) within the cochlea [Verbist et al., 2010a]. Furthermore, a consistent angular position of the round window of 34.6 degrees (SD 0.4 degrees) was found in this study.

The availability of the LUMC cochlear imaging database provides the opportunity to study cochlear morphology and electrode position and their relation to the performance. Electrode position is influenced by the cochlear morphology, implant design, and surgical technique. While many studies have focused on the effect of implant design and surgical technique on position [Arnoldner et al., 2005;Arnoldner et al., 2010;Briggs et al., 2006;Eshraghi et al., 2003;Aschendorff et al., 2007;Tykocinski et al., 2000;Trieger et al., 2010], few have analyzed the effect of cochlear morphology [Escude et al., 2006;Ketten et al., 1998;Wysocki, 1999]. Notably, all these reported studies involved relatively small sample sizes, with some performing their study on no more than 4 patients and one implant type [Baskent and Shannon, 2005]. In addition to the small sample sizes, available studies vary largely in imaging method used (X-ray, MSCT, CBCT, MRI) and evaluation technique, complicating detailed comparison of the outcomes. Therefore, many questions about the actual relation between cochlear morphology, electrode position and performance outcomes remain unanswered.

Ultimately, the goal of research in this field is to gain better speech perception outcomes for cochlear implant patients. We hope to provide more insights on the relation between implant position, anatomy and performance with the studies described in this thesis.

Electrode positioning is suggested as an important factor to influence speech perception outcomes [Finley et al., 2008;Hamzavi and Arnoldner, 2006;Hochmair et al., 2003;Holden et al., 2013;Skinner et al., 2002]. Accurate positioning is also required to minimize intracochlear trauma [Aschendorff et al., 2007;Boyd, 2011;Briggs et al., 2001;Tykocinski et al., 2000], to reduce the applied current [Filipo et al., 2008], and to preserve residual hearing [Baumgartner et al., 2007]. Furthermore, Baskent et al. [2005] and Faulkner et al. [2006] suggest that frequency place matching in full insertions result in better performance. Synchronizing the electrode position with the physiological tonotopic alignment of the basilar membrane would eventually enable cochlear implant users to regain speech perception performance to a level that approximates that of normal hearing individuals.

To acquire the optimal electrode position, all three substitutes that play an influencing part on its position- cochlea, electrode design and the insertion technique of the surgeon - should be studied intensively to gain more control on cochlear implant outcomes.

Performance being influenced by many factors, this research specifically focuses on identifying anatomical and cochlear implant electrode position related factors. Therefore, the studied populations for this thesis existed of implantees with normally developed inner ears without any cochleovestibular anomalies.

The aim of the thesis can be subdivided into three objectives;

1. To explore the clinical value of CT during the postoperative period
2. To develop descriptive modalities for cochlear morphology and its relation to final cochlear implant electrode position
3. To investigate the relationship between several factors related to implant position and performance in terms of speech perception of the implantees.

The proposed three research objectives are further addressed in the next section.

AIMS AND OUTLINE OF THE THESIS

This thesis studies the relation between cochlear morphology, electrode position and performance outcomes in a large study sample of 336 patients implanted between 2000 and 2012, using a the above mentioned cochlear coordinate systems to evaluate pre- and postoperative CT images combined with patient-specific information and performance outcomes. By doing so, it explores the role of CT in the field of cochlear implantation. **Chapters 2** and **3** focus on the first objective and examine the value of CT during the postoperative period. **Chapter 2** describes a study of a population suffering from device failure requiring reimplantation. Previous studies demonstrated good outcomes after reimplantation with an improved implant design. Because an improved implant design was used these good outcomes could be due to the advancements of the device. Although unfortunate for the patients in our study, the device failed within a short time-frame resulting in a reimplantation with exactly the same implant type. This unique situation enabled our centre to study surgical and audiological outcomes after reimplantation without changing the device type.

For the study it was evaluated how precisely a replacement electrode could be inserted relative to the original electrode's position. The changes in speech perception and adaptation time with the new implant were investigated. New findings on electrode position are elucidated using postoperative imaging in the **Chapter 3**. Here, the results of a retrospective study on the stability of the position of the cochlear implant electrode are described. Displacement of the electrode contacts was demonstrated in a significant number of patients and the occurrence of complaints in this population was described. The correlation with implant type and insertion depth was studied and extreme cases were reported. **Chapters 4** and **5** address the second objective of exploring descriptive modalities for cochlear shape. In **Chapter 4,** cochlear morphology is analyzed and its influence on electrode position is investigated. Variations in average cochlear diameters, cochlear canal size and gender differences are studied. In addition, different methods of describing cochlear size and shape are analyzed. The main goal of the study described in **Chapter 5** was to investigate the feasibility of developing a surgical guidance tool to predict electrode position. Such a guidance tool could allow surgeons to more accurately position the electrode. In addition, an optimal range for surgical insertion was identified to minimize overall frequency mismatch. The third objective - investigating the relationship between several implant position related factors and ultimate speech perception performance of the implantees - is explored in **Chapter 6**. This study is performed in a large patient population while controlling for patient specific factors. Thanks to the size of the studied population our outcomes give new insights into the presumed relation between electrode position and performance in comparison to earlier reports of keystone research groups. In **Chapter 7,** the outcomes of this thesis are discussed. Moreover, concluding remarks and recommendations are given and future perspectives are highlighted. **Chapter 8** provides a short summary of the content of this thesis in English and **Chapter 9** presents a summary in Dutch.

REFERENCES

1. Arnoldner C, Baumgartner WD, Gstoettner W, Hamzavi J: Surgical considerations in cochlear implantation in children and adults: a review of 342 cases in Vienna. Acta Otolaryngol 2005;125:228-234.
2. Arnoldner C, Helbig S, Wagenblast J, Baumgartner WD, Hamzavi JS, Riss D, Gstoettner W: Electric acoustic stimulation in patients with postlingual severe high-frequency hearing loss: clinical experience. Adv Otorhinolaryngol 2010;67:116-124.
3. Arweiler-Harbeck D, Monninghoff C, Greve J, Hoffmann T, Goricke S, Arnolds J, Theysohn N, Gollner U, Lang S, Forsting M, Schlamann M: Imaging of Electrode Position after Cochlear Implantation with Flat Panel CT. ISRN Otolaryngol 2012;728205.
4. Aschendorff A: Imaging in cochlear implant patients. GMS Curr Top Otorhinolaryngol Head Neck Surg 2011;;10:Doc07.
5. Aschendorff A, Kromeier J, Klenzner T, Laszig R: Quality control after insertion of the nucleus contour and contour advance electrode in adults. Ear Hear 2007;28:75S-79S.
6. Baskent D, Shannon RV: Interactions between cochlear implant electrode insertion depth and frequency-place mapping. J Acoust Soc Am 2005;117:1405-1416.
7. Baumgartner WD, Jappel A, Morera C, Gstottner W, Muller J, Kiefer J, Van De Heyning P, Anderson I, Nielsen SB: Outcomes in adults implanted with the FLEXsoft electrode. Acta Otolaryngol 2007;127:579-586.
8. Boons T, Brokx JP, Frijns JH, Peeraer L, Philips B, Vermeulen A, Wouters J, van WA: Effect of pediatric bilateral cochlear implantation on language development. Arch Pediatr Adolesc Med 2012;28-34.
9. Boyd PJ: Potential benefits from deeply inserted cochlear implant electrodes. Ear Hear 2011;32:411-427.
10. Briggs RJ, Tykocinski M, Saunders E, Hellier W, Dahm M, Pyman B, Clark GM: Surgical implications of perimodiolar cochlear implant electrode design: avoiding intracochlear damage and scala vestibuli insertion. Cochlear Implants Int 2001;2:135-149.
11. Briggs RJ, Tykocinski M, Xu J, Risi F, Svehla M, Cowan R, Stover T, Erfurt P, Lenarz T: Comparison of round window and cochleostomy approaches with a prototype hearing preservation electrode. Audiol Neurootol 2006;11 Suppl 1:42-48.
12. Crane BT, Gottschalk B, Kraut M, Aygun N, Niparko JK: Magnetic resonance imaging at 1.5 T after cochlear implantation. Otol Neurotol 2010;1215-1220.
13. Djourno A., Eyriès C., Vallancien B.: De l'excitation électrique du nerf cochléaire chez l'homme, par induction a distance, a l'aide d'un micro-bobinage inclus a demeure. C R Soc Biol 1957;423-425.
14. Escude B, James C, Deguine O, Cochard N, Eter E, Fraysse B: The size of the cochlea and predictions of insertion depth angles for cochlear implant electrodes. Audiol Neurootol 2006;11 Suppl 1:27-33.
15. Eshraghi AA, Yang NW, Balkany TJ: Comparative study of cochlear damage with three perimodiolar electrode designs. Laryngoscope 2003;113:415-419.
16. Faulkner A, Rosen S, Norman C: The right information may matter more than frequency-place alignment: simulations of frequency-aligned and upward shifting cochlear implant processors for a shallow electrode array insertion. Ear Hear 2006;27:139-152.
17. Filipo R, Mancini P, Panebianco V, Viccaro M, Covelli E, Vergari V, Passariello R: Assessment of intracochlear electrode position and correlation with behavioural thresholds in CII and 90K cochlear implants. Acta Otolaryngol 2008;128:291-296.

18. Finley CC, Holden TA, Holden LK, Whiting BR, Chole RA, Neely GJ, Hullar TE, Skinner MW: Role of electrode placement as a contributor to variability in cochlear implant outcomes. Otol Neurotol 2008;29:920-928.
19. Greenwood DD: A cochlear frequency-position function for several species--29 years later. J Acoust Soc Am 1990;87:2592-2605.
20. Hamzavi J, Arnoldner C: Effect of deep insertion of the cochlear implant electrode array on pitch estimation and speech perception. Acta Otolaryngol 2006;126:1182-1187.
21. Hassepass F, Stabenau V, Arndt S, Beck R, Bulla S, Grauvogel T, Aschendorff A: Magnet dislocation: an increasing and serious complication following MRI in patients with cochlear implants. Rofo 2014;2014:680-685.
22. Hochmair I, Arnold W, Nopp P, Jolly C, Muller J, Roland P: Deep electrode insertion in cochlear implants: apical morphology, electrodes and speech perception results. Acta Otolaryngol 2003;123:612-617.
23. Holden LK, Finley CC, Firszt JB, Holden TA, Brenner C, Potts LG, Gotter BD, Vanderhoof SS, Mispagel K, Heydebrand G, Skinner MW: Factors affecting open-set word recognition in adults with cochlear implants. Ear Hear 2013;34:342-360.
24. Hopyan T, Manno Iii FA, Papsin BC, Gordon KA: Sad and happy emotion discrimination in music by children with cochlear implants. Child Neuropsychol 2015;1-15.
25. House W.F., Urban J.: Long term results of electrode implantation and electronic stimulation of the cochlea in man. Ann Otol 1973;504-517.
26. Ketten DR, Skinner MW, Wang G, Vannier MW, Gates GA, Neely JG: In vivo measures of cochlear length and insertion depth of nucleus cochlear implant electrode arrays. Ann Otol Rhinol Laryngol Suppl 1998;175:1-16.
27. Kohlberg G, Spitzer JB, Mancuso D, Lalwani AK: Does cochlear implantation restore music appreciation? Laryngoscope 2014;587-588.
28. Li Y, Zhang G, Galvin JJ, III, Fu QJ: Mandarin speech perception in combined electric and acoustic stimulation. PLoS One 2014;e112471.
29. MED-EL. Synchrony Cochlear Implant-Factsheet-1.pdf. 2015. 16-6-2015.
30. Niparko JK, Tobey EA, Thal DJ, Eisenberg LS, Wang NY, Quittner AL, Fink NE: Spoken language development in children following cochlear implantation. JAMA 2010;1498-1506.
31. OPCI. Aantal implantaties in Nederland. 2015. 16-6-2015.
32. Ramsden JD, Gordon K, Aschendorff A, Borucki L, Bunne M, Burdo S, Garabedian N, Grolman W, Irving R, Lesinski-Schiedat A, Loundon N, Manrique M, Martin J, Raine C, Wouters J, Papsin BC: European Bilateral Pediatric Cochlear Implant Forum consensus statement. Otol Neurotol 2012;561-565.
33. Rubenstein Communications Inc. 2013 Lasker Awards honor scientists for pioneering medical research. 9-9-2013. 16-6-2015.
34. Ruivo J, Mermuys K, Bacher K, Kuhweide R, Offeciers E, Casselman JW: Cone beam computed tomography, a low-dose imaging technique in the postoperative assessment of cochlear implantation. Otol Neurotol 2009;30:299-303.
35. Schumann A, Serman M, Gefeller O, Hoppe U: Computer-based auditory phoneme discrimination training improves speech recognition in noise in experienced adult cochlear implant listeners. Int J Audiol 2015;190-198.
36. Skinner MW, Ketten DR, Holden LK, Harding GW, Smith PG, Gates GA, Neely JG, Kletzker GR, Brunsden B, Blocker B: CT-derived estimation of cochlear morphology and electrode array position in relation to word recognition in Nucleus-22 recipients. J Assoc Res Otolaryngol 2002;3:332-350.
37. Smoorenburg GF: Speech reception in quiet and in noisy conditions by individuals with noise-induced hearing loss in relation to their tone audiogram. J Acoust Soc Am 1992;1992:421-437.

38. Snel-Bongers, J. Dual electrode stimulation in cochlear implants : From concept to clinical application. 2013. Thesis
39. Stakhovskaya O, Sridhar D, Bonham BH, Leake PA: Frequency map for the human cochlear spiral ganglion: implications for cochlear implants. J Assoc Res Otolaryngol 2007;8:220-233.
40. Strauss, E. Graeme M. Clark, Ingeborg Hochmair and Blake S. Wilson. For the development of the modern cochlear implant - a device that bestows hearing to individuals with profound deafness. 2013. 16-6-2015.
41. Trieger A, Schulze A, Schneider M, Zahnert T, Murbe D: In Vivo Measurements of the Insertion Depth of Cochlear Implant Arrays Using Flat-Panel Volume Computed Tomography. Otol Neurotol 2010.
42. Tykocinski M, Cohen LT, Pyman BC, Roland T, Jr., Treaba C, Palamara J, Dahm MC, Shepherd RK, Xu J, Cowan RS, Cohen NL, Clark GM: Comparison of electrode position in the human cochlea using various perimodiolar electrode arrays. Am J Otol 2000;21:205-211.
43. van Eijndhoven, M. J. A., Gaasbeek Janzen M.H., and Heymans J. Herbeoordeling standpunt bilaterale cochleaire implantaten bij kinderen (rapport). 16-7-2012. 26-2-2014.
44. Verbist, B M. Cochlear imaging in the era of cochlear implantation : From silence to sound. 2010. Thesis
45. Verbist BM, Joemai RM, Briaire JJ, Teeuwisse WM, Veldkamp WJ, Frijns JH: Cochlear coordinates in regard to cochlear implantation: a clinically individually applicable 3 dimensional CT-based method. Otol Neurotol 2010a;31:738-744.
46. Verbist BM, Skinner MW, Cohen LT, Leake PA, James C, Boex C, Holden TA, Finley CC, Roland PS, Roland JT, Jr., Haller M, Patrick JF, Jolly CN, Faltys MA, Briaire JJ, Frijns JH: Consensus panel on a cochlear coordinate system applicable in histologic, physiologic, and radiologic studies of the human cochlea. Otol Neurotol 2010b;31:722-730.
47. Volta A.: On the electricity excited by mere contact of conducting substances of different kinds. Trans R Soc Phil 1800;403-431.
48. World Health Organization. Factsheet on Deafness and hearing loss. 2013. 19-2-2014.
49. Wysocki J: Dimensions of the human vestibular and tympanic scalae. Hear Res 1999;135:39-46.
50. Xu J, Xu SA, Cohen LT, Clark GM: Cochlear view: postoperative radiography for cochlear implantation. Am J Otol 2000;21:49-56.

Chapter Two

Cochlear Reimplantation with Same Device: Surgical and Audiologic Results

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ABSTRACT

Objectives

To study to what extend it is possible to achieve identical insertion depths and to maintain the same performance after cochlear reimplantation.

Study Design

Outcome research on a retrospective case series in a tertiary university referral centre.

Methods

Data were collected for 12 adults and three children who underwent reimplantation during the last 3 years with a new HiRes90K device with HiFocus1J electrode owing to failure of the feed-through seal. Multi-slice computed tomography scans were used to compare positions of the original and newly placed electrode arrays. The speech-perception scores on a consonant-vowel-consonant word test before and after reimplantation were compared.

Results

All reimplantations were successfully performed by two experienced cochlear implantation surgeons and no complications were observed. Postoperative imaging showed that the average displacement of the new implant was only 0.59 mm. Reactivation of the implant gave immediate open set speech understanding in all patients, and speech perception rapidly returned to the previous level obtained with the original implant within weeks; it was even significantly better at the 3-month follow-up. No relation was found between changes in performance and the amount of displacement of the electrode array.

Conclusions

After cochlear reimplantation with the same device, electrode array position can be accurately replicated and speech perception can be regained or even improved within weeks.

INTRODUCTION

Cochlear implantation has proven to be an excellent therapy for patients with severe to profound sensorineural hearing loss. It restores the ability to hear sound and to understand speech to various degrees. From the beginning of cochlear implantation, many studies have focused on improvements with regard to surgical technique, implant design, and rehabilitation programs to further improve speech perception scores. Still, in certain situations revisions or reimplantations of the implanted device are inevitable. Several circumstances can lead to revision surgery, or even reimplantation, such as optimizing insertion of electrode-array, secondary inflammation after implantation, or the patient's wish to receive an upgraded implant model. The most documented reason for reimplantation is, however, internal device failure [Alexiades et al., 2001;Balkany et al., 1999;Brown et al., 2009;Cote et al., 2007;Fayad et al., 2004;Kim et al., 2008;Lassig et al., 2005]. Although internal device reliability has improved over the years, reimplantation due to device failure is performed repeatedly in many centres. With the growing numbers of cochlear implantation procedures, the revision and reimplantation rate is growing proportionally. Therefore, reviewing and reporting the surgical and audiologic results for this group of patients has become more important.

Although reimplantation is an undesirable consequence of cochlear implantation, many studies have shown good post-reimplantation results in terms of speech perception scores [Alexiades et al., 2001;Balkany et al., 1999;Cote et al., 2007;Gosepath et al., 2009;Lassig et al., 2005]. In those studies, the scores were equal to or better than the speech perception scores before reimplantation. Only a few studies have reported patients who did not achieve the same perception scores after reimplantation [Henson et al., 1999;Miyamoto et al., 1997]. However, in most, if not all, published studies, the period between first implantation, occurrence of the defect, and subsequent reimplantation was fairly long. For that reason, in most cases, a newer type of implant or another brand had become available and was implanted instead of the device that was initially used [Alexiades et al., 2001;Lassig et al., 2005]. As a result, the newer device was an upgraded version of the former device and was coupled with improved software to drive the new implant. Hence, those changes in design, brand, or software could be the explanation of the same, or even better, speech perception scores. Consequently, the confounding variable of a different implant type of implant weakens the comparison between speech perception outcomes from the first implantation and the reimplantation.

In this study, we investigated the effect of reimplantation on speech perception scores while using the same implant type. Our study group showed a confirmed feed-through seal defect in the device [Food and Drug Administration (FDA), 2004], within a relatively short period (9-53 months) after first implantation. Because the defect was manifested within a short time frame, the previously used implant type was still the newest available version and was used again at reimplantation. As a result of this defect, generally known as Vendor B defect, patients had sudden and intermittent complaints of a higher volume of sound, a change in their perception of sound, or failure of the implant-radio frequency (RF) link. Although a device problem could be readily identified, the particular reason behind the problem could not be identified through in vivo tests performed by an audiologist. Still, the Vendor B defect could always be confirmed following explantation and return to the manufacturer. Even though this defect was a very unfortunate outcome for the patients, it did give our center the exceptional chance of evaluating surgical and audiological results after reimplantation in patients with the same type of device within a very short time frame. To our knowledge, research from this unique situation has not been reported before.

In the case of reimplantation in patients with good speech perception scores, we felt that a minimal change in electrode position should be pursued to minimize the risk of deterioration in performance; it is known that a 3 mm displacement in the cochlea would lead to a tonotopic change of 1 octave [Greenwood, 1990]. We believe that hearing with the new implant will be more familiar to the patient if the electrode array is placed at the same location in the cochlea because sound levels and pitch sensations are comparable to the previous situation. This should minimize the rehabilitation and adaptation period with the new implant. Therefore, we used the same type of implant and the same type of electrode array for reimplantation. Pursuing minimal displacement from the original electrode contact locations, we investigated changes in speech perception scores and adaptation time with the new implant. We analyzed to what extent it is possible to position the new array at exactly the same place in the cochlea as the original electrode array. Time between detection of implant failure and reimplantation was evaluated as another performance indicator.

MATERIALS AND METHODS

Patients

In the population of 410 patients who underwent a cochlear implantation between 2000 and 2009 with a CII or HiRes90k at the Leiden University Medical Center, 12 adults and three children with a HiRes90K implant and a HiFocus1J electrode (Advanced Bionics, Sylmar, CA) underwent a reimplantation with the same device and in the same ear without complications (Table I). One adult patient with a Gemini implant (bifurcated electrode array for ossified cochleae) also underwent reimplantation, but those results were not analyzed in this study. These 15 patients all had the specific feed through seal defect, known as Vendor B defect, which was confirmed by intensive testing by the manufacturer, Advanced Bionics, after explantation. All 15 patients underwent their first cochlear implantation procedure at our institution between 2003 and 2006. The 12 adult patients were postlingually deafened. The mean duration of deafness until the first implantation was 22 years (range 5-43 years). At first implantation, the mean age of the adult patients was 49 years (range 22-73 years). The children were 3, 4 and 6 years old at first implantation.

All arrays were fully inserted, which was confirmed with the postoperative computed tomography (CT) scan that was obtained immediately after surgery in children and 1 day after surgery in adults. This imaging technique was chosen, because it provides high-resolution images of the temporal bone on which anatomic landmarks, such as the pyramidal process and round window niche, can be directly visualized. The ability to make multiplanar reconstructions within any desired plane after the scan procedure makes this technique independent of patient positioning and ensures accurate measurements of insertion depth even in serial scans [Verbist et al., 2010a]. The fact that a volume scan contains information of the height of the cochlea CT potentially also provides information on the scalar localization of an electrode contact. However, because we believe that radiation exposure should be as limited as possible, we are currently conducting a study to investigate the value of low-dose CT and cone-beam CT to minimize radiation exposure in future postoperative imaging.

The mean period between initial implantation and detection of the device failure was 2.2 years (range 0.8-4.4 years). Reimplantation was realized within 16 days on average (range 3-30 days) after detection of the failure, with the exclusion of one child whose parents needed more time to consider reimplantation (87 days).

Table I. Demographic information for the subjects who underwent reimplantation

Patient no.	Cause of deafness	Duration of deafness (yrs)	Age at first implantation (yrs)	Ear side	Insertion angle first implant[1] (°)	Recent phoneme score before defect[2] (%)	Time between first implantation and defect (mos)	Time between defect and reimplantation (days)	Insertion angle second implant (°)
Adult 1	Unknown	7	64	Right	500	87.5	9	7	498
Adult 2	Unknown	24	54	Right	491	84.5	14	17	515
Adult 3	Sudden deafness	43	73	Right	479	72.5	41	24	481
Adult 4	Virus	33	50	Left	418	83.0	13	3	418
Adult 5	Unknown Progressive	33	35	Left	406	88.0	10	21	406
Adult 6	Unknown Progressive	15	22	Right	513	80.0	19	30[3]	457
Adult 7	Hereditary progressive	22	65	Left	423	90.0	19	26	430
Adult 8[4]	Iatrogenic antibiotics	36	45	Left	449	24.5	42	8	495
Adult 9	Hereditary progressive	16	36	Right	461	82.5	35	17	388
Adult 10	Hereditary progressive	5	41	Right	485	93.5	36	13	466
Adult 11	Hereditary progressive	24	50	Right	414	74.0	53	18	530
Adult 12	Hereditary progressive	7	50	Left	599[5]	74.5	33	12	594
Child 1	Hereditary Congenital	3	3	Left	509	-	31	11	515
Child 2	Meningitis	6	6	Left	507	-	32	11	516
Child 3	Iatrogenic antibiotics	3	4	Right	511	-	13	87[6]	557

[1] Most recent computed tomography scan before reimplantation. [2] Average phoneme scores (consonant-vowel-consonant monosyllabic words) at 65 and 75 dB sound pressure level in quiet. [3] The period of 30 days was due to a request by the patient himself for private reasons. [4] Patient stated to be postlingually deafened, although his speech production and phoneme scores are more in line with prelingual deafness. [5] During reimplantation it was attempted to restore the insertion angle of first postoperative CT-scan. [6] Parents needed more time to consider reimplantation due to dysfunctional social circumstances.

Reimplantation

After detection of a problem with the internal device, all efforts were made to reimplant within the shortest time. The surgery was performed by two experienced cochlear implantation surgeons to ensure a fastidious and fluent change of arrays. The performance of this delicate procedure by two surgeons facilitates careful removal of the old array and positioning the new array within a very short time frame. After skin incision and elevation of the skin flap, the array was approached and cut as close as possible near the posterior tymponatomy. This enabled coarse manipulation of the implant body, without tension on the intracochlear array and the risk of either inadvertent electrode removal or trauma to the cochlea. Then, after the pocket had been opened, the implant body was removed and the lead withdrawn from the mastoid through a tunnel [Lenarz, 1998]. Next, the area around the cochleostomy was prepared in advance of the array change. If necessary, an incision was made into the fibrous sheath that had formed around the old electrode array. With the new array ready in the insertion tool (tip already slightly protruding), the old array was removed and the new one inserted carefully without disruption of the fibrous sheath. After the old array was removed, it was used for biofilm research [Ruellan et al., 2010], while the body and the attached lead were sent back to the manufacturer for cause-of-failure testing.

Positioning of New Array

To place the new array in exactly the same location as the old array, the position of the old array was evaluated in situ on the CT scan that was obtained after the first implantation. Close attention was paid to the position of the 'jog' of the array in relation to the pyramidal process and the rim of the round window niche (Figure 1). Using this relation, we pursued the identical position during surgery.

Evaluation of Position After Reimplantation

To evaluate the position of the newly placed electrode array, a postoperative CT scan was also obtained after reimplantation. From these scans, multi-planar reconstructions (MPRs) were produced, consisting of consecutive slices through the cochlea along the center of the modiolus and parallel to the basal turn of the cochlea [Verbist et al., 2009]. Using an in-house-designed postprocessing program (Matlab, Mathworks, Novi, MI), the electrode contact positions and their insertion angles were determined in a three-dimensional coordinate system that fulfils the requirements set by an international consensus working group [Verbist et al., 2010b;Verbist et al., 2010a] (Figure 2A and 2B). These data were used to calculate the exact linear displacement of each electrode contact with respect to the previous position at the first implantation. Although the position of the whole electrode array was evaluated, special attention was paid to the position of electrode contact 16, the most basal electrode. During placement, the surgeon was able to see the most basal electrode contact almost until full insertion was reached. The position of this particular electrode contact is most strongly correlated with the surgical variability and is therefore most important in evaluating and influencing electrode array position perioperatively and defining its potential dislocation postoperatively.

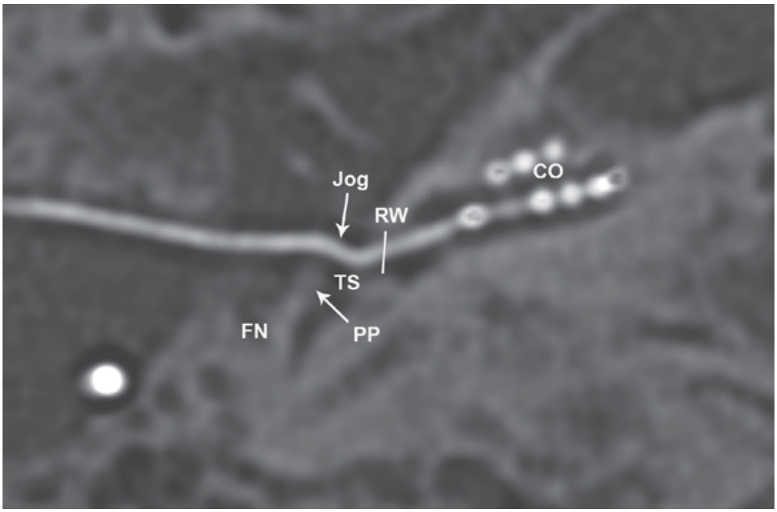

Figure 1. Thick-slice multiplanar reconstruction of an implanted human cochlea. Relation between array (Jog) and surrounding anatomic structures; facial nerve (FN), pyramidal process (PP), tympanic sinus (TS), round window (RW) and cochlea (CO).

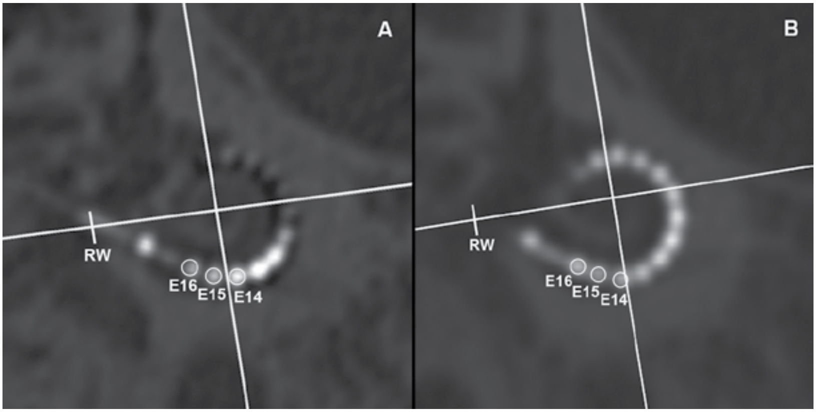

Figure 2. Position of the array before (A) and after reimplantation (B). Electrode-contacts 14-16 and the round windows (RW) are marked to illustrate the displacement.

Rehabilitation and Evaluation

After First Implantation

In general, hookup is carried out within 4 to 6 weeks after implantation. The standard rehabilitation program starts with 30 intensive hearing rehabilitation sessions with a specialized speech therapist during a period of 4 weeks. The rehabilitation program comprises 10 levels, starting with sound detection and ending with telephone training and speech perception in noise. During these training sessions, special attention is paid to speech details, such as consonant identification [Frijns-van Putten et al., 2005]. After this intensive program, frequency of the training sessions is decreased and tailored to each patient's individual needs. From the moment of hook-up, progression of speech perception is tested at set intervals. Speech perception is measured using consonant-vowel-consonant monosyllabic words through the standard Dutch speech audiometric test [Bosman and Smoorenburg, 1995]. All tests are conducted in free field conditions in quiet (65 and 75 dB sound pressure level) and in speech-shaped noise. By using this standardized follow-up program, progress of each patient was carefully examined and documented.

Rehabilitation and Evaluation

After Reimplantation

Because the shorter surgical time without much soft-tissue damage or bone work resulted in a faster healing process, hookup was carried within 2 to 3 weeks of surgery. From the moment of hookup, patients received a less-intensive rehabilitation program (approximately 15 sessions). Speech-training sessions were given daily during the first 2 weeks, reiterating crucial steps from the standard rehabilitation program. After these 2 weeks, additional training sessions were optional and the exercises were adapted to the individual needs of the patient.

In the 12 adults, speech perception was monitored intensively in the first weeks after reimplantation to determine whether (and when) patients recovered to the performance level they had before implant failure. Speech perception was therefore measured only 1 hour after hookup and after 1 week, 2 weeks and 3 months. After these 3 months of intensive measurement, speech perception measurements again fell in line with the standard follow-up scheme in our center. Because of the differences in measures and time scales used to evaluate the children's performance, their speech perception data were not included in the analysis.

Failure Rates

After the feed-through (Vendor B) defect had been recognized in several cochlear implants, every implant recipient with a feed-through by Vendor B was identified and carefully followed because the failure risk was substantially higher than for the non-Vendor B devices. The total failure rate, which is the sum of all failures divided by the total number of patients who underwent implantation at our center, was measured. For this analysis, adults and children were included, as well as every failing device, regardless of device manufacturer. In particular, the Vendor B failure rate, which is the number of failing Vendor B implants divided by the total number of Vendor B implants, was measured.

Statistical Analysis

The most recent speech perception scores with the first functional implant were compared with the scores that were measured at specified times after reimplantation by using a paired *t* test and the nonparametric Wilcoxon signed ranks test. The audiologic outcomes were related to the surgical outcomes to determine whether a correlation existed between changes in performance and the amount of electrode array displacement. For this analysis, the Spearman rank correlation test was applied.

RESULTS

Surgical Outcomes

Each reimplantation was carried out following the procedure described previously. For each reimplantation, full insertions were achieved and no complications were observed. In Figure 3, the displacement of electrode contact 16 between the original and reimplanted electrode arrays is shown. The average displacement was 0.59 mm (approximately 0.5 contact distance), which means a deeper insertion after reimplantation. All but two patients had a displacement of electrode contact 16 between

-2 and 2 mm after reimplantation. One patient (patient no. 12 in Figure 4) showed a displacement of 5.33 mm. For this patient, there were two CT scans available for the first electrode array. The first CT scan was obtained 1 day after surgery, and the second CT scan was obtained several weeks before reimplantation to evaluate the sound-quality complaints of the patient. An obvious difference (6.3 mm) in position of the array between the two CT scans was observed, with the deeper insertion immediately after implantation. Based on this observation, we attempted to restore the first position instead of the most recent position.

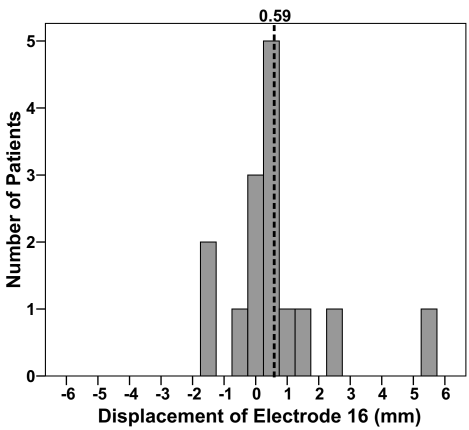

Figure 3.
Displacement of electrode-contact 16. Positive outcomes indicate a deeper insertion at reimplantation. The black dotted line marks the average displacement.

Audiologic Outcomes

In Figure 4, the speech perception scores per adult patient at the different evaluation intervals are shown: 1 hour, 1 week, 2 weeks, and 3 months. The scores of these four measurements were compared to the speech perception score obtained most recently before the device failed. The black line indicates the speech perception before reimplantation. All but one patient (patient no. 3 in Figure 4) reported, at the time of the hookup of the new implant, that the sound was very similar to the sound quality obtained with the previous implant. All patients, with the exception of the low-performing patient (no.8), were able to communicate without lip-reading with their new implant within minutes.

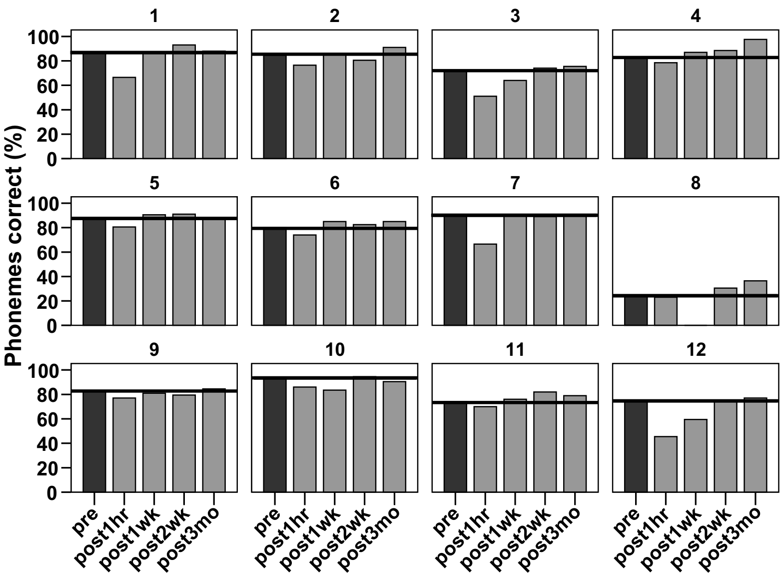

Figure 4. Phoneme scores (monosyllabic consonant-vowel-consonant words) of each patient (1-12) before (dark grey column) and after reimplantation (light grey column). Black line indicates performance level before reimplantation.

In Figure 5, the mean speech perception scores for all 12 adult patients are shown for each test interval. Both a paired *t* test and the Wilcoxon signed ranks test showed a significant difference (p= 0.002) between the mean level before reimplantation and that found 1 hour after hookup of the reimplanted device. The average decline was 11%. However, 3 months after reimplantation there was a significant improvement of 4% on average (p=0.014) relative to the scores before reimplantation.

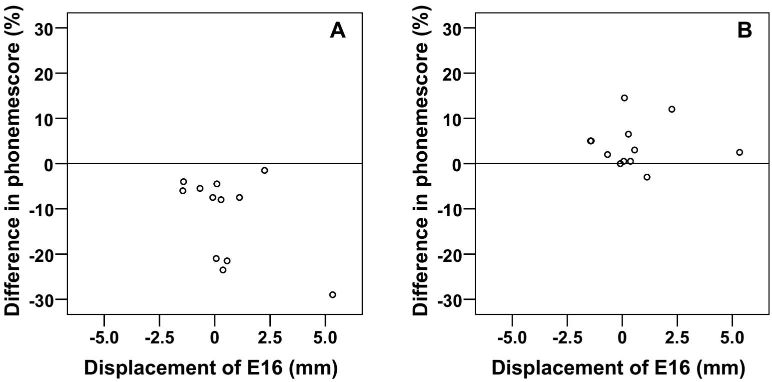

Figure 5. Average phoneme scores (monosyllabic consonant-vowel-consonant words) of the population before and after reimplantation. Black line indicates average performance level before reimplantation. The asterisks indicate a significant (p<0.05) difference compared to the scores before reimplantation.

Correlation Between Surgical Outcomes and Audiologic Outcomes

The audiologic outcomes were compared with the surgical outcomes to determine whether a correlation existed between changes in performance and the amount of electrode array displacement. The results for 1 hour and 3 months after hookup are shown as scatterplots in Figure 6. No significant correlations were found for any of the four measurement intervals.

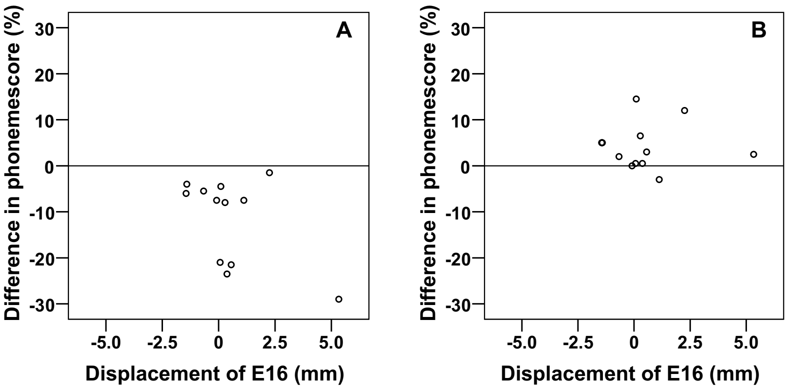

Figure 6. Relationship between displacement of electrode-contact 16 and difference in speech perception score before reimplantation compared to 1 hour (A) and 3 months (B) after hookup.

Device Failure Rates

Between 2000 and 2009, 16 of 410 patients implanted at our center underwent reimplantation, all due to failures of Vendor B devices; the 12 adult patients already discussed, three children and an adult patient with a Gemini implant. Therefore, the total device failure rate in this cohort is 3.9%, with a failure rate of 4.5% in adults and 2.5% in children.

In Figure 7, a Kaplan-Meier plot shows the survival function of the Vendor B devices from the moment of implantation. A total of 60 patients were identified as having a Vendor B feed-through seal. One of those patients had undergone bilateral implantation and received two Vendor B devices; Thus, the Vendor B failure rate was 26%. The remaining patients with Vendor B devices are being closely followed, and any of their complaints will be thoroughly investigated.

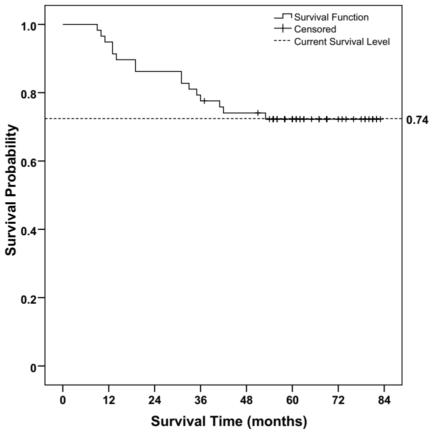

Figure 7. Survival curve of the implants with a Vendor B feed-through.

DISCUSSION

In a group of 15 patients who underwent reimplantation with the same type of implant, the surgical and audiologic outcomes were evaluated. Failure rates within the center's cochlear implant population, as well as within the Vendor B population, were calculated. Analyzing positions of the electrode array showed displacements of between -2 and 2 mm for virtually all of the patients. This demonstrates that it is possible to perform a reimplantation and to replicate the original electrode array position very accurately. For the 12 adult patients, the changes in speech perception scores and adaptation time with the new implant were analyzed. The speech perception scores indicated an initial drop in performance directly after hookup, although all patients except one were able to communicate through sound only within minutes after hookup. Within 2 weeks, most patients had adapted to the new implant and had regained their original performance level, and after 3 months most patients had even a slightly better speech perception than with their old implant.

The revision rate of reimplantation at our center is comparable to that at other centers. In the literature, revision rates of 3.7% to 9.3% have been reported [Brown et al., 2009;Cote et al., 2007;Gosepath et al., 2009;Lassig et al., 2005]. However, the Vendor B failure rate of 26% is considerably higher, despite the relatively short follow-up period (5.8 years on average). Although the failure rate seemed to have stabilized after 50 months (Figure 7), just before submission of this report, another child underwent reimplantation as a result of the Vendor B failure after an implant use of 5.5 years, although this child was not included in this study. Therefore, all patients with Vendor B implants have now been identified and will be tested intensively if they present with sound-quality complaints that could indicate a device failure. In this series, the revision rate of 2.5% among children (mean follow-up, 5.9 years) is low compared to other reported rates. Rates between 5.6 and 15.4% among children have been reported [Arnoldner et al., 2009;Brown et al., 2009;Cote et al., 2007;Fayad et al., 2004;Gosepath et al., 2009;Migirov et al., 2007;Parisier et al., 1996]. Many articles report higher rates of reimplantation in children than in adults as a result of defects due to trauma and breakage of the implant casing [Brown et al., 2009]. In this study, only three children from the total population underwent reimplantation, all owing to the Vendor B failure. However, because of the variability in performance and no technical test option, the detection of a Vendor B failure in children is difficult. Therefore, we continue to be especially careful in monitoring and following the children with a Vendor B feed-through.

When patients first started to present with complaints of sound perception changes, the feed-through seal defect had not yet been uncovered. To analyze the complaints, in some cases an extra CT scan was obtained to check for intracochlear changes and changes in array position. When these scans were analyzed, some were indeed found to show different electrode array positions as compared with the first postoperative scan (0.5-6.3 mm). However, when the complaints intensified and could not be corrected with fitting procedures, the circumstances surpassed beyond what could be expected from and ascribed to shift of electrode array position. Based on these observations, it was concluded that the complaints were the result of a device failure, and reimplantation followed. In all cases, Vendor B failure was subsequently confirmed by the manufacturer following explantation. Further research was started to investigate these array position changes, and findings will be reported in the near future. Nevertheless, when there was a change of array position detected through the second CT scans, the array position was carefully evaluated, and in almost all cases the latest position of the array was pursued during reimplantation.

Although other centers report complications like intraoperative cerebral spinal fluid leakage, epidural haematoma, and postoperative flap breakdowns with implant extrusion [Dodson et al., 2007;Fayad et al., 2004;Gosepath et al., 2009], no such complications were observed in our population. To change the array quickly to prevent contamination or collapse of the fibrous sheath (as previously stated by Henson et al., 1999), all reimplantations were executed by two experienced surgeons. Although we realize operating with two surgeons is a large investment and may not be possible to arrange in all centers, our series of reimplantations indicates that this precaution helps to prevent the reported adverse effects.

We hypothesized that the bigger the displacement, the harder the adaptation to the new tones would be for the patient, but in this study no correlation was found between the change in speech perception and displacement of the array. This was also described by Henson et al. (1999). The fact that no correlation between displacement and speech perception was demonstrated indicates that array position within the small variations (<2mm) in this series does not affect perception and thus adaptation to a new implant; the effect of larger displacements remains unknown. Therefore, we decided to carry on with our exact positioning procedure in future reimplantations to maintain very small displacements.

Interestingly, the mean speech perception score of the adult patients with the Vendor B failure before reimplantation was comparable to the mean scores at 6 months and 2 years, respectively 74.5%, 75.0%, for the total group of adult patients implanted between 2000 and 2009 with a HiRes90K HiFocus1J implant without a Vendor B feed through ($p>0.4$). This means that the patients with the Vendor B device showed no signs of dysfunction or lower performance before the failure of the implant became apparent. This falsifies the hypothesis that the increase in performance after reimplantation was due to lower speech perception scores before detection of the failure. Furthermore, the mean perception score at 3 months after reimplantation compared to the scores of the total group of implanted adults at 6 months, 1 year and 2 years was 4% higher, although this difference was not significant.

However, the improvement of speech perception could be ascribed to the training sessions during the first 2 weeks after hookup, as in these sessions all the crucial steps of the standard rehabilitation program were repeated [Stacey and Summerfield, 2007;Stacey and Summerfield, 2008]. It is interesting to note that reimplantation with limited displacement of the arrays and extra training sessions in all patients led to an improved speech perception.

CONCLUSION

This study confirms that not only the electrode array position can be accurately restored in virtually all reimplantation cases, but also that speech perception performance rapidly returns to at least the level that was obtained with the original implant.

In addition, we conclude that small displacements, like were seen in this series, will not negatively affect speech perception; the effect of larger displacements cannot be predicted from these data. The setup with two experienced surgeons may facilitate this accurate positioning and thereby help to avoid adverse effects. The concomitant short rehabilitation and rapid adaptation to the new implant may justify the additional cost and effort of involving two surgeons.

REFERENCES

1. Alexiades G, Roland JT, Jr., Fishman AJ, Shapiro W, Waltzman SB, Cohen NL: Cochlear reimplantation: surgical techniques and functional results. Laryngoscope 2001;111:1608-1613.
2. Arnoldner C, Helbig S, Wagenblast J, Gstoettner W: Cochlear implant reference electrode migration to dura mater. Otol Neurotol 2009;30:1013-1014.
3. Balkany TJ, Hodges AV, Gomez-Marin O, Bird PA, Dolan-Ash S, Butts S, Telischi FF, Lee D: Cochlear reimplantation. Laryngoscope 1999;109:351-355.
4. Bosman AJ, Smoorenburg GF: Intelligibility of Dutch CVC syllables and sentences for listeners with normal hearing and with three types of hearing impairment. Audiology 1995;34:260-284.
5. Brown KD, Connell SS, Balkany TJ, Eshraghi AE, Telischi FF, Angeli SA: Incidence and indications for revision cochlear implant surgery in adults and children. Laryngoscope 2009;119:152-157.
6. Cote M, Ferron P, Bergeron F, Bussieres R: Cochlear reimplantation: causes of failure, outcomes, and audiologic performance. Laryngoscope 2007;117:1225-1235.
7. Dodson KM, Maiberger PG, Sismanis A: Intracranial complications of cochlear implantation. Otol Neurotol 2007;28:459-462.
8. Fayad JN, Baino T, Parisier SC: Revision cochlear implant surgery: causes and outcome. Otolaryngol Head Neck Surg 2004;131:429-432.
9. Food and Drug Administration (FDA): Advanced Bionics Conducts Voluntary Recall of Cochlear Implants. http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2004/ucm108358.htm.
10. Frijns-van Putten A, Beers M, Snieder SG, Frijns JHM: Hoortraining voor volwassen CI-dragers: Het cochleaire leermodel (in Dutch). Logopedie en Foniatrie 2005;50-59.
11. Gosepath J, Lippert K, Keilmann A, Mann WJ: Analysis of fifty-six cochlear implant device failures. ORL J Otorhinolaryngol Relat Spec 2009;71:142-147.
12. Greenwood DD: A cochlear frequency-position function for several species--29 years later. J Acoust Soc Am 1990;87:2592-2605.
13. Henson AM, Slattery WH, III, Luxford WM, Mills DM: Cochlear implant performance after reimplantation: a multicenter study. Am J Otol 1999;20:56-64.
14. Kim CS, Kim DK, Suh MW, Oh SH, Chang SO: Clinical outcomes of cochlear reimplantation due to device failure. Clin Exp Otorhinolaryngol 2008;1:10-14.
15. Lassig AA, Zwolan TA, Telian SA: Cochlear implant failures and revision. Otol Neurotol 2005;26:624-634.
16. Lenarz T: Cochlea-Implantat. Ein praktischer Leitfaden für die Versorgung von Kindern und Erwachsenen. (in German). Springer, Berlin, Heidelberg, New York (Book), 1998.
17. Migirov L, Taitelbaum-Swead R, Hildesheimer M, Kronenberg J: Revision surgeries in cochlear implant patients: a review of 45 cases. Eur Arch Otorhinolaryngol 2007;264:3-7.
18. Miyamoto RT, Svirsky MA, Myres WA, Kirk KI, Schulte J: Cochlear implant reimplantation. Am J Otol 1997;18:S60-S61.
19. Parisier SC, Chute PM, Popp AL: Cochlear implant mechanical failures. Am J Otol 1996;17:730-734.
20. Ruellan K, Frijns JH, Bloemberg GV, Hautefort C, Van den AT, Lamers GE, Herman P, Huy PT, Kania RE: Detection of bacterial biofilm on cochlear implants removed because of device failure, without evidence of infection. Otol Neurotol 2010;31:1320-1324.
21. Stacey PC, Summerfield AQ: Effectiveness of computer-based auditory training in improving the perception of noise-vocoded speech. J Acoust Soc Am 2007;121:2923-2935.

22. Stacey PC, Summerfield AQ: Comparison of word-, sentence-, and phoneme-based training strategies in improving the perception of spectrally distorted speech. J Speech Lang Hear Res 2008;51:526-538.
23. Verbist BM, Ferrarini L, Briaire JJ, Zarowski A, dmiraal-Behloul F, Olofsen H, Reiber JH, Frijns JH: Anatomic considerations of cochlear morphology and its implications for insertion trauma in cochlear implant surgery. Otol Neurotol 2009;30:471-477.
24. Verbist BM, Joemai RM, Briaire JJ, Teeuwisse WM, Veldkamp WJ, Frijns JH: Cochlear coordinates in regard to cochlear implantation: a clinically individually applicable 3 dimensional CT-based method. Otol Neurotol 2010a;31:738-744.
25. Verbist BM, Skinner MW, Cohen LT, Leake PA, James C, Boex C, Holden TA, Finley CC, Roland PS, Roland JT, Jr., Haller M, Patrick JF, Jolly CN, Faltys MA, Briaire JJ, Frijns JH: Consensus Panel on a Cochlear Coordinate System Applicable in Histologic, Physiologic, and Radiologic Studies of the Human Cochlea. Otol Neurotol 2010b.

Chapter Three

Electrode Migration in Cochlear Implant Patients: Not an Exception

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ABSTRACT

Objective
It was the aim of this study to investigate the occurrence of electrode migration of a cochlear implant in patients with and without complaints.

Methods
We performed a retrospective case review in a tertiary referral center. The electrode position was evaluated in 35 cochlear implantees, 16 with a CII HiFocus1 (non-positioner) and 19 with a HiRes90K HiFocus1J, using multiplanar reconstructions of the postoperative CT scans. Of 5 patients, a second scan was obtained to evaluate complaints of performance drop, vertigo, tinnitus, headache or nonauditory stimulation. Displacements of the electrode contacts were calculated and displacements of >1 mm were considered a migration. The possible correlation with implant type, insertion depth or presence of complaints was analyzed.

Results
Migrations were detected in 10 patients (29%). There was a significant effect of the implant type in favour of the HiFocus1, but no relation with the original insertion depth of the device. In the 5 patients scanned because of complaints, two migrations were detected.

Conclusions
In our patient population, electrode migration was not uncommon and turned out to occur in patients with and without complaints.

INTRODUCTION

Cochlear implantation is a safe and reliable otosurgical procedure to rehabilitate patients with sensorineural hearing loss. Most patients benefit tremendously from this treatment in terms of improved speech perception and quality of life. However, sometimes patients return to the clinic with complaints such as changes in sound perception, performance drop, facial stimulation, vertigo or even pain. Finding the origin of these complaints can be a difficult and time-consuming task, since there are many options to evaluate and resolve these complaints. Electrophysiological and psychophysical testing is most commonly used to evaluate complaints and detect their cause. Adjustments of the speech processor settings tend to solve the complaints in most cases and often restore the original performance level. Nonetheless, in some cases electrophysiological recordings do not result in satisfactory outcomes, or the cause of the complaint is not completely solved with fitting procedures.

When these testing methods have failed, imaging is considered. Imaging provides information about changes in array position or other causal factors, such as ossification around the array, which could also clarify high impedance measurements. In many centers, imaging may be delayed because of the concern of radiation exposure.

It was commonly believed that the electrode array position remained stable following insertion, so postoperative CT imaging to evaluate complaints appeared to be unnecessary [Roland, Jr. et al., 1998]. However, an increasing number of recent papers report cases where an electrode migration was observed in patients with complaints. Moreover, electrode migration, or extrusion, is reported to be the second most common indication for cochlear reimplantation [Brown et al., 2009;Cullen et al., 2008;Rivas et al., 2008;Connell et al., 2008]. Electrode migration is often associated with sudden drops in performance, or elevated electrode contact impedance, although complaints of nonauditory stimulation, pain and vertigo might also be symptoms of electrode migration [Rivas et al., 2008;Connell et al., 2008]. In our population, we discovered electrode migration for the first time during reimplantation surgery necessitated by device failure [van der Marel et al., 2011]. The possibility of electrode migration convinced us to implement a second CT scan before the reimplantation to define the current position of the array. When evaluating the second CT scans, migrations were confirmed in several cases. Information about the current electrode array position ensured accurate replacement of the electrode array during the reimplantation surgery. Since these patients had not noticed any change and showed a stable performance before device failure, our hypothesis was that a migration could also occur without causing complaints, although, to our knowledge, this has never been reported in the literature. To test this hypothesis, we retrospectively identified each patient of the population in our clinic of whom more than one postoperative CT scan was available since the start of our cochlear implantation program in 2000.

In this study, we analyzed how often a migration occurred in patients with and without complaints. In addition, we evaluated which complaints may suggest an electrode migration and when to decide to perform imaging to detect this. Furthermore, we will discuss the implications of detecting an electrode array migration for clinical care and research purposes.

MATERIALS AND METHODS

Patients

A retrospective review of all cases since the start of the cochlear implantation program at the Leiden University Medical Center in 2000 identified 40 cases for which a second postoperative CT scan was obtained. All patients received an Advanced Bionics cochlear implant. Of these 40 cases, 5 patients had implants with a positioner and were analyzed separately because of the fixation by the positioner. Table I shows the characteristics of the remaining 35 patients. This group consisted of 16 patients with a CII implant with a HiFocus1 electrode array and 19 patients with a HiRes90k with a HiFocus1J electrode array.

All patients were under regular follow up. Speech perception was tested with monosyllabic words (sound only, four lists of eleven consonant-vowel-consonant words per condition, scored as the percentage of phonemes correct) at each visit and in between, in case of complaints [Bosman and Smoorenburg, 1995]. In 10 out of the 35 patients, the second CT scan was performed to define the array position prior to reimplantation, and for 5 patients, a second scan was obtained to evaluate complaints of performance drop, vertigo, tinnitus, headache or nonauditory stimulation. In the remaining patients, it was obtained for nonauditory symptoms or reasons unrelated to the performance of the cochlear implant. The patients were implanted at an average age of 45 years (range 0-78). In all patients, the surgery resulted in complete and uncomplicated insertions, using an extended round window approach. The mean period between these two CT scans was 24 months (range 3 days to 90 months). The average insertion angle (of the most apical electrode contact: contact 1) on the first postoperative CT scan, obtained directly after the original implantation, was 479° (range 309-674). The average insertion angle on the second CT scan was 437° (range 199-678).

Calculation of Electrode Migration

To analyze the occurrence of electrode migration, serial multi-planar reconstructions were made using two available postoperative CT scans of each patient [Verbist et al., 2005;Verbist et al., 2010b]. The electrode array positions and insertion angles of each electrode contact were determined in a 3D coordinate system based on international consensus, using an in-house designed post-processing program (Matlab, Mathworks, Novi, Mich). The accuracy of this method was evaluated in a previous study showing good intraclass correlation coefficients and small standard deviations (SD) for both angular (intraclass correlation coefficient 0.74-1, SD<5°) and linear measurements (intraclass correlation coefficient 0.77-1, SD<0.5 mm) within the cochlea [Verbist et al., 2010a]. It is known that a shift of 3 mm in the cochlea would lead to a tonotopic change of 1 octave [Greenwood, 1990;Carlyon et al., 2010].

For analysis of the migration, the displacement of the most basal contact (E16) was used. A displacement of >1 mm (i.e. approx. 1 contact spacing) was considered a migration. If one or more contacts would migrate outside the cochlea, this would result in a smaller stimulation area, which might cause complaints such as performance drop. Figure 1 shows an example of a clear electrode migration, resulting in a shallower insertion on the second CT scan.

Correlations with Electrode Migration

Statistical analysis was done using the statistical software program SPSS, and p-values <0.05 were considered significant. A χ^2 test was used to test whether the occurrence of migration is correlated with the implant type. In addition, a Spearman ranks correlation test was executed to test the hypothesis that the original insertion depth of electrode 1 (E1, the most apical contact) could be related to the amount of migration, as an electrode array experiences more strain when it is inserted deeper into the cochlea, which in turn might lead to further migration.

Additionally, the relation between migration and speech perception was evaluated in 5 symptomatic patients. The medical and audiological follow-up for 2 patients with evidence of migration is described.

Table I. Characteristics of patients

Patient No.	Age at implantation, years	Ear side	Electrode type	Vendor B defect	Insertion angle 1st scan, °	Insertion angle 2nd scan, °	Reason for second scan	Time between scans, months
1	71	Left	HiFocus1	No	329	344	Nonauditory	7
2	23	Left	HiFocus1	No	522	516	Nonauditory	7
3	53	Right	HiFocus1	No	312	313	Nonauditory	7
4	65	Right	HiFocus1	No	318	318	Nonauditory	7
5	47	Left	HiFocus1	No	309	311	Nonauditory	9
6	62	Left	HiFocus1	No	476	370	Nonauditory	8
7	56	Right	HiFocus1	No	531	526	Nonauditory	10
8	64	Right	HiFocus1	No	380	375	Nonauditory	8
9	50	Left	HiFocus1	No	378	376	Nonauditory	9
10	53	Right	HiFocus1	No	358	371	Nonauditory	8
11	60	Left	HiFocus1	No	413	418	Nonauditory	8
12	77	Left	HiFocus1	No	609	599	Nonauditory	7
13	55	Right	HiFocus1	No	674	678	Nonauditory	7
14	40	Left	HiFocus1	No	535	543	Nonauditory	6
15	40	Right	HiFocus1	No	425	403	Nonauditory	0
16	50	Right	HiFocus1	No	672	674	Nonauditory	0
17	47	Left	HiFocus1J	Yes	495	411	Device failure	70
18	42	Left	HiFocus1J	No	536	539	Vertigo	52
19	1	Right	HiFocus1J	No	481	478	Nonauditory	5
20	50	Right	HiFocus1J	Yes	414	389	Device failure	54
21	36	Right	HiFocus1J	Yes	461	419	Device failure	59
22	45	Left	HiFocus1J	Yes	449	423	Device failure	43
23	40	Right	HiFocus1J	Yes	485	438	Device failure	37
24	49	Left	HiFocus1J	Yes	599	354	Device failure	33
25	64	Right	HiFocus1J	No	370	221	Performance drop; Facial stimulation	52
26	70	Right	HiFocus1J	Yes	488	440	Device failure	55
27	4	Right	HiFocus1J	Yes	511	511	Device failure	3
28	6	Left	HiFocus1J	Yes	513	508	Device failure	31
29	66	Right	HiFocus1J	No	519	476	Performance drop	44
30	79	Right	HiFocus1J	No	532	199	Performance drop	18
31	1	Left	HiFocus1J	No	595	588	Nonauditory	3
32	2	Right	HiFocus1J	Yes	632	481	Nonauditory	90
33	1	Left	HiFocus1J	No	408	362	Nonauditory	13
34	49	Right	HiFocus1J	No	559	496	Tinnitus; Headache	5
35	51	Right	HiFocus1J	Yes	464	415	Device failure	76

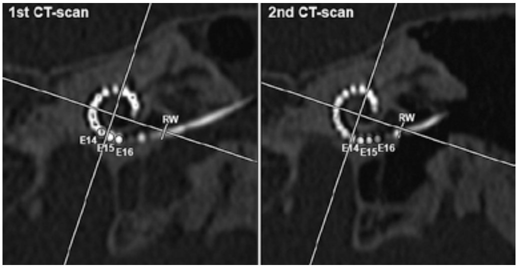

Figure 1. Example of electrode migration. RW = round window.

RESULTS

Migrations of >1 mm were detected in 10 of the 35 patients (29%). The frequency of occurrence and the extent of migration is shown in Figure 2. The results are separated by electrode type and by presence of complaints. Migrations occurred in patients with both electrode array types. However, in the group with a HiFocus1 array, only 1 patient had a migration of >1 mm, compared to 9 patients with a HiFocus1J electrode (p=0.005). None of the patients with a HiFocus1 electrode array had experienced any complaints. In the HiFocus1J group, 7 out of 9 patients showed a migration of E16 of >1 mm without having complaints. This means a migration occurred in 8 out of 35 patients (22%) without symptoms. In none of the 5 patients who have a positioner, a migration occurred.

The Spearman's rank correlation between the insertion depth of E1 and the amount of migration of E16 was not significant (p = 0.60), which rejects the hypothesis that a causal relation exists between the original insertion depth and the frequency and extent of migration.

Out of the 5 symptomatic implantees, 2 had a migration of the electrode of >1 mm, i.e. 11.5 and 4.8 mm, respectively (patient No. 30 and 25). The scores of patient No. 30, expressed as phonemes correct on monosyllabic words, were normal at the initial measurement (55% at 2-week implant experience), but slowly declined to 44% and 32% (3 and 6 months after implantation, respectively), and ultimately dropped to chance level (6%), despite repeated fitting sessions and turning off several electrode contacts. Ultimately, radiological analysis was performed, showing extreme migration with at least 5 extracochlear electrodes. This patient underwent a reimplantation and his first available scores (45% on average) are promising. The speech perception of patient No. 25 dropped from 95% and 86% (6 months and 1 year after implantation, respectively) to a score of 51% (3 years after implantation) despite extensive fitting procedures. In addition, he had facial stimulation. A CT scan showed evident migration with three extracochlear contacts over which high contact impedance values were measured. With that knowledge, the patient received a new fitting with the extracochlear contacts turned off, resulting in an acceptable performance level (66%).

Three other patients (No. 18, 29 and 34) reported complaints, though no substantial migrations were detected with their second CT scans. The first patient reported vertigo. His performance remained stable over the years and no migration was detected.

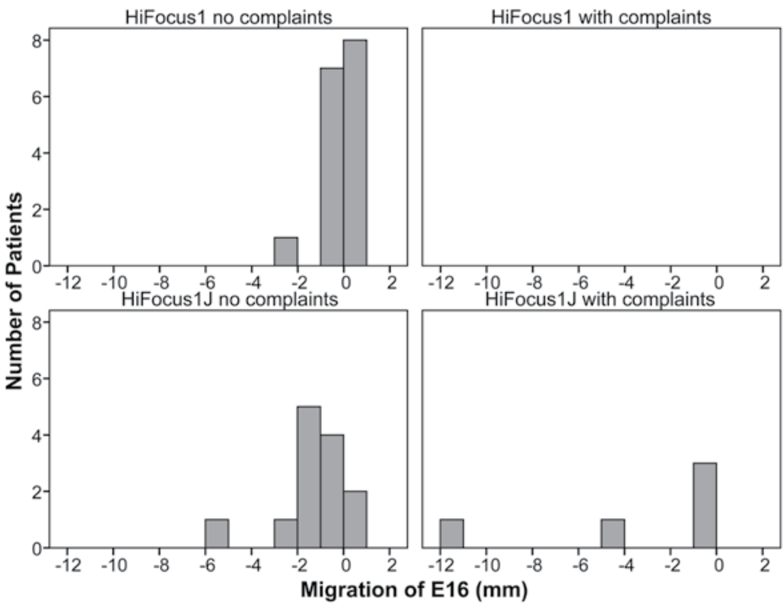

Figure 2. Occurrence of migration separated by electrode type and presence of complaints.

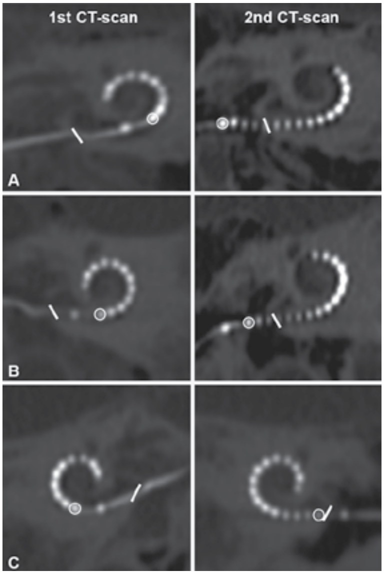

Figure 3.
CT scans of patients No. 30(A), 25(B), and 24(C) showing the extreme migrations.

The second patient (No. 29) showed a clear performance drop, from 88 to 43%, while the migration of the array was no more than 1 mm. New fitting procedures restored speech perception only partly (to 57%).

Additional efforts are currently undertaken to further restore speech perception. The third patient reported an increase of her pre-existent tinnitus and headache, shortly after receiving the cochlear implant, though no migration or any other cause was observed on the CT scan. In only 3 patients, an extreme migration of >4 mm occurred. CT scans of these 3 patients are shown in Figure 3. Two out of them presented themselves at our clinic with sound quality complaints as described in the previous section. Figure 3A shows the two scans of patient No. 30 who had the largest migration of 11.5 mm, resulting in 5 extracochlear electrode contacts, while Figure 3B shows the scans of patient No. 25. The third patient (No. 24, Figure 3C) had no complaints in spite of a migration of 5.9 mm. Fortunately, all electrode contacts were still intracochlear in this case.

DISCUSSION

To our knowledge, this is the first study that reports documented electrode migration in cochlear implant patients without complaints. It retrospectively analyzed all 35 patients in our center, implanted with a HiFocus electrode from Advanced Bionics, for whom two postoperative CT scans were available. Ten patients were identified with a migration of >1 mm, but only two of them experienced a drop in speech perception. Migration turned out to be unrelated to insertion depth, but was shown to occur more frequently with the HiFocus1J array than with its predecessor.

In 2 out of 5 symptomatic implantees, postoperative imaging showed an extreme migration, resulting in very shallow insertions with several extracochlear contacts. Despite a migration of almost 6 mm, the case shown in Figure 3C still had all active contacts inside the cochlea. This patient did not experience any perceptual changes, and speech perception scores were stable. This observation could suggest that performance drops caused by migration only occur if the migration results in extracochlear contacts. On the other hand, the performance drop and migration could also be totally unrelated, as the migration could have occurred before first activation of the implant.

In most cases, drops in speech perception can be resolved with new fittings. If, as in some cases, these adjustments during fitting sessions do not result in acceptable restoration of performance, imaging can provide extra information about the electrode array position. In extreme cases of migration leading to several extracochlear contacts, reimplantation might be the best treatment option.

However, clinicians should be cautious in attributing complaints to a detected migration and always consider other causes of performance drop, such as a technical device failure. This study documents that migration occurs, and that it is associated with certain complaints in a number of patients, but it does not prove beyond doubt that the migration is causing the complaints. The migration could have occurred long before the complaint started, or even before the implant was turned on for the first time. If this is the case, the migration is not likely to have any relation to the complaints of the patient.

Hence, acquiring more insights about the moment of migration is crucial; in cases where the migration occurs during the healing period after surgery, in the period after the first postoperative CT scan and before the first activation of the cochlear implant, the patients will learn to understand speech only with the final electrode contact positions.

This can explain why some patients with a documented electrode migration will never experience any changes in sound quality or performance drops. In our population, we observed this in 8 patients with a migration of >1 mm.

We believe that it is most likely for the array to move in the first weeks after implantation, because at this time it is not yet covered by a fibrous sheath, or otherwise immobilized by ossification [Fayad et al., 2004;Rivas et al., 2008]. Similarly, in the field of neurosurgery, where electrodes are placed as spinal cord stimulator to treat chronic pain, electrode migration is also believed to occur within the first days to weeks after placement until the electrode is covered by a fibrous sheath [Barolat et al., 2005]. In the additional group of 5 patients who received a cochlear implant with a positioner, no migrations were detected. This supports the theory that the occurrence of migration declines after immobilization of the array by ossification, fibrous sheath or, like in these cases, a positioner.

The clinical consequences of migration can be significant, since migration can induce performance drops, pain, vertigo or facial stimulation and eventually can lead to reimplantation [Connell et al., 2008;Brown et al., 2009;Cullen et al., 2008;Rivas et al., 2008;Alexiades et al., 2001]. Moreover, detection of migration is also important in the research setting, in studies that try to relate speech perception or pitch to electrode contact positions or insertion depth. These studies can result in misleading outcomes, if migration occurred after imaging was obtained. This was illustrated in a recent pitch matching study by Carlyon et al. [2010].

The risk of missing a migration or, on the contrary, incorrectly assigning a causal relation to new complaints and a long existing migration forced us to question our postoperative imaging protocol. Comparison of the electrode array position, and thus detection of a migration, is only possible if the postoperative imaging, obtained after implantation, can serve as a baseline measurement. In our center CT imaging is obtained on the first postoperative day to detect kinking, extracochlear contacts or otherwise incorrect insertions of the electrode array; in many centers, a conventional X-ray is made for this purpose. Although this provides immediate information about the surgical result, it might not be the best timing to evaluate the relation between electrode array position and performance. In fact, as we believe that migration is most likely to occur in the first weeks, we will postpone imaging for several weeks until just before activation of the implant. A disadvantage of this change in protocol is that it might reduce intervention possibilities in case of incorrect insertions.

However, we do obtain objective electrical and electrophysiological measures during surgery, which can serve as an alternatively intraoperative evaluation of the implant position and function [Vanpoucke et al., 2011]. In case severe doubts arise during surgery, imaging is available and will be considered. In that situation, plane X-ray is very well applicable to assess electrode position. Moreover, since radiation exposure should be as limited as possible, we are currently conducting a study to investigate the value of low-dose CT and cone-beam CT to minimize radiation exposure in future postoperative imaging.

Many techniques involving placement and fixation of the electrode array have been developed during the past years to reduce the occurrence rate of migration. Surgical factors, such as size and site of the cochleostomy, positioning of the electrode cable and packing of the cochleostomy site, are assumed to have influence on the stability of the electrode array. Due to the single implantation technique used in these patients, the (extended) round window approach, the outcomes cannot be extrapolated to alternate approaches, which involve making a cochleostomy. During surgery, positioning of the lead wire should receive special attention. All efforts must be made to curl up the lead without any withdrawing forces and below the cortical plane of the mastoid to prevent direct electrode migration. Currently, recent changes to the design of the array, such as the wing and stabilizing collar/stopper on the new Nucleus Hybrid L24 electrode and especially the precurved electrode array designs, are expected to lower the migration rate and may overcome the need for fixation [Cullen et al., 2008;Connell et al., 2008].

On the basis of the present study, we conclude that electrode migration is more common than generally presumed. In the studied population, migration occurred in patients with and without complaints. Research with larger patient populations is needed to document the chances of migration for each cochlear implant electrode type separately.

REFERENCES

1. Alexiades G, Roland JT, Jr., Fishman AJ, Shapiro W, Waltzman SB, Cohen NL: Cochlear reimplantation: surgical techniques and functional results. Laryngoscope 2001;111:1608-1613.
2. Barolat G, Peacock WJ, Staudt LA: Pain and Spasticity; in Benzel EC (ed): Spine Surgery; Techniques, Complication Avoidance, and Management. Philidelphia, Elsevier, 2005 pp 1239-1252.
3. Bosman AJ, Smoorenburg GF: Intelligibility of Dutch CVC syllables and sentences for listeners with normal hearing and with three types of hearing impairment. Audiology 1995;34:260-284.
4. Brown KD, Connell SS, Balkany TJ, Eshraghi AE, Telischi FF, Angeli SA: Incidence and indications for revision cochlear implant surgery in adults and children. Laryngoscope 2009;119:152-157.
5. Carlyon RP, Macherey O, Frijns JH, Axon PR, Kalkman RK, Boyle P, Baguley DM, Briggs J, Deeks JM, Briaire JJ, Barreau X, Dauman R: Pitch Comparisons between Electrical Stimulation of a Cochlear Implant and Acoustic Stimuli Presented to a Normal-hearing Contralateral Ear. J Assoc Res Otolaryngol 2010;11:625-640.
6. Connell SS, Balkany TJ, Hodges AV, Telischi FF, Angeli SI, Eshraghi AA: Electrode migration after cochlear implantation. Otol Neurotol 2008;29:156-159.
7. Cullen RD, Fayad JN, Luxford WM, Buchman CA: Revision cochlear implant surgery in children. Otol Neurotol 2008;29:214-220.
8. Fayad JN, Baino T, Parisier SC: Revision cochlear implant surgery: causes and outcome. Otolaryngol Head Neck Surg 2004;131:429-432.
9. Greenwood DD: A cochlear frequency-position function for several species--29 years later. J Acoust Soc Am 1990;87:2592-2605.
10. Rivas A, Marlowe AL, Chinnici JE, Niparko JK, Francis HW: Revision cochlear implantation surgery in adults: indications and results. Otol Neurotol 2008;29:639-648.
11. Roland JT, Jr., Fishman AJ, Waltzman SB, Alexiades G, Hoffman RA, Cohen NL: Stability of the cochlear implant array in children. Laryngoscope 1998;108:1119-1123.
12. van der Marel KS, Briaire JJ, Verbist BM, Joemai RM, Boermans PP, Peek FA, Frijns JH: Cochlear reimplantation with same device: Surgical and audiologic results. Laryngoscope 2011;121:1517-1524.
13. Vanpoucke F, Boermans PP, Frijns J: Assessing the Placement of a Cochlear Electrode Array by Multidimensional Scaling. IEEE Trans Biomed Eng 2011.
14. Verbist BM, Frijns JH, Geleijns J, van Buchem MA: Multisection CT as a valuable tool in the postoperative assessment of cochlear implant patients. AJNR Am J Neuroradiol 2005;26:424-429.
15. Verbist BM, Joemai RM, Briaire JJ, Teeuwisse WM, Veldkamp WJ, Frijns JH: Cochlear coordinates in regard to cochlear implantation: a clinically individually applicable 3 dimensional CT-based method. Otol Neurotol 2010a;31:738-744.
16. Verbist BM, Skinner MW, Cohen LT, Leake PA, James C, Boex C, Holden TA, Finley CC, Roland PS, Roland JT, Jr., Haller M, Patrick JF, Jolly CN, Faltys MA, Briaire JJ, Frijns JH: Consensus panel on a cochlear coordinate system applicable in histologic, physiologic, and radiologic studies of the human cochlea. Otol Neurotol 2010b;31:722-730.

Chapter Four

Diversity in Cochlear Morphology and its Influence on CI Electrode Position

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ABSTRACT

Objectives

To define a minimal set of descriptive parameters for cochlear morphology and study its influence on the cochlear implant electrode position in relation to surgical insertion distance.

Design

Cochlear morphology and electrode position were analyzed using multiplanar reconstructions of the pre- and postoperative CT scans in a population of 336 patients (including 26 bilaterally implanted ones) with a CII HiFocus1 or HiRes90K HiFocus1J implant. Variations in cochlear diameter and cochlear canal size were analyzed. The relationship between the outer and inner walls was investigated. Size differences based on sex, age, and ear side were investigated using linear mixed models. Two new methods, spiral fitting and principal component analysis, were proposed to describe cochlear shape, and the goodness of fit was investigated. The relationship between cochlear shape and electrode position, in terms of modiolus proximity and insertion depth, was analyzed using clustering, one-way analysis of variance (ANOVA) and simple linear regression analysis.

Results

Large variations in cochlear morphology were found, with cochlear canal sizes ranging from 0.98 to 2.96 mm and average cochlear diameters between 8.85 and 5.92 mm (with standard deviations of around 0.4 mm). The outer and inner walls were significantly correlated ($p < 0.01$), and a size difference of 4% in favor of males was found. Spiral fitting shows good alignment of the true measurements, with residuals having a mean of 0.01 mm and a standard deviation of 0.29 mm.

Principal component analysis (PCA) showed that the use of one component, which describes size, is sufficient to explain 93.6% of the cochlear shape variance. A significant sex difference was also found with spiral fitting and PCA. Cochlear size was found to have a significant influence on modiolus proximity and insertion depth of the electrode ($p < 0.01$). Cochlear size explained around 13% of the variance in electrode position. When cochlear size was combined with surgical insertion, more than 81% of the variance in insertion depth can be explained.

Conclusions

This study demonstrates a large variety in cochlear morphology, which significantly impacts electrode position in terms of modiolus proximity and insertion depth. The effect size is, however, relatively small compared with surgical insertion distance. PCA is shown to be an accurate reduction method for describing cochlear shape.

INTRODUCTION

Cochlear Implantation is a well-established therapy for patients with severe to profound hearing loss. Among patients, however, a wide variability in performance is observed. Electrode positioning has been indicated to be one of the factors that influence cochlear implant (CI) performance, and adjusting this may further improve the hearing scores of implantees (Aschendorff et al. 2007; Finley et al. 2008). Three factors that influence electrode position can be identified; cochlear anatomy, surgical insertion, and electrode design. Intracochlear trauma and loss of residual hearing are some of the unfortunate outcomes that can sometimes be prevented by controlled surgical insertion and the use of a patient-appropriate electrode design (Adunka & Kiefer 2006; Aschendorff et al. 2007). Other than its design and surgical insertion, the position of the electrode is also influenced by the morphology of the cochlea (Dimopoulos & Muren 1990; Ketten et al. 1998; Escude et al. 2006). This study investigates a minimal set of descriptive parameters for the human cochlear morphology and its influence on the electrode position in combination with the variability due to surgical insertion distance. Descriptive parameters will facilitate the development of a future predictive model for insertion depth to guide the surgeon during insertion, hopefully thereby creating conditions that help to maximize performance.

Cochlear morphology has been studied by several groups, both radiologically and histologically. The radiological analysis by Escudé et al. (2006) shows a wide spread of about 2.0 mm (95% CI) in overall size of the basal turn of the cochlea. This is in line with the described variations (from 7.08 mm to 9.16 mm) in cochlear basal diameter among the 20 patients studied by Ketten et al. (1998). They also measured cochlear length and found it to range between 29.07 and 37.45 mm. The histological analysis performed by Erixon et al. (2009) showed similar variations in cochlear morphology, including spiral length, and the authors also stated that each cochlea has its own “fingerprint,” an individual design with variable proportions.

Defining the exact cochlear shape with a limited set of parameters remains a challenge. In mathematical studies, cochlear shape has been approximated by different spiral functions, mostly based on either the Archimedean or logarithmic spiral (Ketten et al. 1998; Yoo et al. 2000). These methods result in accurate descriptions, but require elaborate postprocessing procedures. Thus, an easily applicable method for defining cochlear shape is needed for clinical purposes, but is not yet available. Moreover, it is necessary to investigate whether direct size measurements, like cochlear diameters, are sufficient to describe the influence on insertion depth. The primary goal of this study was to identify one or two variables by which cochlear morphology can be best described.

Besides cochlear morphology, surgical insertion technique and electrode design are two other known factors that influence electrode position. Unlike the morphology of the cochlea, which is patient specific and fixed, surgical insertion technique and choice of electrode design are adjustable factors. Various surgical techniques and electrode designs have been developed to facilitate atraumatic or controlled positioning of the electrode (Gstoettner et al. 1997; Tykocinski et al, 2000; Eshraghi et al. 2003; Aschendorff et al. 2007; Rebscher et al. 2008; Verbist et al. 2009; Ibrahim et al. 2011; Iverson et al. 2011; Kahrs et al. 2011). The electrode can be inserted using an round-window approach or via a cochleostomy, with both methods showing comparable outcomes in terms of insertion trauma and residual hearing preservation (Adunka & Kiefer 2006; Skarzynski et al. 2007). Alternatively, the crista ante fenestram can be drilled away, defined as an extended round-window approach, reducing the chances of preserving residual hearing. Analyzing the influence of insertion variations and cochlear morphology on electrode positioning will allow surgeons more control over surgical results (Finley et al. 2008). Moreover, it provides feedback to the surgeon, which might improve surgical skills (Finley et al. 2008).

With regard to electrode design, acquiring more knowledge about cochlear morphology can also be of great value for the surgeon in selecting the patient-appropriate electrode and for development of future implant designs. Escudé et al. (2006) showed a large impact of cochlear size variations on both linear and angular insertion depth for straight and perimodiolar electrode types. Research could either focus on an electrode type that fits most cochleas or develop a tailor-made electrode for each individual patient. The FLEX electrode series of Med-El (Medical Electronics, MedEl, Innsbruck Austria) are an example of such tailor-made electrode types (MED-EL, 2012). Although these electrodes are clinically available for cochlear implantation, few CI centers use individualized, preoperative electrode selection for a standard cochlear implantation. A secondary goal of this study was to determine the degree to which electrode position is influenced by cochlear morphology, and to what extent the final position can be influenced by the surgeon.

To reach these two goals, we searched for a clinically applicable method for defining the shape of an individual cochlea. This method must be available for surgeons during the process of preoperative electrode selection, and consist of only a few variables that can be obtained from clinical images. Several directly measured and some derived variables, based on fitting formulas and reductional statistical analysis, were studied. These derived variables had the advantage of being less correlated to each other than directly measured variables. The correspondence of the derived variables with the directly measured variables was tested. Also, differences in cochlear morphology and its variations (sex, age and ear side) among subgroups were investigated. Finally, the relationship between cochlear shape and final electrode position was illustrated, while controlling for variations in surgical insertion distance.

PATIENTS AND METHODS

Patients

For this study data of 401 patients who sequentially received a CII implant with HiFocus1 electrode or a HiRes90K with HiFocus1J electrode manufactured by Advanced Bionics (Advanced Bionics, Sylmar, CA) between September 2002 and December 2011 at Leiden University Medical Center, The Netherlands, was collected (all without a positioner). The study was restricted to this lateral wall electrode type because of the visibility of the individual contacts on postoperative CT scans. Five cases with abnormal insertion, 26 cases with abnormal cochlear morphology, and 34 cases with poor-quality scans (all obtained during first years of implantation, when the CI scanning protocol was still being fine-tuned) were excluded. In the end, the population consisted of 336 patients, including 26 bilaterally implanted patients, thus 362 implanted cochleas. The CT scans of 671 cochleas were analyzed (for 1 patient there was no scan obtained of the nonimplanted cochlea). Demographic details of the included population are shown in Table I. In all these patients surgery resulted in complete and uncomplicated insertions, using an extended round-window approach.

Image Reconstruction and Analysis

As part of the standard workup for cochlear implantation at our center, all patients are scanned before and 1 day after surgery with a CT scanner (scanner type: Aquilion 4, Aquilion 16, Aquilion 64, Aquilion 1; Toshiba Medical Systems, Otowara, Japan) and multiplanar reconstructions (MPRs, voxel size: 0.015 mm^3) were made from these scans (Verbist et al. 2005, 2010a). To study cochlear sizes and their relationship to insertion depth, the MPRs of each patient were analyzed by applying a three-dimensional coordinate system

(Verbist et al. 2010b). This coordinate system enables surgeons and researchers to assess individual MPRs and measure cochlear sizes and electrode positioning without the use of a universal template (Verbist et al., 2010a, 2010b).
To analyze cochlear size, the outer and inner wall distances to the center of the modiolus were defined by scrolling through the preoperative MPR slices in the plane of the basal turn of the cochlea using an in-house designed postprocessing program (Matlab, Mathworks, Novi, MI; Figure 1A).

Table I. Demographic details of studied patients (N=336)

Gender	N	%
Male	153	46
Female	183	54
Age at implantation (yrs)	**N**	**%**
Age ≤ 2 yrs	51[1]	15
Age > 2 yrs	285[1]	85
	Mean	**SD**
Age at onset of HL (yrs)	13	19
Duration of deafness (yrs)	20	19
Age at implantation (yrs)	41	26
Etiology	**N**	**%**
Congenital	168	50
Hereditary	93	
Acquired	30	
Unknown	45	
Acquired	95	28
Meniere's disease	6	
Infectious	50	
Otosclerosis	6	
Ototoxity	12	
Trauma	8	
Unknown	13	
Unknown	73	22

[1] One child was sequentially implanted and received a second implant at the age of 9 years.

As these distances are measured along four axes, this results in four diameters (=8 radii) and eight cochlear canal sizes for the basal turn of the cochlea. Two of these axes are in accordance with the consensus on cochlear coordinates (Verbist et al. 2010b) and conform to the cross-sections used by Escudé et al. (2006), consisting of a line connecting the center of the round window to the center of the modiolus (radius 1 and 5) in combination with a perpendicular line (radius 3 and 7) lying within the plane of the cochlear basal turn. The other two axes derive from the Leiden coordinate system, as described by Verbist et al. (2005), and are defined by a line connecting the center of the modiolus to the most lateral point of the horizontal semicircular canal (radius 4 and 8) combined with a perpendicular line (radius 2 and 6), again in the abovementioned plane. This system is especially useful for the assessment of postoperative MPRs, as the horizontal semicircular canal remains stable (it can be difficult to identify the center of the round window postoperatively after using a [extended] round window approach). The average rotational angle between the consensus coordinate system and the Leiden coordinate system for the studied population was 33 degrees with a standard deviation of 3.51 degrees. The accuracy of this method was evaluated in a previous study showing good intraclass correlation coefficients (ICCs) and small standard deviations for both angular (ICC 0.74-1; SD<5 degrees) and linear measurements (ICC 0.77-1; SD<0.5mm) within the cochlea (Verbist et al. 2010a). 4

Postoperative MPRs were assessed to visualize several electrode position measurements (Figure 1B). Every indicated position was expressed in an "angular" (degrees from the round window) and "linear" (millimeters between two positions) manner. For each of the 16 electrode contacts the distance from the contact center to the inner wall of the cochlea and center of the modiolus was measured. The position of the most apical contact (electrode contact 1:E1) defined the angular insertion depth. The distance from the round-window center (RW) to the most basal contact (electrode contact 16:E16) can be mostly controlled by the surgeon and is therefore designated by "surgical insertion." To obtain this distance, the spiral length from RW to E16 was calculated using Eq. (1):

$S(\theta) = \left(a \cdot \sqrt{1+b^2} \cdot e^{b\theta(E16)} - 1\right)/b$ *with* $a=r(RW)$ (r is radial distance to center of modiolus) and $b = ln\frac{r(E16)}{r(RW)} \cdot \frac{1}{\theta(E16)}$.

The formerly often used linear insertion depth is the sum of the surgical insertion distance and the standard configuration length of the electrode type (17 mm).

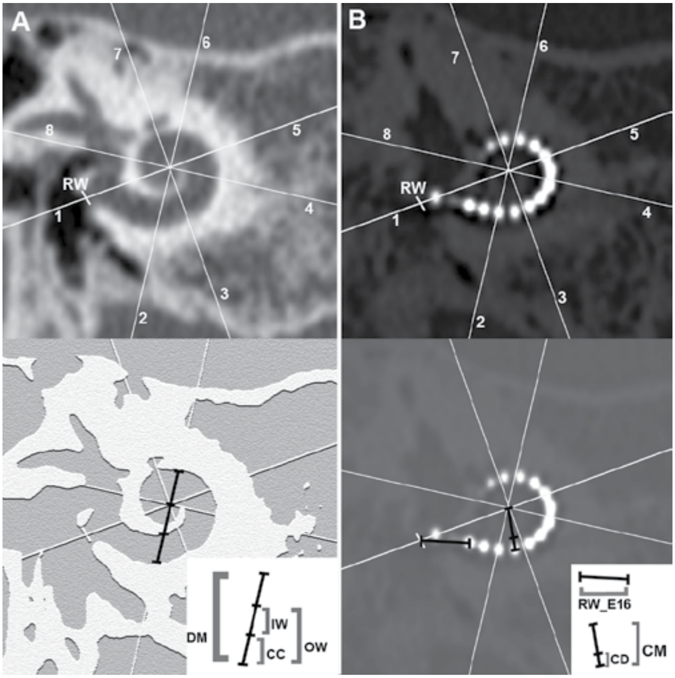

Figure 1. Measurements in preoperative reconstructions (A) and postoperative reconstructions (B). Upper level: True reconstructions with eight radii and round window (RW). Lower level: Schematic illustrations and measurements. The case used to explain the measurements, had an angular insertion depth of 360 degrees. Measurements on reconstruction **A:** DM=diameter, IW=distance inner wall-center modiolus, CC=cochlear canal, OW=outer wall-center modiolus. Diameter 1= OW radius 1+5, Diameter 2= OW radius 2+6, Diameter 3= OW radius 3+7, Diameter 4= OW radius 4+8. Measurements on reconstruction **B:** RW_E16=surgical insertion, CD=contact distance to modiolar wall, CM=contact distance to center of modiolus. Consensus coordinate system: (radii 1 and 5) x (radii 3 and 7). Leiden coordinate system: (radii 4 and 8) x (radii 2 and 6)

Derived Variables

Clustering

To facilitate further statistical analyses, we classified some of the previously described measurements into a few, predefined number of clusters (See Appendix A Cluster Outcomes; final cluster centers and ANOVA tables). The K-sample clustering procedure in SPSS (SPSS 17.0 for Windows; SPSS Inc., Chicago, IL) attempts to identify relatively homogeneous groups of cases based on selected characteristics using a predefined algorithm. Using this procedure, a cochlear size group was obtained consisting of three clusters (small, medium, large) based on the four cochlear diameters. Clustering was also used to form a three-cluster (shallow, average, deep) surgical insertion distance group. Finally, two electrode position clusters (medial, lateral) were formed based on the 16 contact distances to the modiolar wall measured on the postoperative MPRs. The number and percentages of patients assigned to each cluster are presented in Table II and used for analysis of the relationship between cochlear size and electrode position.

Statistical Analysis

The cochlear morphology measurements were analyzed using SPSS with p values less than or equal to 0.05 considered significant. Simple descriptive statistics were used to analyze overall cochlear canal size and diameters.

Size differences based on ear side, age (cutoff 2 years) and sex were analyzed with linear mixed models. This method inherently adjusts for correlations of measurements derived from the two cochleas of a patient, or within the same cochlea. In accordance with the work of Escudé et al (2006), it was also tested whether there was a difference in ratio of diameter 1 divided by diameter 3. The relationship between cochlear morphology and electrode position was analyzed using one-way ANOVA and multiple linear regression analyses.

Table II. Cluster measurements

Cochlear size	N	%
small	117	33
medium	171	47
large	74	20
Surgical insertion	N	%
shallow	46	13
average	162	45
deep	154	43
Electrode position	N	%
Medial	211	58
Lateral	151	42

Methods of Describing Cochlear Shape

Spiral Fitting

Modeling of the human cochlea is most often done by fitting either a logarithmic or Archimedean spiral to the cochlea in question (Skinner et al. 1994; Ketten et al. 1998; Yoo et al. 2000). For this study, in accordance with the work by Yoo et al. (2000), we chose the logarithmic spiral as it represents a more generalized function in comparison to the Archimedean spiral which is a first-order approximation of a logarithmic spiral. A logarithmic spiral is described by Eq. (2): $r(\theta) = ae^{b\theta}$,(2) where r represents the radial distance to the center of the modiolus, θ the corresponding angle and a and b coefficients. Coefficient a is proportional to cochlear size, while coefficient b defines cochlear curvature by quantifying the exponential decline in size of the cochlea with increasing angles. The spiral coefficients a and b were determined by fitting the distances to the modiolus center measured along four axes (8 radii) in the basal turn of the cochlea to an exponential function using logarithmic transformation and regression analysis. Spiral fits were determined for both the outer- and inner-wall radial distances. The goodness of fit of this method was investigated.

Principal Component Analysis

Variation in the shape of the basal turn of each cochlea was also described using principal component analysis (PCA). This method derives a number of mutually orthogonal (uncorrelated) base forms from the set of measurements. For this study, cochlear morphology is analyzed as two separate sets of eight sizes (8 outer- and 8 inner-wall distances to the center of modiolus). An individual cochlea is modeled as a weighted sum of these base forms in relation to the average cochlear shape. When using the complete set of base forms, the cochlear shape can be reshaped identically from its origin. This method was optimized by minimizing the number of base forms while still accounting for 90% of the variation in individual cochlear shape, then testing the resulting goodness of fit.

Relation between Cochlear Size and Electrode Position

The relationship between the cochlear size and electrode position is analyzed in terms of distance to modiolus and insertion depth. To investigate the relationship between cochlear size and distance to modiolus, the distribution of electrode positioning groups in the three cochlear size clusters was tested with a Chi-square test.

To illustrate and analyze the influence of cochlear size on insertion depth, again a post hoc test for trend using one-way ANOVA was executed. The relationship between cochlear size and insertion depth is also emphasized by an "insertion graph" according to the method of Escudé et al. (2006; Figure 3). This was executed by calculating the average insertion depth for each of the three cochlear size cluster groups and plotting the linear insertion depth against the angular insertion depth for all three groups. The difference in angular insertion depth between the large and small cochlear size clusters was determined at the average linear insertion depth of the whole population. This difference was tested by a multiple regression model. The relationship between insertion depth and two of the diameters, the spiral-fit coefficient and the first principal component, was tested by multiple linear regression. In addition, the influence of cochlear size on the insertion depth is presented using scatter plots with the three surgical insertion distance clusters marked by different icons and colors.

RESULTS

Cochlear Size

Figure 2A shows a boxplot of the outer- and inner-wall radial distances, both of which were significantly ($p < 0.001$) correlated on all radii, ranging from Pearson's $R = 0.76$ (radius 1) to $R = 0.45$ (radius 8). Cochlear canal sizes are represented in Figure 2B as radius along each of the eight previously described radii. To quantify the tapering of the cochlea shown in Figure 2, the mean canal sizes decreased from 2.96 (0 degree) to 0.98 mm (327 degrees), and for every radii the mean canal size differed significantly from the mean canal size of adjacent radii ($p<0.003$), except for radii 7 and 8 ($p = 0.95$). The mean cochlear canal size declines, although somewhat surprisingly, nonmonotonously, with increasing angle from 2.07 mm for radius 1 to 1.74 mm for radius 8. Table III shows the preoperative imaging characteristics. The mean cochlear diameter declined from 8.85 to 5.92 mm with standard deviations between 0.37 and 0.45 mm. The mean cochlear diameters were significantly different ($p < 0.001$) between males and females, ranging from a 3.0 to 4.4% larger diameter on average in males. The ratio mean diameter of radius 1 to mean diameter of radius 3 was 1.35 and was not significantly different between males and females ($p = 0.23$). Linear mixed model analyses of cochlear size as related to ear side and age showed no significant size differences ($p = 0.18$; $p = 0.21$). However, the effect of sex on cochlear size is significant ($p < 0.001$), with male cochlea being on average 4% larger.

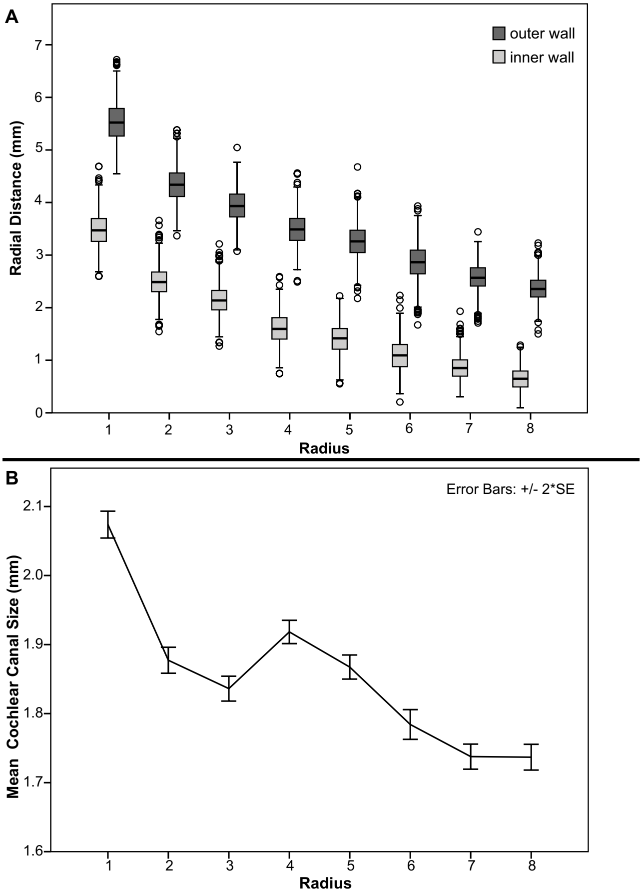

Figure 2. A: Outer and inner wall radial distances. B: Mean cochlear canal sizes for each radius and error bars representing 2*SE (n=671).

Table III. Imaging measurements (N=671)

Cochlear diameter (mm)	Mean (SD)
Diameter 1[1]	8.85 (0.45)
Diameter 2	7.26 (0.45)
Diameter 3[1]	6.58 (0.40)
Diameter 4	5.92 (0.37)

[1] Diameters 1 and 3 are the same as those used by Escudé et al. (2006), where they are referred to as 'distance A' and 'distance B'.

Describing the Cochlear Shape

Spiral Fitting

Using logarithmic transformation and regression analysis, fitting formula coefficients were determined for the basal turn of each implanted cochlea. These coefficients were based on the preoperative outer- and inner-wall measurements. The spiral fitting resulted in two coefficients, a_{outer} and b_{outer}, with average values of 5.19 mm (SD = 0.33, range 4.38; 6.10) and -0.0025 rad^{-1} (SD = 0.00036, range -0.0038; -0.0015), respectively. The inner wall was described by two coefficients, a_{inner} and b_{inner}, with average values of 3.19 mm (SD = 0.48; range 2.86; 5.74) and -0.0052 rad^{-1} (SD = 0.001; range -0.0090; -0.0026), respectively. Figure 3A shows typical examples of true and spiral-fitted cochleas. The goodness of fit of this method is shown in Figure 3B using a histogram of outer wall residuals, which reveals a normal residual distribution with a mean of 0.01 mm and a standard deviation of 0.29 mm. The mean of the inner wall residuals was -0.23 mm with a standard deviation of 0.41 mm. The spread is wider at the basis (radii 1-3) than in the middle (radii 4-8), with outer-wall standard deviations of 0.37 to 0.20 and inner-wall standard deviations declining from 0.59 to 0.20. These larger deviations can also be observed in the fitted cochlear shape examples of Figure 3A.

Each of the four coefficients (a_{outer}, b_{outer}, a_{inner}, b_{inner}) are correlated significantly ($p < 0.001$) with the other three coefficients. The strongest correlation existed between a_{outer} and b_{outer} (R = 0.56). Again, significant differences ($p < 0.001$) in the mean of coefficient a_{outer} and a_{inner} were found between males and females. The mean values of the b coefficients were not significantly different ($p > 0.68$), indicating similar curvature of both outer and inner walls between the two sexes. All four coefficients correlated significantly with the four diameters.

Coefficient a_{outer} showed the strongest correlation with all diameters, ranging from R=0.52 (diameter 2) to R=0.62 (diameter 1). The other coefficient defining cochlear size, a_{inner}, showed the second strongest correlation with all diameters, from R = 0.31 (diameter 1) to R = 0.39 (diameter 4).

Principal Component Analysis

Figure 4A shows the shape of the first three components derived from the PCAs. All components accumulated with the individual factor scores define deviations from the central pathway along the cochlear canal (See Appendix B PCA Outcomes; description of method, component matrix, average PCA scores). As a consequence of analyzing the outer- and inner-wall distances as two times eight recordings, the first component defines cochlear size. Figure 4A shows that the first component remains almost constant for each radius, while the second and third components vary sinusoidally along the measured radii. As component one is constant, it defines general size. Component two has a minimum of -0.24 at radius 6 and a maximum of 0.24 at radius 1, while component three reaches a minimum of -0.18 at

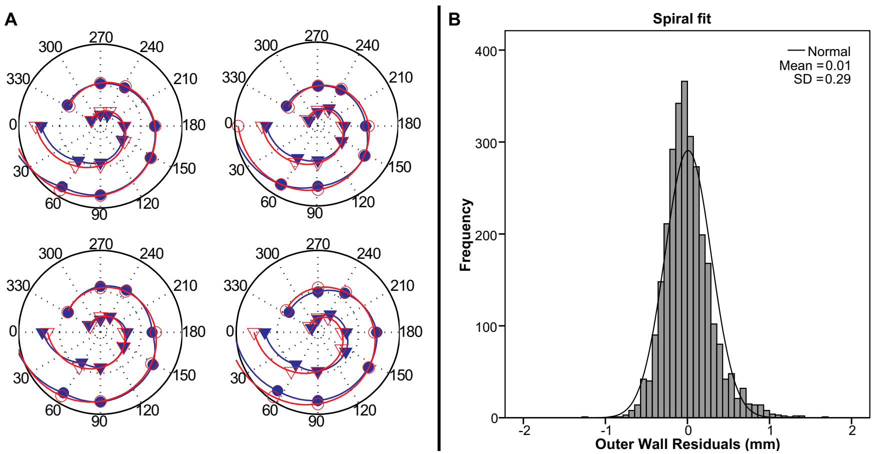

Figure 3. Results of spiral fitting method. **A:** Examples of true (blue lines) and spiral-fitted (red lines) cochlear shapes. The inner wall measurement points are marked by triangles and those of the outer wall by circles. **B:** Histogram of the outer wall residuals with normal distribution curve.

radius 3 and a maximum of 0.15 at radius 7. Via their sinusoidal nature, the second and third components define small broadening and narrowing adjustments at certain locations along the cochlear canal, resulting in the specific fingerprint of each cochlea. The other components define only very small changes along the eight radii. The first component explains 93.6% of the variance in cochlear shape. The second component explains only 3.0% variance and the third component less than 2.0%. On the basis of cumulative explained variance, it is evident that using one component for the outer and another for the inner measurements would sufficiently describe cochlear shape. The first component and the factor scores were used to calculate the fitted PCA outcomes for the outer- and inner-wall distances. Figure 4B shows examples of the true and PCA-fitted cochlear shapes. Figure 4C shows the goodness of fit histograms of the calculated residuals between the true and PCA-fitted outer walls using one, two and three components. The mean of the residuals was 0.02 mm. The standard deviation decreased from 0.27 mm to 0.13 mm with increasing number of components used (1 to 3 components). With component 1, the mean of the residuals between the true and PCA-fitted inner-wall distances was 0.02 mm with a standard deviation of 0.24 mm. The standard deviations did not differ among the different measurement radii.

Again, a significant difference in mean factor scores with component 1 was found for the outer and inner wall between males and females ($p < 0.001$). However, no significant sex difference was found for component 2 or 3 (all: $p > 0.09$). Furthermore, a strong correlation was found between component 1 and all four diameters ($p<0.001$). The correlations between component 1 of the outer walls and the diameters were between R = 0.85 and R = 0.91. For the inner walls, correlations with the diameters were between R = 0.40 and R = 0.55. The other components were not correlated with these diameters.

When clustering into three groups was repeated based on only component 1 and cluster numbers were compared to the original cluster group numbers based on the four diameters, high levels of correspondence were found. Of the small cochleas 90.1% were classified into a small cluster group by both forms of clustering. For the middle-sized cochleas, 94.8% correspondence between two forms of clustering was found with 99.0% correspondence for the large-sized cochleas.

Relation between Cochlear Size and Electrode Position

Influence of Cochlear Size on the Distance to Modiolus

The distribution of the medial and lateral electrode positioning groups in the three cochlear size clusters was tested with a Chi-square test and showed a significant difference in distribution between the three cochlear size cluster groups ($p < 0.001$).

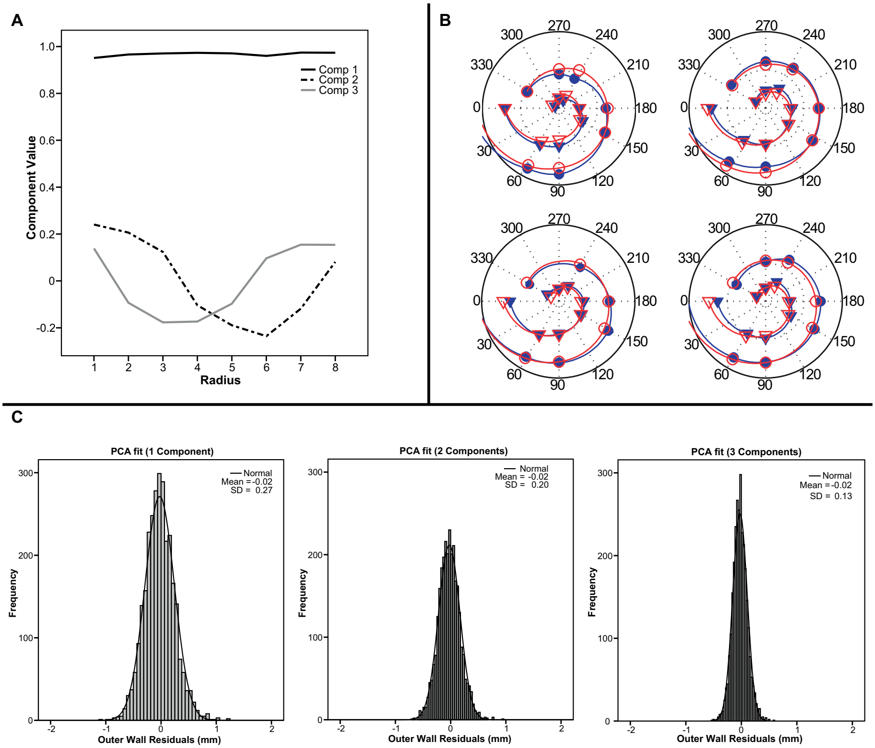

Figure 4. Results of PCA. **A:** Values of the first three components on all radii. **B:** Examples of true (blue lines) and PCA-fitted (red lines) cochlear shapes. The inner wall measurement points are marked by triangles and those of the outer wall by circles. **C:** Histograms of PCA-fitting residuals of the outer walls with 1, 2, and 3 components. The lines represent normal distribution curves.

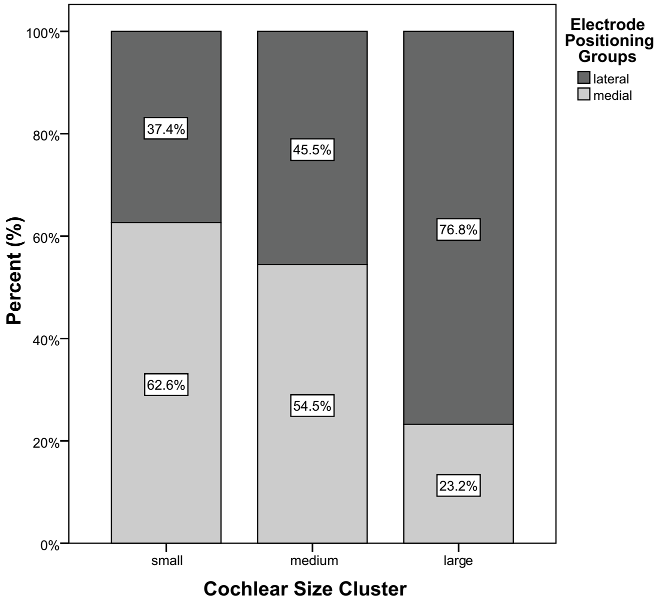

Figure 5. Distribution of electrode positioning groups in the three cochlear size clusters.

The percentages of medial and lateral electrode positioning groups in the small, medium, and large cochleas are shown in Figure 5, illustrating the different distribution among the groups.

Influence of Cochlear Size on the Final Insertion Depth

In addition, the relationships between the cochlear size and shape and their influence on the insertion depth were analyzed. The mean (angular) insertion depth was 480 degrees and the mean surgical insertion distance (distance from round window to most basal contact) was 6.53 mm. All diameters were negatively correlated with insertion depth. For all diameters, the Pearson's correlation coefficients with insertion depth were $R = -0.3$ ($p < 0.001$). Figure 6 shows the insertion depth for each of the three cochlear size groups. The significance of the relationship between cochlear size and insertion depth was supported by a test for trend using a one-way ANOVA ($p < 0.001$).

This relationship is further illustrated by Figure 7, where the linear insertion depth of the most apical electrode contact (E1) is plotted against the angular insertion depth. The different cochlear size clusters are denoted using regression lines and varying symbols. The average value for diameter 1, titled “distance A” by Escudé et al. (2006), was 8.5 mm for small cochleas and 9.4 mm for large cochleas, respectively. For the studied population, the average surgical insertion distance was 6.53 mm and the average linear insertion depth was 23.0 mm. For this average linear insertion depth (vertical line), the average difference in insertion angle between small, medium and large cochleas is shown in the figure, resulting in a difference of 68 degrees between the small and large cochleas (horizontal lines). This difference in angular insertion depth between the small and large cochlear size clusters for all linear insertion depths was highly significant ($p < 0.001$), as demonstrated using a linear regression model.

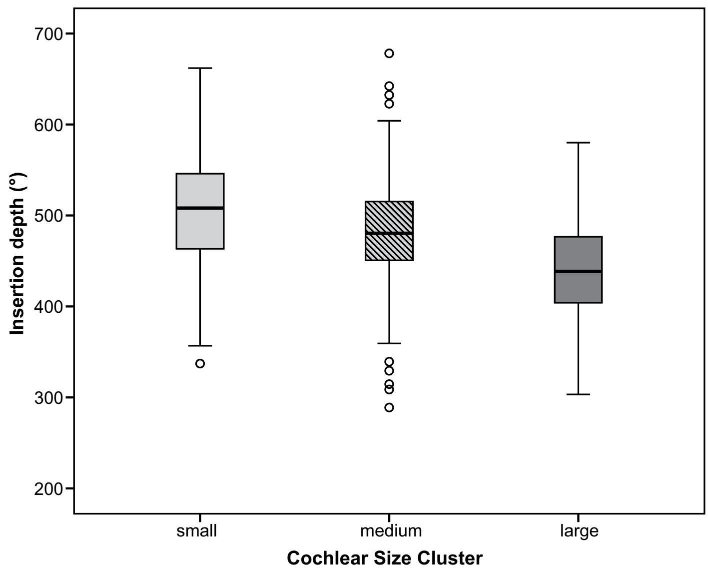

Figure 6. Angular insertion depths of the three cochlear size clusters.

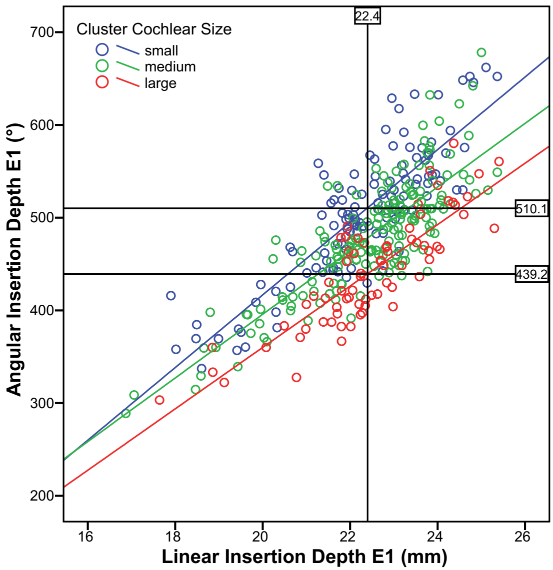

Figure 7. Linear insertion depth of the most apical E1 versus angular insertion depth E1. Vertical line shows the average linear insertion depth of 22.4 mm. The upper horizontal line shows the average insertion angle for the small cochleas group and lower horizontal line shows average angle for large cochleas.

Figure 8 shows the relationship between cochlear sizes and surgical insertion distance on insertion depth. Surgical insertion distance was clustered into the three groups (Table III) and marked with different symbols and colors in the figure. Figure 8A and B show scatterplots of the two cochlear diameters (diameter 1 and 2) versus the insertion depth. The same plots were obtained for the spiral coefficient a_{outer} in Figure 8C and the PCA component 1 in Figure 8D. When surgical insertion distance clusters are analyzed separately, downward trend lines between cochlear size and insertion depth can be observed. The slopes of the downward trend lines for the different surgical insertion distance groups differed between the two diameters (Figure 8A versus 8B). Also, downward trends can be observed when using the spiral- or PCA-fit variables (Fig 8C versus 8D).

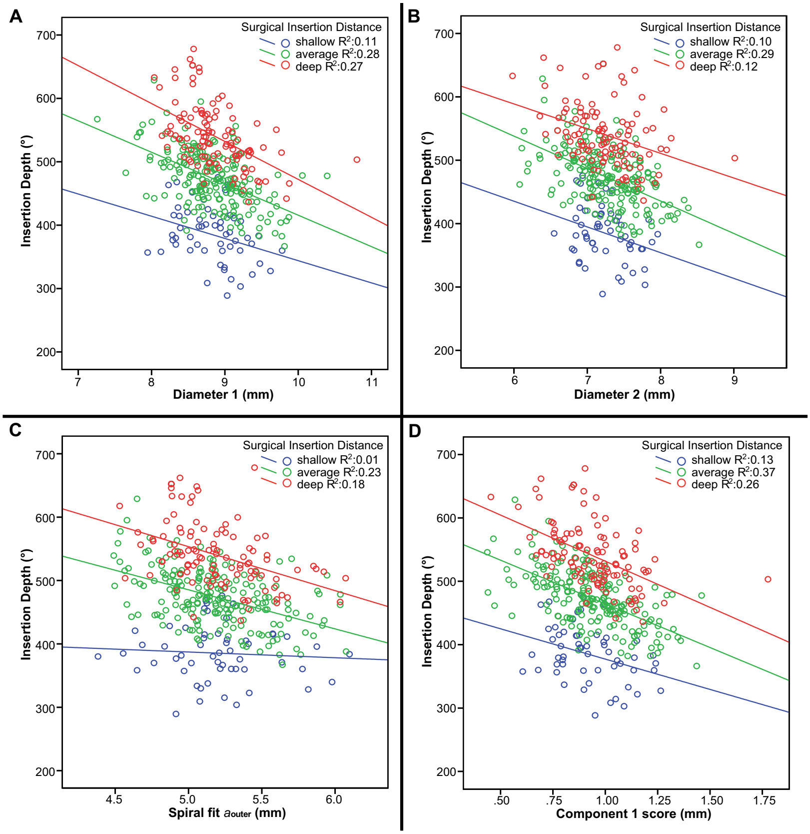

Figure 8. Relationship between the two cochlear diameters 1 (A) and 3 (B), spiral-fit coefficient a_{outer} (C), PCA component 1 (D), and insertion depth, analyzed separately, for different surgical insertion distances. The three surgical insertion distance groups are denoted using varying symbols and colors. A trend line is fitted for each surgical insertion distance group.

However, the spiral-fit trend lines are not as steep as those of the PCA-fit trend lines. In the spiral-fit plot, an almost horizontal trend line can be observed for the shallow surgical insertion distance group, indicating almost no relationship between spiral coefficient and insertion depth. The difference in insertion depth between the different surgical insertion distance clusters, when tested for the diameters 1 and 2, spiral fit a_{outer} and principal component 1 using multiple regression models, was highly significant ($p < 0.001$) in all models, with a mean difference of around 150 degrees between the shallow and deep surgical insertion distance clusters.

The relationship between insertion depth and the two proposed methods for defining cochlear shape was tested by regression analyses (Table IV). This relationship was compared with the relationship between insertion depth and the four cochlear diameters. All analyses showed that cochlear size variables only accounts for a small percentage of variance in insertion depth. A regression model with the four diameters as predictors resulted in 12.1% of explained variance. In that model, only diameter 1 explained a significant part of variance ($p = 0.024$), while the other diameters did not significantly add more explained variance to the model having *p* values of above 0.24. Using only diameter 1 resulted in 10.1% of explained variance. A model using spiral-fitting coefficients a_{outer} and b_{outer} as predictors explained 13.5% of the observed variance and both coefficients showed significant contribution to the model.

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Table IV. Relation between insertion depth, cochlear shape and surgical insertion distance

Regression Models	Explained Variance of Insertion Depth (%)
Diameter 1	10.1 %
Diameter 1 + diameter 2 + diameter 3 + diameter 4	12.1 %
Spiral fit coefficient a_{outer} + coefficient b_{outer}	13.5 %
PCA component 1 + component 2 + component 3	13.1 %
Surgical insertion distance	65.3 %
Surgical insertion distance + diameter 1	78.1 %
Surgical insertion distance + diameters 1 - 4	81.1 %
Surgical insertion distance + spiral fit coefficient a_{outer} + coefficient b_{outer}	78.8 %
Surgical insertion distance + PCA components 1 - 3	80.4 %

In the model with PCA components for the outer wall, 13.1% of the variance was explained. Only component 1 shows a significant contribution to the model. The coefficients of components 2 and 3 were not significant.

Although the amount of explained variance by variables defining cochlear size was demonstrated to be low in all of the formulated models, use of the predictors of the newly proposed methods did not show a decline in the percentages of explained variance, but contributed by slightly higher percentages.

Moreover, the percentage of variance explained rose when surgical insertion distance was added to the three models. The model using four diameters explained 81.1% of variance, with the model using only the first diameter explaining 78.1%. The models with spiral-fitting predictors and PCA predictors, explained 78.8% and 80.4% of variation, respectively. Surgical insertion distance alone explained 65.3% of the variance in insertion depth.

DISCUSSION

This study reports on the diversity in cochlear shape and the impact of cochlear shape on electrode position in a large clinical population. Analysis of CT scans of a large clinical population showed that cochlear sizes were measured along eight measurement radii, resulting in four basal turn diameters and eight cochlear canal sizes. Both diameters and canal sizes showed large variation with standard deviations of 0.4 mm along all radii. A significant sex difference was found, with males having a 4% larger cochlea on average. Spiral fitting and PCAs were shown to be able to reduce the number of variables needed to describe cochlear shape accurately. Using PCA, 93.6% of the variance in cochlear shape can be described with only one component for the outer and one for the inner walls. The size of the cochlea significantly influences electrode position in terms of modiolus proximity and insertion depth. Cochlear size alone explains around 13% of variance in insertion depth. When combined with surgical insertion distance, 75% of the variance can be explained.

Only a few previous studies have reported on anatomical variance in the normally developed cochlea. A diameter of the basal turn of the cochlea, comparable with diameter 1 in this study, was previously measured by Erixon et al. (2009). They reported a mean width of 6.8 mm (SD 0.46 mm) with a range of 5.6 to 8.2 mm. This mean diameter is slightly smaller than the 8.84 mm measured in this study. Escudé et al. (2006) measured two diameters (“A” and “B”) which are comparable with diameters 1 and 3 of this study. The Escudé diameter A mean was 9.23 mm versus a mean diameter 1 in this study of 8.84 mm while Escudé diameter B mean was 6.99 mm (SD = 0.37) compared with 6.58 mm (SD=0.40) for diameter 3 in this study. However, the diameters found in this study were slightly larger than reported by Erixon et al. and smaller than reported by Escudé et al. Moreover, the measured diameter 1 is in line with the reported diameter range of 6.9 to 8.2 mm by Stakhovskaya et al. (2007).

In accordance with the studies by Roland et al. (1998) and Sato et al. (1991), no size differences based on age were found ($p = 0.21$). The left and right cochleae were of similar size in this study ($p = 0.18$), while Escudé et al. (2006) reported a significant ($p<0.001$) mean difference of 0.23 mm for diameter A. In the present (larger) study group, however, only a significant size difference based on sex was found ($p < 0.001$). This size difference between males and females has been reported before by Escudé et al. (differences in diameter A $p < 0.05$ and B $p = 0.01$). Like the present study, the study by Escudé et al. found no significant sex difference in the ratio of A/B. The mean ratio of 1.32 in their study is comparable to the mean of 1.34 reported in the present study. Sato et al. found significant differences in cochlear canal length based on sex ($p < 0.01$) while Ketten et al. (1998) found only a slightly longer cochlear canal length in males, which was not significantly in their study. This study analyzed only the basal turn of the cochlea, thus no comparison of cochlear canal length with the outcomes of Erixon et al. (2009) and Ketten et al. can be made. It seems reasonable, however, to assume that a larger cochlear size corresponds with a larger cochlear canal length.

In this study, multiplanar reconstructions were obtained and the *z* axis was determined during the process of reconstruction. As correctly mentioned by Escudé et al. (2006) and Stakhovskaya et al. (2007) before, comparison of the abovementioned measurements can be easily affected by only a slight shift in chosen angle of view. Moreover, a small rotation of the *z* axis in our study might also affect the measured and fitted curved cross-sectional shape of the cochlear canal, altering the measured individual shape of the cochlea.

The uniqueness of the cochlea's shape, the fingerprint as described by Erixon et al. (2009), emphasizes the need for methods that can accurately describe this shape. The Archimedean and logarithmic spiral are most often used to model the human cochlea (Skinner et al. 1994; Ketten et al. 1998; Yoo et al. 2000). The logarithmic spiral represents a more generalized function and was therefore chosen to model cochlear shape, in accordance with Yoo et al. (2000). This spiral fitting indicated good concordance with the true measurements of the basal turn and the coefficients were all correlated with the measured diameters (Figure 3).

Coefficient a_{outer} [Eq. (2)] defined size, and (like diameters 1 to 4) also differed significantly based on sex (males: 3.4% larger, $p < 0.001$), while b_{outer} describing the curvature along the cochlear canal, was not significantly different between males and females ($p = 0.84$).
As a second descriptive method, PCA was performed. A component matrix and eight components were extracted from the observed measurements. The extent to which various components explained cochlear shape variation was evaluated. One component was found to explain more than 93% of the variation in shape and was sufficient to describe cochlear shape (Figure 4). This component described cochlear size and was strongly correlated with all four diameters. Clustering based on this one component showed strong correspondence (>90% similar groups) with clustering based on four diameters. Again a significant difference of 3.5% in favor of males was found in mean factor scores for component 1 ($p < 0.001$). Component 2 and 3, as these describe the fingerprint and not size, showed no significant difference based on sex ($p > 0.09$), indicating again that the overall shape of male and female cochleae is apparently not different. Components 2 and 3 define locations of broadening and narrowing along the cochlear canal, defining the unique fingerprint of each cochlea as it was named by Erixon et al. (2009). However, these components do not explain more than 3% of variance and were not correlated with the diameters. Describing the cochlear shape using only component 1 and disregarding its unique fingerprint (quantified by components 2 and 3) nonetheless results in good alignment with the true measurements. However in this study, the cochlear shape was only approximated using measurements obtained on the level of the basal turn. Other features characterizing the fingerprint of the cochlea, such as the ascending aspect and tapering of the cochlear canal duct could not be approximated with the available measurements. This study thus confirms that the use of a general template, adjusted in size to fit each cochlea, is a viable option. However, templates like the one being used by Skinner et al. (2007) and Kawano et al. (1996) are derived from a single micro CT scan of one donor and reconstruction of eight male cochleas. An alternative would be to use the more universal component matrix based on the cochleas of 336 patients, as yielded with PCA in the present study.
Comparing spiral fitting to PCA demonstrated that both are suitable for the present purpose, which is to accurately define cochlear shape. The relevant measurements can be easily obtained from reconstructions of clinical CT scans and are reduced to a small number of variables used to describe the cochlear shape without losing much variation. While the spiral-fit variables are still correlated, the PCA components are unrelated to one another. The

four diameters, being highly correlated, are not suitable for multiple regression models as their interaction may mask the true contribution of each variable to the model. Moreover, the standard deviations of the residuals were broader at the basal radii than in the middle, while no differences in standard deviations along the radii were observed for the PCA-fitted residuals. Overall, PCA is preferable because the components are uncorrelated and fewer variables are needed to sufficiently explain a cochlear variance. When analyzing the goodness of fit, the histogram also showed slightly narrower standard deviations compared to those of the spiral fit. Moreover, if desired, one can make PCA fits as accurate as one wishes, by adding more components.

More research is needed to further improve measurements and fits. Improving the software to enable measurements beyond the first turn of the cochlea might lead to more accurate results, especially with deeper inserted electrode designs. Fitting of the outer radii 1 and 8 showed broader standard deviations of the residuals with the present coordinate system. Measuring beyond the basal turn might also lead to a better fit as extrapolation of the currently obtained spiral fits into the second turn shows increasing misalignment the further the fits are extrapolated. This is in accordance with several observations that the width of the cochlear canal does not diminish continuously from base to apex (Zrunek et al. 1980; Wysocki 1999; Erixon et al. 2009). For the basal turn of the cochlea this study also showed a non-continuous narrowing of the cochlear canal (Figure 2B). Moreover, addition of more measurement radii or even development of software, which automatically obtains measurements might lead to more detailed and accurate outcomes. The poor visibility of the inner wall of the modiolus on the clinically available CT scans beyond the first turn may become a limiting factor, when trying to extend the measurements and fits into the second turn.

This study also analyzed the influence of cochlear shape on electrode position. A significant impact was shown for both direct and derived variables. The measured diameters were all negatively correlated to insertion depth with Pearson's correlation coefficients of 0.3 ($p < 0.001$). These coefficients are considerably lower than the significant correlation of 0.51 between diameter A and insertion depth angle as reported by Escudé et al. (2006) in a smaller cohort. Significant differences between the cochlear size cluster groups in both modiolus proximity and insertion depth were found ($p < 0.001$) (Figs. 5 and 6). To illustrate this relationship, the average difference in insertion angle between the small and large cochlea groups was evaluated. For the studied population, differences in cochlear size resulted in a difference of 68 degrees in angular insertion depth on average (Figure 7).

To determine whether there is a need for patient-specific electrode lengths, an extra analysis was performed. The goal being to cover the physiological cochlear frequency range from 200 to 6 kHz, a variation in length of array should be available. To illustrate this, patients with an insertion depth around 400 degrees (>390 degrees and <419 degrees) were selected and the spread of distance from round window to most basal electrode was analyzed. All these patients had the same array with a length of 17 mm in total. To obtain an insertion depth of 400 degrees with this type of array, a variation in length of 19 to 24 mm is needed. Thus, to achieve full coverage of the cochlear canal up to a desired insertion angle, patient-specific electrode lengths would be required. The need for full coverage and the impact of electrode position on performance was not evaluated in this study. However, an average difference of 68 degrees in angular insertion depth or a range of 4 mm in electrode length could have a large impact on performance outcomes (a 3mm shift along the basilar membrane corresponds to a frequency change of 1 octave (Stakhovskaya et al. 2007; Greenwood, 1990)).

This study was performed in patients who received a HiFocus1 or HiFocus1J electrode. Because this electrode is a free-fitted lateral type, the electrode insertion depth can be largely influenced by the surgeon, while cochlear size morphology also have a direct influence. If this study would have been performed using a precurved (modiolus-hugging or mid scalar) electrode type, like the Nucleus Freedom (Cochlear Americas, Denver, CO) or the HiFocus MS of Advanced Bionics, the variability in final electrode position might be smaller. The precurved shape with additional markers to guide the insertion, limits the surgical freedom during insertion, theoretically resulting in a more stable insertion depth with more proximity to the modiolus. Moreover, the built-in electrode curvature is likely to be more important than the details of the cochlear anatomy.

The findings of the present study demonstrating the influence of cochlear shape and surgical insertion distance on electrode position are also essential for the development of insertion models that predict the linear surgical insertion depth necessary to reach a predefined insertion depth angle. These models may provide more control over electrode position to stimulate a desired tonotopic area of the cochlea. The described new methods used to define both cochlear shape and diameters will be considered input parameters in these models. In this study, cochlear size measurements alone describe around 13% of the variance in insertion depth. After adding the surgical insertion distance to the different models, around 80% of the variance can be explained. Compared to surgical insertion distance (65.3%), the variance of cochlear size has only a limited effect on the final insertion depth. Future studies will have to be performed on the development of such insertion models.

Although the relation between performance, insertion depth and cochlear size is very interesting, not much literature is available on this topic. However, the recent study by Holden et al. (2013) showed several relations. In addition, this is also the topic of ongoing research at our center (in preparation).

This study demonstrates a substantial variety in cochlear shape and size and its impact on electrode positioning. A significant size difference of 4% in favor of males was found based on sex with no size difference based on ear side or age being found. Two new methods, spiral fitting and PCAs, were proposed to describe cochlear shape with PCA being the preferred method. Using PCA, a general component matrix, in combination with one individual component score for the outer and another for the inner, can accurately describe the shape of the cochlea. Cochlear morphology was proven in several ways to significantly influence electrode position, both in terms of modiolus proximity and insertion depth.

REFERENCES

1 Finley CC, Holden TA, Holden LK et al. Role of electrode placement as a contributor to variability in cochlear implant outcomes. *Otol Neurotol* 2008;29(7):920-928.

2 Aschendorff A, Kromeier J, Klenzner T et al. Quality control after insertion of the nucleus contour and contour advance electrode in adults. *Ear Hear* 2007;28(2 Suppl):75S-79S.

3 Adunka O, Kiefer J. Impact of electrode insertion depth on intracochlear trauma. *Otolaryngol Head Neck Surg* 2006;135(3):374-382.

4 Escude B, James C, Deguine O et al. The size of the cochlea and predictions of insertion depth angles for cochlear implant electrodes. *Audiol Neurootol* 2006;11 Suppl 1:27-33.

5 Dimopoulos P, Muren C. Anatomic variations of the cochlea and relations to other temporal bone structures. *Acta Radiol* 1990;31(5):439-444.

6 Ketten DR, Skinner MW, Wang G et al. In vivo measures of cochlear length and insertion depth of nucleus cochlear implant electrode arrays. *Ann Otol Rhinol Laryngol Suppl* 1998;175:1-16.

7 Erixon E, Hogstorp H, Wadin K et al. Variational anatomy of the human cochlea: implications for cochlear implantation. *Otol Neurotol* 2009;30(1):14-22.

8 Yoo SK, Wang G, Rubinstein JT et al. Three-dimensional modeling and visualization of the cochlea on the Internet. *IEEE Trans Inf Technol Biomed* 2000;4(2):144-151.

9 Gstoettner W, Plenk H, Jr., Franz P et al. Cochlear implant deep electrode insertion: extent of insertional trauma. *Acta Otolaryngol* 1997;117(2):274-277.

10 Tykocinski M, Cohen LT, Pyman BC et al. Comparison of electrode position in the human cochlea using various perimodiolar electrode arrays. *Am J Otol* 2000;21(2):205-211.

11 Eshraghi AA, Yang NW, Balkany TJ. Comparative study of cochlear damage with three perimodiolar electrode designs. *Laryngoscope* 2003;113(3):415-419.

12 Rebscher SJ, Hetherington A, Bonham B et al. Considerations for design of future cochlear implant electrode arrays: electrode array stiffness, size, and depth of insertion. *J Rehabil Res Dev* 2008;45(5):731-747.

13 Verbist BM, Ferrarini L, Briaire JJ et al. Anatomic considerations of cochlear morphology and its implications for insertion trauma in cochlear implant surgery. *Otol Neurotol* 2009;30(4):471-477.

14 Ibrahim HN, Helbig S, Bossard D et al. Surgical Trauma After Sequential Insertion of Intracochlear Catheters and Electrode Arrays (a Histologic Study). *Otol Neurotol* 2011.

15 Iverson KC, Bhatti PT, Falcone J et al. Cochlear Implantation Using Thin-Film Array Electrodes. *Otolaryngol Head Neck Surg* 2011.

16 Kahrs LA, McRackan TR, Labadie RF. Intracochlear Visualization: Comparing Established and Novel Endoscopy Techniques. *Otol Neurotol* 2011.

17 Skarzynski H, Lorens A, Piotrowska A et al. Preservation of low frequency hearing in partial deafness cochlear implantation (PDCI) using the round window surgical approach. *Acta Otolaryngol* 2007;127(1):41-48.

18 MED-EL (2012). FLEX Portfolio The Softest, Most Flexible Electrode Arrays [MED-EL Web site]. 2012, December 13. Retrieved December 13, 2012 from http://www.medel.com/data/downloads/MAESTRO/23236.pdf.

19 Verbist BM, Frijns JH, Geleijns J et al. Multisection CT as a valuable tool in the postoperative assessment of cochlear implant patients. *AJNR Am J Neuroradiol* 2005;26(2):424-429.

20 Verbist BM, Joemai RM, Briaire JJ et al. Cochlear coordinates in regard to cochlear implantation: a clinically individually applicable 3 dimensional CT-based method. *Otol Neurotol* 2010;31(5):738-744.

21 Verbist BM, Skinner MW, Cohen LT et al. Consensus panel on a cochlear coordinate system applicable in histologic, physiologic, and radiologic studies of the human cochlea. *Otol Neurotol* 2010;31(5):722-730.

22 Skinner MW, Ketten DR, Vannier MW et al. Determination of the position of nucleus cochlear implant electrodes in the inner ear. *Am J Otol* 1994;15(5):644-651.

23 Stakhovskaya O, Sridhar D, Bonham BH et al. Frequency map for the human cochlear spiral ganglion: implications for cochlear implants. *J Assoc Res Otolaryngol* 2007;8(2):220-233.

24 Roland JT, Jr., Fishman AJ, Waltzman SB et al. Stability of the cochlear implant array in children. *Laryngoscope* 1998;108(8 Pt 1):1119-1123.

25 Sato H, Sando I, Takahashi H. Sexual dimorphism and development of the human cochlea. Computer 3-D measurement. *Acta Otolaryngol* 1991;111(6):1037-1040.

26 Skinner MW, Holden TA, Whiting BR et al. In vivo estimates of the position of advanced bionics electrode arrays in the human cochlea. *Ann Otol Rhinol Laryngol Suppl* 2007;197:2-24.

27 Kawano A, Seldon HL, Clark GM. Computer-aided three-dimensional reconstruction in human cochlear maps: measurement of the lengths of organ of Corti, outer wall, inner wall, and Rosenthal's canal. *Ann Otol Rhinol Laryngol* 1996;105(9):701-709.

28 Wysocki J. Dimensions of the human vestibular and tympanic scalae. *Hear Res* 1999;135(1-2):39-46.

29 Zrunek M, Lischka M, Hochmair-Desoyer I et al. Dimensions of the scala tympani in relation to the diameters of multichannel electrodes. *Arch Otorhinolaryngol* 1980;229(3-4):159-165.

30 Greenwood DD. A cochlear frequency-position function for several species--29 years later. *J Acoust Soc Am* 1990;87(6):2592-2605.

31 Holden LK, Finley CC, Firszt JB et al. Factors Affecting Open-Set Word Recognition in Adults With Cochlear Implants. *Ear Hear* 2013.

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APPENDIX A
Cluster Outcomes

Clustering Cochlear Size based on 4 Cochlear Diameters (DM)

Final Cluster Centers			
	Cluster		
	Small	Medium	Large
Diameter 1	8.45	8.87	9.41
Diameter 2	6.81	7.33	7.79
Diameter 3	6.18	6.64	7.08
Diameter 4	5.57	5.96	6.38

ANOVA						
	Cluster		Error			
	Mean Square	df	Mean Square	df	F	Sig.
Diameter 1	20.956	2	.087	359	239.969	.000
Diameter 2	22.550	2	.070	359	321.151	.000
Diameter 3	18.891	2	.054	359	349.591	.000
Diameter 4	14.926	2	.061	359	243.084	.000

Clustering Surgical Insertion (RW_E16)

Final Cluster Centers			
	Cluster		
	shallow	average	deep
Surgical insertion	3.25	6.23	8.69

ANOVA						
	Cluster		Error			
	Mean Square	df	Mean Square	df	F	Sig.
Surgical insertion	561.926	2	.,845	359	665.328	.000

Clustering Electrode Position based on 16 Contact Distances (CD)

Final Cluster Centers		
	Cluster	
	Lateral	Medial
Contact Distance 16	2.24	1.97
Contact Distance 15	2.15	1.85
Contact Distance 14	2.11	1.74
Contact Distance 13	2.04	1.62
Contact Distance 12	1.97	1.50
Contact Distance 11	1.90	1.38
Contact Distance 10	1.79	1.25
Contact Distance 9	1.65	1.12
Contact Distance 8	1.48	.98
Contact Distance 7	1.28	.86
Contact Distance 6	1.08	.78
Contact Distance 5	.93	.74
Contact Distance 4	.83	.70
Contact Distance 3	.77	.65
Contact Distance 2	.75	.61
Contact Distance 1	.73	.58

ANOVA						
	Cluster		Error			
	Mean Square	df	Mean Square	df	F	Sig.
Contact Distance 16	6.214	1	.144	360	43.241	.000
Contact Distance 15	7.924	1	.100	360	79.632	.000
Contact Distance 14	11.790	1	.080	360	147.661	.000
Contact Distance 13	15.467	1	.065	360	238.353	.000
Contact Distance 12	19.484	1	.059	360	329.700	.000
Contact Distance 11	23.897	1	.054	360	439.101	.000
Contact Distance 10	25.836	1	.058	360	448.356	.000
Contact Distance 9	25.563	1	.060	360	427.840	.000
Contact Distance 8	21.657	1	.065	360	335.752	.000
Contact Distance 7	15.201	1	.068	360	222.106	.000
Contact Distance 6	8.208	1	.064	360	127.566	.000
Contact Distance 5	3.473	1	.073	360	47.506	.000
Contact Distance 4	1.588	1	.067	360	23.849	.000
Contact Distance 3	1.260	1	.058	360	21.641	.000
Contact Distance 2	1.713	1	.055	360	31.075	.000
Contact Distance 1	1.841	1	.052	360	35.622	.000

APPENDIX B

PCA Outcomes

Principal Component Analysis

Principal Components Analysis (PCA) is a multivariate statistical technique developed to reduce the dimensionality of the data. This factor extraction method used to form uncorrelated linear combinations of the observed variables. The first component explains the largest amount of variance. Successive components explain progressively smaller portions of the variance and are all uncorrelated with each other. To calculate the PCA fits the factor scores are multiplied with the component matrix, and this is added to the average PCA score. The average PCA score defines the central pathway along the cochlear canal.

Component Matrix

	Component							
	1	2	3	4	5	6	7	8
Radius 1	0.951	0.240	0.139	0.130	0.031	0.016	0.016	-0.001
Radius 2	0.966	0.206	-0.093	-0.076	0.055	0.040	-0.072	0.002
Radius 3	0.970	0.124	-0.177	-0.040	0.018	-0.056	0.080	0.016
Radius 4	0.973	-0.104	-0.173	0.051	-0.055	0.020	-0.007	-0.077
Radius 5	0.971	-0.189	-0.097	0.064	-0.022	-0.010	-0.037	0.078
Radius 6	0.960	-0.236	0.096	-0.040	0.066	0.073	0.048	0.001
Radius 7	0.974	-0.119	0.155	-0.022	0.041	-0.095	-0.035	-0.031
Radius 8	0.973	0.081	0.154	-0.065	-0.132	0.013	0.007	0.013

Average PCA scores for each radius

	Average PCA Scores
Radius 1	4.524
Radius 2	3.433
Radius 3	3.066
Radius 4	2.567
Radius 5	2.352
Radius 6	1.992
Radius 7	1.730
Radius 8	1.525

Chapter Five

Development of Insertion Models Predicting Cochlear Implant Electrode Position

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ABSTRACT

Objectives

To assess the possibility to define a preferable range for electrode array insertion depth and surgical insertion distance for which frequency mismatch is minimalized. To develop a surgical insertion guidance tool by which a preferred target angle can be attained using preoperative available anatomical data and surgically controllable insertion distance.

Design

Multiplanar reconstructions of pre- and postoperative CT-scans were evaluated in a population of 336 patients implanted with the CII HiFocus1 or HiFocus1J implant (26 bilaterally implantees included). Cochlear radial distances were measured on four measurement axes on the preoperative CT-scan. Electrode contact positions were obtained in angular depth, distance from the round window and to the modiolus center. Frequency mismatch was calculated based on the yielded frequency as a function of the angular position per contact. Cochlear diameters were clustered into three cochlear size groups with K-sample clustering. Using spiral fitting and general linear regression modelling the feasibility of different insertion models with cochlear size measures and surgical insertion as input parameters was analyzed. The final developed model was internally validated with bootstrapping to calculate the optimism-corrected R-squared.

Results

Frequency mismatch was minimalized for surgical insertion of 6.7 mm and insertion depth of 484˚. Cochlear size clusters were derived consisting of a 'small' (N=117), 'medium' (N=171) and 'large'(N=74) cluster with mean insertion depths of 506˚, 480˚ and 441˚ respectively. The relation between surgical insertion (L_{E16}) and insertion depth (θ_{E1}) differed significantly between the three clusters ($p<0.01$). The insertion models based on spiral fitting showed an R-squared of 62% with mean of the residuals of -0.5 mm (SD=1.2 mm) between the measured and predicted L_{E16} and a mean of 15˚ (SD=83˚) for θ_{E1}. Using general linear regression modelling resulted in a residual mean of -0.2 µm (SD=0.9 mm) for measured and predicted L_{E16} and 0.01˚ (SD=33˚) for θ_{E1}. The model derived from general linear regression modelling resulted in an R-squared of 78.7% and was validated with bootstrapping. An optimism of 0.6% was calculated using this analysis. The optimism-corrected R-squared of 78.1% defined the estimated performance of the final insertion model in future populations.

Conclusions

A minimal frequency mismatch for an electrode array design can be calculated to define preferable electrode array position within the cochlea. In general, to achieve a minimal frequency mismatch, the surgeon should attempt to insert the HiFocus 1 or 1J array around 6, 7 or 8 mm in case of a 'small', 'medium' or 'large' cochlea, respectively. Development of different insertion models showed the feasibility of obtaining a surgical guidance tool to lead the surgeon during cochlear implantation depending on individual cochlear size and controllable surgical distance. The developed final insertion model predicted 78.1% of the variation in final HiFocus1 or HiFocus1J implant position.

INTRODUCTION

Cochlear implantation as therapy for severe to profound hearing loss generally leads to good auditory performance. However, large variations are still observed among patients, making it difficult to inform candidates about their expected outcome. Electrode position is one of the factors influencing performance. Finley et al. (2008) and Holden et al. (2013) concluded that lower performance outcomes are associated with larger insertion depth and a high number of contacts located within the scala vestibuli. The advantages of scala tympani over scala vestibuli insertions on speech performance results were also demonstrated by Aschendorff et al. (2007). The debate about the optimal surgical insertion distance and insertion depths is still ongoing. In our previous study (Marel 2014), it was illustrated that more than 81 % of the variance in insertion depth can be explained when cochlear size is combined with the surgical insertion. This study aims to develop a surgical guidance model that, on the basis of a pre-operative CT scan, will provide the surgeon with an insertion distance so that the implant will reach a specific target insertion depth. The goodness-of-fit of this prediction model is evaluated with postoperative images.

Poor CI performance outcomes can partially be explained by large discrepancies between the natural tonotopic organization of the cochlea and the frequency setting of the individual electrode contacts (Baskent & Shannon, 2005; Faulkner et al. 2006; Carlyon et al. 2010). Each implant design has its own frequency configuration for the electrode contacts along the electrode array, determined by the manufacturer. A non-optimal insertion results in a 'frequency mismatch,' defined as the error between the frequency attributed to the specific contact and the physiological tonotopic frequency corresponding to that cochlear location. This was also concluded by Baskent et al. (2005) who showed that for complete insertions, frequency-place matching produced better speech recognition than compression of the full speech range onto the array, ignoring the actual electrode to frequency-place map. A recent prospective study of Buchman et al. (2014) comparing two electrode lengths found faster time to asymptotic speech perception levels in users of longer CI electrodes. In theory, the relation between insertion depth and 'frequency mismatch' would be described by a U-shaped function, as for each electrode type there is an optimal insertion depth range where frequency mismatch is minimal and deviations from this optimum would result in more mismatch both ways (shallower or deeper insertions). The location and magnitude of the minimum of the function is influenced by the electrode design (length and contact spacing), the lateral-to-medial position of the array in the cochlea and cochlear geometry. Electrode position depends on three factors; cochlear morphology, electrode design, and the surgeon's insertion technique. The influence of these factors on electrode position and its relation to the occurrence of intracochlear trauma and residual hearing preservation is well documented (Briggs et al. 2001; Eshraghi et al 2003; Arnoldner et al. 2010; Biedron et al. 2010).

The relation of cochlear morphology and size to electrode position has been described for different electrode designs (Escude et al. 2006; Biedron et al. 2010; Van der Marel et al. 2014). Both insertion depth and modiolus proximity are influenced by cochlear size. Even with a fixed position of the most basal electrode contact this may result in insertion depth differences of over 73˚ for a particular electrode (Escude et al. 2006; Van der Marel et al. 2014). Also the risk for translocation to a scala vestibuli position and the occurrence of intracochlear trauma is related to cochlear morphology. Individual variations in micromorphology and distinct narrowing of cochlear diameter in the ascending basal turn may contribute to the occurrence of insertion trauma (Biedron et al. 2010). In addition, Verbist et al. (2009) concluded that the irregularly ascending lumen of the cochlea towards the helicotrema, leads to pressure points at certain locations, especially in the upper basal turn, thus increasing the risk of insertion trauma during cochlear implantation.

CI design is a second factor influencing position. Currently available arrays include straight and precurved designs with large differences in length, thickness and stiffness, theoretically enabling surgeons to choose an individually appropriate design. Various studies on the relation between electrode configuration and cochlear trauma or residual hearing preservation have been conducted (Boex et al., 2006; Briggs et al., 2006; Gstoettner et al., 2004). However, the different study designs, array types and primary outcomes measures, complicate detailed comparison of the outcomes. Nonetheless, from these studies it can be concluded in general that electrode characteristics have a large impact on intracochlear position in terms of modiolus proximity, scalar location, and insertion depth, which in turn have a clear impact on the risk of intracochlear trauma and loss of residual hearing.

Another factor influencing electrode position is the surgeon's choice between cochleostomy versus a round window approach for array insertion. The choice of surgical approach affects electrode position, especially basal modiolus proximity and insertion depth (Briggs et al. 2006). In addition to the surgical approach, the surgeon must also decide how far and consequently what angle to insert the electrode array into the cochlea.

Various schools of thought exist with regard to optimal insertion depth, with electrode array lengths varying widely among the different manufacturers. While Hamzavi et al. (2006) and Hochmair et al. (2003) concluded that stimulating apical regions improves speech perception, studies of Finley et al. (2008) and Radeloff et al. (2008) suggest the opposite and warn that deeper insertions might be related to increased intracochlear trauma and loss of residual hearing. Adunka et al. (2006) studied the effect of surgical technique and insertion depth on intracochlear trauma and found evidence that trauma increases with deep insertions. They advise to stop at point of first resistance, while Baskent et al. (2005) and Faulkner et al. (2006) suggest completing full insertions in order to reach full coverage of the auditory nerve. The length difference between the cochlear duct (2 ¾ turns) and the spiral ganglion (1 ¾ turns) adds an additional level to this discussion (Stakhovskaya et al. 2007). Furthermore, there is evidence that insertion beyond the end of the spiral ganglion (630^0) will not result in additional discernible percepts (Kalkman et al. 2014, Boyd 2011).
This study analyzed the relation between electrode position of the physiological frequency-place map of each cochlea, for the HiFocus 1 and 1J electrode (Advanced Bionics Corp., Valencia, CA), which only differ in the way the lead is attached to the array. The first goal was to study whether or not it is possible to define an optimal range for surgical insertion distance or insertion angle by which overall frequency mismatch averaged for all active contacts is minimized. The development and validation of a more accurate, individualized prediction model relating the final insertion depth of the apical contact to the surgically controllable insertion distance of the most basal contact, which may facilitate optimal electrode insertion was the second goal of this study.

MATERIAL AND METHODS

Patients

For this study the data of 401 patients, implanted with an Advanced Bionics (Valencia, CA, USA) implant between 2002 and 2011 at Leiden University Medical Center (LUMC) and of whom a pre- and postoperative CT-scan was available, were collected. Patients with abnormal cochlear morphology (N=26), abnormal insertion (e.g., tip fold-over or incomplete insertions) (N=5) or poor quality scans (N=34) were excluded. In total, 336 patients (153 male, 183 female) who received a CII implant with HiFocus1 electrode without positioner or a HiRes90K with HiFocus1J electrode were included. Both outer wall electrodes have the same contact size and spacing. Of this population, 26 patients were bilaterally implanted, and thus 362 implanted cochleas were analyzed. In all these patients the surgery, performed by three surgeons, resulted in complete and uncomplicated insertions, using an extended round window approach. The surgical approach consisted of exposure of the round window niche by performing a mastoidectomie and a posterior tympanotomy. After opening the round window membrane, the crista fenestrae was drilled away, creating an anterior inferior extension of the round window so that the electrode array could be inserted inside the cochlea.

Image Reconstruction and Analysis

All CT-scans (scanner type: Aquillion 4, Aquillion 16, Aquillion 64, Aquillion 1; Toshiba Medical Systems, Otawara, Japan) were obtained according to the standard cochlear implant imaging protocol in the LUMC (Verbist et al., 2005; Verbist et al. 2010b). Multi-planar reconstructions (MPRs) were made of both the preoperative and postoperative scans. The first step in the analysis of the MPRs was applying a 3-dimensional coordinate system (Verbist et al. 2010a). The outer and inner wall distances to the center of the modiolus were determined by scrolling through the slices of the preoperative MPR and selecting the largest diameters found along 4 predefined coordinate axes (e.g., 8 radii) using an in-house designed post processing program (Matlab, Mathworks Inc., Natick, MA, USA)(Figure 1A). This results in 4 diameters (i.e., 8 radii) for the cochlea (Figure 1). Two of these coordinate axes (i.e., 4 radii, radius 1,3,5 and 7) are in accordance with the consensus on cochlear coordinates (Verbist et al. 2010a), consisting of a line connecting the center of the round window to the center of the modiolus (radius 1 and 5=diameter D_1) in combination with a line perpendicular to it (radius 3 and 7=diameter D_3). This way, the center of the round window (RW) defines the zero reference point (insertion angle $\theta=0^\circ$). The other 2 coordinate axes (i.e., 4 radii, radius 2,4,6 and 8) are defined by a line connecting the center of the modiolus to the most lateral point of the horizontal semicircular canal (radius 4 and 8=diameter D_4) combined with a line perpendicular to it (radius 2 and 6=diameter D_2). These axes originate from the Leiden coordinate system, as described by Verbist et al. (2005, 2010a).

On the postoperative MPRs, the position of each electrode contact was expressed in two ways; in an 'angular' (degrees from the round window) and a 'linear' (millimeters between two positions) manner (Figure 1B and 1C). The linear position of the most basal electrode contact (E16) can be mostly controlled by the surgeon and is therefore referred to as 'surgical insertion' depth. Direct measurement of this distance on the MPR showed to be unreliable for some implanted cochleas, especially the deeply inserted ones (θ_{E16}>100˚). For those cochleas a straight line to E16 would run through the modiolus and did therefore not represent the true curved route of the electrode lead. Therefore this distance (L_{E16}) was obtained by calculating the spiral length from the round window (RW) to E16, using:

$$L_{E16} = \frac{\left(a \cdot \sqrt{1+b^2} \cdot e^{b\theta_{E16}} - 1\right)}{b}, \tag{1}$$

with the corresponding angle of E16, a=r(RW), r is radial distance to center of modiolus and $b = \ln\frac{r(E16)}{r(RW)} \cdot \frac{1}{\theta_{E16}}$. The formula of Equation 1 is based on the function of a logarithmic spiral, which is often used to fit into the curvature of the cochlea (Yoo et al. 2000; Van der Marel et al. 2014).

The linear insertion depth (L_{E1}) is the sum of the surgical insertion (L_{E16}) and the standard configuration length of the electrode type (17 mm). The 'insertion depth' is defined as the angle θ_{E1} from the round window to the most apical electrode contact (E1).

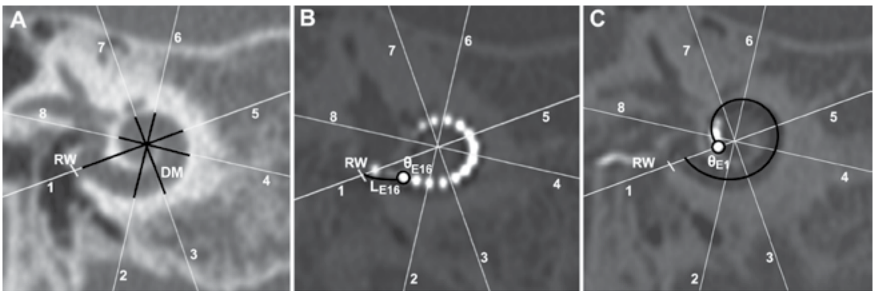

Figure 1. **A.** Preoperative reconstruction with measurements on 8 radii in a basal turn cross-section, **B.** Postoperative reconstruction with measurement of 'surgical insertion distance' (L_{E16}) in a basal turn cross-section **C.** Postoperative reconstruction with measurement of insertion depth (θ_{E1}) in an apical turn cross-section. 1-8=radii; RW=round window; DM=diameter; Diameter 1=radius 1+5, Diameter 2=radius 2+6, Diameter 3=radius 3+7, Diameter 4=radius 4+8. Consensus coordinate system: (radius 1 and 5) x (radius 3 and 7); Leiden coordinate system: (radius 4 and 8) x (radius 2 and 6) θ_{E16}=insertion depth from the round window to the most basal electrode contact 16; θ_{E1}=insertion depth from the round window to the most apical electrode contact 1. In this specific case the following metrics were measured; Figure 1A: DM 1=9.78 mm; DM 2=7.74 mm; DM 3=7.19 mm; DM 4=6.31 mm; Figure 1B: L_{E16}=2.36 mm; θ_{E16}=17˚; Figure 1C: θ_{E1}=360˚ ; A rather shallow inserted cochlea was chosen for this example to show many electrode contacts with enough detail.

Frequency Mismatch

The Leiden University Medical Center maintains a large database of postoperative CT-scans of cochlear implant patients. For a subsample of the implantees implanted between 2002 and 2008 (N=222), the 'frequency mismatch' was calculated by comparison of the implant settings and the electrode place pitch. The implant settings needed for this analyses were available for the population that was implanted between 2002 and 2008 and described by Van der Beek et al. (2015). Therefore, this subsample of patients was used for the frequency mismatch analyses, but they were also all included in the total studied population for this study.

The cochlear frequency-to-position function of Greenwood (1990), where acoustic frequency 'f' (kHz) is related to a certain point 'x' along the basilar membrane, was used as a starting point. This function is given by:

$$f(x)=A\cdot(10ax - k), \tag{2}$$

with A=0.1654 kHz, a=2.1 and k=0.88 the parameters for the human cochlea from Greenwood, 1990. Here 'x' represents a proportion of the complete basilar membrane from apex to the position that is requested (x=0 for the apex; x=1 for the basal end of the basilar membrane).

In a recent modelling study by Kalkman et al. (2014), this Greenwood function was combined with histological data from Stakhovskaya et al. (2007) and geometrical data from several 3D models of the human cochlea to produce a SG-based version of the Greenwood function. This adjusted Greenwood function describes the characteristic place pitch at the spiral ganglion (SG) as a function of cochlear position:

$$f_{SG}(\varphi) = A\left(10^{a\left(1-\frac{\varphi-\sqrt{\varphi^2-4A_S B_S}}{2B_S}\right)} - k\right) \tag{3}$$

where A_S and B_S are constants taken from Stakhovskaya et al. (2007), with values A_S=0.22 and B_S=-0.93. The cochlear position is parameterized by , which is defined as a function of cochlear angle θ by:

$$\varphi(\theta) = \sqrt{\frac{ln(1+\delta)-\varepsilon}{ln\left(\frac{\theta}{\theta_t}+\delta\right)-\varepsilon\frac{\theta}{\theta_t}}} - 1 + A_S + B_S \tag{4}$$

where δ=1.031, ε=0.4621 and θ_t is the assumed termination angle of the SG, set at 630° (Kalkman et al., 2014). The angles θ and θ_t are measured from the center of the round window. Equation 3 was used to determine the predicted place pitch at the spiral ganglion for each electrode contact, based on their angular positions ($f_{SG}(\theta_i)$). Additionally, the center frequency of the sound processing filter of each electrode contact was obtained from the filter map assigned to the implant's channels by the manufacturer. These center frequencies are referred to as $f_{MF}(i)$, where i represents the contact number (1 through 16). The overall frequency mismatch (ΔF) in each patient in semitones was obtained by calculating the difference (Δf_i) between $f_{MF}(i)$ and $f_{SG}(\theta_i)$ in semitones with:

$$\Delta f_i = 12 \cdot {}^2log\, f_{MF}(i) - 12 \cdot {}^2log\, f_{SG}(\theta_i), \tag{5}$$

and from this, the root mean square (RMS) with:

$$\Delta F = \sqrt{\frac{1}{N}\sum_{i=1}^{N} \Delta f_i^{\,2}}, \tag{6}$$

where N = number of active contacts as used in the patients program. In addition, the relation between the average frequency mismatch (ΔF), surgical insertion distance (L_{E16}), and insertion depth (θ_{E1}) was analyzed.

Spiral Fitting

The logarithmic spiral, often used for describing the curvature of the cochlea (outer wall radii) (Yoo et al. 2000; Van der Marel et al. 2014), can also be used to predict the electrode trajectory within the cochlea. For this purpose, first the spiral fit coefficients (a_{outer} and b_{outer}) derived from the outer wall spiral fitting were used to calculate the arc length of the outer wall (L_{arc}) from the center of the round window to a specific target angle for the most apical electrode (θ_{E1}) by:

$$L_{arc}(\theta_{E1}) = \frac{\left(a_{outer} \cdot \sqrt{1 + b_{outer}^2} \cdot e^{b_{outer}\theta_{E1}} - 1\right)}{b_{outer}} \tag{7}.$$

Insertion Model based on Spiral Fit

As both the HiFocus 1 and 1J are lateral wall electrodes, they will follow the outer wall of the cochlea but with a smaller curvature. The first insertion model is derived from this knowledge. In equation 7 the arc length of the outer wall to the targeted insertion depth is calculated. It is assumed that the length difference between the outer wall and the final electrode trajectory can be approximated by a linear correction function:

$$L'_{E1} = c \cdot L_{arc} + d, \tag{8}$$

where L'_{E1} is the estimated insertion length measured from the round window, c and d are regression coefficients of the model. The regression coefficients result from general linear regression model with the true linear insertion depth (L_{E1}) as determined from the CT as dependent variable and L_{arc} as independent variable. The surgical insertion distance (L'_{E16}) was predicted using the above formula (8), with subtraction of the electrode configuration length of 17 mm.

Multi-Dimensional Linear Regression Insertion Model

The anatomical measurements, e.g., four diameters (or eight radii) of the cochleas, were considered as anatomical input parameters in a prediction model. These input parameters were first further analyzed. For this purpose the cochleas were also clustered into 3 cochlear size clusters (small, medium and large) based on the sum of the four diameters, with the K-sample clustering procedure of SPSS (SPSS 17.0 for Windows; SPSS Inc., Chicago, IL, USA). The relation between surgical insertion (L_{E16}), cochlear size clusters and insertion depth was analyzed using one-way analysis of variance (ANOVA) and multiple linear regression analyses. The surgical insertion L_{E16} was combined with one or more of the cochlear diameters and radial distances in order to predict the insertion depth (θ_{E1}) using general linear regression modeling.

Model Validation

The described models produce an estimated surgical insertion distance (L'_{E16}) based on a target angle. Using the post-operative data set it is possible to do a validation of the models by inserting the actual insertion angle θ_{E1} of a patient and thereby predicting the surgical insertion distance (L'_{E16}). The difference between the actual recorded surgical insertion distance (L_{E16}) and the predicted one is a measure for the accuracy. A second estimator of accuracy used the surgical insertion distance (L_{E16}) and the model to estimate the insertion angle θ'_{E1}. This served the purpose of illustrating the variance in the target angles if the 'prescribed surgical insertion distance' would have been used (and achieved) by the surgeon. For this purpose the two insertion models were inverted.

Validation using Bootstrapping

Finally, the prediction model with the highest R-squared, defining the explained variance by the model (R^2), was further analyzed. To assess the risk of 'overfitting', i.e., using too many parameters in the prediction model, resulting in predictions from the model that do not generalize to new patients outside the sample, the model was internally validated with bootstrapping as described in Steyerberg 'Clinical Prediction Models' (Steyerberg, 2009). This was performed for 1000 samples with the 'validate.ols function' of the 'rms package' by F.E. Harrell Jr. in R statistical software (R version 2.15.0; R Foundation for Statistical Computing, Vienna, Austria). The average performance of these bootstrap samples was used to quantify the 'optimism', i.e., the difference between 'apparent' performance in the bootstrap samples and true performance in the original sample. This optimism of the prediction model is subtracted from the original estimate of R^2 to obtain the optimism-corrected R^2, which represents the estimate of the performance in future cases.

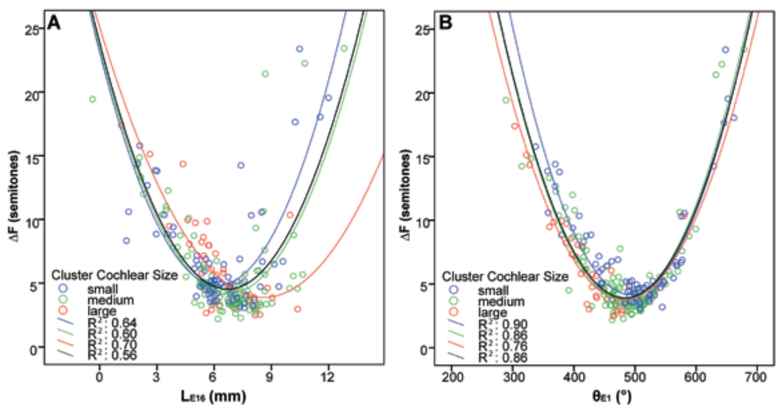

Figure 2. A. Relation between surgical insertion distance (L_{E16}) and frequency mismatch (ΔF). B: Relation between insertion depth (θ_{E1}) and frequency mismatch (ΔF). Lines represent the fitted quadratic functions with calculated R-squared and the cochlear cluster sizes are marked by color (blue=small, green=medium, red=large). The black line represents the fitted function of the total population.

Table I. Relation between frequency mismatch and surgical insertion distance

Group	a	b	c	$L_{E16(min)}$	R^2
Total population (N=222)	0.43	-5.78	23.91	6.7	0.56
Small cluster (N=117)	0.48	-5.92	23.14	6.2	0.64
Medium cluster (N=171)	0.42	-5.70	23.42	6.8	0.60
Large cluster (N=74)	0.29	-4.93	25.09	8.5	0.70

Table II. Relation between frequency mismatch and insertion depth

Group	d	e	f	$\theta_{E1(min)}$	R^2
Total population (N=222)	0.000519	-0.50	125.24	484	0.86
Small cluster (N=117)	0.000565	-0.56	141	496	0.90
Medium cluster (N=171)	0.000530	-0.51	127	481	0.86
Large cluster (N=74)	0.000465	-0.45	112	484	0.90

RESULTS

Frequency Mismatch

The cochleas were clustered into 3 cochlear size groups ('small' N:117, 'medium' N:171, 'large' N:74), with mean D_1=8.5 mm, 8.9 mm and 9.4 mm, respectively. In Figure 2 the overall frequency mismatch (ΔF) is plotted as a function of surgical insertion distance (Figure 2A) and as function of the insertion depth (Figure 2B). The black line shows the quadratic fit of the total population and the colored lines show the fits of the cochlear size clusters.

The mean frequency mismatch for the studied electrode array type was 6.3 semitones (N=222). The data shows the expected U-shape described in the introduction, as illustrated by the fitted quadratic functions. The fitted quadratic function between frequency mismatch and surgical insertion distance (Figure 2A) was given by;

$$\Delta F = a \cdot (L_{E16})^2 + b \cdot (L_{E16}) + c \quad (9).$$

Table I shows the values of the coefficien^{t}s, the R2 and the surgical insertion distance that gives the minimum frequency mismatch ($L_{E16(min)}$) for the total population and cluster size groups separately. The fitted quadratic function of the total population (N=222) showed an R^2 of 0.56 ($p<0.01$).
The correlation function between frequency mismatch and insertion depth was defined by;

$$\Delta F = d \cdot (\theta_{E1})^2 + e \cdot (\theta_{E1}) + f, \quad (10)$$

and the total population yielded an R^2 of 0.86 ($p<0.01$). Table II shows the values of the coefficients, the R^2 and the insertion depth belonging to the minimum of the quadratic functions ($\theta_{E1(min)}$) for the total population and cluster size groups. The minimum mismatch in frequency for this electrode design is found to be at a surgical insertion distance of 6.7 mm (Figure 2A) and an insertion depth of 484° (Figure 2B).

An additional analysis, however, could not demonstrate any significant correlation (p= 1.0) between the frequency mismatch and final phoneme scores (average scores for 65dB SPL and 75dB SPL between 1 and 2 years after implantation). This analysis was performed in the subsample of postlingually deaf adults (N=123), analyzed for a previous study by Van der Marel et al. (2015), for which frequency mismatch data and long-term follow-up data were available.

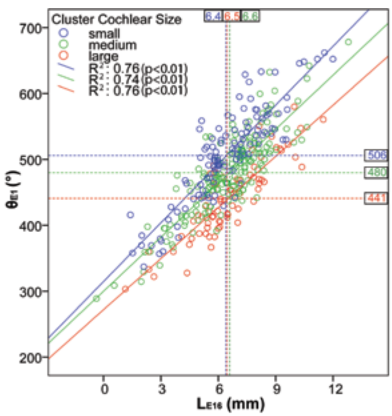

Figure 3.
Relation between surgical insertion distance (L_{E16}) and insertion depth (θ_{E1}), with cochlear cluster sizes marked by color (blue=small, green=medium, red=large). Straight lines represent the fitted linear regression fits with calculated R-squared per cluster. The horizontal and vertical dashed reference lines represent the mean values for each cochlear cluster size.

Influence of Cochlear Size on Insertion Depth

In Figure 3 the relation between surgical insertion distance (LE16) and insertion depth (θ E1) is shown, with different cochlear size clusters marked by colors. The mean insertion depth (θ E1) was 480˚ and the mean surgical insertion distance (LE16) was 6.5 mm (N=362).
The mean surgical insertion distance (LE16) per cluster was 6.4 mm for 'small' cochleas, 6.6 mm for 'medium' cochleas and 6.5 mm for 'large' cochleas. This mean surgical insertion distance did not significantly differ between the cochlear cluster size groups as determined by one-way ANOVA ($F(2,359) = 0.241$, $p = 0.79$).
Linear regression lines were calculated per group, and within group correlations turned out to be highly significant ($R^2=0.76$ ($p<0.01$) for 'small', $R^2=0.74$ ($p<0.01$) for 'medium' and $R^2=0.76$ ($p<0.01$) for 'large' cochleas). Furthermore, these regression lines were significantly

different between the groups ($p<0.01$), demonstrating an influence of cochlear size on the insertion depth. The mean insertion depth (θ_{E1}) per cluster was 506˚ for 'small' cochleas, 480˚ for 'medium' cochleas and 441˚ for large cochleas. The mean insertion depths were significantly different between the cochlear cluster size groups as determined by one-way ANOVA ($F(2,359) = 23.101$, $p<0.01$).

Spiral Fitting Model

As described in Materials and Methods, for the Spiral fitting model the length of the spiral fit along the outer wall until the targeted insertion angle was corrected to represent the length of the inserted electrode array. As both the length along the outer wall and the actual insertion length could be determined, the parameters of the correction function in equation 8 could be calculated. This resulted in a value of $c = 0.748$ and of $d = 4.009$.

Using this model it is possible to 'predict' the required insertion length from electrode 16 to the round window (L'_{E16}) and compare it to the actual insertion depth achieved during surgery (L_{E16}). Figure 4A shows a histogram of the residuals between predicted (L'_{E16}) and measured surgical insertion distance (L_{E16}). The mean of the residuals was -0.5 mm and the standard deviation was 1.2 mm. The R^2, representing the performance of this method, was 62%. 5

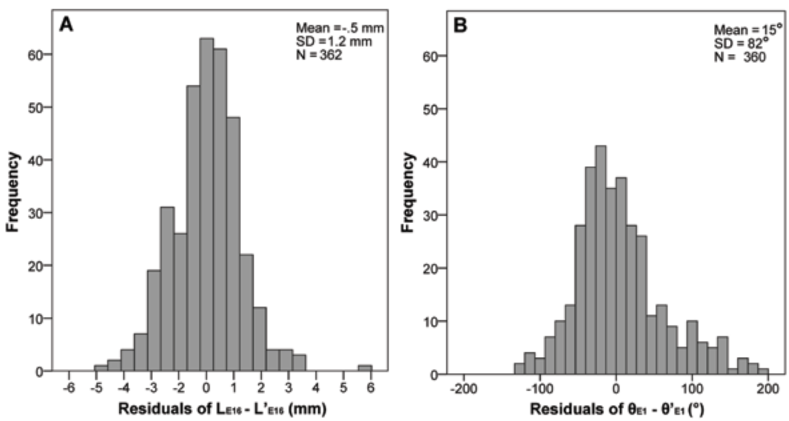

Figure 4. Histogram showing the residuals between the predicted and true surgical insertion distance (L'_{E16} - L_{E16}) using the spiral fitting method (A) and showing the residuals between the predicted and true insertion depth (θ'_{E1} - θ_{E1}) (B). The residuals of 12 cochleas are not shown in this histogram, as the outcome was beyond 200˚.

Using the inverse of the prediction model the predicted insertion depth (θ'_{E1}) of this spiral fitting method was calculated with the measured L_{16} as input parameter and compared to the true insertion depth (θ_{E1}). The histogram in Figure 4B shows the residuals between these two variables. The mean of the residuals was 15˚ with a standard deviation of 83˚. For 2 cochleas the input term for the logarithm in the inversed function resulted in 0 or lower (as a consequence of the inherent extrapolation involved) and therefore the residuals could not be calculated. For 12 cochleas the results showed such outliers (residuals>200˚), that they were not depicted by this histogram, but were included in all performed analyses. These specific cases had a relatively deep insertion with many electrodes beyond the first turn of the cochlea, which resulted in poorer fitting with the spiral fitting method since these electrode positions were predicted by extrapolation.

Multiple Linear Regression Model

The other approach for developing a surgical guidance tool consisted of testing several multiple linear regression models, using either each diameter separately or combinations of them. In addition, the eight radii were analyzed separately, as well as several subsets. The explained variances in surgical insertion distance of each combination of parameters in the regression model are shown in Table III.

Table III. Development of surgical guidance tool

Regression Models	Explained variance of surgical insertion distance (%)
Insertion depth θ_{E1} + Diameter 1	75.7 %
Insertion depth θ_{E1} + Diameter 1 + 3	77.5 %
Insertion depth θ_{E1} + Radii 1-8	79.2 %
Insertion depth θ_{E1} + Diameter 1 + 3 + 4 (final)	78.7 %

Table IV. Parameter estimates of final prediction model (N=336)

Parameter	B	Significance (p)
Intercept	-21.681	<0.01
D_1	0.715	<0.01
D_3	0.486	0.012
D_4	0.923	<0.01
θ_{E1}	0.028	<0.01

Table V. Defining model performance by bootstrapping.

Prediction Model (R^2)	Apparent (%)	Training (%)	Test (%)	Optimism (%)	Optimism corrected (%)
Surgical Insertion Distance (L'_{E16})	78.7	79.0	78.4	0.6	78.1

The resulting prediction model using three diameters as parameters ($p<0.05$), except for D_2 ($p=0.6$), explained 78.7% of variance in surgical insertion distance (L'_{E16}). The predictive value of this model was higher than if 1 diameter ($R^2=0.757$) or 2 diameters ($R^2=0.775$) were used. The use of all of the eight radii separately in the model resulted in a comparable R^2 (79.2%), so the three diameters were favored as input parameters in the final model. This model predicted surgical insertion (L'_{E16}) in mm for a desired insertion depth θ_{E1}(in degrees) by the following regression function:

$$L'_{E16} = -21.681 + (0.715 \cdot D_1) + (0.486 \cdot D_3) + (0.923 \cdot D_4) + (0.028 \cdot \theta_{E1}) \qquad (11).$$

5

The significance levels of the different parameters of equation 11 are shown in Table IV. The residuals between the predicted surgical insertion distance L'_{E16} and the true distance L_{E16} are shown in Figure 5A. The mean of the residuals was -0.2 µm with standard deviation of 0.9 mm. As a validation step, a predicted insertion depth θ'_{E1} on the basis of actual surgical insertion depth L_{E16} was also rendered and compared with the true insertion depth (θ_{E1}) using the inverse formula of equation 11. The residuals of this calculation are shown in Figure 5B, with a mean of 0.01° and standard deviation of 33°.

The model was further analyzed with bootstrap validation to obtain an estimate of how optimistic this original observed explained variance (R^2) is. The outcome of this analysis is shown in Table V. The original data was resampled a 1000 times and a bootstrap regression model was rendered. The averaged R^2 was obtained from this procedure, referred to as 'Training R^2'. Then, the bootstrap regression model was applied onto the original data set, resulting in the 'Test R^2'. By subtracting this Test R^2 from the Training R^2, the 'Optimism' of the model as calculated was 0.6%. Therefore, the optimism-corrected R^2 of the model was 78.1%.

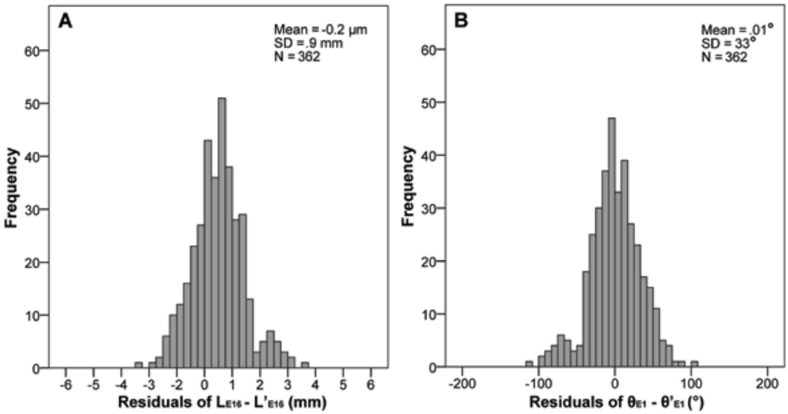

Figure 5. Histograms of the final insertion model showing residuals for predicted and true surgical insertion distance (L'_{E16} -L_{E16}) (**A**) and insertion depth (θ'_{E1} - θ_{E1}) (**B**).

DISCUSSION

Only a few studies have investigated the influence of cochlear size on electrode position (Escude et al. 2006; Van der Marel et al. 2014), although it is well known that the morphology of the cochlea can vary substantially (Ketten et al. 1998; Escude et al. 2006; Erixon et al. 2009). Van der Marel et al. (2014) concluded that over 81% of the variability of insertion depth could be explained from the surgical insertion distance and cochlear size. In the present paper an insertion model was developed that predicts the required surgical insertion distance L_{E16} (distance from round window to most basal electrode contact) necessary to reach a targeted insertion depth θ_{E1} of the most apical contact for the HiFocus 1 and 1J electrode arrays. It uses information about cochlear morphology from pre-operative CT-scans. For this purpose two different methods were tested, the spiral fit method and the multiple linear regression method. The best result with the linear regression method uses three diameters as input parameters. The accuracy of this regression model was tested using bootstrap validation to obtain the optimism-corrected R^2. This revealed that the model will predict up to 78.1% of the variation in surgical insertion distance (L_{E16}) in future data, i.e., very close to the 81% which could maximally be explained in view of Van der Marel et al. (2014). Using one diameter less, which is comparable to the method of Escudé (2006), would result in a predictive loss of 0.6%, and predicts 77.5% of the variations in L_{E16}:

$$L'_{E16} = -21.246 + (0.970 \cdot D_1) + (0.920 \cdot D_3) + (0.027 \cdot \theta_{E1}) \quad (12).$$

Using only one diameter as input, which may be most practical for clinical purposes in terms of making a balance between predictability and applicability, would result in a prediction of 75.7% of the variance:

$$L'_{E16} = -19.605 + (1.498 \cdot D_1) + (0.027 \cdot \theta_{E1}) \quad (13).$$

In this respect it is important to realize that the diameter(s) in equations 11, 12 and 13 can be measured directly from the pre-operative scan without the need of special programs, while it provides a guidance for the surgeon to control the insertion depth.

As an alternative approach for development of an insertion guidance tool, the spiral fitting method was evaluated, which was an extension to fitting a logarithmic spiral to the outer wall curvature as described by Van der Marel et al. (2014). General linear regression modelling was applied to adjust the arc length, i.e., the predicted linear insertion depth (L_{E1}), to the more medial position of the electrode array. However, using this method, the residuals between the predicted and true surgical insertion distance showed standard deviations of 1.2 mm, which are greater than the standard deviations of 0.9 mm of the final model using multiple regression analysis. In line with this, the goodness-of-fit when predicting the insertion depth was better for the regression model (mean residual error 0˚, SD 33˚) than for the spiral model (mean residual error 15˚, SD 82˚).

The poorer predictive performance of the spiral fitting method could be due to the fact that the coefficients are determined by fitting a spiral on the basis radial distances which are only measured within the basal turn of the cochlea. These coefficients are then used for predictions of the arc length from the center of the round window to a target angle, which in most cases, is located far beyond the basal turn of the cochlea. Although the method was shown to be accurate in describing the outer wall arc length in the basal turn of the cochlea, predictions of arc length far beyond this point may not be as accurate. This accuracy might be improved by adding more measurements in the basal turn and/or by extending the measuring into the second turn of the cochlea to achieve better spiral fits, which would then be based on more and wider spread measurement points. Extension of measurements into the (much smaller) second turn of the cochlea may be complicated by voxel size limitations of clinical CT-scans.

Many studies have described that the type of implant influences electrode position (Tykocinski et al. 2000; Kos et al. 2005; Radeloff et al. 2008). The fact that the present study is limited to the highly comparable HiFocus1 and HiFocus1J electrodes of Advanced Bionics and uses a uniform surgical approach, enabled clear evaluation of the feasibility and performance of a predictive model. On the other hand, this puts also a limit to the interpretation of the data, as on the basis of the present study no assumptions can be made for other implant types or surgical techniques. Adjustments to the current model are probably necessary. These adjustments may be provided by manufacturers when introducing a new implant type on the market, as they exhaustively test new prototypes in temporal bone studies and afterwards have access to large patient populations from multiple cochlear implant centers that may use a different surgical technique.

The analysis on frequency mismatch (ΔF) between mapped frequency and physiological frequency showed that there exists a relatively broad range of insertion depths for which the mismatch is 2 to 6 semitones, but ΔF was up to 23 semitones in the study sample. The clinical relevance of having a small mismatch is still under discussion in the field of cochlear implantation and this study does not provide any evidence that it results in better performance outcomes of CI patients.

It is important to note that the frequency mismatch calculations were based on the model predictions that the spiral ganglion is the target of electrical stimulation (Kalkman et al. 2014, Stakhovskaya et al. 2007). To minimize frequency mismatch for the studied HiFocus 1 or 1J array estimated insertion distance and angular insertion depth of 6.7 mm and 484°, respectively would be required. However, if the basilar membrane (BM) is assumed to be target site of excitation a shift in these estimations is observed. In that case, the estimated optimal insertion distance and insertion depth to minimize frequency mismatch would be 8.4 mm and 537 ° (data not presented in the figures). So, the frequency mismatch outcomes strongly depend on assumptions about the hypothetical stimulation target.

For the studied population the mean insertion distance and insertion depth with the HiFocus 1 or 1J array were 6.5 mm and 480°; in case of the SG as target site the average electrode array is already optimally positioned, whereas in case of the BM the position is clearly suboptimal. Moreover, it should be noted that the average achieved insertion depth with a certain electrode type also varies among different CI centers influencing the frequency mismatch (Landsberger et al. 2015).

Apart from another potential advantage of the use of insertion models in cochlear implantation surgery, it supports the need for availability and development of electrode arrays of varying lengths to accommodate different cochlear sizes. Because frequency-mismatch is a function of both insertion depth and electrode length, it is hypothesized that changing the array length adjusting to cochlear size might further minimize it.

Although the analysis on the relationship between the frequency mismatch and final speech perception in quiet showed no significant correlation, it is hypothesized on the basis of available research with vocoder simulations that the patients with a small frequency mismatch may show a faster initial increase in phoneme scores than the patients with a larger frequency mismatch and/or better speech perception in noise (Baskent & Shannon, 2007; Li & Fu, 2010). However, the current dataset does not provide the information required to perform such an analysis. Further studies are currently conducted on this topic.

This study applied two different methods (spiral fitting and multiple linear regression) to develop insertion models, which could assist the surgeon during surgery in reaching the preferred position of the electrode array within the cochlea. In a previous study principal components (PCA) and spiral fitting coefficients of the outer cochlear wall were considered as input parameters in regression models (Van der Marel et al. 2014). However, those variables required a more time-consuming analysis, and did not lead to substantially higher correlation coefficients compared to the direct cochlear size measures. Therefore they were discarded as input parameters in the present study.

To summarize, the present study has led to the formulation of insertion models of varying complexity (Eqs. 11-13) which are expected to predict over 75% to 78% of the variation in insertion depth by providing an estimated surgical insertion distance (L'_{E16}) in future data. Further prospective research is needed to analyze the validity of the model and to evaluate whether this guidance tool will lead to better performance of implantees.

At the risk of over-simplifying, the following general guidelines for everyday clinical practice can be formulated on the basis of this study, which will help surgeons to more consistently reach the preferred position of HiFocus 1 and 1J electrode arrays in future surgeries:

- The HiFocus 1 or 1J array of Advanced Bionics should be positioned at a surgical insertion distance of 5.5 to 8 mm to achieve minimal frequency mismatch. A deeper insertion is likely to result in a large frequency mismatch, which might influence performance outcomes adversely.
- If a specific insertion depth is aimed at, the optimal surgical insertion distance differs approximately 2.5 mm between a 'small' and a 'large' cochlea (e.g., between 5.5 mm and 8 mm for 480°) (Figure 3).
- Therefore, it is beneficial to determine cochlear size with preoperative imaging (based on diameter measurements), as it can tell the surgeon whether he/she should try to achieve a surgical insertion distance of around 6, 7 or 8 mm for a 'small', 'medium' or 'large' cochlea, respectively, in order to reach an optimal tonotopic position (Figure 2).

REFERENCES

1. Adunka, O. & Kiefer, J. (2006). Impact of electrode insertion depth on intracochlear trauma. *Otolaryngol.Head Neck Surg., 135,* 374-382.
2. Arnoldner, C., Helbig, S., Wagenblast, J., et al. (2010). Electric acoustic stimulation in patients with postlingual severe high-frequency hearing loss: clinical experience. *Adv.Otorhinolaryngol., 67,* 116-124.
3. Aschendorff, A., Kromeier, J., Klenzner, T., et al. (2007). Quality control after insertion of the nucleus contour and contour advance electrode in adults. *Ear Hear., 28,* 75S-79S.
4. Baskent, D. & Shannon, R. V. (2005). Interactions between cochlear implant electrode insertion depth and frequency-place mapping. *J.Acoust.Soc.Am., 117,* 1405-1416.
5. Baskent, D. & Shannon, R. V. (2005). Combined effects of frequency compression-expansion and shift on speech recognition. *Ear Hear., 28,* 277-289.
6. Boex, C., Baud, L., Cosendai, G., Sigrist, A., Kos, M. I., & Pelizzone, M. (2006). Acoustic to electric pitch comparisons in cochlear implant subjects with residual hearing. *J.Assoc.Res.Otolaryngol., 7,* 110-124.
7. Boyd, P. J. (2011). Potential benefits from deeply inserted cochlear implant electrodes. *Ear Hear., 32,* 411-427.
8. Biedron, S., Prescher, A., Ilgner, J., et al. (2010). The internal dimensions of the cochlear scalae with special reference to cochlear electrode insertion trauma. *Otol. Neurotol., 31,* 731-737.
9. Briggs, R. J., Tykocinski, M., Saunders, E., et al. (2001). Surgical implications of perimodiolar cochlear implant electrode design: avoiding intracochlear damage and scala vestibuli insertion. *Cochlear.Implants. Int., 2,* 135-149.
10. Briggs, R. J., Tykocinski, M., Xu, J., et al. (2006). Comparison of round window and cochleostomy approaches with a prototype hearing preservation electrode. *Audiol. Neurootol., 11 Suppl 1,* 42-48.
11. Buchman CA, Dillon MT, King ER, Adunka MC, Adunka OF, Pillsbury HC. Influence of cochlear implant insertion depth on performance: a prospective randomized trial. *Otol Neurotol* 2014;35:1773-1779.
12. Carlyon, R. P., Macherey, O., Frijns, J. H., et al. (2010). Pitch Comparisons between Electrical Stimulation of a Cochlear Implant and Acoustic Stimuli Presented to a Normal-hearing Contralateral Ear. *J.Assoc.Res. Otolaryngol., 11,* 625-640.
13. Erixon, E., Hogstorp, H., Wadin, K., et al. (2009). Variational anatomy of the human cochlea: implications for cochlear implantation. *Otol.Neurotol., 30,* 14-22.
14. Escude, B., James, C., Deguine, O., et al. (2006). The size of the cochlea and predictions of insertion depth angles for cochlear implant electrodes. *Audiol. Neurootol., 11 Suppl 1,* 27-33.
15. Eshraghi, A. A., Yang, N. W., & Balkany, T. J. (2003). Comparative study of cochlear damage with three perimodiolar electrode designs. *Laryngoscope, 113,* 415-419.
16. Faulkner, A., Rosen, S., & Norman, C. (2006). The right information may matter more than frequency-place alignment: simulations of frequency-aligned and upward shifting cochlear implant processors for a shallow electrode array insertion. *Ear Hear., 27,* 139-152.
17. Finley, C. C., Holden, T. A., Holden, L. K., et al. (2008). Role of electrode placement as a contributor to variability in cochlear implant outcomes. *Otol.Neurotol., 29,* 920-928.
18. Greenwood, D. D. (1990). A cochlear frequency-position function for several species--29 years later. *J.Acoust.Soc.Am., 87,* 2592-2605.
19. Gstoettner, W., Kiefer, J., Baumgartner, W. D., Pok, S., Peters, S., & Adunka, O. (2004). Hearing preservation in cochlear implantation for electric acoustic stimulation. *Acta Otolaryngol., 124,* 348-352.
20. Hamzavi, J. & Arnoldner, C. (2006). Effect of deep insertion of the cochlear implant

electrode array on pitch estimation and speech perception. *Acta Otolaryngol., 126,* 1182-1187.

21. Hochmair, I., Arnold, W., Nopp, P., et al. (2003). Deep electrode insertion in cochlear implants: apical morphology, electrodes and speech perception results. *Acta Otolaryngol., 123,* 612-617.
22. Holden, L. K., Finley, C. C., Firszt, J. B., et al. (2013). Factors affecting open-set word recognition in adults with cochlear implants. *Ear Hear., 34,* 342-360.
23. Kalkman, R. K., Briaire, J. J., Dekker, D. M. T., et al. (2014). Place pitch versus electrode location in a realistic computational model of the implanted human cochlea. *Hear.Res. 315,* 10-24.
24. Ketten, D. R., Skinner, M. W., Wang, G., et al. (1998). In vivo measures of cochlear length and insertion depth of nucleus cochlear implant electrode arrays. *Ann.Otol.Rhinol. Laryngol.Suppl, 175,* 1-16.
25. Kos, M. I., Boex, C., Sigrist, A., et al. (2005). Measurements of electrode position inside the cochlea for different cochlear implant systems. *Acta Otolaryngol., 125,* 474-480.
26. Landsberger DM, Svrakic M, Roland JT, Jr., Svirsky M. The Relationship Between Insertion Angles, Default Frequency Allocations, and Spiral Ganglion Place Pitch in Cochlear Implants. *Ear Hear* 2015;36:e207-e213.
27. Li, T. & Fu, Q.J. (2010). Effects of spectral shifting on speech perception in noise. *Hear. Res., 270*, 81-88.
28. Radeloff, A., Mack, M., Baghi, M., et al. (2008). Variance of angular insertion depths in free-fitting and perimodiolar cochlear implant electrodes. *Otol.Neurotol., 29,* 131-136.
29. Stakhovskaya O, Sridhar D, Bonham BH, Leake PA (2007). Frequency map for the human cochlear spiral ganglion: implications for cochlear implants. *J Assoc Res Otolaryngol., 8*, 220-233.
30. Steyerberg, E. W. (2009). Overfitting and Optimism in Prediction
31. Models. In *Clinical Prediction Models; A Practical Approach to Development, Validation, and Updatig* (XXVIII ed., pp. 83-100). Springer.
32. Tykocinski, M., Cohen, L. T., Pyman, B. C., et al. (2000). Comparison of electrode position in the human cochlea using various perimodiolar electrode arrays. *Am.J.Otol., 21,* 205-211.
33. van der Beek F. B., Briaire J. J., Frijns J. H. (2015). Population-based prediction of fitting levels for individual cochlear implant recipients. *Audiol Neurootol*., 20, 1-16.
34. van der Marel, K. S., Briaire, J. J., Wolterbeek, R., et al. (2014). Diversity in cochlear morphology and its influence on cochlear implant electrode position. *Ear Hear., 35,* e9-e20.
35. van der Marel KS, Briaire JJ, Verbist BM, Muurling TJ, Frijns JH. The influence of cochlear implant electrode position on performance. *Audiol Neurootol* 2015;20:202-211.
36. Verbist, B. M., Ferrarini, L., Briaire, J. J., et al. (2009). Anatomic considerations of cochlear morphology and its implications for insertion trauma in cochlear implant surgery. *Otol.Neurotol., 30,* 471-477.
37. Verbist, B. M., Frijns, J. H., Geleijns, J., et al. (2005). Multisection CT as a valuable tool in the postoperative assessment of cochlear implant patients. *AJNR Am.J.Neuroradiol., 26,* 424-429.
38. Verbist, B. M., Joemai, R. M., Briaire, J. J., et al. (2010a). Cochlear coordinates in regard to cochlear implantation: a clinically individually applicable 3 dimensional CT-based method. *Otol.Neurotol., 31,* 738-744.
39. Verbist, B. M., Skinner, M. W., Cohen, L. T., et al. (2010b). Consensus panel on a cochlear coordinate system applicable in histologic, physiologic, and radiologic studies of the human cochlea. *Otol.Neurotol., 31,* 722-730.
40. Yoo, S. K., Wang, G., Rubinstein, J. T., et al. (2000). Three-dimensional geometric modeling of the cochlea using helico-spiral approximation. *IEEE Trans.Biomed.Eng, 47,* 1392-1402.

Chapter Six

The Influence of Cochlear Implant Electrode Position on Performance

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ABSTRACT

Objectives

To study the relation between variables related to cochlear implant electrode position and speech perception performance scores in a large patient population.

Design

The study sample consisted of 203 patients implanted with a CII or HiRes90K implant with a HiFocus 1 or 1J electrode of Advanced Bionics. Phoneme and word scores average for 1- and 2-years of follow-up were calculated for 41 prelingually deaf and 162 postlingually deaf patients. Analyses to reveal correlations between these performance outcomes and six position-related variables (angle of most basal electrode contact, surgical insertion angle, surgical insertion, wrapping factor, angular insertion depth, linear insertion depth) were executed. The scalar location, as an indication for presence of intracochlear trauma, and modiolus proximity beyond the basal turn were not evaluated in this study. In addition, different patient-specific variables (age at implantation, age at onset of hearing loss, duration of deafness, preoperative phoneme and word scores) were tested for correlation with performance.

Results

The performance scores of prelingual patients were correlated with age at onset of hearing loss, duration of deafness and preoperative scores. For the postlingual patients performance showed correlations with all 5 patient-specific variables. None of the 6 of the position-related variables influenced speech perception in cochlear implant patients.

Conclusions

Although several patient-specific variables showed correlations with speech perception outcomes, not one of the studied angular and linear position-related variables turned out to have a demonstrable influence on performance.

INTRODUCTION

Cochlear implantation has become a widely accepted therapy for patients with severe-to-profound hearing loss. Since the introduction of this therapy, continuous modifications to design, fitting modalities and surgical techniques have led to gradual improvements in performance outcomes in terms of speech understanding. Still, large individual variations in performance persist among patients. The influence of one of the identified variables affecting CI performance, namely the electrode position, is investigated in this study in a large patient population.

The relation between electrode position and speech perception is an often studied one [Aschendorff et al., 2007; Baskent and Shannon, 2005; Finley et al., 2008; Skinner et al., 2007; van der Beek et al., 2005; Yukawa et al., 2004]. Frequency alignment, the prevention of intracochlear trauma and the preservation of residual hearing are important topics related to this matter. Different aspects of electrode position are studied, such as modiolus proximity, scalar location and insertion depth.

Close proximity to the modiolus has been shown to lower M levels or C levels (depending on the brand) and electrically evoked compound action potential thresholds, which facilitate more focused stimulation and optimization of pulse width [Dorman et al., 2007; Filipo et al., 2008; van der Beek et al., 2005; van Wermeskerken et al., 2009]. According to Briggs et al. [2001], proximity to the modiolus can be achieved without intracochlear damage, provided a free-fitting electrode array of appropriate size and shape is used and inserted in the scala tympani. The findings of van der Beek et al. [2005] are in line with these recommendations. They concluded that electrode designs which are located perimodiolar in the basal region of the cochlea improve speech perception results, as was the case for the Clarion HiFocus 1 with positioner.

Scalar location is also reported to be an influential factor. Radeloff et al. [2008] reported that scala vestibuli insertions often showed greater insertion depths as compared to comparable scala tympani insertions and that angular insertion beyond 390° often suggests scala vestibuli insertions. This, in turn, is reported by Finley et al. [2008] in patients with an Advanced Bionics electrode and Asschendorff et al. [2007] in patients with either Nucleus Contour or Contour Advanced electrode to be associated with poorer speech perception.

The influence of insertion depth remains controversial and the optimal electrode position has yet to be found. In some studies, deep insertions were associated with decreased basal

stimulation [Finley et al., 2008], apical pitch confusion [Gani et al., 2007] and increased intracochlear trauma [Adunka and Kiefer, 2006]. Also, Finley et al. [2008] reported poorer performance outcomes in cases of greater insertion depths of the Advanced Bionics electrodes. On the other hand, deeper insertions are recommended by Baskent and Shannon [2005] and Faulkner et al. [2006] to reduce frequency misalignment and to reach full coverage of the cochlea. Additionally, they suggest that in case of shallow insertions, listening experience and mild frequency compression for the lower frequencies can improve speech perception. Hochmair et al. [2003] concluded from their study on patients with a Med-el Combi 40+ electrode that the apical region supports a significant degree of speech understanding and that distributing contacts over the entire length of the cochlea improves speech perception in both quiet and noisy situations. In accordance with this finding, Yukawa et al. [2004] and Hamzavi and Arnoldner [2006] found deeper insertions to be related to better speech perception outcomes.
Nevertheless, several other studies [Hodges et al., 1999; Kos et al., 2005; Lee et al., 2010] did not find any correlation between speech perception performance and electrode position for several implant types. Moreover, the study of Gani et al. [2007] reports on improvement of speech understanding after deactivation of apical electrodes in some patients with very deep insertions possibly to reduce pitch confusions among their most apical electrodes. The study of Boyd [2011] reports that there is evidence that deeply inserted electrodes of currently available designs produce more intracochlear trauma than shorter arrays. This can result in loss of residual acoustic hearing, reducing potential performance benefits.
Notably, the previously reported studies involved relatively small sample sizes, some of the analyses having been performed on no more than 4 patients with 1 implant type [Baskent and Shannon, 2005]. Hamzavi et al. [2003] studied performance in the largest group, consisting of 66 patients, though implanted with 6 implant designs. Most studies were unable to report a significant influence of electrode position-related factors alone and found only associations with speech perception performance if these factors were combined with other patient specific variables [Yukawa et al., 2004]. Also, controlling for various implant types or other patient-specific influential factors, like duration of deafness or age at implantation, is not possible without a large sample size. Thus the relation between electrode position and speech perception performance remains unclear.

For this reason, the goal of this study was to analyze the relation between speech perception performance (phoneme and word scores) and variables defining the electrode position in a large patient population, while controlling for patient-specific variables like duration of deafness, age at onset of hearing loss, age at implantation and etiology of deafness. This study investigates the influence of electrode position-related variables suggested by previous studies to influence speech perception, like angular and linear insertion depth, wrapping factor (modiolus proximity), surgical insertion distance, surgical insertion angle and angle of most basal electrode contact, while minimizing variability by restricting to a single electrode design.

METHODS

Patients

For this study, 203 patients implanted between 2002 and 2011 at the Leiden University Medical Center with a CII or HiRes90K implant with a HiFocus 1 or 1J electrode of Advanced Bionics were included. Preoperative imaging of these patients showed no anatomical anomalies and the surgery, performed by three surgeons using an extended round window (RW) insertion, resulted in complete and uncomplicated insertions. The surgical approach consisted of a mastoidectomy and a posterior tympanotomy resulting in exposure of the RW niche. This was followed by drilling away of the subiculum, the bony overhang over the RW, and the crista ante fenestram, an anterior inferior extension of the RW, ensuring that the electrode array could be securely inserted inside the cochlea. Cochlear malformations and abnormal or incomplete insertions were reasons to exclude patients from this study. Only patients of whom speech perception scores of at least a 1-year follow-up were available were included. Bilaterally implanted patients and children younger than 12 years at time of measuring the 1-year follow-up speech perception scores were excluded from this study. Demographic details with regard to the hearing loss of the studied population are shown in table I. In the table, details are separately for prelingual and postlingual patients. Here, prelingual deafness was defined as the presence of bilateral, moderate (40-60 dB) to profound (>90 dB) hearing loss at or before the age of 4 years. By applying this definition, the studied population consisted of 41 prelingual patients and 162 postlingual patients.

Table I. Demographics of the patients (n=203)

	Prelingual	Postlingual
Gender	Patients N (%)	
Male	12 (29)	73 (45)
Female	29 (71)	89 (55)
Age at onset of hearing loss, years	1 ± 1	20 ± 19
Duration of deafness, years	37 ± 12	22 ± 18
Age at implantation, years	39 ± 12	56 ± 15
Etiology		
Congenital	30 (73)	56 (35)
Hereditary	11	45
Syndromic	2	4
Non-syndromic	1	1
Unknown	8	40
Acquired	6	5
Hyperbilirubinemic encephalopathy	1	-
Infectious	3	5
O_2-deficience	1	-
Unknown	1	-
Unknown	13	6
Acquired	4 (10)	53 (33)
Infectious	2	22
Meningitis	2	17
Other Infection	-	5
Ototoxity	2	8
Trauma	-	7
Skull base fracture	-	3
Other trauma	-	4
Otosclerosis	-	6
Meniere's disease	-	5
Unknown	-	5
Unknown	7 (17)	53 (33)

Values are patient numbers with percentages in parentheses or means ± SD.

Speech Perception

Patients implanted at the Leiden University Medical Center receive intensive rehabilitation training after cochlear implantation, starting at hook-up, 4-6 weeks after the implantation. The rehabilitation program consists of 4 weeks of intensive daily hearing rehabilitation sessions with a specialized speech therapist. After this intensive program, the frequency of training sessions is decreased and tailored to the patient's needs. Especially during the first weeks, regular implant fittings (up to 9 in the first year) are scheduled to optimize speech perception.

Speech perception is tested at set intervals to evaluate and document the progress. Table II shows the mean preoperative and postoperative test scores for the prelingual and postlingual patients. A standard Dutch speech audiometric test of the Dutch Society of Audiology, consisting of phonetically balanced monosyllabic CVC word lists, is used to measure speech perception [Bosman and Smoorenburg, 1995]. All material is presented through a loudspeaker, 1 m in front of the patient, in quiet (65 and 75 dB SPL) and in the speech-shaped noise from the same recording. To improve test accuracy, 4 lists (44 words) are administered for each condition and the test scores obtained at 65 and 75 dB are averaged.

For this study the phoneme and word scores, quantified as percentage phoneme and words correct, measured 1 and 2 years after implantation, were used as performance outcome. If speech perception was tested in both years, the scores were averaged. The speech perception scores at 1 and 2 years represent steady-state outcomes, which were confirmed with paired t tests between both scores, if available, showing nonsignificant differences between the phoneme and word scores measured 1 and 2 years after implantation using SPSS (SPSS version 17.0 for Windows; SPSS Inc., Chicago, Ill., USA). The phoneme scores did not differ significantly between the first and second year: 1-year phoneme score at 65dB SPL, mean = 70.34, SD = 20.91, and 2-year phoneme score, mean = 70.60, SD = 21.18, $t(126) = -0.33$, $p = 0.74$; 1-year phoneme score at 75 dB SPL, mean = 67.07, SD = 20.81, and 2-year phoneme score, mean = 68.22, SD = 20.44, $t(120) = -1.64$, $p = 0.10$.

Also, no significant difference in word scores was found between the measurements at the first and second year after implantation: 1-year word score at 65 dB SPL, mean = 49.46, SD = 25.57, and 2-year word score, mean = 49.84, SD = 25.67, $t(126) = -0.36$, $p = 0.72$; 1-year word score at 75 dB SPL, mean = 45.31, SD = 24.93, and 2-year word score, mean = 46.26, SD = 24.96, ($t(120) = -0.84$, $p = 0.40$. For 76 patients, however, only the first- or the second-year measurement was available, so only 1 score was used in the following analysis.

Table II. Mean speech perception scores

	Prelingual (n=41)		Postlingual (n=162)
Preoperative (% correct)		Mean (SD)	
Phoneme score	15.2 (10.8)[1]		29.8 (17.9)[2]
Word score	2.6 (4.0)[1]		10.1 (11.1)[2]
Postoperative [3](% correct)		Mean (SD)	
Phoneme score	39.1 (22.9)		73.6 (18.6)
Word score	17.2 (20.2)		53.6 (21.9)

[1] Preoperative scores of 4 prelingual patients missing. [2] Preoperative scores of 12 postlingual patients missing. [3] Average of 1 and 2 year post implantation test scores, if both scores were available.

Electrode Position Analysis

All of the studied patients were implanted with a HiFocus 1 (n = 14) or HiFocus 1J (n = 189) electrode array of Advanced Bionics without a positioner. The HiFocus 1 and HiFocus 1J arrays are almost identical except for the configuration of silicone at the jog region, i.e. the forward superior side of the proximal end was removed on the 1J for better visibility. The distance from the non-stimulating marker to the jog is 2 mm longer on the HiFocus 1J than on the HiFocus 1. The 16 active electrode contacts are placed medially, spanning a distance of around 17 mm. The distance from the center of one contact to the next is approximately 1.1 mm. The distance from electrode 16 to the nonstimulating marker is approximately 2 mm, and the distance from the marker to the jog is approximately 3 mm. The approximate angular insertion depth is intended to be between 400 and 500° into the cochlea [Skinner et al., 2007]. Oblique multiplanar reconstructions, parallel to the basal turn of the cochlea, were created of the postoperative CT scans on a Vitrea work station (Vitrea 2; Vital Images, Minnetonka, Minn., USA). The multiplanar reconstructions were analyzed with a Matlab postprocessing program (Matlab, Mathworks, Novi, Mich., USA), developed in-house, by applying a 3-dimensional coordinate system [van der Marel et al., 2014; Verbist et al., 2010a]. This coordinate system, shown in Figure 1, is a combination of the 2 axes (4 radii, i.e. radii 1, 3, 5 and 7) derived from the consensus panel on cochlear coordinates [Verbist et al., 2010b] and the 2 axes (radii 2, 4, 6 and 8) of the Leiden coordinate system of Verbist et al. [2010a]. The electrode position of each contact was determined on the reconstructions (multiplanar reconstructions, voxel size: 0.015 mm^3) in an angular and linear manner, as shown in Figure 1.

On the cross section through the basal turn, shown in Figure 1A, the distance from the RW to the most basal electrode contact 16 (E16), indicated as RW_E16, was calculated using the angles and radial distances to the center of the modiolus. This distance (RW_E16) was referred to as 'surgical insertion'. For shallow insertions a linear approximation of this distance would suffice. However, for deeply inserted arrays, the linear distance from RW to E16 crosses the modiolus, hereby underestimating the true length along the cochlear spiral. The arc along the spiral from RW to E16 can be approximated by fitting an Archimedean spiral through both points [van der Marel et al., 2014]. The distance (RW_E16) along the spiral from RW to E16 is then the given by:

$$S(\theta) = \left(a \cdot \sqrt{1+b^2} \cdot e^{b\theta(E16)} - 1\right)/b, \quad (1)$$

with a=$r(RW)$ and $b = ln\frac{r(E16)}{r(RW)} \cdot \frac{1}{\theta(E16)}$, where θ_{E16} is the corresponding angle of E16 measured from RW, $r(E16)$ is the radial distance from E16 to modiolus center, $r(RW)$ is radial distance from center of the RW to the modiolus center. From the defined 'surgical insertion', one can calculate the linear insertion depth by adding the length of the array (17 mm for the implant used in this study). This value is added to the results as this is often the reported variable in the literature.

The insertion angle by which the surgeon inserts the array is defined as the angle ϕ between the tangent and the radial line of the fitted spiral from RW to E16. This angle is described by $\phi = \arctan\frac{1}{b}$. This angle is referred to as 'surgical insertion angle', as this influences the direction by which the electrode is inserted into the cochlear canal and the position where it reaches the outer wall of the canal.

In the cross section at the level of the upper basal to middle turn, depicted in Figure 1B, the positions of the more apical electrode contacts of the array were determined. The angle measured from the RW to the most apical electrode contact is designated the 'angular insertion depth'. The linear distance from the RW to the most apical electrode contact was referred to as 'linear insertion depth'. This linear insertion depth was derived from the sum of the surgical insertion distance (RW_E16) and the active array length of the HiFocus 1 or 1J electrode of 17 mm. In line with the method of Holden et al. [2013], the so-called 'wrapping factor' was calculated; this is a ratio between 0 and 1 classifying the position of the electrode array from a complete lateral (1) to a more medial position along the first turn (Figure 1c). According to this method, the distance along the electrode array from the RW to the 360° position (gray line) was divided by the corresponding circumference along the outer wall of the cochlea (white line). Thus, if the electrode lies completely against the outer wall of the cochlea in the basal turn, its position would be described as completely lateral and the wrapping factor would be 1. The closer the electrode is located to the modiolus, the smaller becomes the distance along the array to the 360° position (gray line), resulting in a smaller ratio (<1). In 5 patients, the insertion was shallow, and the angular insertion depth of the array was <360°, so for those cases the wrapping factor could not be determined. Since the average angular insertion depth was not significantly different ($p = 0.35$) between the HiFocus 1 (insertion depth in degrees: mean = 497, SD = 108, min. = 358, max. = 678) and the HiFocus 1J patients (insertion depth in degrees: mean = 479, SD = 64, min. = 303, max. = 648) further analyses were performed for the complete population of 203 patients. The average outcomes for the electrode positioning variables are shown in table III. The average angular insertion depth was 480° (SD = 67, R = 375), the angular depth of the most basal electrode contact (E16) was 76° (SD = 28, R = 171) and the wrapping factor was

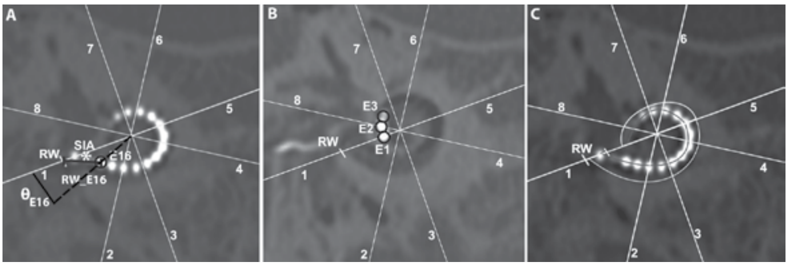

Figure 1. Electrode position measurements on postoperative multiplanar reconstructions. **A** Surgical insertion (RW_E16), angle of E16 and surgical insertion angle (SIA) on the basal turn cross section. The surgical insertion is indicated by the black arc (RW_E16), and the surgical insertion angle is the angle between the tangent and the radial line of the fitted spiral from RW to E16, indicated by the white asterisk. The angle of electrode 16 (θ_{E16}) is the angle between radius 1 and the dotted line through the center of E16; **B** Angular insertion depth (θ_{E1}) and linear insertion depth (from RW to most apical electrode contact 1), where the most apical electrode is indicated by the black circle around E1 on the middle to apical turn cross section; **C** Wrapping factor measurements, where the electrode array length until 360° (gray line) was divided by the cochlear outer wall length until 360° (white line); E1, E2, E3 = Apical electrode contacts 1, 2 and 3.

Table III. Electrode positioning variables

Electrode positioning	Mean (SD)
Angle E16 (θ_{E16}) (degrees)	76 (28)
Surgical Insertion Angle (SIA)(°)	64 (11)
Surgical Insertion (mm)	6.4 (1.9)
Wrapping Factor[1]	.90 (.04)
Insertion Depth (θ_{E1})(°)	480 (67)
Linear Insertion Depth (mm)	23.4 (1.9)

[1] For 5 patients wrapping factors could not be calculated because insertion depth was <360°.

0.9 (SD = 0.04, R = 0.29). The surgical insertion angle was 64° (SD = 11, R = 70) on average. Furthermore, the average surgical insertion was 6.4 mm (SD = 1.9, R = 11.7), resulting in a linear insertion depth of 23.4 mm.

Statistical Analyses

Correlations between patient-specific variables and performance were calculated using SPSS (SPSS version 17.0 for Windows; SPSS Inc., Chicago, Ill., USA) and p value of <0.05 was considered significant. Since previous studies have revealed the positive influence of certain patient-specific variables, for this analysis correlation coefficients were calculated using a 1-tailed test. In addition, a Bonferroni correction was applied to lower the p values to a more conservative significance level. Since the influence of 5 patient-specific variables was analyzed, the significance level of <0.5 was divided by 5 resulting in $p < 0.01$ to be considered significant. In addition, the relation between electrode position and performance was analyzed. Partial correlation coefficients with performance were calculated for all position-related variables, while controlling for patient-specific variables that showed significant correlation with performance. Since not much is known about the possible relation between these position-related variables and performance, for these analyses correlation coefficients were calculated using 2-tailed tests. A Bonferroni correction was applied post hoc, and so the significance level was changed by dividing the p value of 0.05 by 6 (number of position-related variables), resulting in a p value of <0.008 to be considered significant.

RESULTS

In table IV, the outcomes of the analyses between patient-specific variables and performance scores are presented, separately for prelingual and postlingual patients. The relation was analyzed by calculation of the correlation coefficients. In the prelingual patient group, phoneme scores were correlated with age at onset of hearing loss ($R^2 = 0.31$; $p = 0.02$), duration of deafness ($R^2 = 0\text{-}.26$; $p = 0.05$), preoperative phoneme score ($R^2 = 0.46$; $p < 0.01$) and preoperative word score ($R^2 = 0.37$; $p = 0.01$). After Bonferroni correction, only preoperative phoneme score remained significantly correlated with the postoperative phoneme scores. The word scores of this prelingual group were correlated with the same patient-specific variables, except for duration of deafness ($p = 0.15$). After Bonferroni correction, the word scores were also only significantly correlated with preoperative phoneme score.

In the postlingual patient group, all tested patient-specific variables were significantly correlated with performance at the significance level op $p < 0.05$, except for age at implantation. Age at implantation showed a p value of 0.05 ($R^2 = -0.13$) when correlated to postoperative phoneme score. The phoneme scores showed strong correlations ($p < 0.01$) with duration of deafness ($R^2 = -0.34$), and with preoperative phoneme ($R^2 = 0.22$) and word scores ($R^2 = 0.20$) and remained significant after the Bonferroni correction.

Table IV. Correlations between patient-specific variables and performance

	Prelingual (n=41) Speech perception scores (% correct)		Postlingual (n=162) Speech perception scores (% correct)	
Correlations	Phoneme score *R (p-value)*	Word score *R (p-value)*	Phoneme score *R (p-value)*	Word score *R (p-value)*
Age at implantation (Yrs)	-.22 (.09)	-.13 (.21)	-.13 (.05)	-.17* (.01)
Age at onset of HL (Yrs)	.31*(.02)	.28*(.04)	.17* (.02)	.17* (.01)
Duration of deafness (Yrs)	-.26*(.05)	-.17 (.15)	-.34 ** (.00)	-.37** (.00)
Preoperative phoneme score (% correct)[1]	.46**(.00)	.40**(.00)	.22**(.00)	.21** (.00)
Preoperative word score (% correct)[1]	.37*(.01)	.35*(.02)	.20**(.00)	.20** (.00)

One-tailed correlation coefficients (R) with p-value in the parenthesis. (*p<.05; **p<.01). The significance level after Bonferroni correction was p<0.01. [1] Preoperative scores of 4 prelingual and 12 postlingual patients were missing.

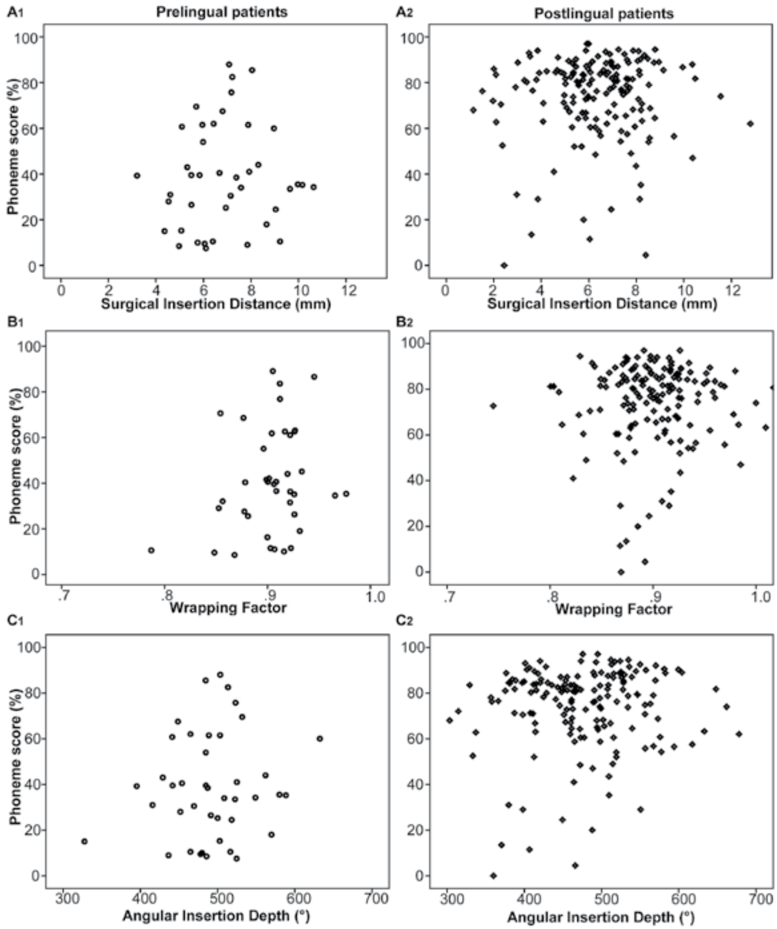

Figure 2. Scatterplots of the relation between electrode position variables (A Surgical insertion; B Wrapping factor; C Angular insertion depth) and phoneme scores for prelingual (A1, B1, C1) and postlingual (A2, B2, C2) patients.

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The word scores also showed strong correlations with these variables ($p < 0.01$). In Figure 2, phoneme scores were plotted against 3 of the position-related variables: surgical insertion distance (A), wrapping factor (B) and angular insertion depth (C). Both for the prelingual (A1, B1, C1) and postlingual (A2, B2, C2) patients, no relation can be observed between phoneme scores and surgical insertion distance, wrapping factor or angular insertion depth, respectively.
Next, the relation between electrode position-related variables and performance was analyzed in more detail by calculating correlation coefficients with 2-tailed tests. Partial correlations were calculated, while adjusting for the patient-specific variables that showed significant correlations with performance in the previous analysis. As shown in table V, none of the position-related variables was significantly correlated with performance. Even without controlling for the patient-specific variables, no correlation was found between electrode position-related variables and performance.

DISCUSSION

This is the first study that evaluated the relation between electrode position-related variables and performance in a large population of cochlear implant patients implanted with a straight electrode design, while also controlling for other influential patient-specific variables (age at implantation, age at onset of hearing loss, duration of deafness, preoperative phoneme and word scores). The influence on performance of several patient-specific variables known from the literature was confirmed by significant correlations, both for prelingually and postlingually deaf patients, but no relation between electrode position-related variables and performance could be demonstrated.
For postlingually deaf patients, after Bonferroni correction 3 of the 5 patient-specific variables, i.e. duration of deafness and preoperative phoneme and word scores, were significantly correlated with performance, both with phoneme and word scores. The outcomes of this study, performed in a large homogenous population, are in line with findings of Lee et al. [2010], Gomaa et al. [2003] and Finley et al. [2008]. The variable age at implantation was also found to correlate with performance by Lee et al. [2010], though in their study this relation disappeared after elimination of 2 very good performers. Gomaa et al. [2003] and Finley et al. [2008] found duration of deafness and preoperative performance to be correlated with

Table V. Partial correlations between electrode position and performance

	Prelingual (n=37)[1] Speech perception scores (% correct)		Postlingual (n=146)[2] Speech perception scores (% correct)	
Partial Correlations	Phoneme score[3] *R (p-value)*	Word score[3] *R (p-value)*	Phoneme score[4] *R (p-value)*	Word score[4] *R (p-value)*
Angle E16 (θ_{E16})(°)	.02 (.93)	.02 (.90)	-.002 (.98)	.002 (.98)
Surgical Insertion Angle (SIA) (°)	-.12 (.51)	-.16 (.38)	.02 (81)	.03 (.67)
Surgical Insertion (mm)	.008 (.96)	.03 (.88)	-.02 (.86)	-.005 (.95)
Wrapping Factor[1]	.35 (.03)	.29 (.09)	.04 (.67)	.03 (.69)
Insertion Depth(θ_{E1}) (°)	.02 (.90)	.07 (.69)	.02 (.85)	.01 (.89)
Linear Insertion Depth (mm)	.008 (.96)	.03 (.88)	-.02 (.86)	-.005 (.95)

Two-tailed partial correlation coefficients (R), adjusted for patient-specific variables with p-value in the parenthesis. After Bonferroni correction a significance level of $p<0.008$ was considered significant (*$p<.008$). [1] Controlling variable preoperative phoneme scores was missing for 4 patients. [2] Controlling variable preoperative phoneme scores was missing for 12 patients and wrapping factors could not be calculated due to shallow insertions for 4 patients. [3] Prelingual speech perception scores with controlling variable: preoperative phoneme score. [4] postlingual speech perception scores with controlling variables: duration of deafness, preoperative phoneme score and preoperative word score.

postoperative outcomes. On the contrary, Hamzavi et al. [2003] and Lee et al. [2010] found no such association with duration of deafness. The study performed by Hodges et al. [1999] found none of the patient-specific variables to be related with performance, while Waltzman et al. [1995] did find significant, although weak correlations between patient characteristics and performance, including the same variable as in this study, duration of deafness and age at implantation. Overall, this study did reveal significant influence of patient-specific variables on performance, thus confirming the need to control for these variables when analyzing relations with other variables.

In the prelingually deaf patients group, consisting of 41 patients, after Bonferroni correction, significant correlations were only found between performance and preoperative phoneme scores. These findings are in contrast with the previous study by Klop et al. [2007], who reported no correlations between several patient factors (age at implantation, duration of deafness, preoperative CVC scores) and performance in 8 studied prelingual adolescents. Van Dijkhuizen et al. [2011] concluded that for prelingual patients, preoperative speech perception does predict speech perception outcomes with an implant.

While controlling for patient-specific variables, the relation between electrode position-related variables and performance was analyzed and showed no significant correlations. Even without adjusting for the patient-specific variables, no correlation between electrode position and performance was observed. This finding is in line with studies by Hodges et al. [1999], Kos et al. [2005] and Lee et al. [2010]. However, the results are in contrast with those of Skinner et al. [2002] who found insertion depth as a percentage of total cochlear length to be correlated significantly with word scores. Finley et al. [2008] also reported that lower outcome scores were associated with greater insertion depths. Moreover, Yukawa et al. [2004] also reported significant correlations between a combination of duration of deafness and insertion depth and performance in patients with a Nucleus 22 or 24 cochlear implant with straight electrode. However, they only report on the combination rather than the singular correlation between insertion depth and performance. Their analysis was also performed in the current study population, and neither insertion depth nor an interaction term between insertion depth and duration of deafness reached significance in the regression model with performance as depending variable ($p > 0.6$ and $p > 0.3$, respectively). Duration of deafness, however, was the only significant independent variable showing a very strong relation to performance (R^2 for phoneme scores of -0.26 and -0.34 for pre- and postlingually deaf patients, respectively). Repeating the analysis in this larger study sample thus strongly suggests that the correlation reported by Yukawa et al. [2004] may be completely explained by duration of deafness alone.

The present study was performed among patients who all received a HiFocus electrode, using a controlled surgical technique (extended RW approach with only three surgeons involved), narrowing the spread of surgical insertion angle. The surgical and anatomical factors influencing the final insertion depth were analyzed in depth in two separate studies. It turned out that anatomical factors accounted for approximately 13% of the variance, while surgical ones explained 65% of the variance [van der Marel et al., 2014]. When using a prediction model consisting of anatomical and surgical variables combined, it is possible to explain 78% of the variance in insertion depth [van der Marel, submitted; van der Marel et al., 2014]. The uniformity of the surgical approach and the electrode array allowed clear interpretations of the relation between electrode position and performance without the interfering impact of different implant types. However, it also implicates that conclusions about the relation between performance and electrode position can only be applied to this specific electrode type and surgical technique. It will be left to future studies to analyze this relation for other implant types, preferable also in a population large enough to enable controlling for other influential factors.

The variation in position between different electrode types was also illustrated by calculations of the wrapping factors, when comparing the outcomes of Holden et al. [2013] and this study. The study of Holden et al. [2013] was performed mainly in patients with a Nucleus Contour electrode, which is a tightly wrapped electrode, while the straight HiFocus electrode of Advanced Bionics in this study is much more loosely wrapped around the modiolus. Logically, there was not much overlap, as Holden et al. [2013] found wrapping factors between 0.54 and 0.85, and in this study wrapping factors ranged from 0.74 to 1. Also, precurved designs will generally result in smaller wrapping factors and possibly also in deeper insertions. The findings on the HiFocus MS will follow soon from studies currently performed at our center.

The HiFocus electrode, being a free-fitting electrode, is designed to reach an average depth of approximately 23 mm, which may explain why the study failed to find any relation between position and performance. A negative relation with performance may only be detectable in cases of extreme positioning, either very shallow or very deep insertions, for which the specific implant type is not configured. Indeed, in studies of patients with a Med-El Combi40+ electrode, much deeper insertion depths with averages around 630° are described [Baumann and Nobbe, 2006; Gani et al., 2007; Hamzavi and Arnoldner, 2006; Kos et al., 2005; Radeloff et al., 2008; Vermeire et al., 2008], yet speech perception outcomes remain comparable to those reported with HiFocus implants. This supports the hypothesis that not factors such as electrode length, contact number or intercontact spacing, but rather large discrepancies between the implant configuration (which frequencies are stimulated by which contact) and the position within the cochlea affect performance. Focusing more on frequency place matching could improve performance outcomes, as suggested by Baskent and Shannon [2005].

In this study, an average angular insertion depth of 480° was reached with the HiFocus electrode, and no correlation between basal angle of contact 16 or angular insertion depth with performance was found. However, the same implant type with comparable average angular insertion depth was studied by Finley et al. [2008]. They found that consonant-nucleus-consonant word recognition decreased significantly with increased basal electrode angular depth. This difference may be explained by the fact that they evaluated a small group of patients for whom the basal contacts were on average positioned deeper than in our study. Furthermore, the group of Finley et al. [2008] also found increased basal electrode angular depth to be significantly related to total number of contacts in the scala vestibuli.

In addition, Radeloff et al. [2008] reported that insertions in the scala vestibuli are more likely to result in greater insertion depths. In their study with the C40+ (Med-El, Innsbruck, Austria) and the Contour Soft-Tip (Cochlear Ltd., Lane Cove, N.S.W., Australia) electrodes, an insertion angle of greater than 390° often indicated that the array was located within the scala vestibuli. Therefore, scalar localization may in turn be the underlying factor explaining differences in observed correlations between insertion depths and performance [Aschendorff et al., 2007; Finley et al., 2008]. However, scalar location and intracochlear trauma was not addressed in the present study. Future studies, carried out in a large patient population, are needed to investigate the relation between these factors and performance.

On the basis of this present study, performed in a relatively large and homogeneous patient group, it is concluded that neither measures of linear and angular insertion depth nor the wrapping factor could be identified as significant factors influencing speech perception, both in prelingually and in postlingually deaf patients.

REFERENCES

1. Adunka O, Kiefer J: Impact of electrode insertion depth on intracochlear trauma. Otolaryngol Head Neck Surg 2006;135:374-382.
2. Aschendorff A, Kromeier J, Klenzner T, Laszig R: Quality control after insertion of the nucleus contour and contour advance electrode in adults. Ear Hear 2007;28:75S-79S.
3. Baskent D, Shannon RV: Interactions between cochlear implant electrode insertion depth and frequency-place mapping. J Acoust Soc Am 2005;117:1405-1416.
4. Baumann U, Nobbe A: The cochlear implant electrode-pitch function. Hear Res 2006;213:34-42.
5. Bosman AJ, Smoorenburg GF: Intelligibility of Dutch CVC syllables and sentences for listeners with normal hearing and with three types of hearing impairment. Audiology 1995;34:260-284.
6. Boyd PJ: Potential benefits from deeply inserted cochlear implant electrodes. Ear Hear 2011;32:411-427.
7. Briggs RJ, Tykocinski M, Saunders E, Hellier W, Dahm M, Pyman B, Clark GM: Surgical implications of perimodiolar cochlear implant electrode design: avoiding intracochlear damage and scala vestibuli insertion. Cochlear Implants Int 2001;2:135-149.
8. Dorman MF, Spahr T, Gifford R, Loiselle L, McKarns S, Holden T, Skinner M, Finley C: An electric frequency-to-place map for a cochlear implant patient with hearing in the nonimplanted ear. J Assoc Res Otolaryngol 2007;8:234-240.
9. Faulkner A, Rosen S, Norman C: The right information may matter more than frequency-place alignment: simulations of frequency-aligned and upward shifting cochlear implant processors for a shallow electrode array insertion. Ear Hear 2006;27:139-152.
10. Filipo R, Mancini P, Panebianco V, Viccaro M, Covelli E, Vergari V, Passariello R: Assessment of intracochlear electrode position and correlation with behavioural thresholds in CII and 90K cochlear implants. Acta Otolaryngol 2008;128:291-296.
11. Finley CC, Holden TA, Holden LK, Whiting BR, Chole RA, Neely GJ, Hullar TE, Skinner MW: Role of electrode placement as a contributor to variability in cochlear implant outcomes. Otol Neurotol 2008;29:920-928.
12. Gani M, Valentini G, Sigrist A, Kos MI, Boex C: Implications of deep electrode insertion on cochlear implant fitting. J Assoc Res Otolaryngol 2007;8:69-83.
13. Gomaa NA, Rubinstein JT, Lowder MW, Tyler RS, Gantz BJ: Residual speech perception and cochlear implant performance in postlingually deafened adults. Ear Hear 2003;24:539-544.
14. Hamzavi J, Arnoldner C: Effect of deep insertion of the cochlear implant electrode array on pitch estimation and speech perception. Acta Otolaryngol 2006;126:1182-1187.
15. Hamzavi J, Baumgartner WD, Pok SM, Franz P, Gstoettner W: Variables affecting speech perception in postlingually deaf adults following cochlear implantation. Acta Otolaryngol 2003;123:493-498.
16. Hochmair I, Arnold W, Nopp P, Jolly C, Muller J, Roland P: Deep electrode insertion in cochlear implants: apical morphology, electrodes and speech perception results. Acta Otolaryngol 2003;123:612-617.
17. Hodges AV, Villasuso E, Balkany T, Bird PA, Butts S, Lee D, Gomez O: Hearing results with deep insertion of cochlear implant electrodes. Am J Otol 1999;20:53-55.
18. Holden LK, Finley CC, Firszt JB, Holden TA, Brenner C, Potts LG, Gotter BD, Vanderhoof SS, Mispagel K, Heydebrand G, Skinner MW: Factors affecting open-set word recognition in adults with cochlear implants. Ear Hear 2013;34:342-360.
19. Klop WM, Briaire JJ, Stiggelbout AM, Frijns JH: Cochlear implant outcomes and quality

of life in adults with prelingual deafness. Laryngoscope 2007;117:1982-1987.
20. Kos MI, Boex C, Sigrist A, Guyot JP, Pelizzone M: Measurements of electrode position inside the cochlea for different cochlear implant systems. Acta Otolaryngol 2005;125:474-480.
21. Lee J, Nadol JB, Jr., Eddington DK: Depth of Electrode Insertion and Postoperative Performance in Humans with Cochlear Implants: A Histopathologic Study. Audiol Neurootol 2010;15:323-331.
22. Radeloff A, Mack M, Baghi M, Gstoettner WK, Adunka OF: Variance of angular insertion depths in free-fitting and perimodiolar cochlear implant electrodes. Otol Neurotol 2008;29:131-136.
23. Skinner MW, Holden TA, Whiting BR, Voie AH, Brunsden B, Neely JG, Saxon EA, Hullar TE, Finley CC: In vivo estimates of the position of advanced bionics electrode arrays in the human cochlea. Ann Otol Rhinol Laryngol Suppl 2007;197:2-24.
24. Skinner MW, Ketten DR, Holden LK, Harding GW, Smith PG, Gates GA, Neely JG, Kletzker GR, Brunsden B, Blocker B: CT-derived estimation of cochlear morphology and electrode array position in relation to word recognition in Nucleus-22 recipients. J Assoc Res Otolaryngol 2002;3:332-350.
25. Van der Beek FB, Boermans PP, Verbist BM, Briaire JJ, Frijns JH: Clinical evaluation of the Clarion CII HiFocus 1 with and without positioner. Ear Hear 2005;26:577-592.
26. Van der Marel KS, Briaire JJ, Wolterbeek R, Snel-Bongers J, Verbist BM, Frijns JH: Diversity in cochlear morphology and its influence on cochlear implant electrode position. Ear Hear 2014;35:e9-e20.
27. Van Dijkhuizen JN, Beers M, Boermans PP, Briaire JJ, Frijns JH: Speech intelligibility as a predictor of cochlear implant outcome in prelingually deafened adults. Ear Hear 2011;32:445-458.
28. Van Wermeskerken GK, van Olphen AF, Graamans K: Imaging of electrode position in relation to electrode functioning after cochlear implantation. Eur Arch Otorhinolaryngol 2009.
29. Verbist BM, Joemai RM, Briaire JJ, Teeuwisse WM, Veldkamp WJ, Frijns JH: Cochlear coordinates in regard to cochlear implantation: a clinically individually applicable 3 dimensional CT-based method. Otol Neurotol 2010a;31:738-744.
30. Verbist BM, Skinner MW, Cohen LT, Leake PA, James C, Boex C, Holden TA, Finley CC, Roland PS, Roland JT, Jr., Haller M, Patrick JF, Jolly CN, Faltys MA, Briaire JJ, Frijns JH: Consensus panel on a cochlear coordinate system applicable in histologic, physiologic, and radiologic studies of the human cochlea. Otol Neurotol 2010b;31:722-730.
31. Vermeire K, Nobbe A, Schleich P, Nopp P, Voormolen MH, Van de Heyning PH: Neural tonotopy in cochlear implants: an evaluation in unilateral cochlear implant patients with unilateral deafness and tinnitus. Hear Res 2008;245:98-106.
32. Waltzman SB, Fisher SG, Niparko JK, Cohen NL: Predictors of postoperative performance with cochlear implants. Ann Otol Rhinol Laryngol Suppl 1995;165:15-18.
33. Yukawa K, Cohen L, Blamey P, Pyman B, Tungvachirakul V, O'Leary S: Effects of insertion depth of cochlear implant electrodes upon speech perception. Audiol Neurootol 2004;9:163-172.

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Chapter Seven

Concluding Remarks and Future Perspectives

In this thesis we explored the role of computed tomography imaging in the field of cochlear implantation. The field of cochlear implantation evolves continuously due to extending treatment indications, augmenting insights in surgical approaches and the availability of new sophisticated electrode designs. Imaging will continue to play an important role during these developments. Overall, these developments have one fundamental goal; improving of the performance outcomes of cochlear implantees.

While patients with similar implant types and similar patient specific factors show large variation in performance, the research described in this thesis focused on the possible contribution of electrode position to this matter. This electrode position is known to depend on three factors, namely the cochlea, the design of the electrode and the surgeon. To study the effects of the electrode position, CT scans obtained before and after implantation were evaluated using in house designed software. The LUMC has built up a large imaging database over the years providing the special chance of performing research within a large study sample, while being able to control for other influential variables if necessary. The implementation of a cochlear coordinate system to the post processing software allows good comparison with the outcomes of other studies.

By applying the coordinate system to both preoperative and postoperative CT scans the diversity in cochlear morphology and its influence on CI electrode position was investigated. Since the coordinate system provides many cochlear measurements, several methods of summarizing the cochlear morphology were tested. Two methods of describing cochlear shape, spiral curve fitting and principal component analysis, were evaluated with principal component being the most optimal reduction requiring only 1 principal component, reflecting cochlear size, to explain 93.6% of the variance in outer wall shape of the cochlea. The study discloses the second objective of this thesis by demonstrating individual varieties in cochlear morphology which significantly influences electrode position with regard to modiolus proximity and insertion depth.

The first objective of the thesis was partly answered by the study on the stability of the electrode, where a migration of the electrode was incidentally detected in a patient with device failure. This observation encouraged us to retrospectively identify all patients of whom more than one postoperative CT scan was available and investigate the stability of the electrode. An electrode migration had occurred in 29% of the studied patients. Interestingly, only two of these patients had reported complaints. Therefore, electrode migration was concluded to be more common than previously assumed and showed to occur with and without causing complaints. Supported by these findings, it was hypothesized that after insertion the electrode might need some time to stabilize and that its final position can differ from the position as inserted by the surgeon. This hypothesis might be tested by future prospective research studying electrode stability using multiple postoperative imaging moments.

In addition to the first objective, postoperative imaging was assessed using the extensive database to study various electrode position related variables and their possible relation with speech perception scores. This study, revealing the answers to the third objective, confirmed the influence of several patient-specific variables in both prelingual and postlingual patients and controlled for these influences when studying the relation between electrode position and performance. However, the study found no correlations between electrode-position related variables and performance. Even when the analysis was performed without controlling for patient specific variables, none of the electrode-position related variables showed any correlation to performance. This might be explained by the relative similar electrode position within the studied population. Possibly, only extreme electrode position may be found to correlate with performance outcome.

In line with this, a study performed among patients with device failure showed that the electrode position can be restored very accurately during a reimplantation. Prior to reimplantation the postoperative CT scan was extensively studied to acquire a similar position with the new implant. After reimplantation, new imaging was obtained which confirmed almost similar or small displacements in every case. More importantly, the performance was restored within weeks to at least the level obtained with the original implant. This study covered the other part to the first objective of examining the value of CT during the postoperative period.

These outcomes encouraged us to study the feasibility of developing a surgical guidance tool predicting final electrode position for an individual patient based on preoperative available variables. Such a model could allow surgeons greater control over the ultimate position. Since cochlear size was found to have a significant influence on modiolus proximity as well as insertion depth, several variables describing this size were evaluated as predictors in the insertion model. This study established an extension to the second objective next to the study on cochlear morphology. A surgical guidance tool predicting surgical insertion distance necessary to reach a predefined insertion depth was developed. For this model a combination of 4 cochlear diameters and the preferred insertion depth was able to predict up to 78.1% of the variation in surgical insertion distance.

The research described in this thesis was performed among patients who received a HiRes90K implant with HiFocus electrode using one surgical approach, the extended round window insertion. As described by previous studies, design of the implant and surgical approach are important factors influencing electrode position. Performing the studies under these controlled circumstances allowed clear interpretations of the outcomes. Though, it also implies that conclusions about the outcomes can only be applied to the specific electrode design inserted under the same circumstances. It will be left to future research to analyze these topics with other designs and surgical techniques.

While performing the study on the relation between electrode position and performance, we also found some leads on the most preferable position with regard to minimal frequency mismatch. It is important to note that the goal of this research was not to determine the optimal electrode position. However, for the studied population the analysis of the relation between surgical insertion distance and insertion depth respectively, to frequency mismatch illustrated a range of positions, either measured as distance from round window or insertion depth, wherein minimal frequency mismatch may occur. Positioning of the electrode within this range might thereby provide optimal chances of obtaining good performance with the implant. Future studies focusing on the relation between frequency mismatch and performance, instead of a direct relation between electrode position and performance might reveal new insights.

This research found no relation between any of the electrode position related variables and performance. This outcome may be explained by the fact that for many of the studied patients the electrodes where positioned within this observed range of insertion depth and surgical insertion distance where frequency mismatch is minimal.

Nonetheless, the calculated frequency mismatch might in fact be different considering the findings of the study on electrode stability. This study raised doubts about the actual electrode position as migrations had often occurred when comparing the CT scan obtained 1 day after surgery with a later performed CT scan. The insight that a migration could occur after postoperative imaging was obtained, made us realize that there was a significant chance that the actual electrode position differed from the position detected with imaging. This weakens all previous studies which used direct postoperative imaging to define electrode position and investigate any relations between position and performance.

Indeed, this important finding encouraged us to evaluate our own imaging protocol. Given the chance of migration within the first weeks and the fact that implant is activated around

4-6 weeks after surgery we considered postponing imaging until just before this implant activation. This would allow research on the relation of position with performance and also better evaluation of later occurring performance complaints. Though, implementing this in the protocol inhibits direct postoperative surgical evaluation. This might be solved by introducing a conventional X-ray directly postoperatively to allow confirmation of intracochlear location. On the contrary, direct postoperative evaluation still does not allow direct correction of any unwanted position, while intra-operative imaging does allow this. Radiation exposure is also an important aspect in this matter and forms a difficult task to find a balance between gathering enough knowledge and limiting side-effect as for instance radiation. Cone beam CT may compose the best solution to this dilemma and current research is performed to evaluate the suitability of this imaging technique in cochlear implantation (Hodez 2011, Ruivo 2009).

Anyhow, imaging developers should keep up with implant developers. The development of promising new imaging techniques, like for instance imaging robots (Hussong 2009, Rau 2010, Stieger 2011), are as essential as new implant designs since more detailed and direct information about temporal bone anatomy and electrode position is desired to improve overall outcomes in cochlear implantation. In this research, the available scanner and post-processing software used did not allow detection of intrascalar position or studying of intracochlear trauma. With the prospects of even thinner electrodes with lesser inter-contact spacing in the near future, the quality of imaging may form a limiting factor.

This thesis described great variations in normal developed cochlea's and its influence on electrode position. As indications for cochlear implantation become broader and even patients with single sided deafness, residual hearing and malformed cochleas are now considered a suitable candidate, the role of imaging will logically become even larger. Moreover, these specific cases form an even greater challenge for the surgeon to accurate insert an electrode. This thesis proposes a surgical guidance tool to enable surgeons to simplify this immensely difficult task. Such a guidance tool predicting necessary insertion distance to reach a certain depth for an individual patient is even more crucial in complex cases such as patients with malformed cochleas or residual hearing. Moreover, preoperatively analyzing of cochlear morphology and using an individually adjusted surgical guidance tool might help to prevent intracochlear trauma.

In short, the complex goal of surgeon is to insertion the electrode into the cochlea, placing it close to the modiolus and reaching an insertion depth where a complete frequency range is stimulated without interruption of the delicate intracochlear structures. Considering the diversity in normal cochlear shape combined with the extension in treatment indications with malformed cochlea's or patients with residual hearing, manufacturers of electrodes will probably shift from developing a 'one size fits all' to a 'tailor-made' electrode design. This shift has already begun as Med-El introduced 4 lengths for the Flex electrode, allowing surgeons to choose the suitable length based on cochlear duct length. Future possibilities for new design may include adjustable contact spacing, newer material to reduce trauma, including sensors which guide insertion or shape memory material.

Overall, since restoring hair cell function by stem cell therapy remains uncertain and clinical application is still years from now, cochlear implantation will remain the best treatment of choice to rehabilitate severe to profound hearing loss. A combination of continuous improvements in the fields of imaging, design development, and surgical skills and implant software will hopefully result in optimization of electrode positioning ultimately leading to better performance outcomes in cochlear implant patients.

Chapter Eight

Summary

Disabling hearing loss affects 5% of the world's population, counting for 360 million individuals (328 million adults and 32 million children) as stated by the Worlds Health Organization (WHO 2013). This group has sincerely better prospects on hearing rehabilitation thanks to the availability of cochlear implants nowadays. The expected performance outcomes with this inner ear electrical hearing device are ascertained by the innovative imaging modalities emerging over the same years as the evolvement of the cochlear implant itself. As of today, CT and MRI are complementary used prior to the implantation surgery. These modalities each deliver their own unequivocal insight on the temporal bone anatomy to enable cautious insertion of the implant electrode within the cochlea. Although new CI designs and MRI techniques evolved that enable the use of MRI afterwards without a risk of compromising the implant position, CT has mostly been applied postsurgical if detailed information about the implant or surrounding anatomical structures is desired. The continuous process of expanding treatment indications, improving electrode design, surgical techniques and electrophysiological software enhancements strengthen the role of imaging even more. At the same time, these inventions form a challenging task and might also highlight limitations to current imaging modalities to be assessed in the field of cochlear implantation. The benefits and drawbacks of using CT to evaluate and improve the results of cochlear implantation were the topic of the studies described in this thesis. This thesis unravels the knowledge on cochlear shapes and implant electrode position that can be obtained with computed tomography.

The introduction of this thesis provided by **Chapter 1** formulates the three main objectives of this research and shortly outlines general background information on hearing loss and normal hearing physiology, combined with an overview of the past and present of the cochlear implant, its function, and the implantation procedure in Leiden. Then, a demonstration of standardized imaging and reconstructive techniques of the cochlea, including the applied cochlear coordinate system are presented.

The suspicion of device failures is a common reason to perform postoperative CT to detect or reject this very undesirable event. Though this being a rare event, **Chapter 2** describes anatomical and speech perception performance outcomes in 15 patients who experienced a failure of the HiFocus1J electrode (Advanced Bionics) caused by a defective feed through seal. Comparisons of the electrode position with high resolution CT scans of the original and replacement electrode revealed that the average displacement of the implant was only 0.59 mm. The accurate replacement of the electrode was translated into a rapid restoration of previous speech perception levels, without revealing any relation between the amount of displacement and the performance changes. The reimplanted patients even showed significant improved speech perception scores. This result could possibly be ascribed to the two week period of extra training sessions to rehearse crucial steps of the standard rehabilitation program. The overall lesson that could be learned from these patients was that an unfortunate reimplantation surgery resulting in limited displacement of the electrode will probably lead to rapid adaptation to the new implant and restoration of the speech perception performance when combined with some extra training sessions.

Another phenomenon that is revealed by CT is electrode migration. The finding that electrode migration even occurs in some patients without any changes to performance or causing complaints was documented for the first time by the study described in **Chapter 3**. The migrations were revealed by a retrospective case review of 35 patients (5 patients with complaints; 30 patients without) with two available sequentially obtained postoperative CT scans. In 10 out of the 35 patients a migration (displacement of most basal contact of more than 1 mm) was detected (29%). Two of these migrations were observed because these patients were complaining of performance drop. The other eight patients did not subjectively give any reason to question the previous noted implant position (protocolled obtained one day after surgery). The study of this group showed that the occurence of migration was unrelated to insertion depth, though the newer HiFocus 1J array showed a higher frequency of migration than the predecessor (HiFocus1). This chapter also illustrates an extreme observation of three very large electrode shifts (more than 4 mm displacement when comparing both scans). The fact that in two of these cases several extracochlear contacts were detected could be the explanation for the performance drop reported by these particular patients. The general observation of migration designates first postoperative observation of implant position to be less reliable in some cases and may have large impact on research relating implant position to stimulated tonotopic frequencies and even speech perception performance outcomes.

The preoperative value of CT is delineated in **Chapter 4**, where cochlear morphology is studied and described in various ways. In this chapter the large CT database was first inquired consisting of CT of all CI users since 2000. Pre- and postoperative CT scans of 336 patients were analyzed to detect variations in cochlear diameter, cochlear canal size and outer to inner wall relations. Furthermore, the relation between cochlear shape and electrode position, depth and modiolus proximity, were investigated. Analysis showed that cochlear canal size augments from 0.98 to 2.96 mm and cochlear diameters diminish from 8.85 mm to 5.92 mm. Significant correlations between the inner and outer cochlear wall measurements ($p<0.01$)

and a size difference in favor of males of 4% by linear mixed model analysis were found. No relation was found between cochlear size and ear size or sex respectively. To simplify cochlear size description, two new descriptive methods, spiral fitting and principal component analysis (PCA) were introduced to compile the actual amount of measurements into a smaller set of descriptive variables. Spiral fitting is constituted by the adaption of the logarithmic spiral onto the natural cochlear shape, while principal component analysis derives a requested number of uncorrelated components which can recompose the cochlear shape when multiplied with a component matrix. All spiral fitting coefficients and the first principal component coefficient were significantly correlated with the four measured cochlear diameters. In addition, in this study the relation between cochlear size and electrode position was investigated, showing a distinct difference in distribution in modiolus proximity (medial versus lateral) and insertion depth when the studied cochleas were divided into three size groups (small, medium and large).

In **Chapter 5** the aim of inventing a surgical guidance tool predicting final electrode position was approached two methodological ways using preoperatively measurable cochlear size parameters. The described spiral fitting method was reassembled to predict insertion depth of the most apical electrode contact. However, the predictive performance of this method was found to be poorer than using a general linear regression model with the four cochlear diameters as input parameters combined with the preferred insertion depth. The final model was able to predict up to 78.1% of variance in final electrode array position. To form the basis for obtaining more surgical control over final implant position an analysis was performed on the optimal insertion depth regarding a minimal so-called frequency mismatch, e.g. difference in stimulated frequency by the contact related to the anatomically frequency belonging to the position within the cochlea. This part of the study also supported the need for variable electrode lengths with different contact spacing options.

A study on the influence of cochlear implant electrode position on performance is described in **Chapter 6**. Indeed conform previous reports; several patient related variables did show to have influence on performance outcomes (age at onset of hearing loss, duration of deafness, preoperative phoneme & word scores). However, as opposed to the conclusions from many studies in the past years, this study found none of the implant position variables to be related to performance outcomes.

In **Chapter 7** the concluding remarks of this thesis were provided. This chapter was extended with some future perspectives. Regarding the three objectives formulated in the introduction CT imaging is a valuable evaluation modality providing major information about the cochlear spirals and implant electrode position of CI patients. It depicts surgical results after reimplantation surgery and helps to guide the surgeon prior to this necessary second surgery to replace the electrode accurately. It also may reveal an electrode migration which in some cases explains individual complaints such as performance drop. Using the detailed CT scanning of the cochlea prior to surgery enables a range of descripting possibilities for the cochlear shape and size. The variations found in cochlear size are proven to influence final implant electrode position and are thereby a factor that is not often accounted for in cochlear implant studies. The third objective stated in the introduction also delivered the most surprising outcome. Based on the findings of Chapter 6 there seems to be no direct relation between cochlear implant electrode position and speech perception performance. An important strength of this research was the uniformity among the studied implantees. Performing the studies on one implant design (HiRes90K HiFocus implant of Advanced Bionics) and using the (extended) round window insertion technique allowed clear interpretations insured by this controlled study design. However, using this study design implies that the derived new insights can only be applied to candidates undergoing surgery in the comparable situation. Regarding the possibility of electrode migration without giving complaints weakens the final study outcomes of chapter 6 and previous published studies on the relation with performance. The broader availability of cone beam CT possibly composes a better future imaging option to lessen radiation exposure. The innovative current and future perspectives of availability of tailor-made electrode lengths, automatically post-processing CT and electrophysiological fitting software and even hair cell regeneration establish the hope of gaining better performance for implantees in the years to come.

Chapter Nine

Nederlandse Samenvatting

Invaliderend gehoorverlies komt voor bij 5% van de wereldbevolking, uitkomend op 360 miljoen mensen (328 miljoen volwassenen en 32 miljoen kinderen), zoals is vastgesteld door de Wereld Gezondheid Organisatie (WHO 2013). Deze groep heeft beduidend betere vooruitzichten op gehoorrevalidatie dankzij de beschikbaarheid van cochleaire implantaten tegenwoordig. De verwachte spraakverstaan prestaties met dit elektrisch hoortoestel voor het binnenoor worden gegarandeerd door de innovatieve beeldvormingsmodaliteiten, welke zijn ontstaan gedurende dezelfde jaren als de ontwikkeling van het cochleaire implantaat zelf. Tegenwoordig worden CT en MRI complementair gebruikt voorafgaand aan de implantatie ingreep. Deze modaliteiten leveren elk hun eigen specifieke kijk in de temporale bot anatomie om nauwkeurige insertie van de implantaat elektrode in de cochlea mogelijk te maken. Hoewel nieuwe CI ontwerpen en MRI technieken beschikbaar zijn gekomen die toepassing van MRI na de ingreep zonder risico op het compromitteren van de implantaat positie toestaan, wordt toch vooral CT gebruikt na implantatie indien gedetailleerde informatie over het implantaat of omliggende anatomische structuren is gewenst. Het voortdurende uitbreidingsproces van behandelingsindicaties, verbeterde elektrode designs, chirurgische technieken en elektrofysiologische software aanpassingen versterkt de rol van beeldvorming aanzienlijk. Tegelijkertijd vormen deze ontwikkelingen een uitdagende opdracht en brengen mogelijk tevens beperkingen aan het licht bij de huidige beeldvormingsmodaliteiten die gebruikt worden in het veld van cochleaire implantatie. De voordelen en tegenvallers van het CT gebruik om de resultaten van cochleaire implantatie te evalueren en verbeteren vormden het onderwerp van de studies die beschreven worden in dit proefschrift. Dit proefschrift ontrafelt de kennis van cochleaire vormen en implantaat electrode positie die verkregen kan worden met CT.

De inleiding van dit proefschrift beschreven in **Hoofdstuk 1** formuleert de drie doelstellingen van dit onderzoek en geeft in het kort een overzicht van achtergrondinformatie over gehoorverlies en normale gehoor fysiologie, gecombineerd met een overzicht van de verleden en tegenwoordige feiten over het cochleair implantaat, de functie, en de implantatie procedure in Leiden. Vervolgens, wordt een demonstratie van de gestandaardiseerde beeldvorming en reconstructie technieken van de cochlea, samen met het toegepaste coördinatenstelsel gegeven.

De verdenking op implantaat falen is een veelvoorkomende reden om postoperatief een CT uit te voeren om deze mogelijke zeer ongewenste gebeurtenis te detecteren of te verwerpen. Hoewel dit een zeldzame gebeurtenis is, beschrijft **Hoofdstuk 2** anatomische en spraakverstaan uitkomsten van 15 patiënten die getroffen werden door een defecte HiFocus1j elektrode (Advanced Bionics) als gevolg van een defecte draadisolatie. Vergelijkingen van de elektrode positie met hoge resolutie CT scans van de originele en vervangende elektrode resulteerde in een gemiddelde verplaatsing van niet meer dan 0.59 mm. De nauwkeurige vervanging van de elektrode werd vertaald in een vlot herstel van het eerdere spraakverstaan niveau, zonder een relatie tussen de grootte van de verplaatsing en veranderingen in spraakverstaan te laten zien. De gereimplanteerde patiënten lieten zelfs significant verbeterde spraakverstaan scores zien. Deze bevinding dient mogelijk toegeschreven te worden aan de tweeweekse periode van extra training sessies om cruciale stappen van het standaard revalidatie programma op te halen.

Een ander fenomeen dat werd ontdekt met CT is elektrode migratie. De bevinding dat elektrode migratie zelfs voorkomt in sommige patiënten zonder te leiden tot veranderingen in spraakverstaan of klachten werd voor het eerst gedocumenteerd in de studie beschreven in **Hoofdstuk 3**. De migraties werden zichtbaar tijdens een retrospectief casus onderzoek welke 35 patiënten (5 patiënten met klachten; 30 patiënten zonder) betrof met twee beschikbare sequentieel verkregen postoperatieve CT scans. In 10 van de 35 patiënten werd een migratie (verschuiving van het meest basale contact van meer dan 1 mm) vastgesteld (29%). Twee van deze migraties werden ontdekt omdat deze patiënten klaagden over achteruitgang in spraakverstaan. De overige acht patiënten gaven individueel geen enkele aanleiding om de eerder vastgestelde implantaat positie (geprotocolleerd vastgesteld één dag na de operatie) in twijfel te trekken. De studie bij deze groep toonde aan dat het voorkomen van migratie niet gerelateerd aan insertiediepte, echter de nieuwere HiFocus1J electrode liet een hogere migratie frequentie dan zijn voorganger zien (HiFocus1). Dit hoofdstuk toont ook een extreme observatie van drie zeer grote elektrode verschuivingen (meer dan 4 mm verschuiving bij vergelijking van beide scans). Het feit dat in twee van deze gevallen verschillende extracochleaire contacten werden gedetecteerd zou de verklaring kunnen vormen voor de spraakverstaan achteruitgang die werd gerapporteerd door de betreffende patiënten. Het voorkomen van migratie over het algemeen, betekent dat de origineel vastgelegde postoperatieve implantaat positie mogelijk minder betrouwbaar is in sommige gevallen en dit kan een grote impact hebben op onderzoek dat implantaat positie relateert aan gestimuleerde tonotopische frequenties en zelfs spraakverstaan uitkomsten.

De preoperatieve waarde van CT wordt onderschreven in **Hoofdstuk 4**, waarin cochleaire morfologie bestudeerd en op verschillende manieren omschreven wordt. In dit hoofdstuk

wordt de uitgebreide CT database voor het eerst geraadpleegd, waarin CT beelden van alle CI-gebruikers zijn opgenomen sinds 2000. Pre- en postoperatieve CT scans van 336 patiënten werden geanalyseerd om variaties te vinden in cochleaire diameter, cochleaire kanaal grootte en buiten en binnenwand relaties. Daarnaast werd de relatie tussen cochleaire vorm en elektrode positie, diepte en modiolus nabijheid onderzocht. Analyse toonde dat cochleaire kanaal grootte toeneemt van 0.98 naar 2.96 mm en cochleaire diameters afnemen van 8.85 mm naar 5.92 mm. Significante correlaties werden gevonden tussen de cochleaire binnen- en buitenwand ($p<0.01$) en een grootte verschil ten gunste van mannen van 4% middels linear mixed model analyses. Er werd geen relatie gevonden tussen cochleaire grootte en oorzijde of sekse. Om de cochleaire grootte omschrijving te vereenvoudigen werden twee nieuwe beschrijvingsmethoden, spiral fitting en principal component analyse (PCA) geïntroduceerd om de werkelijke hoeveelheid maten te beperken tot een kleinere set beschrijvende getallen. Spiral fitting is gebaseerd op het toepassen van een logaritmische spiraal op de natuurlijke cochleaire vorm, terwijl principal component analyse een gewenst aantal gecorreleerde componenten levert welke de cochleaire vorm kunnen heropbouwen indien ze worden vermenigvuldigd met een component matrix. Alle spiral fit coëfficiënten en eerste principal component coëfficiënt waren significant gecorreleerd met de vier gemeten cochleaire diameters. Aanvullend, werd in deze studie de relatie tussen cochleaire grootte en elektrode positie onderzocht, waarbij een opvallend verschil in verdeling naar modiolus nabijheid (mediaal versus lateraal) en insertiediepte werd gevonden wanneer de cochleas werden ingedeeld in drie grootte groepen (klein, middel en groot).
In **Hoofdstuk 5** was het doel om een chirurgisch sturingshulpmiddel te ontwikkelen dat uiteindelijke elektrode positie voorspeld op twee methodologische wijzen benaderd, gebruikmakend van preoperatief meetbare cochleaire grootte parameters. De beschreven spiral fit methode werd toegepast om insertiediepte te voorspellen van de meest apicale elektrode contact. Desalniettemin, bleek de voorspellende kwaliteit van deze methode slechter dan het gebruik van een general linear regression model met vier cochleaire diameters als input parameters gecombineerd met de gewenste insertiediepte. Het finale model was in staat tot 78.1% van de variantie in uiteindelijke elektrode array positie te voorspellen. Om als basis te dienen bij het verkrijgen van meer chirurgische controle over de uiteindelijke implantaat positie werd een analyse uitgevoerd naar de optimale insertiediepte met betrekking tot het verkrijgen van een minimale zogenoemde ‘frequentie-mismatch’, betekenend het verschil in gestimuleerde frequentie bij het contact in relatie

tot de anatomische frequentie behorend bij de betreffende positie in de cochlea. Dit deel van de studie onderbouwde het belang voor het bestaan van variërende elektrode lengtes en contact-afstand opties.

Een studie naar de invloed van de CI elektrode positie op spraakverstaan prestaties is beschreven in **Hoofdstuk 6**. In overeenstemming met eerdere publicaties werd inderdaad aangetoond dat verscheidene patiënt gerelateerde variabelen invloed hebben op spraakverstaan prestaties (leeftijd van ontstaan van de doofheid, duur van doofheid, preoperatieve foneem & woord scores). Echter, in tegenstelling tot de conclusies uit vele studies van de afgelopen jaren, vond deze studie dat geen van de implantaat positie gerelateerde variabelen een relatie hebben met spraakverstaan prestatie uitkomsten.

In **Hoofdstuk 7** worden de concluderende opmerkingen over dit proefschrift beschreven. Dit hoofdstuk werd uitgebreid met enkele toekomstperspectieven. Met betrekking tot de drie in de introductie geformuleerde doelstellingen is CT een waardevolle evaluatiemodaliteit welke majeure informatie verschaft over cochleaire spiralen en implantaat elektrode positie van cochleaire implantatie patiënten. Het geeft de chirurgische resultaten na een herimplantatie weer en ondersteunt de chirurg voorafgaand aan deze noodzakelijke tweede operatie om de elektrode nauwlettend te herplaatsen. Het kan een elektrode migratie aan het licht brengen in sommige casussen welke een goede verklaring vormen voor individuele klachten over spraakverstaan achteruitgang. Het uitvoeren van de gedetailleerde CT van de cochlea voorafgaand aan de ingreep biedt tal van beschrijvende mogelijkheden ten aanzien van cochleaire vorm en grootte. Van de gevonden variaties in cochlea grootte is aangetoond dat zij van invloed zijn op de uiteindelijke elektrode positie en vormen daardoor een factor die niet vaak wordt meegenomen in CI-studies. De derde doelstelling leverde tevens de meest verrassende uitkomst. Berustend op de bevindingen van hoofdstuk 6 blijkt er geen directe relatie te bestaan tussen CI-elektrode positie en spraakverstaan prestaties. Een belangrijke kracht van dit onderzoek was de uniformiteit tussen de bestudeerde CI-patiënten. De uitvoering van de studies naar één type implantaat (HiRes90K HiFocus implantaat van Advanced Bionics) en enkel het gebruik van de (uitgebreide) ronde venster insertie techniek maakte heldere interpretaties mogelijk. Maar, het gebruik van deze gecontroleerde studie opzet bepaald ook dat de hieruit ontleende nieuwe inzichten alleen toepasbaar zijn op kandidaten die de ingreep in de vergelijkbare situatie ondergaan. Met het oog op de mogelijkheid van migratie zonder het veroorzaken van klachten maken de uitkomsten van hoofdstuk 6 en eerder gepubliceerde studies naar de relatie met spraakverstaan prestaties minder sterk. De bredere beschikbaarheid van ‘cone beam CT’ vormt mogelijk een betere beeldvormingsoptie in de toekomst om radiatie blootstelling te beperken. De innovatieve huidige en toekomstige ontwikkelingen op gebied van beschikbaarheid van op maat gemaakte elektrode lengtes, geautomatiseerde verwerking van CT en elektrofysiologische fitting software en zelfs haarcelregeneratie vormen de hoop op het verkrijgen van betere prestatie mogelijkheden voor geïmplanteerde in de voor ons liggende jaren.

Appendices

Pubmed Literature Search

List of Publications

Curriculum vitae

Dankwoord

PUBMED LITERATURE SEARCH

The search in PubMed consists of six separate queries. These queries combine the following subjects and were limited to articles written in english:
1. Cochlear implantation or Cochlear implants
2. Cochlea and Electrodes
3. Inner ear implants
4. (1 or 2 or 3) and Performance
5. Computed tomography and Cochlear implantation
6. Cochlear implantation and Angle, Array, Position

These queries in full are as follows:

1. (cochlear implantation OR cochlear implant electrodes OR cochlear implant electrode OR cochlear implant OR cochlear implants OR cochlea implant OR cochlea implants OR cochlea implantation OR "Cochlea/anatomy and histology"[Mesh]) AND **english**[la]

2. ((cochlea OR cochlear) AND (electrode OR electrodes OR electrod*)) AND **english**[la]

3. (inner ear OR basilar membrane OR cochlear aqueduct OR cochlear duct OR "Organ of Corti" OR round window OR scala tympani OR scala vestibuli OR spiral ganglion OR spiral lamina OR semicircular canals OR semicircular ducts OR labyrinth vestibule OR oval window OR saccule OR utricle OR vestibular aqueduct) AND (implant OR implants OR implantation OR implant*) AND english[la]

4. ((cochlear implantation OR cochlear implant electrodes OR cochlear implant electrode OR cochlear implant OR cochlear implants OR cochlea implant OR cochlea implants OR cochlea implantation OR "Cochlea/anatomy and histology"[Mesh] OR ((cochlea OR cochlear) AND (electrode OR electrodes OR electrod*)) OR ((inner ear OR basilar membrane OR cochlear aqueduct OR cochlear duct OR "Organ of Corti" OR round window OR scala tympani OR scala vestibuli OR spiral ganglion OR spiral lamina OR semicircular canals OR semicircular ducts OR labyrinth vestibule OR oval window OR saccule OR utricle OR vestibular aqueduct) AND (implant OR implants OR implantation OR implant*))) AND (performance OR performances OR "phoneme scores" OR "phoneme score" OR outcome[ti] OR outcomes[ti] OR result[ti] OR results[ti] OR "speech perception" OR "speech understanding")) AND english[la]

5. ((((computed tomography OR hrct OR cat scan OR cat scans OR computer tomography OR computerized tomography OR ct scan OR ct scans OR cine-ct OR cine ct OR electron beam tomography OR computed tomographic OR computer tomographic OR computerized tomographic OR computer assisted tomography OR (CT[tw] AND (spiral OR preoperative OR postoperative))) AND (cochlear implantation OR cochlear implant electrodes OR cochlear implant electrode OR cochlear implant OR cochlear implants OR cochlea implant OR cochlea implants OR cochlea implantation OR "Cochlea/anatomy and histology"[Mesh] OR ((cochlea OR cochlear) AND (electrode OR electrodes OR electrod*)) OR ((inner ear OR basilar membrane OR cochlear aqueduct OR cochlear duct OR "Organ of Corti" OR round window OR scala tympani OR scala vestibuli OR spiral ganglion OR spiral lamina OR semicircular canals OR semicircular ducts OR labyrinth vestibule OR oval window OR saccule OR utricle OR vestibular aqueduct) AND (implant OR implants OR implantation OR implant*)))) AND english[la]

6. ((cochlear implantation OR cochlear implant electrodes OR cochlear implant electrode OR cochlear implant OR cochlear implants OR cochlea implant OR cochlea implants OR cochlea implantation OR "Cochlea/anatomy and histology"[Mesh] OR ((cochlea OR cochlear) AND (electrode OR electrodes OR electrod*)) OR ((inner ear OR basilar membrane OR cochlear aqueduct OR cochlear duct OR "Organ of Corti" OR round window OR scala tympani OR scala vestibuli OR spiral ganglion OR spiral lamina OR semicircular canals OR semicircular ducts OR labyrinth vestibule OR oval window OR saccule OR utricle OR vestibular aqueduct) AND (implant OR implants OR implantation OR implant*))) AND (angle OR angles OR insertion OR depth OR position OR placement OR array OR arrays OR positions OR positioned OR "coordinate system" OR "coordinate systems")))) AND english[la]

LIST OF PUBLICATIONS

Van der Marel, K. S., Briaire, J. J., Verbist, B. M., Joemai, R. M., Boermans, P. P., Peek, F. A. and Frijns, J.H. (2011). Cochlear reimplantation with same device: Surgical and audiologic results. *Laryngoscope, 121*, 1517-1524.

Van der Marel, K. S., Verbist, B. M., Briaire, J. J., Joemai, R. M., & Frijns, J. H. (2012). Electrode Migration in Cochlear Implant Patients: Not an Exception. *Audiol.Neurootol., 17*, 275-281.

Van der Marel, K. S., Briaire, J. J., Wolterbeek, R., Snel-Bongers, J., Verbist, B. M., & Frijns, J. H. (2014). Diversity in cochlear morphology and its influence on cochlear implant electrode position. *Ear Hear., 35*, e9-e20.

Van der Marel, K.S., Briaire, J. J., Wolterbeek, R., Verbist, B. M., & Frijns, J. H. (in press). Development of Insertion Models predicting Cochlear Implant Electrode Position. *Ear Hear*.

Van der Marel, K.S., Briaire, J. J., Wolterbeek, R., Verbist, B. M., Muurling T. & Frijns, J. H. (2015). The Influence of Cochlear Implant Electrode Position on Performance. *Audiol. Neurootol.*20(3):202-11.

Van der Beek, F.B., Briaire, J. J., **Van der Marel, K.S.**, Verbist, B. M., & Frijns, J. H. (in press). Intra-cochlear position of cochlear implants determined using CT-scanning vs fitting levels: higher threshold levels at basal turn. *Audiol.Neurootol.*

CURRICULUM VITAE

Kim van der Marel was born on February 13th (1985) in Haarlem, the Netherlands. She graduated from Atheneum College Hageveld (Heemstede) in 2003. Later that year, she started her medical study at the Leiden University. During this study, she worked in a nursing home in Heemstede and later as a medical doctor in an acute psychiatric hospital. Between 2007 and 2009 she followed internships in several hospitals near Leiden. In 2008 she went to Suriname where she followed internships in community and family medicine. In Paramaribo, she worked at a pediatric consultation clinic, an occupational health foundation, a general medical practice, and inland, at the Medical Mission in the Upper Suriname Region (Laduani). Her internships in Otorhinolaryngology at the Antoni van Leeuwenhoek Center (AvL, Amsterdam) and Leiden University Medical Center (LUMC, Leiden) inspired her to pursue a career in this area of medicine. In 2009 she started as a PhD student at the Otorhinolaryngology Department under the supervision of professor Johan Frijns. She gained her scientific skills while being mentored by dr. Jeroen Briaire and dr. Berit Verbist. Between 2009 and 2012 the foundation of this thesis was laid. During this period, Kim gave multiple oral presentations at national and international conferences and followed several courses in English and statistics.

In 2012 she started her medical residency at the Department of Otorhinolaryngology and Head and Neck surgery at the LUMC (Leiden), followed by a period at the Groene Hart Ziekenhuis (GHZ, Gouda) in 2014. She currently works at the LUMC and in 2017 she will continue her residency at the Alrijne Ziekenhuis (Leiderdorp).

Kim is married to Michiel de Roij. Together they have a son named Ravel (2015) and live in Heemstede.

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