Challenging indications for cochlear implantation

Asymmetrical hearing loss
Far-advanced otosclerosis
Postmeningitic hearing loss

Maarten Caspar van Loon

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To my parents

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Chapter 1

Introduction

1

HEARING PHYSIOLOGY

Hearing is the result of the transduction of sound pressure waves into action potentials which are processed further upwards the auditory pathway to the brain where sound is perceived (Figure 1). The pinna acts as a funnel which assists in transferring sound pressure waves through the ear canal to the tympanic membrane. Consequently, the tympanic membrane vibrates and passes on these vibrations to the middle ear ossicles: the malleus, the incus and the stapes, respectively. Acoustic vibrations of the tympanic membrane are amplified and conducted by the ossicular chain. The stapes footplate conveys these vibrations to the oval window membrane where sound the mechanical vibrations are transferred to the fluid containing cochlea.

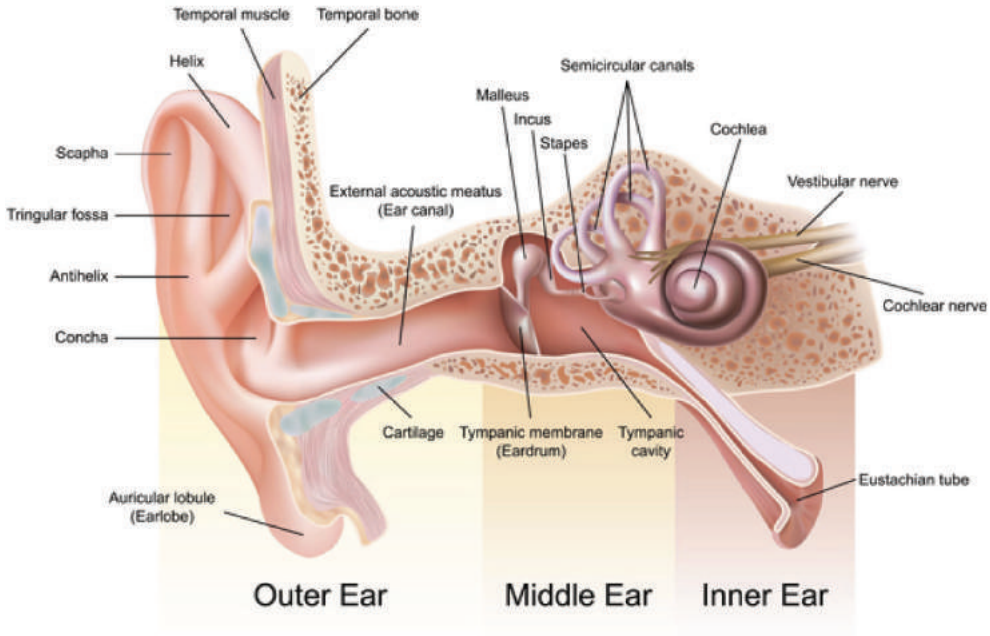

Figure 1: Overview of the anatomy of the outer, middle and inner ear. *Illustration adapted from the "Sensory and Motor Mechanisms" series by Neil Campbell and Jane Reece. Slideshare.net.*

The cochlea is a coiled snail shell-like structure of approximately 35mm long embedded in the temporal bone. Three fluid containing compartments, the scala media, scala vestibuli and scala tympani, make up the cochlear turn which spirals approximately two and a half turns around the central modiolus. The scala media houses the sense organ of hearing, the organ of Corti, which rests on the basilar membrane (Figure 2). Oscillation of the stapes footplate results in fluid movement within the cochlea followed by movement of the basilar membrane. The stiffness and wideness of the basilar membrane varies from base to apex.

As a result, high-frequency sounds cause maximum vibration of the basilar membrane close to the oval window while low-frequency sounds predominantly cause vibrations at the cochlear apex. This separation of frequencies across the cochlea is referred to as tonotopy. Two types of hair cells are distinguished within the organ of Corti: one row of inner hair cells and three rows of outer hair cells. The outer hair cells have the ability to contract and selectively amplify the movement of the basilar membrane. The inner hair cells are the actual sensory receptors of sound.

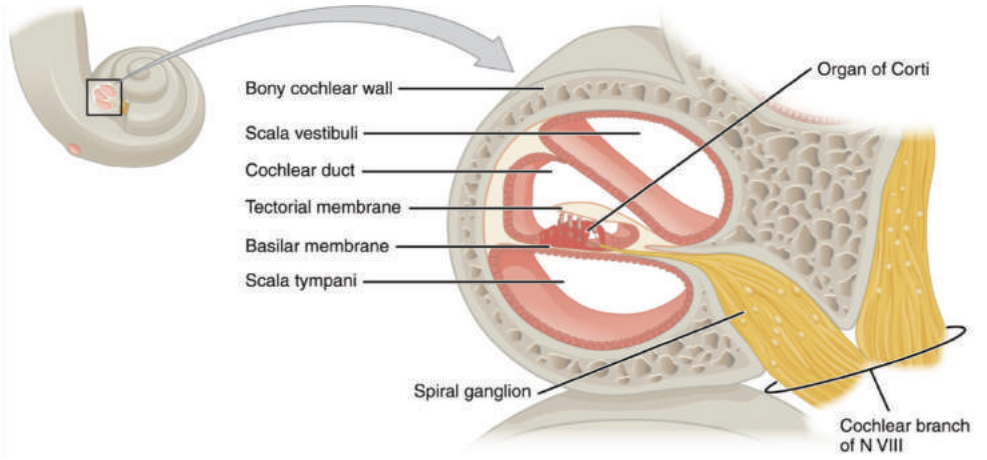

Figure 2: Cross sectional image of the cochlea showing the position of the organ of Corti located on the basilar membrane. The hair cells of the organ of Corti are innervated by the spiral ganglion cells of which the afferent axons form the auditory nerve (N VIII). *Illustration adapted from the "Sensory and Motor Mechanisms" series by Neil Campbell and Jane Reece. Slideshare.net.*

As the basilar membrane vibrates, the inner hair cells of the organ of Corti move back and forth and evoke action potentials. The hair cells of the organ of Corti are innervated by the spiral ganglion cells located in the central modiolus. Afferent axons from the spiral ganglion cells, which innervate the approximately 3000 inner hair cells, constitute the cochlear nerve which is joined by the vestibular nerves forming the vestibulocochlear nerve. Auditory information synapses to the cochlear nuclei located in the rostral medulla where most nerve fibers cross to the contralateral side (Figure 3). Both crossed and uncrossed nerve fibers from the cochlear nuclei synapse in the olivary nuclei located in the pons. This is the first place in the ascending pathway to receive bilateral input from both ears. The olivary nuclei projects to the nuclei of the lateral lemniscus and inferior colliculus, and the signal finally terminates in the auditory cortex via the medial geniculate body. The tonotopic organization of nerve fibers is roughly preserved throughout the auditory pathway as different frequencies corresponds to specific anatomical location of the auditory cortex.

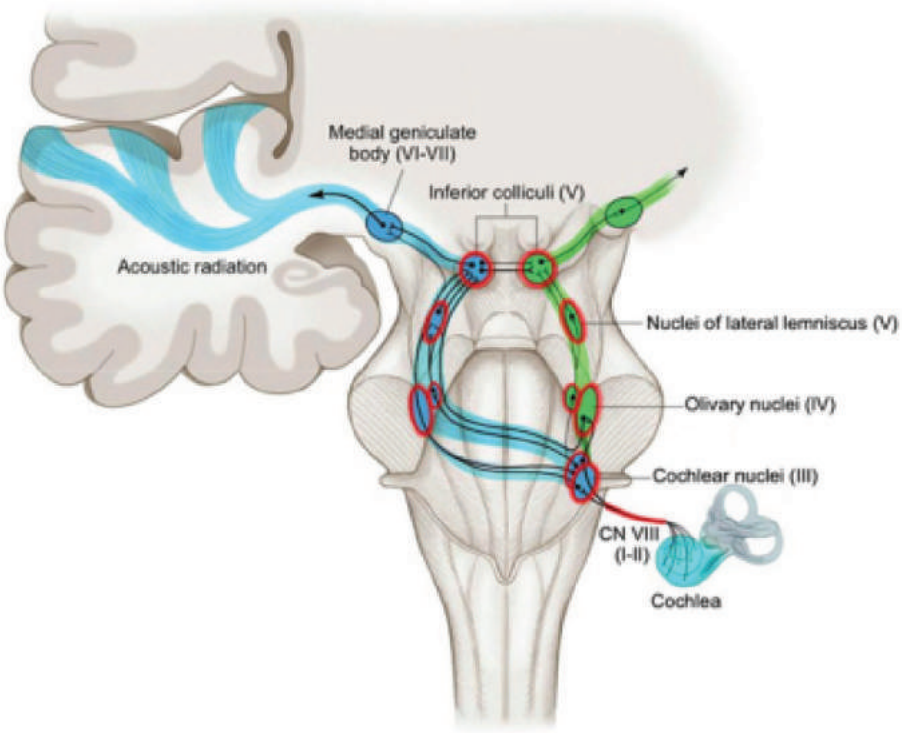

Figure 3: Schematic diagram of the auditory pathway from cochlea to the auditory cortex. Input from both ears travels up the ipsilateral and contralateral central auditory pathways where signals are processed at multiple nuclei (numbers I-VII) before reaching the auditory cortex. CN VIII=, vestibulocochlear nerve. *Illustration adapted from the "Ear Anatomy" series by Robert Jackler and Christine Gralapp.*

BINAURAL HEARING

Binaural hearing allows listeners to segregate the target signal from disturbing background noise and assists in identifying the location of sound sources[1]. Input from both ears travels up the ipsilateral and contralateral central auditory pathways where signals are processed at multiple nuclei before reaching the auditory cortex (Figure 3). Comparison of subtle interaural cues allows the listener to separate the input originating from each ear and binaural processing further improves auditory performance. Binaural processing improves speech recognition in quiet and noise[2-4] and results in better performance when speech and disturbing noise are spatially segregated[5,6]. Three binaural phenomena are responsible for this superior binaural performance: the better-ear-effect, binaural squelch and binaural

summation. Whereas the better-ear-effect is a physical phenomenon, binaural summation and binaural squelch require binaural integration.

The *better-ear-effect* is caused by the physical presence of the head which creates a difference in signal-to-noise ratio (SNR) between both ears when two competing sounds are spatially separated. The ear closest to the originating sound will have a favorable SNR as compared to the contralateral ear. The listener can select the ear with the most favorable SNR, while ignoring the ear with the poorer SNR. Depending on the origin of the sounds and the position of the head, this effect can contribute 3.0-15.7 dB to the speech reception threshold (SRT)[7-9]. *Binaural squelch* is also based on interaural differences in phase and intensity to suppress the impact of disturbing noise, resulting in a SRT-improvement of 0.9-2.3 dB[7-9]. In complex listening conditions (i.e., when both ears receive a signal with a different SNR), patients can select the ear with the most favorable SNR using the better-ear-effect and use the information from the ear with the least favorable SNR to further increase intelligibility using the squelch effect. *Binaural summation* is defined as the capacity to centrally integrate identical input from both ears to improve the speech reception in diotic listening conditions (i.e., when both ears receive identical stimuli). As a result, binaural summation yields 2.1-3.0 dB improvement of the SRT[7-9].

Binaural processing also assists in the localization of sounds which is strongly dependent on interaural differences[10,11]. For frequencies below 800Hz, the auditory system relies mainly on phase delays caused by interaural time differences, whereas for frequencies exceeding 1600Hz, it primarily relies on interaural level differences[12]. Binaural processing is typically present in normal-hearing listeners but binaural effects are, to a lesser extent, also observed in patients using hearing aids or cochlear implants[1,13-16].

HEARING LOSS

According to the World Health Organization, over 5% of the world's population, 328 million adults and 32 million children, suffer from disabling hearing loss[17]. Disabling hearing loss refers to hearing loss greater than 40dB in the best hearing ear in adults and a hearing loss greater than 30dB in the best hearing ear in children. Hearing loss may be caused by an impairment of any of the components in the auditory pathway, from the pinna to the auditory cortex. Loss in the conduction of sound pressure waves to the cochlea results in conductive hearing loss, for instance caused by otitis media (with effusion), impacted cerumen, a perforated or atelectatic tympanic membrane, otosclerosis or cholesteatoma. This type of hearing loss may be remedied by removal of the pathology, restoration of the

components of the sound conduction system (i.e. the tympanic membrane or the ossicles), or acoustic amplification using hearing aids. Impaired cochlear function and pathologies affecting the cochlear nerve or central auditory pathway result in sensorineural hearing loss (SNHL). By far the most common cause of SNHL is the loss or damage of inner and/or outer hair cells of the cochlea. Numerous etiologies have been identified that affect hair cells including presbyacusis, a genetic predisposition of loss hair cell function, noise exposure, bacterial toxins or ototoxic medications. Partial loss of hair cells can be compensated by acoustic amplification with hearing aids in patients with moderate SNHL. Patients with severe-to-profound SNHL however insufficiently benefit from hearing aids because too little hair cells remain to successfully process acoustic amplification. The preferred intervention in this group of patients is cochlear implantation (CI) which bypasses cochlear hair cells and directly stimulates the spiral ganglion cells of the cochlear nerve.

HISTORY OF COCHLEAR IMPLANTATION

Cochlear implants are commercially available for a few decades, however the idea of using electrical rather than an acoustic stimulation to activate the auditory system dates back several centuries. Around 1800 Alessandro Volta, an Italian physicist, developed the first electric battery and experimented with electrical stimulation of the ear. He connected metal rods to a battery and inserted them in his ears causing him to lose consciousness. He remembered hearing “a boom within the head” followed by a hissing sound similar “to a thick soup boiling”[18].

Figure 4: An Italian banknote of 10.000 Lire showing a portrait of physicist Alessandro Giuseppe Antonio Anastasio Volta (18 February 1745 - 5 March 1827). Also illustrated is the Voltic pile, the first electrical battery, consisting of several pairs of alternating copper and zinc discs separated by cloth. When the top and bottom contact were connected by a wire, a continuous electrical current flowed through the Voltic pile. (*GNU Free Documentation License).*

Almost two centuries later, the French electrophysiologist André Djourno and French otolaryngologist Charles Ayriès were the first to experiment with direct electrical stimulation of the auditory nerve. In 1957 they placed a single copper wire on the stump of the auditory nerve of a patient who lost hearing after bilateral temporal bone resection because of cholesteatomas. After electrical current was applied, the patient was able to hear sounds like "a roulette wheel" and "crickets" and detection of high and low frequencies was possible[19]. The implanted electrode broke down after a few weeks though Djourno and Ayries predicted the imminent development of cochlear implants as they concluded in their first paper: "The electrical stimulation of the cochlea itself, in analogous conditions, would without doubt allow the construction of a possible mechanism for electrical hearing."

The first actual CI was developed in 1961 by otolaryngologist William House in collaboration with neurosurgeon John Doyle and his brother James Doyle, an electrical engineer[20]. The team from Los Angeles inserted a gold five-wire electrode in the cochlea through the round window. They noted that loudness changed with level of stimulation and the pitch of the stimulus changed with variation in the rate of stimulation[21]. The device assisted in the detection of sound and assisted in lip reading. Speech recognition was not possible because all five wires of this single-channel device stimulated subpopulations of the auditory nerve simultaneously. In 1962, otolaryngologist Blair Simmons and engineer Robert White, both affiliated to the Stanford University, conducted experiments in a patient undergoing explorative craniotomy under local anesthesia after cerebellar ependymona surgery. They used a multichannel device consisting of six electrodes that could be stimulated separately and positioned it on the auditory nerve. Consequent stimulation of the different electrodes caused the patient to be able to discriminate different frequencies using the tonotopic organization of the auditory nerve[22]. The first commercially available cochlear implant was the House/3M single-channel device which was introduced in 1972. Over the next years, several patients were permanently implanted with the House/3M devices by either William House, or Robert Michelson and his team from the University of California- San Francisco[23].

A turning point in the development of the CI came in 1975, when the National Institutes of Health sponsored Robert Bilger to initiate a detailed evaluation of all thirteen patients who had received a single-channel CI thus far. Although the Bilger report concluded that cochlear implantation did not result in better speech recognition, it did conclude that CI resulted in better speech production, supported in lip reading abilities and improved the quality of life[24]. The interest for cochlear implantation as well as the funding increased after the Bilger report and several groups started working on the development of multichannel CI devices. Inspired by the work of his American colleagues, Australian otolaryngologist Graeme Clarke from the Melbourne University independently started working on the

development of his own implantable multichannel device. Graeme Clarke performed his first cochlear implantation in 1978 and in 1981 he proved that open-set speech recognition was possible without lip reading[25]. Technological advancement created by the aerospace and computer industry resulted in smaller implants and improved durability of the electrode array. The developments in the United States and separately in Australia later resulted in the introduction of Advanced Bionics™ Clarion® and the Cochlear™ Nucleus® devices respectively. In the following years the 3M/Vienna and Neurelec/MXM multichannel devices were developed in Austria and France, eventually resulting in the formation of MED-EL™ and Neurelec™ companies, the latter now known as Oticon. The American Food and Drugs Administration (FDA) approved CI as a safe device for implantation in 1985 for adults and in 1990 for children. Cochlear implantation has proven its effectiveness over the last decades and the number of people who received a CI is estimated to be around 324.000 in 2012[26]. The competitive CI industry is constantly evolving and over the last decades continuous advancements in hardware and software have been issued. Recent developments include Bluetooth® connections with other devices, waterproof processors, synchronization with contralateral hearing aids, advanced noise cancelling software and directional hearing with multiple microphones.

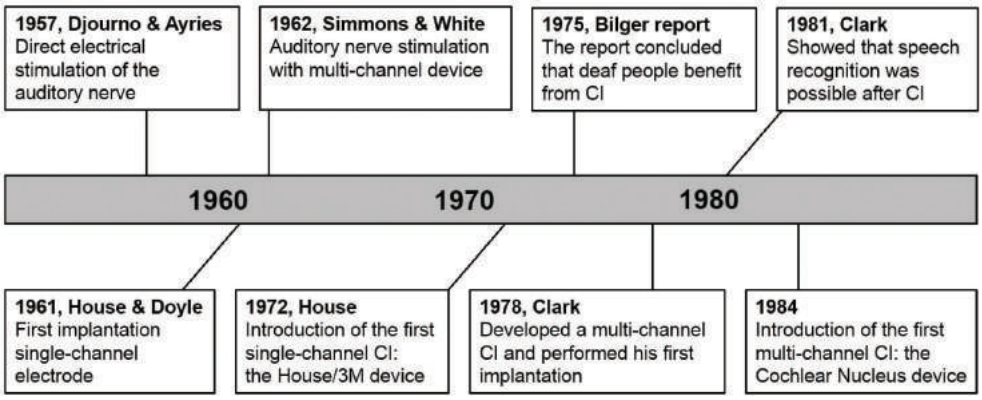

Figure 5: Timeline illustrating the early milestones in the development of cochlear implants from the first electrical stimulation of the auditory nerve in 1957 till the introduction of the first multichannel device in 1984.

CURRENT COCHLEAR IMPLANTATION

A cochlear implant consist of an external part and a surgically implanted device (Figure 6). The external part is commonly worn on top of the pinna like a conventional hearing aid and comprises a microphone, a speech processor and has a short lead to an electromagnetic

coil (Figure 7a). The implanted device contains the receiver-stimulator (Figure 7b), which is surgically implanted underneath the temporal muscle and skin, in a surgically drilled bone bed. An electrode array (Figure 7c) is inserted in the cochlea and an extracochlear ground electrode allows current return. Sound is picked up by the microphone and encoded to a digital code by the speech processor. The signal is encoded in such way that different frequencies stimulate different electrodes of the array. The digital information is transmitted through the skin to the subcutaneous receiver via the magnetic coil. The receiver of the CI decodes the signal and sends electrical impulses across a lead to the electrode array within the cochlea to stimulate the spiral ganglion cells. Modern electrode arrays consist of up to 21 stimulation electrodes and one ground electrode. The stimulation electrodes stimulate specific locations across the cochlear turns utilizing the tonotopy of the cochlea (Figure 7d).

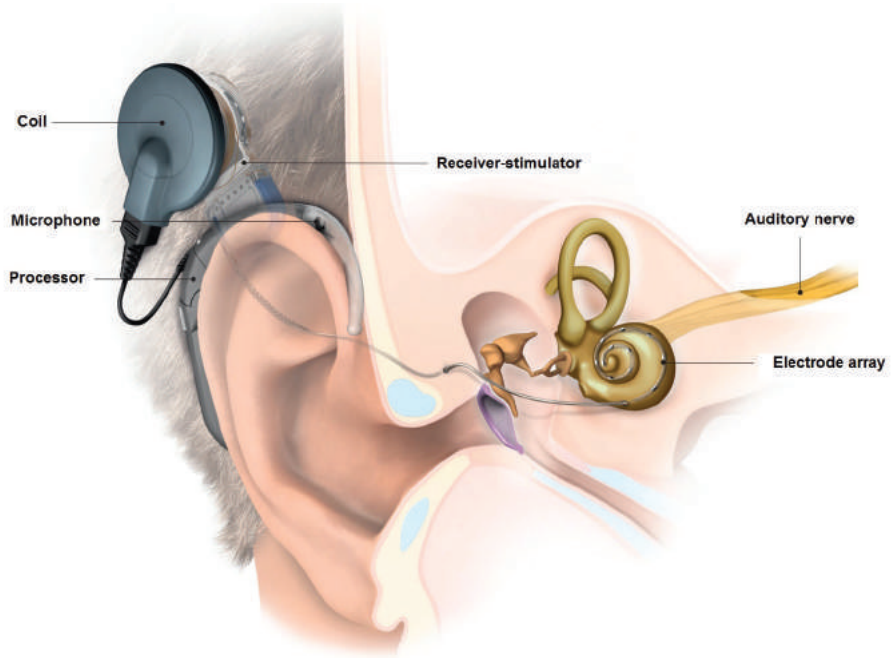

Figure 6: Schematic overview of a cochlear implant with its components. Sounds are picked up by the microphone in the audio processor. The signal is sent to the electromagnetic coil and transmitted transcutaneous to the implanted device. This receiver-stimulator sends electrical pulses along the electrode array. Stimulation of cochlear spiral ganglion cells results in action potentials in the auditory nerve. *Image retrieved from the website of Med-El™*.

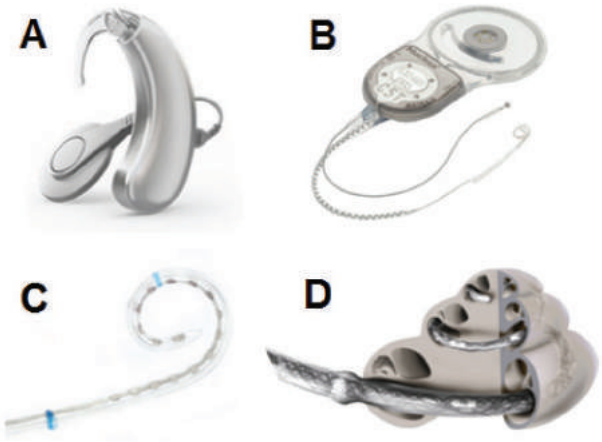

Figure 7: The components of a cochlear implant system from different manufacturers. A: the external speech processor (Oticon Medical™ Neuro One®). B: the implanted device with electrode array and ground electrode (Cochlear™ Nucleus® with CI24RE electrode). C: a close-up view of the HiFocus® Mid-Scala electrode array (Advanced Bionics™,). D: Illustration of an implanted electrode located in the cochlea (Med-El™). *Images retrieved from the websites of Oticon Medical™ (A), Cochlear™ (B), Advanced Bionics™ (C) and Med-El™ (D).*

The most commonly used surgical technique for implantation is a mastoidectomy followed by a posterior tympanotomy for adequate exposure of the cochlear promontory and round window, in order to allow for the insertion of the electrode into the cochlea via the mastoid in a correct angle [27,28]. The electrode array is preferably inserted in the scala tympani by either a direct round window approach or via a separate cochleostomy through the promontory. In case of ossification of the cochlear lumen, which sometimes can be seen in case of otosclerosis, posttraumatic-, postinflammatory- or postmeningitic hearing loss, extra drilling might be necessary to create sufficient lumen for an electrode insertion. In difficult cases with abnormal anatomy, the electrode can also be inserted in the scala vestibuli[29]. A double array electrode might be indicated when cochlear obliteration is severe. This device consists of two separate electrode arrays which are placed through two separate cochleostomies in the basal and second cochlear turn[30,31].

The performance of CI recipients has been analyzed extensively and several factors have been identified to influence the outcome of CI. The most significant factor associated with a poorer CI outcome is a longer duration of deafness[32]. Age of implantation also negatively correlates to the performance if the recipient is older than sixty[33]. Other negative predictors include a prelingual onset of deafness, limited amount of residual hearing, a partial electrode insertion, poor overall medical condition, impaired cognitive capacity and the presence of inner ear malformations[34-36]. Cochlear implantation is considered to be a safe procedure, albeit that it carries a small risk of per- and postoperative complications[37,38]. Major

complications of cochlear implantation include meningitis, flap necrosis, device failures and facial nerve injury. Tinnitus, vertigo, taste disturbance and facial nerve stimulation are considered minor complications.

INDICATIONS FOR COCHLEAR IMPLANTATION

At the beginning of the CI era, CI was only available for postlingually deafened adults with bilateral profound hearing loss and no open-set speech recognition ability with hearing aids[39]. As the proven benefit of CI has increased substantially over the last decades, worldwide criteria for CI have become less stringent. Patients who have been advised against cochlear implantation in the past, may therefore be considered suitable candidates nowadays. Presently, congenitally deaf children, patients with residual hearing and prelingually deafened patients are also being indicated for CI[40]. This thesis focusses on cochlear implantation in three specific groups of patients: (1) patients with asymmetrical hearing, (2) patients with far-advanced otosclerosis and (3) patients with deafness caused by bacterial meningitis. The specific challenges and considerations in the decision making will be further discussed in the paragraph “thesis outline” of this introduction.

Criteria for CI in adults

The Dutch criteria for CI are established by the federation of the eight tertiary CI centers in the Netherlands located in Amsterdam, Groningen, Leiden, Maastricht, Nijmegen, Rotterdam and Utrecht (CI Overleg Nederland, CI-ON). According to the current guidelines in the Netherlands, unilateral CI is indicated for patients with bilateral aided speech recognition scores of less than 50%[41]. Speech recognition is measured after hearing aid fitting, using CVC-words (consonant vowel consonant) in free-field audiometry at 65 dB SPL. Physicians are allowed to diverge from the criteria in some specific cases such as patients with progressive hearing loss. Bilateral cochlear implantation is currently only reimbursed in adults with bilateral SNHL caused by meningitis, as imminent cochlear ossification might preclude CI in the future[42]. An exception is also made for deaf adults with a severe visual handicap (<10% vision and/or <10 degrees field of view of the best eye) as bilateral auditory input in these patients yields a critical advantage for the spatial orientation and localisation[43].

The international availability of cochlear implants is often dependent on guidelines created by local governments or insurance companies[44]. As a result, the criteria for cochlear implantation for adults vary widely across different countries. The audiometric selection of candidates occurs often by using hearing threshold measurements, speech recognition scores or a combination of both. The most conservative audiometric cut offs are applied

in The United Kingdom and Belgium where CI is allowed if the bilateral hearing thresholds are higher than 85-90dB[45,46]. Countries such as Australia and Italy maintain less stringent audiometric cut off levels of hearing thresholds exceeding 70-75dB[47,48]. Variations across countries also apply with respect to the frequency at which hearing loss is measured. Italian and Belgian guidelines, for example, refer to thresholds between 500-2000 Hz[45,47], whereas the United Kingdom maintains thresholds between 2000-4000 Hz[46]. Speech recognition scores are included in most guidelines, though international differences can be seen in the way they are incorporated. The FDA advocates cochlear implantation in patients with an open set speech recognition of less than 60%[49], while Belgium maintains the most stringent criterion of less than 30% speech renognition[45]. Some guidelines use sentences for open set speech recognition, rather than monosyllabic words. This may allow individuals to use their linguistic knowledge to fill in the blanks resulting in an underestimation of the hearing loss. The German approach does not specify audiologic criteria, allowing physicians more freedom in their clinical assessment of the patient. An overview of the international differences regarding the current criteria for CI in adults is provided in Table 1.

Table I: Criteria for cochlear implantation across different countries

Country	Hearing threshold	Speech recognition
Australia	Bilateral >70dB loss above 1500Hz	PS <45% WE, <65% BE
Belgium	Bilateral >85dB loss at 500-2000Hz	Phoneme score <30% WE
Germany	Not specified	Not specified
Italy	Bilateral >75dB loss at 500-2000Hz	Sentence score <50% WE
The Netherlands	Bilateral >85dB loss at 2000-4000Hz	Phoneme score <50% WE
United Kingdom	Bilateral >90dB loss at 2000-4000Hz	Sentence score <50% WE
United States	Bilateral >70dB loss at 500-2000Hz	Sentence score <50-60% WE

WE = worst hearing ear, BE = best hearing ear.

Most countries offer no reimbursement for a second cochlear implant in adults despite several meta-analysis have determined the benefit and cost-effectiveness of a second CI[49-51]. Currently, only the Austrian, Swiss, Swedish and German guidelines, allow for bilateral cochlear implantation. Recent studies also present benefits of CI for patients with single-sided deafness, with or without tinnitus in the deaf ear. Localization abilities significantly improved after cochlear implantation and a substantial suppression of tinnitus was observed[52-54]. Improved speech recognition in noise was also observed although the better performance was often dependent on the spatial configuration of signal and noise[53-55]. Hence, cochlear implantation could be a good method to rehabilitate patients with single-sided deafness as it is currently the only method to restore bilateral input in these patients.

Criteria for CI in children

Cochlear implantation enables deaf children to develop speech and language skills and increases the likelihood of children to obtain conventional education[45,56-58]. Cochlear implantation in children has proven to be highly cost-effective as it often allows children to eventually participate in mainstream society. In the Netherlands, CI is currently reimbursed for children with bilateral aided speech recognition scores of less than 50% or a bilateral hearing threshold of more than 85dB at 2000 and 4000Hz[59]. The application of CI criteria in children can be challenging as measuring pure-tone audiometry and speech recognition scores can be unreliable or even impossible. It is therefore critical to use an age-appropriate test battery for young CI candidates. Newborns in the Netherlands are tested by measuring oto-acoustic emissions (OAEs), in some cases followed by automated auditory brainstem response (AABR) or brainstem evoked response audiometry (BERA). An older age enables alternative assessment of the auditory performance with, for instance, (aided) free field audiometry or closed set picture identification. Objective measurements are complemented by the auditory development of the child.

Numerous studies evaluated the benefit and cost-effectiveness of bilateral CI in children and confirmed the additional value of bilateral CI in children. A second CI in children results in significant better language development, better speech recognition in noise and increased localization abilities as compared to unilateral CI[60-62]. As a result, standard reimbursement for a second implant in children is available in most first world countries. Bilateral CI is in the Netherlands reimbursed for children up to five years of age since 2012[59]. Bilateral cochlear implantation in children between the age of 5 and 18 is allowed since 2014 though this requires independent assessment by a second cochlear implant centre[42].

Patient selection in adults

The selection of adult patients in the Netherlands consists of multidisciplinary evaluation by an audiologist, ENT-surgeon, speech therapist and psychosocial support. The purpose of patient selection is to assess the current hearing performance and to determine whether it is likely that cochlear implantation results in better performance as compared to the situation with best fitted hearing aids or other hearing solutions. The hearing assessment includes pure-tone audiometry, unaided speech recognition in quiet and aided speech recognition in quiet. Prior to hearing assessment, the performance of the hearing aids is optimized. If the current hearing aid offers inadequate amplification, patients are fitted with the best available hearing aids. The ENT surgeon assesses the technical feasibility of cochlear implantation, as well as the preferred operation technique. A CT-scan, and often also a MRI-scan, are made to evaluate the condition of the cochlea and mastoid as well as the condition of the cochlear nerve with respect to electrode insertion and surgical

approach. Imaging may sometimes also reveal the etiology of the hearing loss. On indication patients may be referred for assessment of the vestibular function. Preoperative counseling includes explanation of the assessment process, the surgical procedure including risks of surgery, the rehabilitation period and the expected performance with the cochlear implant. Additionally, the social worker and speech therapist determine whether candidates have realistic expectations of the outcome and evaluate if an adequate social network is available to optimally fulfill the intensive rehabilitation program. Once patients have fulfilled the selection program, patients are appraised by a multidisciplinary CI team followed by an advice of the team.

Patient selection in children

All newborns in the Netherlands are screened for hearing loss within the first days after birth. Early detection of hearing loss allows for a swift workup which might ultimately result in a timely referral to a CI center. In the Netherlands, OAEs are used to screen newborns within the first days after birth. The absence of OAEs indicates a hearing loss greater than 25dB. If OAE measurement are repeatedly negative, they are followed by AABR, which measures the brainstem response after a 35dB click stimulus. When two consecutive AABRs reveal insufficient hearing, infants are referred to an audiology center for further hearing assessment including tympanometry and BERA. Infants with bilateral severe-to-profound hearing loss are referred to one of the eight tertiary CI centers in the Netherlands for etiological diagnosis and to evaluate whether cochlear implantation is necessary and feasible.

THESIS OUTLINE

The decision to perform cochlear implantation can be relatively straightforward in some patients, but for others it can be difficult to determine the best modality and timing for optimal hearing revalidation. This thesis evaluates diagnostic and treatment strategies in several challenging groups of cochlear implant candidates. Three specific groups of patients will be evaluated: (1) patients with asymmetrical SNHL, (2) patients with far-advanced otosclerosis and (3) patients with deafness caused by bacterial meningitis.

Cochlear implantation in patients with asymmetrical SNHL

Patients with severe asymmetric SNHL (i.e., unaidable profound SNHL in one ear and aidable severe hearing loss in the contralateral ear) are often not eligible for cochlear implantation due to the remaining hearing abilities of the best hearing ear. These patients are stuck with monaural input and consequently do not benefit from binaural processing. The speech

recognition abilities in quiet are often relatively good, but speech recognition deteriorates in the presence of background noise. These patients seem to fall between two stools as they are not considered CI candidates but fail to achieve a satisfactory performance with hearing aid fitting in normal day-to-day life. This problem may be solved by cochlear implantation in the functionally deaf ear, combined with acoustic amplification in the contralateral side, which could restore bilateral hearing through bimodal stimulation. In **Chapter 2** we present the results of a prospective study which addresses the outcome of bimodal stimulation in patients with asymmetric SNHL.

According to the current guidelines in the Netherlands, bilateral CI is only reimbursed for children up to eighteen years of age. Due to these restrictions, adult patients with bilateral unaidable profound SNHL who already received a CI are deprived of a second CI. These unilateral CI-users are left with unilateral input and typically experience difficulties in challenging listening conditions and the localisation of sounds is severely impaired. To improve the performance of these patients, one could fit a second microphone on the non-implanted side of CI users. Analogue to the CROS (Contralateral Routing Of Signal) option to restore bilateral input in hearing aid users, the signal of the satellite microphone can be transmitted to the CI on the contralateral side (CI-CROS). CI-CROS allows for the detection sound from both sides. In **Chapter 3** we evaluate whether CI-CROS option is an improvement and if CI-CROS could be an alternative to bilateral cochlear implantation.

Cochlear implantation patients in far-advanced otosclerosis

Otosclerosis or otospongiosis is characterized by bone resorption of the otic capsule followed by a reparative response that causes thick, irregular bone formation. The most commonly affected location is fissula ante fenestram just anterior of the oval window (antefenestral otosclerosis). The majority of the otospongiotic lesions remain small and asymptomatic[63]. Expansion of the lesion can result in stapes footplate fixation and consequently cause conductive hearing loss. Otosclerosis accompanied by hearing loss has a prevalence of 0.3-0.5% in de Caucasian population[64]. For these patients stapes surgery is the preferred surgical intervention in which the fixated stapes is replaced with a prosthesis thereby reducing the conductive hearing loss. Dr. John J. Shae introduced the stapedectomy in 1956 in which the complete stapes, including the stapes footplate, was removed[65]. After the stapedectomy, the oval window is covered with a vein graft and a Teflon prosthesis is attached to the incus and placed on the oval window. Dr. Jean Marquet presented the stapedotomy technique in 1965[66]. In case of a stapedotomy, only the suprastructure of the fixated stapes is removed and the stapes footplate remains in situ. A small fenestration is made in the fixed footplate with a micro drill, laser, needle or micro perforator. Subsequently, a piston prosthesis is placed through the fenestration and clipped on the long process of

the incus (Figure 8). Both the stapedectomy and a stapedotomy are considered excellent techniques for closure of the air-bone gap in patients with otosclerosis and are nowadays widely used.

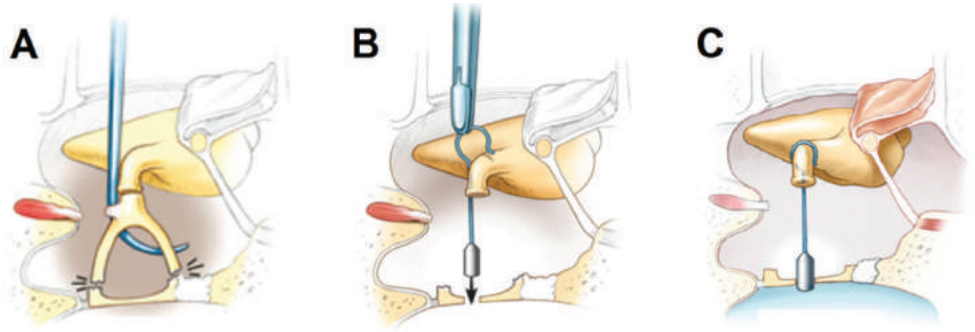

Figure 8: An overview of the surgical steps during a stapedotomy procedure. (A) The suprastructure of the stapes is fractured and removed. (B) A fenestration is made in the fixed footplate and the piston prosthesis is placed though the fenestration and attached to the long process of the incus. (C) Illustration of the altered anatomy of the middle ear after stapedotomy. *Images adapted from "Atlas of Skull Base Surgery and Neurotology" by Robert K. Jackler.*

In some patients, otosclerotic foci also affect the cochlea with additional SNHL loss as a result[67,68]. How otospongiosis can lead to SNHL is not fully elucidated, but a current hypothesis states that SNHL in otosclerosis is thought to be the result of calcification of the cochlear lumen thereby distorting the movement of the basilar membrane[67]. Alternatively, an intracochlear immune reaction could be responsible, through lytic enzymes that are released into the perilymph from otosclerotic foci[69]. Patients suffering from long-term otosclerosis accompanied by severe mixed hearing loss can eventually develop far-advanced otosclerosis (FAO). FAO is defined as an air conduction threshold of more than 85dB and an immeasurable bone conduction threshold[70].

Patients suffering from FAO may eventually meet the criteria of cochlear implantation. However, in some cases a stapedotomy combined with hearing aid fitting could also have satisfactory results. Selecting the best treatment option in FAO can be difficult because it is hard to predict the success rate of stapedotomy in severe mixed hearing loss[71-73]. On the other hand, cochlear implantation can be technically challenging due to extensive otospongiotic and otosclerotic lesions around the otic capsule. Even after a successful cochlear implantation, the rehabilitation of patients with otosclerosis can be challenging because progressive otosclerotic changes in the cochlea can affect the performance of the implant[74-75]. Despite several publications over the last decades, there seemed no consensus regarding the outcome of stapedotomy in patients with FAO. We performed a systematic review of the literature to assist physicians in selecting the optimal treatment strategy for

patients with FAO. In **Chapter 4** we propose an algorithm for the treatment with either CI or stapedotomy of patients with FAO based on pre-operative speech recognition and the otospongiotic abnormalities as seen on HRCT. We initially opted for cochlear implantation in all patients with an aided speech recognition score lower than 30%. Since then, Lachance et al. published a study in which they reported outstanding results of stapedotomy in a group of severely affected patients which, according to our algorithm, were candidates for CI[73]. In follow-up of our algorithm, we performed a meta-analysis of the literature to evaluate the effectiveness of a stapedotomy combined with hearing aid fitting in cochlear implant candidates with FAO. The results of this meta-analysis and our own recent experience of stapedotomy in CI candidates are presented in **Chapter 5**.

Cochlear implantation after bacterial meningitis

One of the severe sequelae of bacterial meningitis is the occurrence of SNHL. The hearing loss is caused by bacterial endotoxins and the subsequent immune reaction, affecting not only the meninges and the brain but also the cochlea[76]. The cochlear inflammation takes place at an early stage of meningitis and SNHL can be present as soon as two days after onset of meningitis. Severe bilateral SNHL occurs in up to 9% of the postmeningitic patients[77] and the preferred method for rehabilitation of these patients is cochlear implantation.

After bacterial meningitis, cochlear inflammation can result in fibrosis, calcification or even ossification of the cochlear lumen[76,78]. If obliteration occurs, it usually starts directly after onset of the meningitis, and ossification of the cochlear lumen can be complete within weeks. If this cochlear obliteration is ongoing, the chances of an uncomplicated successful cochlear implantation may diminish over time. Extra drilling, a scala vestibuli approach or a double array placement is sometimes necessary to achieve an optimal electrode insertion after meningitis. The timing of cochlear implantation in postmeningitic SNHL is therefore crucial as patients should preferably be implanted before the cochlear lumen patency diminishes[79,80]. HRCT is able to detect calcification or ossification of the cochlear lumen. Once detected, cochlear implantation is already more difficult. It would be helpful to be able to predict at an earlier stage whether cochlear patency is diminished. Magnetic resonance imaging (MRI) may be a valuable tool in predicting hearing loss and cochlear obliteration in the follow-up of patients after meningitis. Heavily weighted T2 MRI images (T2MRI) visualize fluid distributions within the cochlea and can detect loss of cochlear fluid caused by either fibrosis or ossification (Figure 9)[81,82]. Additionally, gadolinium-enhanced T1-weighted MRI (GdMRI) can reveal increased perfusion of the striae vascularis which is an indication of active cochlear inflammation (Figure 10)[81,83]. In **Chapter 6** we evaluate the role of GdMRI and T2MRI in (post)meningitic patients with regard to the development of SNHL and the degree of cochlear obliteration encountered during cochlear implantation.

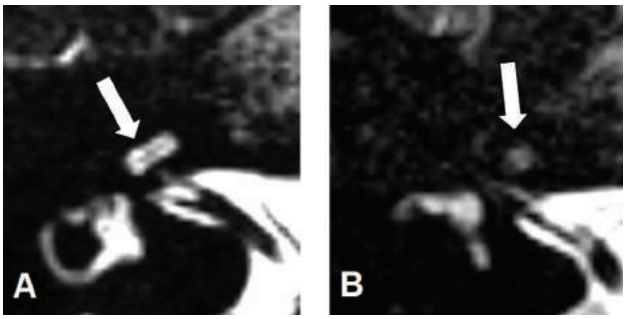

Figure 9: Axial 3D heavily T2-weighted MRI images showing a hyperintense signal within the cochlea indicative of a cochlear lumen containing fluid (A); loss of the hyperintense signal within the cochlea implicating severe loss of intracochlear fluid caused by fibrosis or ossification (B).

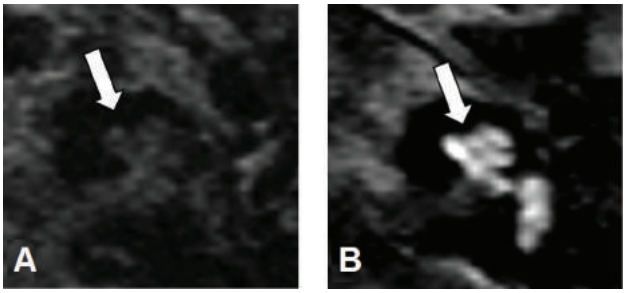

Figure 10: Axial gadolinium enhanced T1-weighted MRI showing the normal situation without cochlear enhancement (A); severe cochlear enhancement caused by increased cochlear perfusion due to inflammation (B).

Bacterial meningitis predominantly affects young children. Whereas in congenitally deaf patients, the preferred age of implantation is between 9 and 12 months, impending cochlear obliteration can necessitate cochlear implantation in postmeningitic patients at an even younger age. A swift diagnostic workup and CI implantation is therefore mandatory in order to minimize the risk of a complicated electrode insertion caused by postmeningitic fibrosis or ossification. These very young patients pose a challenge to the CI team because of their anatomy, physiology, the additional sequelae of meningitis, and the limited time interval between the onset of meningitis and cochlear implantation. In **Chapter 7** we discuss specific diagnostic, anesthesiologic and surgical considerations which should be taken into consideration when performing cochlear implantation in young (postmeningitic) patients under the age of 9 months.

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Chapter 2

Cochlear implantation in adults with asymmetric hearing loss: benefits of bimodal stimulation

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ABSTRACT

Objective: This study addresses the outcome of cochlear implantation in addition to hearing aid use in patients with asymmetric sensorineural hearing loss.

Study Design: Prospective longitudinal study.

Setting: Tertiary referral center.

Patients: Seven adults with asymmetric sensorineural hearing loss, i.e. <30% aided speech recognition in their worst hearing ear and 60-85% speech recognition in their best hearing ear. All patients had a postlingual onset of their hearing loss and less than twenty years of auditory deprivation of their worst hearing ear.

Intervention: Cochlear implantation in the functionally deaf ear.

Main Outcome measures: Speech recognition in quiet, speech recognition in noise, spatial speech recognition, localization abilities, music appreciation and quality of life. Measurements were performed before cochlear implantation and three, six and twelve months after cochlear implantation.

Results: Before cochlear implantation, the average speech recognition of the ear fitted with a hearing aid was 74%. Cochlear implantation eventually resulted in an average speech recognition of 75%. Bimodal stimulation yielded speech recognition scores of 82%, 86% and 88% after three, six and twelve months, respectively. At all time-intervals, bimodal stimulation resulted in a significantly better speech recognition as compared to stimulation with only hearing aid or only CI. Speech recognition in noise and spatial speech recognition significantly improved as well as the ability to localize sounds and the quality of life.

Conclusion: This study demonstrated that patients are able to successfully integrate electrical stimulation with contralateral acoustic amplification and benefit from bimodal stimulation. Therefore we feel that cochlear implantation should be considered in this particular group of patients, even in the presence of substantial residual hearing on the contralateral side.

Key Words: asymmetric, bimodal, binaural, cochlear implantation, localization, quality of life, sensorineural hearing loss.

INTRODUCTION

It is well known that patients with bilateral severe-to-profound sensorineural hearing loss (SNHL) are suitable candidates for cochlear implantation. In most countries, it is therefore standard care to offer cochlear implantation to this group of patients. Patients with severe asymmetric hearing loss (i.e., unaidable profound SNHL in one ear and aidable hearing loss in the contralateral ear) are often not eligible for cochlear implantation due to the remaining hearing abilities of the best hearing ear. Because of monaural input, these patients lack the ability to benefit from bilateral hearing and binaural processing. The speech recognition abilities in quiet are often relatively good, but speech recognition becomes poor in the presence of background noise. The absence of bilateral input also results in impaired localization abilities and reduced speech recognition when speech and background noise are spatially separated. Patients often have to wait until their best hearing ear deteriorates further to meet the standard cochlear implant (CI) criteria. This delay in cochlear implantation has several disadvantages. First, patients may not benefit from bimodal stimulation during this period. Second, a longer period of auditory deprivation is associated with poorer CI outcome[1, 2]. Third, the risks of CI surgery increase with age and older patients might have more difficulties with the intensive rehabilitation period after cochlear implantation.

To improve the hearing abilities of patients with asymmetric SNHL, CI could be considered in the functionally deaf ear before the standard CI criteria are met. The synergistic effect of low-frequency acoustic amplification and contralateral electrical stimulation may yield a significant benefit through bimodal stimulation[3-6]. Bimodal stimulation restores bilateral input which is assumed to provide benefits associated with binaural hearing. Consequently, patients can use bimodal stimulation to achieve better performance in challenging listening conditions. The improved performance can be attributed to three binaural phenomena: the better-ear-effect, binaural squelch and binaural summation. These binaural advantages are typically present in normal-hearing listeners but are, to a lesser extent, also observed in patients with bimodal stimulation[3,4]. The better-ear-effect is caused by the physical presence of the head which results in an interaural difference in signal-to-noise ratio (SNR) when signal and noise originate from different spatial locations. Consequently the ear with the best SNR can be used for speech recognition. The squelch-effect reduces the impact of disturbing noise by using the additional input from the ear with the least favorable SNR. In dichotic listening conditions, patients can thus select the best hearing using the better-ear-effect while using the contralateral input to further increase intelligibility with the squelch effect. The summation-effect is the capacity to centrally integrate identical binaural input to improve the speech reception in diotic listening conditions. Besides the possible advantages

of bilateral input, patients with severe asymmetric hearing loss could also benefit from a CI when the CI outperforms the contralateral ear fitted with a hearing aid.

The goal of this study is to determine the performance of patients with severe asymmetric SNHL after cochlear implantation. Outcome measures include speech recognition in quiet, speech recognition in noise, spatial speech recognition and sound localization abilities. Patients are monitored extensively during the first year after implantation to assess the effects of bimodal stimulation at different time intervals. In addition to functional measurements, the quality of life and music appreciation are measured to evaluate the subjective advantage patients experience from bimodal stimulation.

MATERIAL AND METHODS

Participants

The inclusion of the patients was based on aided speech recognition scores, using CVC-words, at 65dB SPL. Patients were included if the aided speech recognition score for their worst ear was <30% and the speech recognition score for the best hearing ear was between 60% and 85%. Excluded were prelingually deafened patients or patients with more than 20 years of auditory deprivation of the worst ear. Patients followed the standard assessment for CI candidates in our department which included evaluation by an ENT-surgeon, audiologist, speech therapist and social worker. All patients have given their informed consent and the study protocol was approved through the Medical Ethics Committee of the VU University Medical Center in Amsterdam (2012-184).

Seven adults were included in this study with a mean age of 60 years (range 33-72 years). The mean unaided pure-tone average threshold (PTA) in the best ear was 83dB HL (range 70-95dB HL). The mean PTA of the worst hearing ear was 108dB HL (range 104-115dB HL). Average aided speech recognition of the best ear was 76% (range 66-85%). None of the patients used a hearing aid in their worst hearing ear, resulting in no speech recognition at 65dB SPL. The etiology of the hearing loss remained unknown for four patients, one patient was deafened by Meniere disease and two patients were diagnosed with otosclerosis. Bilateral stapedotomy was previously performed in one patient (P4) but did not yield a satisfactory speech recognition. In the other patient with otosclerosis (P5), stapedotomy was only performed in the best hearing ear. Demographic information and individual measurements of the participants of this study are presented in Table 1.

Table 1: demographic information and individual measurements

No	Age (years)	Etiology	Speech recognition*(%)		Pure-tone average** (dB HL)		Auditory deprivation (years)	Hearing aid
P1, ♀	64	Unknown	0	72	115	94	6	Phonak Naïda
P2, ♀	65	Unknown	0	70	105	76	12	Oticon Epoq
P3, ♀	33	Unknown	0	73	104	94	20	Phonak Naïda
P4, ♂	61	Otosclerosis	0	72	109	70	4	Phonak Naïda
P5, ♀	60	Otosclerosis	0	66	109	95	1	Phonak Naïda
P6, ♂	68	Ménière	0	85	101	76	1	Phonak Bolero
P7, ♂	72	Unknown	0	81	110	74	9	Phonak Naïda

** = measured in best aided condition, in free field with CVC words at 65dB SPL, ** = average threshold across 500Hz, 1000Hz, 2000Hz, ♂ = male, ♀ = female.*

Cochlear implantation and rehabilitation

Patients were implanted with an Advanced Bionics® HiRes 90K™ implant with 1J™ electrode and fitted with the Advanced Bionics® Naida CI Q70™ speech processor (Advanced Bionics, Valencia, USA). The classic mastoidectomy with posterior tympanotomy approach was used and a full electrode insertion was achieved in all patients. Patients were enrolled in our CI rehabilitation program including frequent fitting by an audiologist and extensive training with a speech therapist. To achieve the optimal performance of the implant, patients were instructed not to use their hearing aid at the start of the rehabilitation period. When speech recognition score of the implanted ear exceeded speech recognition of the contralateral ear, or when stable CI performance was achieved, patients were instructed to simultaneously use their CI and contralateral hearing aid to get accustomed to bimodal stimulation.

Measurements

Measurements were performed before cochlear implantation and three, six and twelve months after cochlear implantation. The most extensive assessment was made before cochlear implantation and after twelve months of use. An overview of data collection at the different time intervals is presented in Table 2. At three and six months only measurements with bimodal stimulation were performed. After twelve months, speech recognition in noise and spatial speech recognition were tested in three listening conditions: with cochlear implant alone, with hearing aid alone and using bimodal stimulation.

Table 2: data collection at different time intervals

	Pre-CI	3 months	6 months	12 months
Pure-tone audiometry	X			X
Speech recognition in quiet	X	X	X	X
Speech recognition in noise	X	X	X	X
Spatial speech recognition	X	X	X	X
Localization abilities	X			X
Music appreciation	X			X
Quality of Life questionnaires	X		X	X

CI = cochlear implant. Data collection at the different time intervals. The most extensive assessment was made before cochlear implantation and after twelve months of CI use.

Audiometry

The test battery comprised pure-tone audiometry, speech recognition in quiet, speech recognition in noise, spatial speech recognition, localization abilities, music appreciation and quality of life questionnaires.

Speech recognition in quiet was measured with monosyllabic words of the consonant-vowel-consonant type (CVC)[7]. Each syllable consists of three phonemes and each list consist of twelve meaningful words pronounced by a female speaker. Patients were seated in a soundproof booth facing a loudspeaker one meter in front. Words were presented at 65dB SPL. The percentage of correctly repeated phonemes of three consecutive lists resulted in the speech recognition score.

The digits-in-noise test (DIN-test) was used to measure speech recognition in noise and spatial speech recognition8. This test consists of 24 digit triplets in a background of steady-state noise presented at a fixed level of 65dBA. All three digits had to be repeated correctly to qualify the response as correct. A one-up, one-down adaptive tracking procedure was used wherein the signal-to-noise ratio (SNR) varied by 2dB. The SNR at which 50% of the triplets were correctly identified resulted in the speech reception threshold (SRT). Evaluations were made in three different listening conditions as demonstrated in Figure 1.

To assess localization abilities, the participant was seated in the middle of an eight loudspeaker array that spaced 45 degrees apart in a circle around the participant. A distinct sound (ringing bell) randomly originated from one of the eight loudspeakers and the participants were instructed to point to the loudspeakers of which they thought the sound originated. Each loudspeaker played the sound three times resulting in a total of 24 presentations. Localization ability was presented as the root mean square (RMS) error in degrees azimuth between the target speakers and the response of the patient.

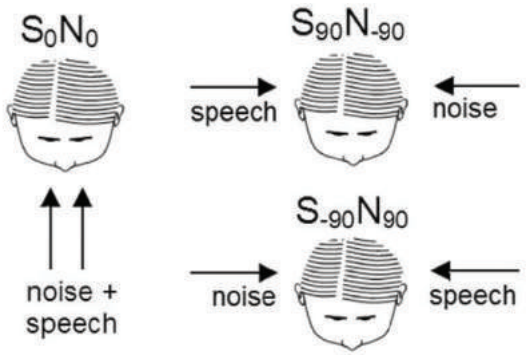

Figure 1: Schematic overview of the setup for speech recognition in noise and spatial speech recognition testing. S_0N_0: speech and noise both presented in front of the listener, $S_{90}N_{-90}$: speech presented at the right side and noise at the left side, $S_{-90}N_{90}$: speech presented at the left side and noise at the right side.

Questionnaires

Quality of life was measured using the Nijmegen Cochlear Implant Questionnaire (NCIQ)[9], the International Outcome Inventories – Cochlear Implants (IOI-CI)[10] and the Health-Utility Index questionnaire Mark 3 (HUI3)[11]. The NCIQ questionnaire measured the quality of life in six subdomains: basic sound perception, advanced sound perception, speech production, activity, social functioning and self-esteem. The IOI-CI questionnaire contains seven items with a scale of answers varying from 1.0 – 5.0 with low scores indicating the worst results. This questionnaire assesses two domains wherein the first domain describes the relation between the user and his cochlear implant (daily usage, benefit, satisfaction, life quality). The second domain addresses the relation between the user and his social environment (limitations, restriction of participation, and impact on others). A descriptive analysis is applied in which individuals with scores lower than 2.5 were considered dissatisfied and individuals with the scores exceeding 2.5 were considered satisfied. The HUI3 questionnaire consists of seventeen questions across eight general domains: vision, hearing, speech, ambulation, dexterity, emotion, cognition and pain. The overall health-related quality of life is calculated with a multi-attribute utility function. A score of 1.00 represents perfect health and a score of 0.00 signifies most disability possible. The single-attribute score represents the quality of life for a single domain.

The ability to appreciate music was measured with a questionnaire developed by Advanced Bionics®[12]. Patients were asked how frequently they listened to music, the overall enjoyment of listening to music, the participation in musical activities and the perception of specific musical features. Patients rated questions on a scale of 0-10 with respect to their current hearing status and to their recollections of music prior to their hearing loss. Additionally, three different music styles (i.e., jazz, classical music and female vocal) were played and

patients were asked about the quality, clarity and appreciation of this music before cochlear implantation and with bimodal stimulation.

Statistical analysis

The Wilcoxon signed rank test was used to test for statistical differences. Results were computed with IBM SPSS statistics software (version 21); a p-value of < 0.05 was used as level of significance. Speech recognition was measured at different time intervals after cochlear implantation (i.e., three, six and twelve months). At these time intervals, the bimodal effect was calculated comparing bimodal speech recognition to monaural speech recognition at the same time interval. Pure-tone thresholds, localization abilities and quality of life were only measured after twelve months and compared to the outcome before cochlear implantation. After twelve months, measurements were performed in different listening conditions: with CI only, with hearing aid only and with bimodal stimulation. Bimodal benefits were calculated by subtracting the SRT measured in the bimodal condition from the preoperative (hearing-aid-only) SRT.

RESULTS

Speech recognition in quiet

The average speech recognition scores in quiet at different time intervals following cochlear implantation are shown in Figure 2. The preoperative average speech recognition score (with a unilateral hearing aid) was 74% (range 66-85). After cochlear implantation, the average speech recognition of the implanted ear was 70% (range: 20-89) at three months, 73% at six months (range: 42-89), and reached 75% after twelve months (range: 42-88). The average speech recognition of the ear fitted with a hearing aid after twelve months (60%) was lower than before cochlear implantation (74%), although not significantly. Bimodal stimulation yielded speech recognition scores of 82%, 86% and 88% after three, six and twelve months, respectively. At all time-intervals, bimodal stimulation resulted in a significantly better speech recognition as compared to stimulation with only hearing aid or only CI.

Individual speech recognition scores after twelve months are shown in Figure 3. In four patients (P2, P5, P6, P7), the speech recognition score with CI was better than with hearing aid. Two patients (P1, P4) showed rather equal performance and one patient (P3) demonstrated better speech recognition with the hearing aid.

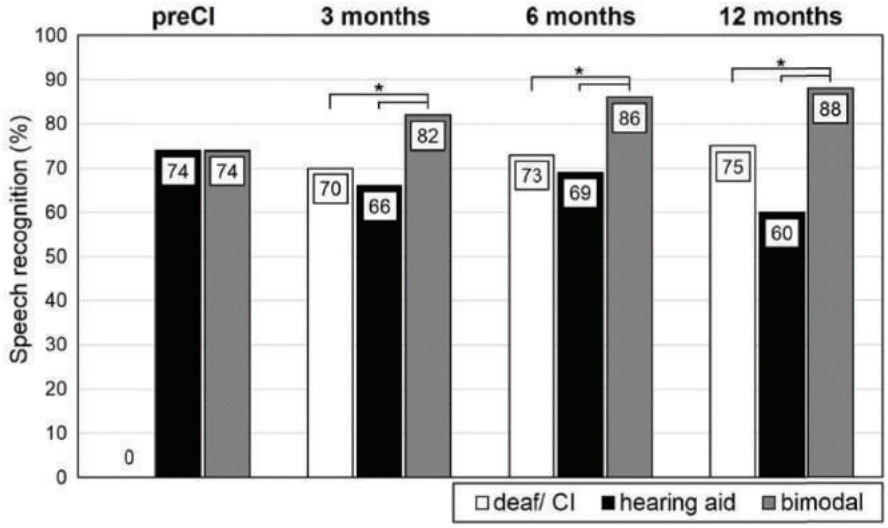

Figure 2: Average speech recognition scores in quiet at different time intervals following cochlear implantation: before CI, after 3 months, after 6 months and after 12 months. At all time internals, bimodal stimulation resulted in significantly better speech recognition as compared to unilateral input.

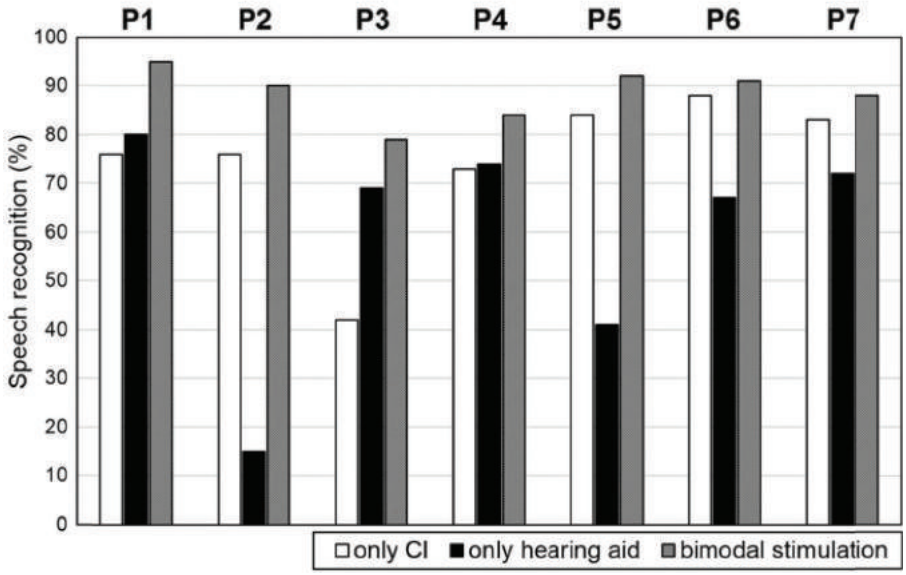

Figure 3: individual speech recognition scores in quiet after twelve months measured with only CI, only hearing aid and in the bimodal condition. Note that all patients demonstrated better bimodal speech recognition as compared to their best performing ear.

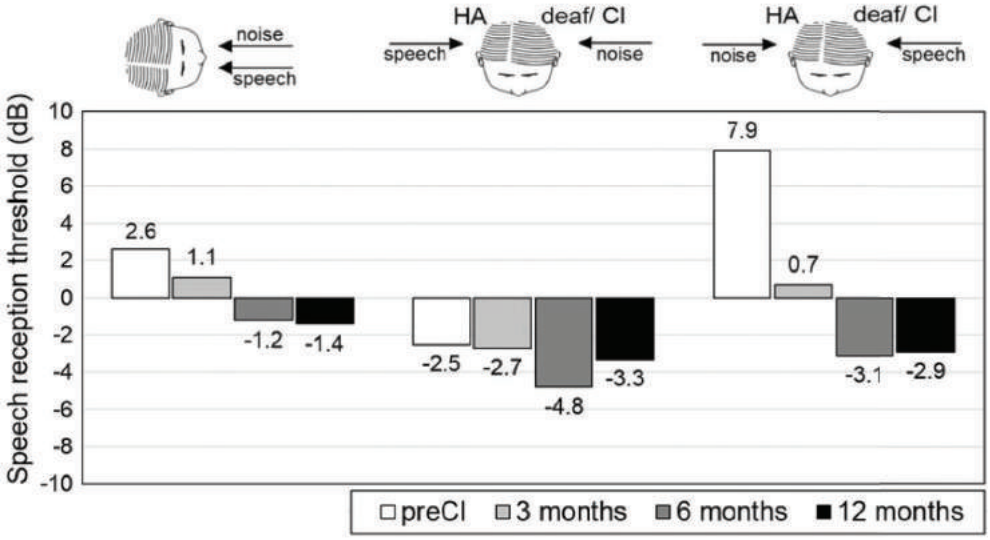

Figure 4: Average SRT for different spatial listening conditions before CI, after 3 months, after 6 months and after 12 months of bimodal stimulation. A lower outcome corresponds to a better performance. HA = hearing aid, CI = cochlear implant.

Speech recognition in noise and spatial speech recognition

Average speech reception thresholds (SRT) for different listening conditions are shown in Figure 4. Note that a lower SRT represents a better performance. When speech and noise were presented in front of the listener, the average SRT before cochlear implantation, with hearing aid alone, was +2.6dB. After three, six and twelve months, the SRT had significantly improved to +1.1dB, -1.2dB and -1.4dB, respectively. Speech presented to the only hearing ear (before cochlear implantation), and noise originating from the deaf side resulted in an average SRT -2.5dB. The SRT was not significant different after twelve months. Finally, a +7.9dB SRT was observed when noise originated from the only hearing ear and speech was presented to the deaf side. Bimodal stimulation resulted in significant better performance as the average SRT decreased to -2.9dB after twelve months.

Bimodal performance after twelve months

After twelve months, measurements were performed in different listening conditions: with CI only, with hearing aid only and using bimodal stimulation. Consequently, the beneficial effects of bimodal stimulation compared with stimulation with only a hearing aid could be determined. The summation effect was determined by evaluating the difference in SRT between the bimodal and hearing-aid-only condition when speech and noise were presented in front of the listener (i.e., the effect of adding an ear with the same SNR). The average summation effect was 3.4 dB but could not be determined statistically. The squelch effect

and the better-ear-effect were calculated in the test condition in which speech originated from one side of the listener, while noise was presented from the contralateral side. Bimodal squelch was determined as the improvement in SRT after adding the ear with the least favorable SNR. The better-ear-effect was calculated as the improvement in SRT after adding the ear with the best SNR. A significant better performance attributed to both the squelch effect (1.9dB better performance) as the better-ear-effect (8.8dB better performance) was observed (Table 3).

Table 3: bimodal performance after 12 months

	HA-only SRT (dB)	Bimodal SRT (dB)	SRT-difference (dB)	p-value
Bimodal summation	+2.0	-1.4	3.4	0.06
Bimodal squelch	-1.4	-3.3	1.9	0.03
Better-ear-effect	5.9	-2.9	8.8	0.02

SRT = speech reception threshold. A p-value of less than 0.05 was chosen as the level of significance.

Localization abilities

Figure 5 illustrates patients' ability to localize sounds before cochlear implantation and with bimodal stimulation after twelve months. The localization abilities improved for all patients. Before cochlear implantation patients demonstrated an average RMS-error of 100 degrees azimuth. Bimodal stimulation led to a significant (p=0.02) better localization ability as the average RMS-error decreased to 63 degrees azimuth.

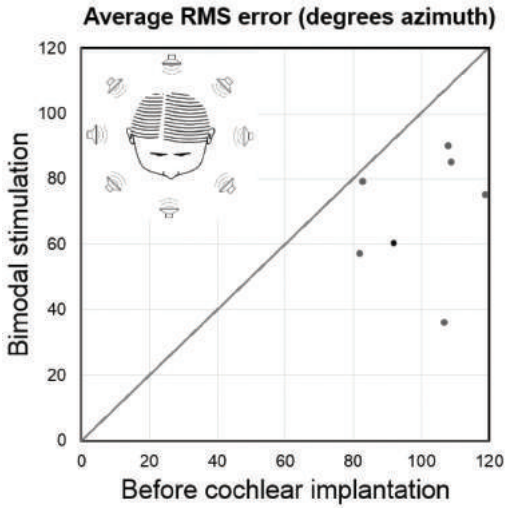

Figure 5: Localization before cochlear implantation and using bimodal stimulation. Bimodal stimulation resulted in significant better localization abilities as the average RMS error in localization decreased from 100 to 63 degrees azimuth.

Music Appreciation

Before the onset of their hearing loss, patients often listened to music (mean score of 6.8/10) and patients considerably enjoyed listening to music (mean score of 7.6/10). The development of SNHL caused a decrease in listening to music (mean score of 3.2/10) and on average patients found listening to music a lot less enjoyable (mean score of 3.3/10). After bimodal stimulation, patients listened to music more often (mean score 6.0/10) and reported an increased enjoyment of listening to music (mean score of 6.3/10). In conclusion, the frequency and satisfaction of listening to music increased after cochlear implantation but did not reach the same level as before the onset of hearing loss. Bimodal stimulation also resulted in better quality, clarity and appreciation of different music styles.

Quality of life

Bimodal stimulation yielded a significant better outcome for the following subdomains of the NCIQ questionnaire: basic sound perception, advanced sound perception, self-esteem activity, and social interactions (Figure 6). Only the speech production was not significantly higher after cochlear implantation. Participants of this study were satisfied with their cochlear implant after six months as all scored high outcomes on both subdomains of the IOI-CI. The average appreciation of the cochlear implant was 4.3/5 (range: 3.5 – 4.5) and patients scored 3.6/5 (range: 2.3 – 4.3) for their relation with the social environment. The HUI3 questionnaire demonstrated an overall health-related quality of life score of 0.63 before cochlear implantation, and 0.70 after (not significantly different). Although overall quality of life did not significantly improve, a significant increase in the score belonging to the hearing domain was observed: 0.45 before cochlear implantation to 0.68 with bimodal stimulation.

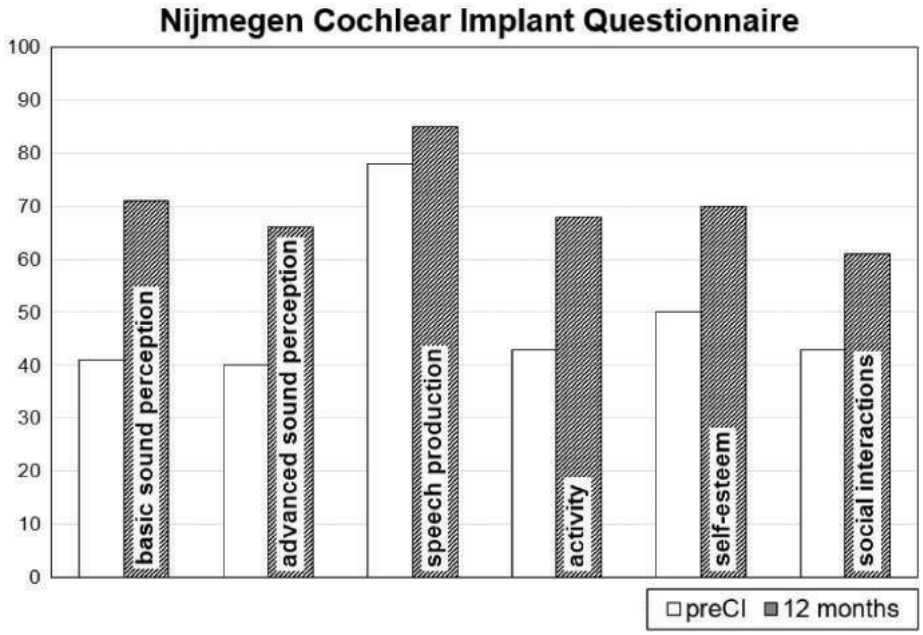

Figure 6: Quality of life with only hearing aid (preCI) and with bimodal stimulation (12 months) as measured with the Nijmegen Cochlear Implant Questionnaire. Patients demonstrated a statistical significant increase for all subdomains of this questionnaire except for speech production.

DISCUSSION

Several studies have evaluated the benefit of using a contralateral hearing aid in unilateral CI-users[3,6,13,14]. In general it is recommended that bimodal stimulation should be considered for CI recipients with contralateral residual hearing. The present study differs in that it addresses the effect of cochlear implantation in patients with fairly good hearing in the best hearing ear. Therefore, the focus is not on the effect of wearing a contralateral hearing aid in CI users, but on the addition of a CI in unilateral hearing aid users. Cochlear implantation is not always standard care in these patients because the hearing performance, which is based on bilateral speech perception scores in quiet, is considered too good.

CI performance

Postlingually deafened adults with less than twenty years of auditory deprivation were included in this study. This increased the probability of good performance after cochlear implantation as a shorter period of auditory deprivation results in better CI performance[1-4,15]. Especially in patients with residual hearing in the contralateral ear, it is important to notice that cochlear implantation actually contributes to a better performance. Almost all

patients in this study demonstrated excellent (70-88%) postoperative speech recognition with their CI. For one patient however (P3), cochlear implantation yielded only 42% speech recognition. This patient was 33 years old and she did not wear a hearing aid since childhood. The etiology of her hearing loss was unknown but in retrospect it is possible that she was prelingually deaf on that side hence explaining the poorer outcome. This outcome is in line with observations made by Cadieux et al. (2013) and Firszt et al. (2012) who both included pre- and postlingually deafened patients[1,2]. Both studies show poor CI speech recognition of <10%, hardly contributing to bimodal hearing, for patients with prelingual onset of hearing loss[1,2].

Speech recognition in quiet

Bimodal stimulation resulted in significant better speech recognition as compared to the condition before CI (88% vs 74%, Figure 2). The benefit of bimodal stimulation on speech recognition is in line with recent observations by Sanhueza et al. (2016) who reported an average bimodal speech recognition of 86% as compared to a preoperative speech recognition of 76%[15]. The actual benefit of bimodal stimulation is however better determined by comparing bimodal performance after twelve months to the hearing-aid-only condition at the same moment. This comparison, which reflects patients' performance if they would not have received a CI, shows that bimodal stimulation results in an average increase in speech recognition score of 28% (88% vs 60%, Figure 2).

A notable observation is that the average speech recognition score of the ear fitted with a hearing aid was lower after twelve months (74% to 60%, Figure 2), an observation shared with Sanhueza et al. (2016)[15]. The fact that the patients were used to bimodal stimulation and only temporarily used monaural input for the testing procedure might partly contribute to this, not statistically significant, poorer outcome. The decrease in performance is predominantly caused by the results of two patients (P2 and P5) who showed significant deterioration of their contralateral ear, probably caused by the natural progression of their hearing loss. The speech recognition of the best hearing ear even decreased to below 50% in these two patients, and at this point they would have been considered suitable candidates for cochlear implantation according to the current Dutch criteria. This emphasizes the importance to consider cochlear implantation for patients with asymmetric SNHL. Early cochlear implantation in patients with progressive hearing loss means that they can benefit from bimodal stimulation when the better ear still has functional hearing. If their hearing decreases to a point that it does not contribute significantly anymore, patients already have a functioning CI on the contralateral side.

Bimodal hearing

Bimodal stimulation resulted in better speech recognition in noise and spatial speech recognition, indicating that patients are able to successfully integrate the signals from two different modes of stimulation (Figure 4). A significant squelch-effect and better-ear-effect were observed when adding the cochlear implant in addition to the hearing aid (Table 3). Morera et al. (2005) also assessed bimodal advantages and observed significant bimodal summation and bimodal squelch[16]. A significant better-ear-effect could not be determined, possibly caused by the setup of the test situation. Whereas the head shadow was maximized in the current study by presenting noise and speech from both sides of the head, Morera et al. (2005) used a test setup in which speech was presented in front and noise originated from the left or right[16]. This test condition causes the head shadow effect to be less prominent, resulting in a more equal SNR arriving at both ear therefore reducing the extent of the better-ear-effect. On the contrary, this test condition yields a greater squelch-effect because speech does not have to travel around the head to reach the contralateral ear. Since Morera et al. (2005) used speech recognition percentages in noise and speech-reception-thresholds were used in this study, a direct comparison of the bimodal outcome could not be made[16]. A recent study by Dincer d'Allessandro et al. (2015) also reported a significant bimodal squelch-effect and better-ear-effect[17]. This study only determined the value of using a hearing aid in addition to a contralateral CI. Based on the PTA however, which was much worse for the ear with hearing aid, it is likely that using a CI in addition to a contralateral hearing aid, would result in similar or even better bimodal benefits. Other studies which evaluated bimodal stimulation in patients with substantial hearing in the ear fitted with hearing aid, did not determine bimodal advantages[1,2,15]. Bilateral hearing is crucial for the localization of sounds. This study confirmed that bimodal stimulation results in significant better localization abilities, a conclusion shared by several other authors[1-3,13]. Both Cadieux et al. (2013) and Firszt et al. (2012) showed that the increased localization ability was predominantly present in postlingually deafened adults[1,2], stressing the need to take the duration of deafness into consideration when deciding to perform cochlear implantation.

Clinical recommendation

Bimodal stimulation in patients with asymmetric SNHL results in a significant better speech recognition (in quiet, noise and spatial), better localization abilities and an improvement in quality of life. Therefore, we feel that cochlear implantation should be considered for patients with asymmetric SNHL, even if there is substantial residual hearing on the contralateral side. Current CI criteria, which are based on speech recognition in quiet, underestimate the hearing disabilities of this group of patients. A more appropriate method to select patients would be to include speech recognition abilities in noise as this better reflects the actual performance in daily life.

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Chapter 3

The addition of a contralateral microphone for unilateral cochlear implant users: not an alternative for bilateral cochlear implantation

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Otology & Neurotology. 2014; 351: 233-9

ABSTRACT

Objective: This study aimed to investigate whether unilateral cochlear implant (CI) users benefit from the addition of a contralateral microphone (CI-CROS) for spatial speech recognition.

Setting: Tertiary referral otology and cochlear implant center.

Methods: The digits-in-noise test was used to measure speech in noise recognition abilities. Evaluations were made in three conditions: speech and noise presented from the front of the listener (S_0N_0) and with spatial separation of speech and noise ($S_{90}N_{-90}$ and $S_{-90}N_{90}$). The performance of CI patients using CI-CROS was compared to their unilateral CI condition (n=10), normal-hearing subjects (n=12) and bilateral CI users (n=5). The presence and extent of several binaural phenomena (binaural summation, binaural squelch and the better-ear-effect) were evaluated.

Results: CI-CROS only provided a benefit in the listening situation wherein speech originates from the side of the CROS microphone, however this benefit was repealed by disadvantages in other listening conditions. With CI-CROS the hearing of patient is essentially monaural, albeit with bilateral input, therefore patients were not able to benefit from the same binaural advantages as normal-hearing subjects and bilateral CI users. Moreover, patients using CI-CROS lost the ability to choose the optimal listening condition in order to perform as well as unilateral CI users.

Conclusion: We conclude that CI-CROS is not advisable for unilateral CI users. Bilateral cochlear implantation would be a better alternative for the rehabilitation of patients with unaidable hearing on the contralateral side.

INTRODUCTION

Cochlear implantation is an effective treatment for children and adults with bilateral severe-to-profound sensorineural hearing loss (SNHL). Currently, the majority of adults receive a cochlear implant (CI) in one ear only. If the contralateral ear has residual hearing, a hearing aid can be fitted to restore bilateral hearing by bimodal stimulation. However, if the contralateral ear has no residual hearing, bimodal stimulation is not possible, and bilateral cochlear implantation can be considered. Several studies have demonstrated the effectiveness of bilateral cochlear implantation to further improve the performance of adult unilateral CI users[1-3]. Nonetheless, bilateral cochlear implantation is not always the standard treatment for adults with severe-to-profound bilateral SNHL, predominantly because of reimbursement restrictions. Many unilateral CI users are left with monaural hearing and typically experience difficulties in hearing sounds from the nonimplanted side and in localization of the sound source. Moreover, their auditory performance deteriorates considerably in the presence of background noise. Especially in situations with spatially separated speech and noise, they do not benefit from three binaural phenomena: the better-ear effect binaural squelch, and binaural summation. The better-ear effect is caused by the physical presence of the head, which creates a head-shadow resulting in a difference in signal-to-noise ratio (SNR) between both ears when two competing sounds are spatially separated. In the case of binaural hearing, the listener can use the ear with the most favorable SNR, while ignoring the ear with the poorer SNR. Depending on the origin of the sounds and the position of the head, this effect can contribute 3.0 to 15.7 dB to the speech reception threshold (SRT) [3-5]. Binaural squelch is based on subtle interaural differences in time, intensity, and phase of both the target speech and the masker arriving at both ears. Consequently, central auditory processing of both signals can yield approximately 0.9 to 2.3 dB SNR improvement[3-5]. Finally, binaural summation results in an increase of loudness when an identical signal is processed by both ears and yields a 2.1 to 3.0 dB improvement of the SRT[3-5].

In patients with unaidable unilateral hearing loss, a microphone can be fitted on the deaf side to transmit the signal from this satellite microphone to the normal hearing ear. This contralateral routing of signal (CROS) has been available for decades, and mixed results have been reported. Some studies conclude that CROS is beneficial for patients with single-sided deafness[6,7] whereas other studies report less benefit or even worse outcome with CROS[8,9]. If hearing loss is present in the better hearing ear, a CROS microphone on the deaf side can be connected to a contralateral hearing aid, which receives the signal and also provides amplification to the better ear (BI-CROS). Previous studies have demonstrated that BICROS provides a satisfactory outcome in 73% to 95% of the patients[10,11]. Consequently,

we speculated about the potential of a CROS microphone in unilateral CI users (CI-CROS). Unilateral CI users are, after successful rehabilitation, still stuck with unaidable hearing on the contralateral side and therefore resemble patients with single-sided deafness. In this group of patients, CI-CROS could be a (very) cost-effective alternative to bilateral cochlear implantation. A CROS microphone eliminates the head shadow effect, thus resulting in an improved signal-to-noise ratio (SNR) when speech is presented to the CROS microphone and noise comes from the side fitted with a cochlear implant. However, when noise is presented to the CROS-side and speech comes from the CI side, the use of bilateral microphones should provide poorer outcome because the relatively clear speech signal received from the CI will be masked by the poorer signal originating from the CROS microphone.

A literature search revealed that only two studies have examined the use of a CROS microphone in CI users. Ching et al.[12] evaluated the benefits of a CROS microphone for unilateral CI users and compared the outcome with bimodal stimulation. A significant advantage in speech perception was described for both CI-CROS and bimodal stimulation when speech was presented to the nonimplanted side. Bimodal stimulation was most favorable because this offered a better outcome in localization and functional performance. Most patients in their study had residual hearing in the contralateral ear, making this recommendation not useful for patients with unaidable hearing in the contralateral ear. A recent study by Arora et al.[13] reported a significant improvement when speech was presented at the CROS side; however, an adverse effect was described when noise was presented at the CROS side. Unfortunately, both studies did not compare the outcome with bilateral CI users, making it impossible to determine whether CI-CROS might be a valuable alternative for bilateral CI. The aim of the current study is to evaluate the additional value for speech recognition of a CROS microphone for unilateral cochlear implant recipients with unaidable hearing on the contralateral side. Speech recognition abilities in noise will be evaluated in several listening conditions, and the results will be compared with a group of normal-hearing subjects and a case series of five (young) bilateral CI users.

MATERIAL AND METHODS

Participants

Three subject groups participated in this study: normal-hearing subjects (n=12), unilateral CI users (n=10) and bilateral CI users (n=5). The normal-hearing group consisted of four men and eight women, with a mean age of 26 years (range 21-32). All subjects had a mean pure-tone threshold ≤20 dB HL at octave frequencies from 250-8000 Hz. The second group contained

ten patients (mean age 51, range 25-76) with severe bilateral SNHL who previously received a unilateral cochlear implant. The last group consisted of five patients (mean age 20, range 4-54) using bilateral cochlear implants. All CI users (unilateral and bilateral) were implanted with a Cochlear Nucleus Contour Advance electrode (Cochlear, Sydney, Australia) and had completed the rehabilitation programme. One patient used the Nucleus 5 sound processor and the remaining patients used the Nucleus Freedom sound processor (Cochlear, Sydney, Australia). Table 1 presents an overview of the demographic details of the unilateral and bilateral CI users.

Table 1: Demographic details of unilateral- and bilateral CI users

Subject	CI ear	Sex	Age (years)	Aetiology of SNHL	CI use (months)	CVC (%)
1	Right	F	76	Idiopathic	4	85
2	Right	F	41	Meningitis	13	92
3	Right	M	62	Otosclerosis	13	82
4	Left	M	78	Idiopathic	15	80
5	Left	M	64	ISSHL	25	98
6	Left	M	38	Meningitis	61	69
7	Left	F	39	Idiopathic	108	92
8	Right	M	35	Meningitis	42	76
9	Right	M	25	Meningitis	14	79
10	Right	F	54	Idiopathic	50	80
11	Both	M	5	Pendred	5, 42	100, 97
12	Both	F	19	Idiopathic	45, 18	71, 72
13	Both	F	54	Idiopathic	50, 7	85, 84
14	Both	M	4	Congenital	30, 30	89, 94
15	Both	M	16	Meningitis	62, 62	100, 100

SNHL = sensorineural hearing loss, CI = cochlear implant, M = male, F = female, ISSHL = idiopathic sudden sensorineural hearing loss, CVC = speech recognition score using consonant-vowel-consonant words, tested in free field audiometry at 65 dB SPL.

Preparation

Subjects were seated in a quiet room during testing, three speakers (Tannoy, Scotland) were positioned at a distance of approximately two meters on the left (-90° azimuth), on the right (+90° azimuth) and in front (0° azimuth) of the listener. Subjects were instructed not to move their heads during testing. Normal-hearing subjects were tested in the monaural and the binaural condition. To test the monaural condition, one ear was muted with a foam earplug and a 3M PeltorOptime earcap (3M, Diegem, Belgium) which resulted in an attenuation of 40-55 dB (confirmed by pure-tone audiometry at frequencies between 250 and 8000 Hz) and a reduction of 40-50 dB for speech recognition in free field audiometry. Unilateral CI

users were tested using their CI with unilateral microphone input and after the addition of a CROS microphone (CI-CROS). For examining the CI-CROS condition, a double external Cochlear Nucleus Freedom Lapel Microphone (Cochlear, Sydney, Australia) was developed in-house by connecting the wires of two microphones. To eliminate any differences between the internal microphone and the external microphones, the internal microphone of the CI was substituted with the two external microphones. These microphones were placed on the implanted side in conditions testing the unilateral-CI-condition, whereas they were positioned on both sides of the head for testing the CI-CROS-condition. If residual hearing was present on the non-implanted side, a foam plug was positioned in the ear canal. Bilateral CI users were tested while using both implants and while using only one CI (the first received CI or, in case of simultaneous implantation, the best performing CI).

Test battery

The digits-in-noise test[14] (DIN test) was used to measure speech recognition in noise. This test consists of 24 triplets of digits presented at a fixed level of 65 dBA in a background of steady-state noise. All three digits had to be repeated correctly to qualify the response as correct. An one-up, one-down adaptive tracking procedure was used wherein the signal-to-noise ratio (SNR) varied by 2 dB. The SNR at which 50% of the triplets were correctly identified resulted in the SRT. The SRT was determined by averaging the SNR values starting at the fifth triplet (i.e., the last 20 triplets). In the group of normal-hearing subjects, each condition was measured twice, and the results were averaged. Evaluations were made in three conditions: in one condition, speech and noise were presented from the front of the listener (S_0N_0). In the other condition, speech recognition was measured with spatial separation of speech and noise: speech was presented to the right at 90-degree azimuth and noise originated from the left side at -90-degree azimuth ($S_{90}N_{-90}$) or vice versa ($S_{-90}N_{90}$) (Figure 1). The order of the conditions was counterbalanced across subjects. For purposes of clarity in the remaining of this paper, for some subjects, the results of the $S_{90}N_{-90}$ condition were presented as the $S_{-90}N_{90}$ condition and vice versa. Hence, for all unilateral CI users, $S_{90}N_{-90}$ was the condition in which speech was presented to the CI side and noise was presented to the CROS- or deaf side. Additionally, for bilateral CI users, $S_{90}N_{-90}$ was the condition in which speech was presented to the CI and noise to the deaf side or second CI. For normal-hearing subjects, $S_{90}N_{-90}$ was the condition in which noise was presented to the muted ear if subjects were tested monaurally.

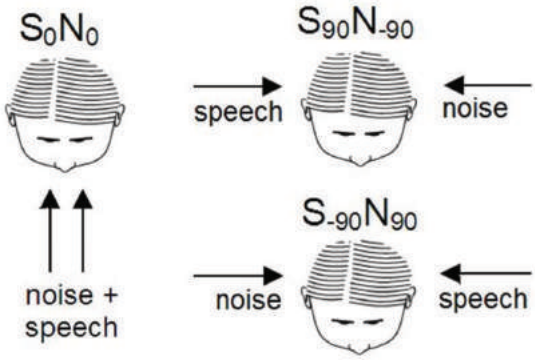

Figure 1: Schematic overview of the setup for speech recognition testing. S0N0: speech and noise both presented in front of the listener, S90N-90: speech presented at the right side and noise at the left side, and S-90N90: speech presented at the left side and noise at the right side. Each group of patients was tested in 2 listening conditions (normal-hearing subjects: monaural versus binaural, unilateral CI users: CI-only versus CI-CROS, bilateral CI users: unilateral CI versus bilateral CI).

Statistical analysis

The analysis was based on the comparison between unilateral and bilateral input for each subject group: normal-hearing subjects (monaural versus binaural), unilateral CI users (CI-only versus CI-CROS), and bilateral CI users (unilateral CI versus bilateral CI). Each group of patients was tested in 3 listening conditions: S_0N_0, $S_{90}N_{-90}$, and $S_{-90}N_{90}$. The Wilcoxon signed rank test was used for the comparison between unilateral and bilateral input for each subject group in each testing condition. Binaural summation was determined by calculating the SRT increase after adding an ear with equal SNR (binaural advantage in S_0N_0 condition). Binaural squelch was calculated as the improvement in SRT after adding the ear with the least favorable SNR (binaural advantage in $S_{90}N_{-90}$ condition). The better-ear effect was calculated as the improvement in SRT after adding the ear with a better SNR (binaural advantage in $S_{-90}N_{90}$ condition). The Kruskal-Wallis test was applied to determine differences between the 3 groups of subjects for each testing condition. The Bonferroni correction was used to adjust for multiple comparisons. Results were computed with the IBM SPSS statistics software (version 21); a $p < 0.05$ was chosen as the level of significance.

RESULTS

Normal-hearing subjects: monaural vs binaural

Figure 2 shows the mean monaural and binaural SRT for normal-hearing subjects in each listening condition. A lower SRT corresponds to better performance. When speech and

noise were both presented from the front (S_0N_0), the mean monaural and binaural SRT were -8.5 and -9.4 dB, respectively, yielding a significant binaural advantage of 0.9 dB (p = 0.02). Noise presented to the muted ear ($S_{90}N_{-90}$) resulted in a monaural SRT of -18.0 dB. Removal of the earcap yielded a SRT of -18.8 dB, a non-significant advantage of 0.9 dB (p = 0.08). Finally, when speech was presented at the muted ear (S-90N90), the monaural SRT was -5.9 dB. Removing the earcap resulted in a significantly improved SRT of -19.2 dB (p = 0.002). Normal-hearing subjects showed significantly better SRTs in all tested conditions, both in the binaural and monaural situation, as compared with unilateral and bilateral CI users.

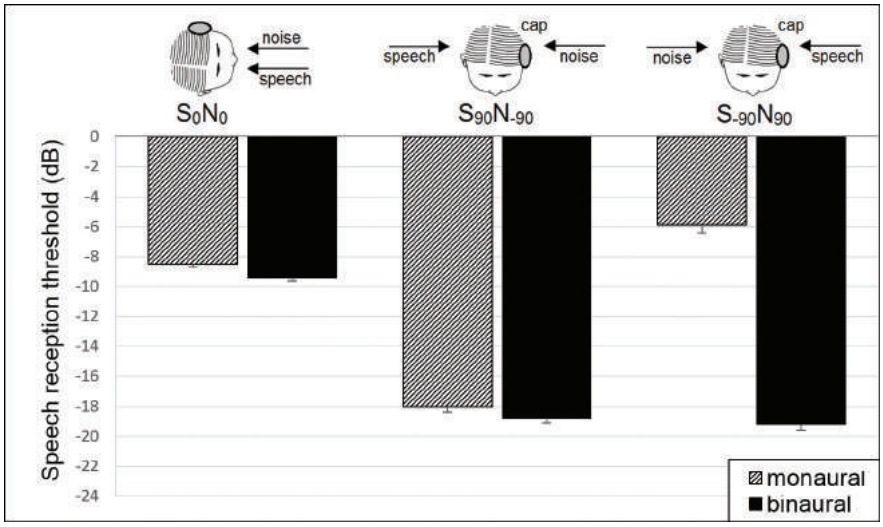

Figure 2: Average speech reception thresholds for normal-hearing subjects in different listening conditions. S_0N_0 = speech and noise presented in front; $S_{90}N_{-90}$ = speech presented to the right ear, noise on the left (hearing/ muted) ear; and $S_{-90}N_{90}$ = speech presented to the left (hearing/muted) ear, noise on the right ear. Error bars represent standard error of the mean.

Unilateral CI users: unilateral CI vs CI-CROS

Figure 3 shows the SRTs for unilateral CI users that were tested with only their CI and after the addition of a CROS microphone. Speech and noise presented from the front (S_0N_0) resulted in a SRT of -1.3 dB, adding a CROS microphone yielded a SRT of +0.1 dB (significant difference, p = 0.005). Speech presented to the CI side and noise to the deaf side ($S_{90}N_{-90}$) resulted in a SRT of -6.1 dB. The addition of the CROS microphone caused significant worse speech recognition: SRT = -0.4 dB (p = 0.005). Presenting noise to the CI side and speech to the deaf side ($S_{-90}N_{90}$) resulted in a SRT of +6.3 dB, adding the CROS microphone led to a significant improvement in speech recognition: SRT = -0.4 dB (p = 0.005). In conclusion, adding a CROS microphone resulted in a SRT advantage of 6.7 dB when speech was presented to the CROS side. However, when noise was presented to the CROS side, a SRT disadvantage of 5.7 dB was observed.

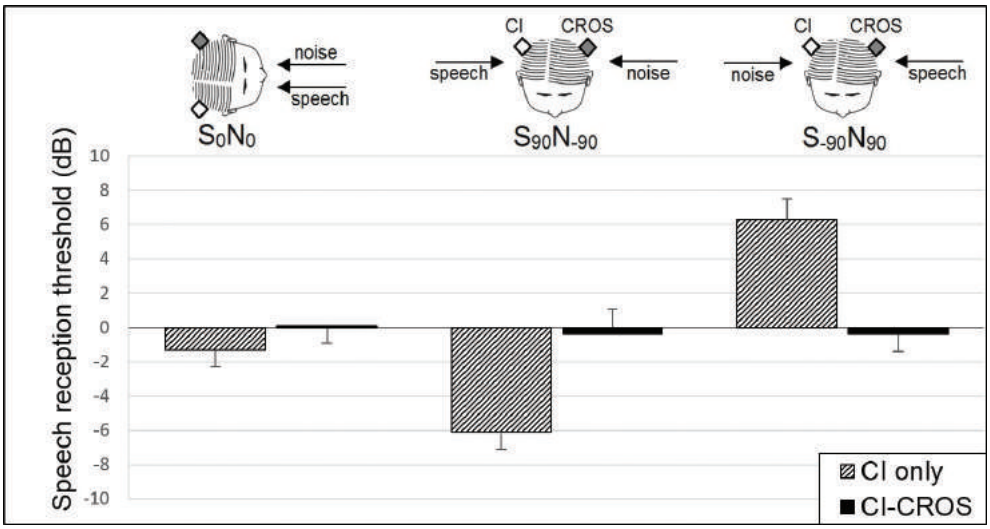

Figure 3: Average speech reception thresholds for unilateral CI users in different listening conditions. S_0N_0 = speech and noise presented in front; $S_{90}N_{-90}$ = speech presented to the CI side, noise on the CI-CROS/deaf side; $S_{-90}N_{90}$ = speech presented to the CI-CROS/ deaf side, noise on the CI side. CI = cochlear implant (white diamond); CROS = contralateral routing of signal microphone (gray diamond). Error bars represent standard error of the mean.

Bilateral CI users: unilateral CI vs bilateral CI

Figure 4 illustrates the SRTs of the five bilateral CI users, measured with either one or both cochlear implants. Speech and noise presented from the front (S_0N_0) resulted in a SRT of +0.4 dB (unilateral CI) and -1.0 dB (bilateral CI). If speech and noise were spatially separated and speech was presented to the CI side and noise to the deaf side ($S_{90}N_{-90}$), the SRT was -4.6 dB. The addition of the second CI in this condition led to a SRT of -6.4 dB; however, this difference is not significant ($p = 0.14$). When only one CI was used and noise was presented to this side and speech to the deaf side, a SRT of +5.6 dB was observed. Adding a second CI yielded a SRT of -6.4 dB, a significant 12 dB improvement as compared with using only one CI ($p = 0.04$).

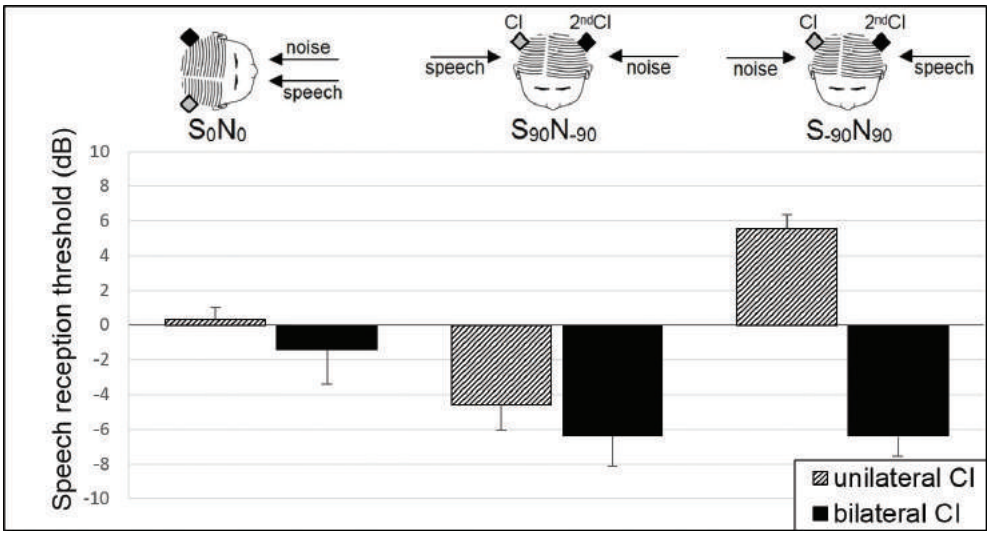

Figure 4: Average speech reception thresholds for bilateral CI users in different listening conditions. S_0N_0 = speech and noise presented in front; $S_{90}N_{-90}$ = speech presented to the first CI, noise on the second CI/ deaf side; and $S_{-90}N_{90}$ = speech presented to the second CI/ deaf side, noise on the first CI. CI = cochlear implant (first CI = gray diamond, second CI = black diamond). Error bars represent standard error of the mean.

DISCUSSION

The effects of a adding a CROS microphone

This study aimed to investigate the use of a CROS microphone for unilateral CI users. The main effect of a CROS microphone is the elimination of the head shadow effect. Patients using CI-CROS have a significantly better SRT when speech is presented to the CROS microphone as compared with the unilateral-CI condition in which speech is presented to the deaf ear (SRT advantage, 6.7 dB). However, when not speech but noise is presented to the CROS microphone instead, CI-CROS results in a significant decrease in speech recognition compared with the unilateral CI condition wherein noise would be presented to the deaf ear (SRT disadvantage: 5.7 dB). Thus, in some listening situations, a CROS microphone results in better performance; however, in some conditions, it is better not to use a CROS microphone. This observation is in agreement with the results of Lin et al. (2006) who used the ABHAB questionnaire and showed that CROS yielded no benefit in different listening situations[9]. However, our measurements seem in disagreement to other studies who reported rather good patient satisfaction of CROS amplification[6,10,11]. This inconsistency might be explained by the subjective methods for outcome testing in these studies, which were based on physician

recommendations and questionnaires rather than objective measurements. It is known from other studies and clinical experience that the localization of sounds is not improved by the use of a CROS microphone since interaural differences are required for localizing sounds. This finding has already been described in other studies [12,13], and therefore, localization tests were not included in this study.

The addition of a CROS microphone provides one ear with an unweighted mixed input picked up from both sides. As a result, the clear signal (of the ear with the best SNR) could be masked with the poor signal (of the ear with a poorer SNR). This mixed input provides no bilateral cues that can be processed and, hence, cannot be used for true binaural hearing. Because CI-CROS eliminates the head shadow, subjects scored similar in the S0N0, S90N-90 and S-90N90 condition (SRTs of approximately 0 dB). Contrary to the CI-CROS users, unilateral CI users can benefit largely from spatial separation of the speech and noise. The average SRT changes from +6.3 dB to -6.1 dB when the head is positioned differently between speech and noise source. In everyday listening situations, unilateral CI users can use this difference to choose an optimal listening position using the head shadow effect to block interfering noise. As Brimijoin et al. (2012)[15] have shown that listeners do not always choose the optimal listening position, unilateral CI users might benefit from training in positioning their head to maximize their hearing potential, looking for an optimum in combination with other aspects like lip reading. Patients using a CROS microphone lose the ability to benefit from spatial separation of speech and noise because the CROS microphone eliminates the positive effect of the head shadow. Therefore, patients using CI-CROS are not able to acquire the optimal listening condition to achieve a SRT as well as unilateral CI users. A device in which one microphone could be switched on and off in specific situations could overcome this limitation. Adaptive noise reduction technologies or directional microphones such as those designed for hearing aids could further increase the performance of the CI-CROS and should be a topic for further research.

Binaural advantages

The addition of a CROS microphone provides bilateral information but processed by one CI. Therefore, CICROS users are by definition not able to benefit from the binaural advantages that normal-hearing subjects and bilateral CI recipients have, such as binaural summation, binaural squelch and the better-ear effect. For normal hearing subjects, binaural summation resulted in a significant SRT improvement of 0.9 dB as compared with the unilateral situation. The average SRT increase for bilateral CI users was 1.8 dB, although this advantage was not significant, possibly because of the small sample size (n = 5). The extent of binaural summation is in concordance with other studies who reported a benefit of 1.1 to 1.2 dB for normal-hearing subjects[4,16] and 1.6 to 2.7 dB for bilateral CI users [2,5,16]. Normal-hearing

subjects showed a 0.9 dB SRT improvement as result of binaural squelch, similar to values as reported before: 0.6 to 2.3 dB[4,16]. The squelch-effect for bilateral CI users was 1.8 dB, also similar as reported in literature[4,16]. The better-ear effect is predominantly based on the presence of the head shadow, which results in a greater SNR difference between the left and right ear. In our study population, the better-ear effect for normal-hearing subjects was 13.3 dB. For bilateral CI users, we found a better-ear effect of 12.0 dB, in line with the model predictions of 12 dB as reported by Culling et al. (2012)[17]. This substantial binaural benefit was caused by the broad separation of signal and noise on both sides of the head. Many other studies used a test setup in which speech was presented in front while noise originated either from the left or the right. Consequently, such a setup ensued a lower attenuation of the speech resulting in a substantially lower head-shadow effect of only 4.6 to 7.4 dB[2,4,5,16]. An overview of the binaural advantages for each subject group is presented in Figure 5. Note that the group of bilateral CI users consisted predominantly of children and that the calculated advantages of bilateral CI might increase with the child's ongoing development of binaural processing.

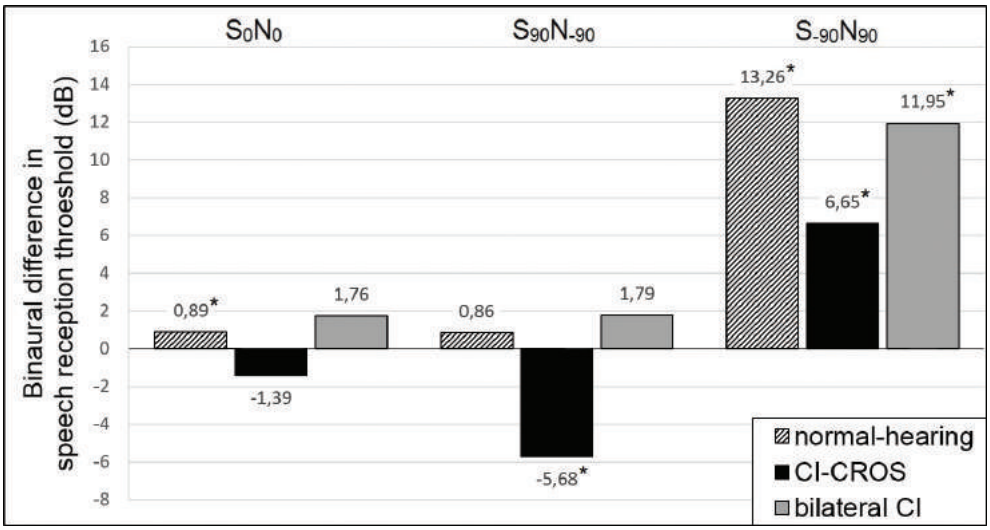

Figure 5: Mean binaural advantages in different listening conditions, dots represent individual data of the bilateral CI users (numbers correspond to subjects as addressed in Table 1). The SRT-advantage in S0N0 corresponds to binaural summation, $S_{90}N_{-90}$ to binaural squelch, and S-90N90 to the better-ear effect. Each group was tested with unilateral and bilateral input (normal-hearing subjects: monaural versus binaural, unilateral CI users: CI-only versus CI-CROS, bilateral CI users: unilateral CI versus bilateral CI). Asterisk = significantly different from zero ($p < 0.05$).

Clinical implications and conclusion

CI-CROS provides a benefit for spatial speech recognition in noise only if speech originates from the side of the CROS microphone. This benefit is repealed by a similar disadvantage

in the listening condition wherein noise is presented to the CROS microphone. Moreover, patients using CI-CROS lose the ability to choose the listening condition that is acoustically optimal and are therefore less able to achieve the most favorable signal (i.e., the highest SNR) compared with unilateral CI users without CI-CROS. Therefore, CI-CROS is not advised for unilateral CI users. Because patients using CI-CROS have monaural hearing, albeit with bilateral input, patients are also not able to benefit from binaural advantages. Bilateral CI users, even children, can benefit from binaural summation, binaural squelch, and the better-ear effect, which leads to better speech recognition in every day listening conditions. Hence, a better option to rehabilitate unilateral CI users would be bilateral cochlear implantation resulting in improved spatial speech recognition and the ability to benefit from binaural advantages. Unfortunately, because of local reimbursement restrictions, this is not always a viable option, and further research to expand the guidelines for bilateral cochlear implantation is warranted.

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Chapter 4

Decision making in advanced otosclerosis: an evidence based strategy

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ABSTRACT

Objectives: To propose an evidence-based strategy for the management of patients with advanced otosclerosis accompanied by severe to profound hearing loss.

Study design: Systematic review of the literature and development of treatment guidelines.

Materials and methods: A systematic review was conducted on (advanced) otosclerosis and cochlear implantation or stapedotomy. We focussed on hearing results, radiological findings and surgical complications. Based on the results of the literature review and our own experience we suggest a strategy to make decisions for the treatment of patients with advanced otosclerosis.

Results: In case of severe mixed hearing loss due to advanced otosclerosis, hearing aids may not result in optimal hearing rehabilitation and cochlear implantation can be considered. However, there could be specific surgical dilemmas concerning cochlear implantation in advanced otosclerosis due to otospongeotic foci around-, and otosclerotic foci within the cochlea. Decision making in these patients can be difficult, especially because a stapedotomy may be still an effective treatment next to hearing aids. An algorithm is presented, based on the speech discrimination score, CT classification and the air-bone gap, which will guide the surgeon to either cochlear implantation, stapedotomy or a hearing aid and follow-up

Conclusion: In order to achieve optimal hearing with minimal disadvantages in patients with otosclerosis and severe to profound hearing loss, an algorithm can help in the selection of patients for either cochlear implantation, stapedotomy or hearing aids and follow up.

Keywords: Cochlear implantation, stapedotomy, guidelines, speech perception, CT classification.

INTRODUCTION

Otosclerosis is the process of bone resorption of the petrous bone (spongiosis), followed by replacement with thick irregular sclerotic bone (sclerosis), often leading to hearing loss. The most commonly affected location is around the oval window, which can result in conductive hearing loss due to stapes footplate fixation (fenestral otosclerosis). In approximately 10% of the patients, otosclerotic foci will also affect the otic capsule (retrofenestral otosclerosis) resulting in cochlear otosclerosis accompanied by sensorineural hearing loss[1]. Next to the radiological diagnosis, there exists a functional diagnosis for otosclerosis with severe mixed hearing loss called far advanced otosclerosis (FAO). FAO was first described by House and Sheehy[2] as an air conduction threshold of at least 85 dB and a nonmeasurable bone conduction threshold (due to the limitations of the audiometer at that time). Nowadays, in the era of cochlear implantation, speech discrimination (SD) scores are more likely to be used instead of pure-tone thresholds. Therefore, the term FAO is not applicable, and in this article we will use the term advanced otosclerosis when referring to patients with sensorineural hearing loss and diminished (<100%) SD scores.

Unfortunately, there are no standard guidelines regarding the rehabilitation of advanced otosclerosis. In advanced otosclerosis there are three treatment options to propose to the patient: (1) no intervention and continue hearing aids, (2) stapedotomy and hearing aid use, or (3) cochlear implantation (CI). In some patients with advanced otosclerosis, the decision can be difficult because of two factors. First, with mixed hearing loss it is hard to predict the success rate of stapedotomy, especially if compared to CI as an alternative intervention. Second, extensive otosclerotic foci around the otic capsule can lead to surgical complications during implantation[1,3,4]. Not only the success rate plays a role in the decision; each intervention has specific advantages and disadvantages. Stapedotomy is a relatively simple, safe, and lowcost procedure that can accomplish very good results. However, the results after stapedotomy in severe mixed hearing loss are unpredictable and variable because stapedotomy is not applicable for the treatment of sensorineural hearing loss[5,6]. Moreover, a feared complication of stapedotomy is an increase of sensorineural hearing loss, which in advanced otosclerosis could result in a functionally deaf ear. CI has yielded excellent results and seems to be an good treatment for patients with advanced otosclerosis[7-9]. On the contrary, it is an expensive and complex procedure that requires experienced surgeons, especially because spongiosis and sclerosis can cause problems during implantation. Furthermore, programming of the CI can be challenging because the progression of otosclerosis can cause postoperative failure of the CI[10].

We have conducted a systematic review to help us with the following questions: Are the results of stapedotomy in advanced otosclerosis good enough to postpone CI? Should patients with advanced otosclerosis receive a CI early because progressive otosclerotic changes could diminish the success rate of CI in the future? Are the surgical risks in patients with advanced otosclerosis and extensive retrofenestral otosclerotic lesions high enough to advise CI in an early stage? Ultimately, guidelines to counsel patients with advanced otosclerosis will be presented, based on a systematic review.

MATERIAL AND METHODS

Search strategy & selection

A systematic review of the literature was conducted using the databases of PubMed, Embase, and the Cochrane Library on October 26, 2010. We searched for articles about the treatment of otosclerosis (domain) with cochlear implantation (intervention) and subsequently, searched for articles about advanced otosclerosis (domain) and stapedotomy (intervention). We did not include the outcome in our search syntax due to the therapeutic design of this paper. The syntax with the key search terms and their synonyms are presented below. Possible duplicates were excluded by using Refworks (www.refworks.com). Articles were included if they contained a combination of domain and determinant. Articles were excluded if the main subject was not in relation to our domain in combination with determinant or in case of languages other than English, Dutch, German, or French. Reviews, and children and animal studies were excluded as well (Figure 1). We screened references and related articles to verify if all valuable articles were included.

The results, acquired from the systematic literature review, will predominantly be presented in tables. We assessed and compared the hearing performance and SD ability after CI and stapedotomy in patients with (advanced) otosclerosis. In addition to the hearing performance, we evaluated the surgical complications during cochlear implantation.

Search syntax

The search syntax was as follows:

([(cochlear AND implant) OR (cochlear AND implants) OR (cochlear AND implantation) OR (cochlear AND implantations) OR (cochlear AND prostheses) OR (cochlear AND prosthesis) OR (auditory AND implant) OR (auditory AND implants) OR (auditory AND implantation) OR (auditory AND implantations) OR (auditory AND prostheses) OR (auditory AND prosthesis)] AND [(otoscleroses) OR (otosclerosis) OR (otospongioses) OR (otospongiosis)])

([(stapedotomy) OR (stapedectomy) OR (stapedectomies) OR (stapedotomies) OR (“stapes surgery”)] AND [(‘‘advanced otoscleroses’’) OR (‘‘advanced otosclerosis’’) OR (‘‘advanced otospongioses’’) OR (‘‘advanced otospongiosis’’) OR (‘‘profound otoscleroses’’) OR (‘‘profound otosclerosis’’) OR (‘‘profound otospongioses’’) OR (‘‘profound otospongiosis’’) OR (‘‘cochlear otoscleroses’’) OR (‘‘cochlear otosclerosis’’) OR (‘‘cochlear otospongioses’’) OR (‘‘cochlear otospongiosis’’)])

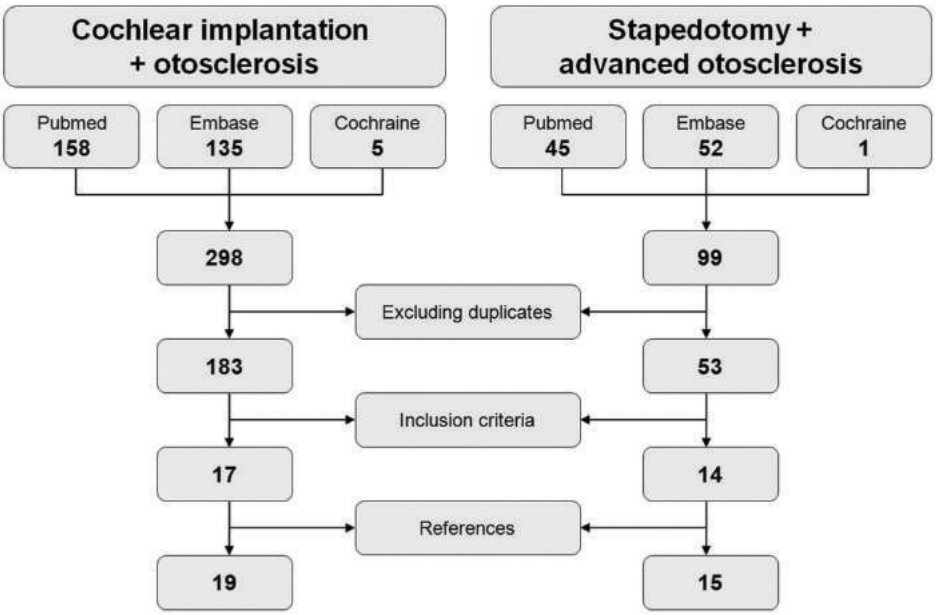

Figure 1: Methodological flow chart of the systematic literature review. For search syntax, see corresponding paragraph in the Material and Methods section. Articles were included if they contained a combination of domain ([advanced] otosclerosis) and determinant (stapedotomy or CI). Articles were excluded if the main subject was not in relation to our domain and in combination with the determinant, or in cases of languages other than English, Dutch, German, or French. Reviews, children, and animal studies were not in the inclusion criteria and were excluded as well. Finally, important references mentioned in the selected articles were added to the search. The numbers refer to the number of articles.

RESULTS

Search strategy & selection

The first search (CI and otosclerosis) resulted in 158, 135 and five articles in Pubmed, Embase, and the Cochrane Library, respectively. After eliminating duplicates, 183 articles remained. Subsequently we assessed these articles on exclusion criteria and checked related articles and references. This resulted in 19 valuable articles about CI in otosclerosis. The second

search (stapedotomy and advanced otosclerosis) resulted in 99 articles, of which eventually 15 articles were used for further analysis. The methodological flow chart of the systematic literature review is presented in Figure 1. A review of the 34 included articles follows.

Cochlear implantation and speech discrimination abilities in otosclerosis patients

The hearing improvement and SD scores after CI in patients with otosclerosis are presented in Table I. We have exclusively presented the SD scores that were measured with tests based on words or sentences. Some authors did not report the SD scores before surgery, because the comparison of pre-and postoperative SD was not the focus of their study. Moreover, nine articles are not mentioned in the table because they did not refer to SD as outcome. In all patients with otosclerosis, CI resulted in better hearing[5–7,9,11,12]. The SD scores after CI had a wide range: 45% to 98% depending on the test used. As expected, patients scored better when the test was based on sentences instead of words. A significant increase in speech perception after CI was reported in studies that compared the pre- and postoperative SD[5–7,9,11]. It was stated that patients with otosclerosis can expect similar benefits from CI in comparison to control patients without otosclerosis[3,8,9,13]. Sainz et al.[9] described two otosclerosis patients with complications: one patient with partial electrode insertion and one patient with facial nerve stimulation, requiring deactivation of the causative electrode. Unfortunately, these patients were not described separately, as these factors would most likely have influenced the outcome.

Stapedotomy and speech discrimination abilities in advanced otosclerosis

The effects of stapedotomy on the hearing improvement and SD scores in patients with advanced otosclerosis are presented in Table II. The SD abilities were measured with hearing aids. One article is not mentioned because the author did not describe the SD scores. The results after stapedotomy were variable: 46% to 100% of the patients achieved an improvement in hearing[5,6,14–25]. The SD scores after stapedotomy were between 38% and 75%[5,6,17,18,21–24]. Shea et al[25]. divided their patients into different cohorts based on the air- and bone-conduction thresholds. They reported a reverse correlation between the severity of the hearing loss and the improvement after stapedotomy; severe hearing loss resulted in lower success percentages and lower SD scores.

Table I: Results of cochlear implantation in patients with otosclerosis

Author	N	Patients hearing improved (%)	Average speech discrimination score before surgery, % (SD)	Average speech discrimination score after surgery, % (SD)	Test
Fayad[11]	16	-	-	45 (17)	MSW
Ruckenstein[12]	8	8 (100)	0 (0)	77 (29)	SEN
Berrettini[5]	5	5 (100)	4 (5)	98 (3)	TSW
Marshall[13]	25	-	-	75 (-)	SEN
Quaranta[8]	9	-	-	60 (22)	TSW
Quaranta[8]	9	-	-	83 (19)	SEN
Rama-Lopez[7]	30	30 (100)	20 (13)	54 (16)	TSW
Rama-Lopez[7]	30	30 (100)	32 (28)	72 (23)	SEN
Calmels[6]	7	7 (100)	0 (0)	80 (15)	TSW
Mosnier[14]	15	15 (100)	-	70 (21)	TSW
Mosnier[14]	15	15 (100)	-	89 (11)	SEN
Psillas[3]	5	-	-	61 (-)	SEN
Sainz[9]	15	15 (100)	0 (0)	79 (-)	TSW
Sainz[9]	15	15 (100)	0 (0)	62 (-)	MSW

N = number of operated ears, SD = standard deviation,; - = not mentioned, MSW = mono-syllable words test, SEN = sentences test, TSW = two-syllable words test.

Table II: Results of stapedotomy in patients with advanced otosclerosis

Author	N	Patients hearing improved (%)	Average speech discrimination score before surgery, % (SD)	Average speech discrimination score after surgery, % (SD)	Test
House[15]	4	3 (75)	-	-	-
Myers[16]	26	14 (54)	-	-	-
Sheehy[17]	67	31 (46)	-	-	-
Wiet[18]	2	2 (100)	-	58 (2)	MSW
Iurato[19]	4	3 (100)	0 (0)	75 (22)	TSW
Frattali[20]	9	7 (78)	-	-	-
Lippy[21]	73	56 (77)	-	-	-
Glasscock[22]	15	9 (82)	4 (6)	38 (26)	MSW
Ghonim[23]	8	8 (100)	33 (20)	71 (20)	SDS
Khalifa[24]	8	6 (75)	5 (7)	49 (29)	SDS
Lippy[25]	24	23 (96)	31 (25)	48 (25)	MSW
Shae[26]	78	52 (67)	-	-	-
Berrettini[5]	6	6 (100)	18 (14)	61 (31)	TSW
Calmels[6]	7	4 (57)	6 (10)	54 (34)	TSW

N = number of operated ears, SD = standard deviation, - = not mentioned, MSW = mono-syllable words test, TSW = two-syllable words test, SDS = speech discrimination score.

Stapedotomy vs cochlear implantation in advanced otosclerosis

CI resulted in better hearing in 100% of the patients, whereas the results after stapedotomy were poorer (46%– 100%). The speech perception after CI varied between 45% and 98%, whereas the speech perception after stapedotomy was between 38% and 75%. The improvement in speech perception was 34% to 94% after CI. Stapedotomy resulted in a slightly poorer improvement of between 17% and 75%. Two studies that compared stapedotomy with CI directly described significantly better performance scores in patients treated with CI[5,6]. In general, the improvement in hearing and the improvement in speech perception seemed to be better after CI than after stapedotomy.

Surgical difficulties and management in cochlear implantation in advanced otosclerosis

Many authors have described surgical difficulties during CI in otosclerosis patients, such as fenestral and basal turn ossification, the necessity for extra drilling, partial electrode insertion, and scala vestibuli insertion. Table III shows the incidence of these difficulties and the occurrence of postoperative facial nerve stimulation (FNS) as reported in the literature. Fenestral ossification frequently requires extra drilling to identify the lumen of the scala tympani to achieve a successful electrode insertion[1,5,7,8,26]. Unfortunately, there are no standard criteria for the action of extra drilling, and the observation is often reported on arbitrary terms. Therefore, the exact number of patients requiring extra drilling remains unknown. Osteoneogenesis can also cause basal turn ossification, a serious pathology as almost all patients (80%–100%) with a partial electrode insertion or misplacement during surgery had basal turn ossification[1,9]. Obliteration of the scala tympani required a scala vestibuli electrode insertion in 2% to 25% of the cases[1,5,11].

Postoperatively, an electrical shunt between the implant and the facial nerve can cause FNS. FNS is an apprehensive complication of CI occurring on average in 20% of the patients with otosclerosis[1,3,5,8,9,11,12,27–29]. The incidence of FNS is significantly higher in patients with otosclerosis compared to control patients, in whom FNS is a rarely reported complication[3,8,9,13,27–29]. This high occurrence of FNS can be explained by an increased conductivity of the otospongiotic bone, making it easier to stimulate the facial nerve[30]. The management of facial nerve stimulation consists of a reduction in stimulus levels of the cranially located electrodes, totally deactivating the causative electrodes or reı¨mplantation[1,9,27–29].

Table III: Surgical difficulties and complications after cochlear implantation in patients with otosclerosis

Author	N	Fenestral oss. (%)	Basal turn oss (%)	Extra drilling (%)	Partial insertion (%)	Scala vestibuli insertion (%)	FNS (%)
Fayad[11]	20	12 (60)	6 (30)	6 (30)	0 (0)	0 (0)	0 (0)
Muckle[28]	38	-	-	-	-	-	4 (11)
Bigelow[27]	4	-	-	-	-	-	3 (75)
Ruckenstein[12]	8	-	3 (38)	1 (13)	0 (0)	2 (25)	2 (25)
Rayner[29]	14	-	-	-	-	-	8 (57)
Berrettini[5]	5	2 (40)	3 (60)	3 (60)	0 (19)	1 (20)	2 (40)
Rotteveel[1]	53	4 (8)	17 (32)	17 (32)	10 (19)	1 (2)	20 (38)
Marshall[13]	30	-	3 (30)	3 (30)	0 (0)	0 (0)	5 (17)
Quaranta[8]	9	8 (89)	-	0 (0)	0 (0)	0 (0)	3 (33)
Rama-Lopez[7]	30	3 (30)	1 (3)	4 (13)	0 (0)	0 (0)	0 (0)
Mosnier[14]	16	-	6 (38)	6 (38)	0 (0)	0 (0)	1 (6)
Psillas[3]	5	0 (0)	-	2 (40)	0 (0)	0 (0)	1 (20)
Sainz[9]	15	-	3 (20)	-	1 (7)	0 (0)	1 (7)

N = number of operated ears, oss = ossification, - = not mentioned, FNS = facial nerve stimulation

CT classification

High-resolution computed tomography scanning (HRCT) can reveal subtle bone formations and demineralization of the cochlea. Therefore, it is considered to be the imaging technique of choice for the diagnosis of otosclerosis with a sensitivity of 66% to 95%[8,13,26,31,32]. Because HRCT can detect subtle otosclerotic foci in and around the cochlea, HRCT may predict the risk of complications during surgery. For instance, the necessity for extra drilling to achieve a successful electrode insertion is related to the extent of fenestral involvement and/or narrowing of the basal turn[7,13,26], and both can be seen on HRCT. Different grading systems (Rotteveel[1] and Symons/Fanning[13]) are available for the classification of otosclerosis. Both are based on the location of the otosclerotic lesions: solely fenestral (grade 1), patchy retrofenestral (grade 2), and diffuse confluent retrofenestral involvement (grade 3) [1,13,32,33]. Difficulties in electrode insertion tend to be associated with cochlear involvement on computed tomography (CT) (grade 2 and 3); however, this is not significant[1,32]. The severity of otosclerosis on CT is also associated with the risk of postoperative FNS, as patients with a higher CT classification are significantly more likely to develop FNS[1,13,32].

Algorithm

Based on the findings in the literature and our own experience, we propose an algorithm for the treatment of patients with advanced otosclerosis (Figure 2). Patients are divided into three main groups using standard speech audiometry[34] (open-set monosyllables[34]): maximum SD scores of <30%, 30% to 50%, and 50% and 70%. Based on the radiological findings and

the extent of the airbone gap, patients will be treated with either CI, stapedotomy, or by a hearing aid and follow-up.

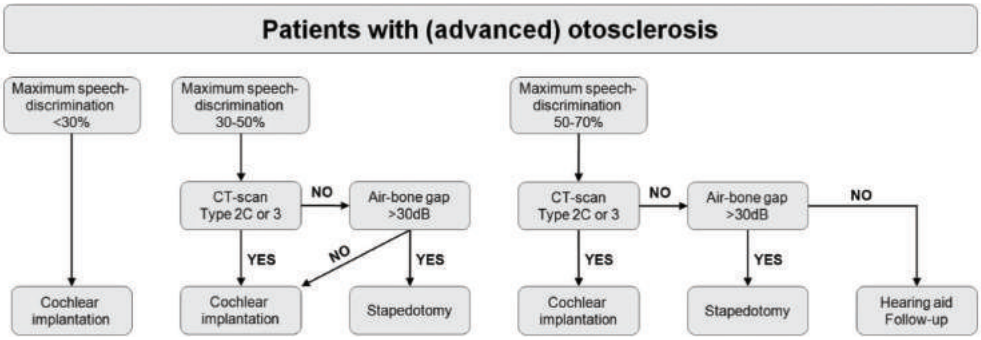

Figure 2: Algorithm guideline to counsel patients with (advanced) otosclerosis. Algorithm is based on the speech discrimination score, computed tomography (CT) classification, and the air-bone gap, and will guide the surgeon to either cochlear implantation, stapedotomy, or a hearing aid and follow-up.

DISCUSSION

Treatment of otosclerosis

In approximately 10% of the patients with otosclerosis, otospongiotic foci will affect the otic capsule (retrofenestral otosclerosis), resulting in cochlear otosclerosis with sensorineural hearing loss.1 In advanced otosclerosis, characterized by mixed hearing loss, hearing aids alone often do not result in optimal hearing rehabilitation, and surgery becomes an option. Nowadays, two surgical techniques are available: stapedotomy or CI. The decision for the appropriate treatment for each patient can be challenging given that both interventions differ in costs, risks, and success rate.

Stapedotomy is a relatively simple and inexpensive procedure that can achieve satisfactory results in patients with otosclerosis. Even in advanced otosclerosis with mixed hearing loss, the surgical correction of only the conductive component can be effective enough to achieve acceptable hearing[5,6,18,19,21–25]. However, in patients with severe mixed hearing loss this treatment would be unsatisfactory because stapedotomy has no influence on the sensorineural component of the hearing loss. Furthermore, the great variability of success rate makes it hard to predict the outcome after stapedotomy in patients with advanced otosclerosis.

Nowadays, an alternative option for patients with advanced otosclerosis is cochlear implantation. Treatment with a CI has resulted in excellent hearing revalidation in advanced otosclerosis and other diseases resulting in sensorineural hearing loss[8,9,13]. However, CI is an expensive procedure and requires experienced surgeons because otosclerotic foci can cause certain surgical problems during implantation. Ossification of the round window or the basal turn requires extra drilling to identify the scala tympani[1,5,7,8,26]. Some patients with severe osteoneogenesis require a scala vestibuli approach to achieve a full insertion (Figure 3C) [1,5,11]. Otosclerosis can also lead to obliteration at the apical regions of the cochlea, which may result in an incomplete electrode insertion. Confluent otospongiotic lesions can surround the cochlea, resulting in pericochlear hypodensity and an osteolytic cavity (double ring or halo effect) [1,32,33]. Because this double ring runs parallel to the basal turn of the cochlea, and the round window has often vanished in a sclerotic plaque, the halo can resemble an opening in the basal turn resulting in an electrode misplacement in this false lumen (Figure 3B) [1,32,33]. It is also possible that an electrode is inserted in the basal turn, that it penetrates the cochlear endosteum, and eventually enters the osteolytic cavity or even the internal auditory canal[4]. Even after a successful implantation, the rehabilitation of patients with otosclerosis is challenging because progressive otosclerotic changes in the cochlea can affect the performance of the implant[10]. Reprogramming with higher stimulus levels might be required to obtain auditory responses,[9,10] although these high stimulus levels increase the risk of facial nerve stimulation. In general, the incidence of facial nerve stimulation in patients with otosclerosis is high[1,3,5,8,9,11–13,27–29].

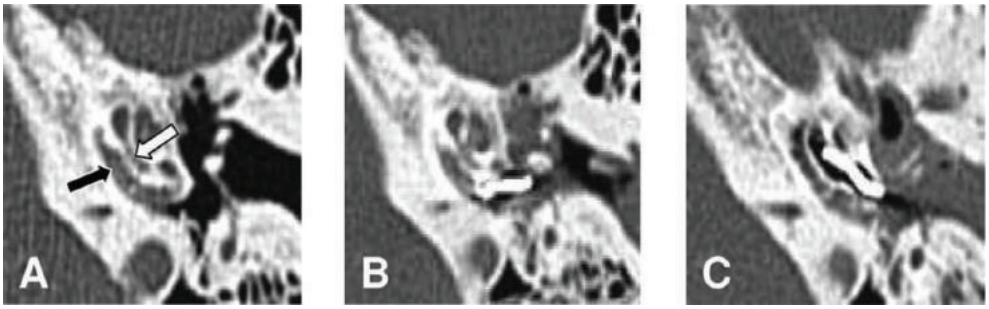

Figure 3: Axial computed tomography (CT) scan of the petrous bone in a patient with retrofenestral otosclerotic lesions: pre-, peri-, and postoperative. (A) Preoperative CT scan: grade 2C retrofenestral otosclerosis (according to Rotteveel classification): double ring (black arrow) and basal turn narrowing (white arrow). (B) Perioperative CT scan of the same patient with the electrode entering a false lumen due to the thickened round window, sclerotic scala tympani, and otospogeotic double ring surrounding the cochlea. (C) Postoperative CT image with a complete electrode insertion in the scala vestibuli.

CT classification

Various authors have used different CT grading systems for the classification of advanced otosclerosis. The CT grading system of Rotteveel[1] is partially based on location and on the

type of lesion: solely fenestral (grade 1) (Figure 4A), retrofenestral: double ring or halo effect (grade 2A) (Figure 4B), narrowed basal turn (grade 2B) or both (grade 2C) (Figure 3A), and diffuse confluent retrofenestral involvement (grade 3) (Figure 4C). One disadvantage of the Rotteveel classification is that subtle erosions around the cochlea are not possible to classify because only a double ring or a narrowed basal turn are included. Symons and Fanning[13] proposed a classification similar to Rotteveel, except grade 2 is based on anatomic location instead of the type of lesion: basal turn (2A), middle/apical turns (2B), both basal and middle/ apical turns (2C). Nonetheless, we prefer to use Rotteveel classification in our algorithm because we believe that the type of lesion is of greater influence on the success rate of CI than the location of the lesion. Subtle erosions in the cochlea, without basal turn narrowing or the halo effect, are not likely to cause considerable problems during electrode insertion.

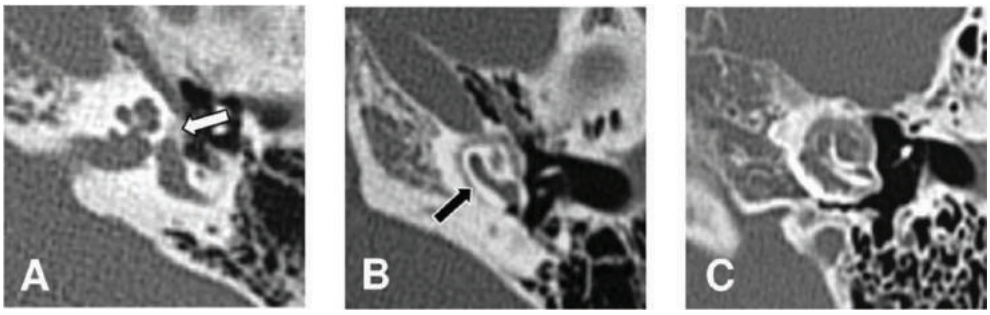

Figure 4: Axial computed tomography scan of the petrous bone in patients with otosclerosis. (A) Grade 1: solely fenestral involvement, otospongiotic lesion on the anterior border of the vestibulum (white arrow). (B) Grade 2A: double ring effect (black arrow). (C) Grade 3: diffuse confluent cochlear involvement with an unrecognizable cochlea.

Algorithm

The presented algorithm divides patients in three main groups based on maximum SD scores: <30%, 30% to 50%, and 50% to 70% (Figure 2). Patients with SD scores of <30% often suffer from severe sensorineural hearing loss, and as has been shown in the literature, the most effective therapeutic intervention for these patients is CI because stapedotomy does not overcome the sensorineural component (Tables I and II). Patients with an SD between 30% and 50% may be treated with either CI or stapedotomy. In cases of severe retrofenestral otosclerosis on HRCT (Rotteveel grade 2C or 3), CI is the better option because of the very good results on hearing and the likely progression of cochlear malformations that could make CI very difficult if postponed. If the CT scan shows less cochlear involvement (Rotteveel grade 1, 2A, or 2B), the air-bone gap (ABG) will guide the surgeon to either stapedotomy or CI. If the ABG is 30 dB or more, a stapedotomy seems to be a cost-effective option with good chances of improvement of hearing. If hearing remains insufficient or decreases with

time after stapedotomy, patients can still be treated with CI. If the ABG is 30 dB or less, patients should be treated with CI rather than stapedotomy because in this patient group stapedotomy yields insufficient improvement of hearing. We believe that patients with an SD of 50% to 70% are candidates for stapedotomy, rehabilitation with hearing aids, or in some cases even CI. Patients with limited cochlear involvement on HRCT (Rotteveel grade 1, 2A, or 2B) and an ABG of 30 dB or more should be treated with stapedotomy. When the ABG is 30 dB or less, and HRCT shows limited cochlear involvement, patients will generally benefit from hearing aids and follow-up. If, on the other hand, HRCT shows extensive retrofenestral otosclerosis (Rotteveel grade 2C or 3), CI seems a viable option in this patient group. To date, SD scores of 50% to 70% are not universally accepted as an indication for CI, and in some countries reimbursement may be a problem. However, we believe that extensive cochlear involvement on HRCT with impending cochlear obliteration may constitute an indication for CI because speech perception and the chances of successful cochlear implantation will diminish further with time. There seems to be a window of opportunity for successful implantation, and CI should therefore be considered as a treatment option in this category of patients[1,32]. The algorithm that is presented here is based on the best evidence currently available. Prospective studies are needed to evaluate this strategy and asses the applicability in a clinical setting.

CONCLUSION

In the absence of management guidelines for patients with advanced otosclerosis, selecting the best treatment modality with optimal hearing results and minimal disadvantages can be challenging. An algrithm based on three parameters: speech performance, CT classification, and the extent of the ABG, ill guide the surgeon to either cochlear implantaion, stapedotomy, or a hearing aid and follow-up.

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Chapter 5

Stapedotomy in cochlear implant candidates with far advanced otosclerosis: a systematic review of the literature and meta-analysis.

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ABSTRACT

Objective*:* To evaluate the effect of stapedotomy in cochlear implant candidates with far-advanced otosclerosis (FAO).

Design*:* Systematic review of literature and meta-analysis.

Data sources*:* PubMed, EMBASE and Cochrane databases were searched on "stapedotomy" and "far-advanced otosclerosis" and their synonyms. The search was carried out on November 28th 2013, no language restrictions were applied.

Study selection*:* The initial search yielded 243 articles, a total of nine articles met our inclusion criteria (i.e., patients with FAO and aided speech recognition scores of 50% or less) and were included in this review. Additionally, a group of five patients (seven stapedotomies) of our own center was also included in this meta-analysis.

Data extraction*:* The methodological quality of included studies was assessed by examining study design, level of evidence, method of measurement and the adequacy of outcome reporting. The speech recognition scores before- and after stapedotomy as well as the pure-tone average (PTA) before- and after stapedotomy were extracted.

Data synthesis*:* A random effects model was fitted for calculating weighted means. The mean preoperative speech recognition score was 11%, stapedotomy resulted in a mean postoperative speech recognition score of 59%. The mean pre- and postoperative PTAs were 112 dB HL and 80 dB HL, respectively. 72% of the patients no longer met the criterion for cochlear implantation (i.e., less than 50% speech recognition) and 35% of the patients reached a postoperative aided speech recognition of more than 80%.

Conclusion: Stapedotomy combined with hearing aid fitting results in a good outcome in a substantial amount of CI-candidates with FAO. We feel that a stapedotomy should be attempted before considering CI in all patients with FAO. In patients with bilateral otosclerosis, a contralateral stapedotomy may offer patients the benefits of binaural processing. If bilateral stapedotomy yields an unsatisfactory outcome, the option for CI is still open.

INTRODUCTION

Otosclerosis, or otospongiosis, is an osteoclast-driven disorder resulting in bone resorption of the otic capsule followed by a reparative response that causes irregular bone formation. Otosclerosis occurs bilaterally in the majority of patients, with a reported bilateral incidence of 76-88%[1,2]. The most commonly affected location is just anterior from the oval window (antefenestral otosclerosis) causing bone formation around the oval window and stapes footplate fixation, resulting in a conductive hearing loss. Stapedotomy yields excellent results in these patients with primarily conductive hearing loss. Additional sensorineural hearing loss (SNHL) develops in approximately 10% of the patients[3,4]. Patients suffering from long-term otosclerosis accompanied by severe mixed hearing loss can eventually develop far-advanced otosclerosis (FAO). FAO was first defined by House and Sheehy as an air conduction threshold of more than 85dB and an immeasurable bone conduction threshold[5] (due to the technical limitations of the audiometer). In the era of cochlear implantation (CI), speech recognition scores are more frequently used than pure tone-thresholds for the choice of rehabilitation in patients with severe-to-profound hearing loss. Nowadays, the term FAO is often used to describe otosclerotic patients with severely decreased speech recognition abilities[6].

CI has proven to be a good treatment option for patients with FAO[3,7,8]. However, CI is an expensive procedure accompanied by an intensive rehabilitation period and some authors report disappointing results because otospongiosis may hamper the electrode insertion and CI performance[9,10]. Alternatively, patients may be treated with stapedotomy and fitted with hearing aids. Stapedotomy is a relatively simple and cost-effective procedure which can result in a good outcome in patients with FAO[11,12]. Nonetheless, the performance after stapedotomy can be disappointing since it is hard to predict the outcome of stapedotomy in patients with mixed hearing loss[13,14,15].

According to the current guidelines in the Netherlands, CI is indicated in patients with aided speech recognition scores of 50% or less. For patients with FAO referred to our CI center, we discriminated between either patients with a functionally deaf ear (i.e., aided speech recognition scores lower than 30%) or patients with aided speech recognition scores of 30-50%. Until recently, we indicated a CI in the first category of patients. For patients with speech recognition scores between 30-50%, we based our decision on the extent of the air-bone-gap and findings on high-resolution CT scanning (HRCT). Patients with an air-bone gap of less than 30dB and/or severe cochlear otospongiosis on HRCT received a CI, in the remaining patients we performed a stapedotomy first[16]. Recently, Lachance et al. published a study in which they reported outstanding results of stapedotomy in a group of patients

with FAO that met our criteria for CI[6]. Despite several publications over the last decades, there is no consensus regarding the outcome of stapedotomy in patients with FAO. The aim of the current study was to conduct a systematic review of the literature to evaluate the potential of stapedotomy in patients with FAO whom are nowadays often referred for CI. Subsequently, we combined the results of the review with our own recent experience in a meta-analysis to determine the best method to rehabilitate patients with FAO.

MATERIALS AND METHODS

Literature search

A systematic search of the literature was conducted by one of the authors (MvL) assisted by a professional librarian, the databases searched included PubMed, EMBASE and the Cochrane Library. Databases were searched for all articles published up to November 28th, 2013, no language restriction was applied. To identify all relevant studies that described the results of stapedotomy in patients with far-advanced otosclerosis, articles were selected on the following terms and synonyms in their title, abstract, keywords or medical subjects heading (MeSH) terms: “stapedotomy” or “stapedectomy” and “far-advanced otosclerosis” or “cochlear otosclerosis”.

Study selection

Two investigators (MvL, EH) independently assessed publications for eligibility. Titles and abstract were screened and, if deemed relevant, full text articles were retrieved and evaluated. Studies of interest were observational studies that included patients with FAO whom underwent stapedotomy. Conference abstracts, animal studies, comments, case-reports and reviews were excluded. Because this study focusses on the improvement in speech recognition, papers not reporting both preoperative and aided postoperative speech recognition scores were excluded. For example, studies which only described the mean improvement in speech recognition in a (heterogeneous) group of patients were excluded. If multiple articles describing the same population of patients were identified, only the most recent publication was included. Finally, the references in selected articles were screened manually. Disagreement over in- and exclusion of articles was resolved by consensus among authors.

Data extraction

Individual patient data were extracted from the publications. The following study-variables were abstracted in a standardized form: author, year of publication, study design, inclusion

criteria, sample size, gender, age, method of speech recognition testing and outcome measurements. Only patients with FAO who were candidates for CI (i.e., patients with an aided speech recognition score of 50% or less) were included in this systematic review. For studies which measured speech recognition at multiple time intervals, we included the most recent measurement which corresponds to the longest duration after stapedotomy. The following outcome variables were collected: pre- and postoperative speech recognition scores, pre- and postoperative pure-tone average (PTA). PTA was calculated by averaging the air-conduction thresholds at 500, 1000 and 2000Hz. Patients with FAO occasionally do not hear pure-tones at maximum output levels of the audiometer (120 dB HL). To provide an estimate of the degree of hearing loss, a 125 dB HL air-conduction threshold was assigned to these non-perceived frequencies. The primary outcome was the speech recognition score (pre- and postoperative), the secondary outcome included the PTA (pre- and postoperative). In addition to the articles derived from the literature search, a group of five patients (seven stapedotomies) of our own department was also included in this meta-analysis.

Assessment of methodological quality

The methodological quality was determined by examining the study design, level of evidence (according to the Oxford Centre for Evidence-based medicine[17]), and method of speech recognition measurement. Finally, the adequacy of outcome reporting was scored by determining whether pre- and postoperative data were available for all operated ears and consequently assessing the cause of missing data.

Patients of our department included in this meta-analysis

In our department, we tended to perform CI in all otosclerotic patients with a functionally deaf ear (i.e., lower than 30% speech recognition). Based on recent publications, we offered a stapedotomy to patients with FAO and explained that CI could still be performed if stapedotomy resulted in an unsatisfactory outcome. Five patients who met our criteria for CI opted for a stapedotomy (Table II). In these 5 patients, we performed 7 stapedotomies (2 patients received bilateral stapedotomies). The patient data derived from the systematic review, combined with our own experience at the VU University Medical Center (VUmc), will be presented in this meta-analysis.

Data synthesis

All studies which were included in this meta-analysis used different methods of speech recognition testing (words or sentences, monosyllables or disyllables, different languages of test battery). Heterogeneity in outcome measures across studies precluded the use of a fixed effect model for data-pooling. Consequently, a random effects model with fixed intercept and random effects for the different studies was fitted for data-pooling of the

speech recognition data. This method takes into account both within and between variations of studies as well as different sample sizes between studies. Also for the PTA measurements, we determined heterogeneity across studies, even though the method of pure-tone audiometry was comparable. Hence, also for pooling PTA outcomes a mixed model was fitted. The weighted means for speech recognition scores and PTA (both pre- and postoperative) were calculated, 95% confidence intervals provide an estimate of the spread across studies. Additionally, the percentage of patients which demonstrated an increase in speech recognition scores more than 30% or more than 50% was calculated. The percentage of patients which reached a postoperative speech recognition score higher than 50% or higher than 80% was calculated as well. These dichotomous outcomes were analysed with generalized estimating equations. A logit function was used to link the patients' data nested within each study to the outcome and an independent correlation structure was chosen.

5

RESULTS

Identification of eligible studies

The initial search yielded a total of 214, 203 and 1 articles in EMBASE, PubMed and the Cochrane Library, respectively. After excluding duplicates, 243 articles remained of which nine articles were suited eligible for this review as they met the inclusion criteria. There was an excellent interobserver reliability and consensus was reached on all articles. All of the included studies showed a low level of evidence (Table I). We identified only one case-control study (level 3b) and the remaining eight studies used a retrospective case series design (level 4). Consequently, studies were scored on the method of speech recognition testing and the adequacy of outcome reporting. Both pre- and postoperative speech recognition scores were available for all patients in 7/9 studies (A). One study omitted speech recognition scores for one patient due to a language barrier (B) [6], and one study was biased because four patients who initially were treated by stapedotomy received a CI though the post-stapedotomy outcome was not presented (C)[18].

The included studies described a total 98 patients in which 17 patients were subjected to bilateral stapedotomy, resulting in a total of 115 stapedotomies. All studies reported predominantly on patients with FAO, defined as an air-conduction threshold of more than 85dB and an immeasurable bone-conduction threshold. Some studies also included patients with conventional otosclerosis and thus also ears with a speech recognition score higher than 50% were presented. We excluded these ears (n=23) from further analysis[6,11,19]. In summary, the literature search identified 92 ears with FAO in which a stapedotomy was

performed. In combination with the seven stapedotomies of our own center, a total of 99 operated ears were available for further analysis.

Table I: Included studies en quality assessment

Author	Total ears operated	Included in review	Study design	Level of evidence*	Method of SR testing	Adequacy of SR reporting
Berrettini et al.	9	9	RS,CI	4	WRS	A
Calmels et al.	11	7	RS,CI	4	DSW	C
Ghonim et al.	12	9	RS	4	SDS	A
Glasscock et al.	15	15	RS	4	WRS	A
Iurato et al.	34	18	RS,CC	3B	WRS	A
Iurato et al.	4	4	RS,CS	4	WRS	A
Khalifa et al.	9	9	RS	4	SDS	A
Lachance et al.	19	18	RS	4	SEN	B
Wiet et al.	2	2	RS,CS	4	MSW	A

** = According to the Oxford Centre of Evidence-based Medicine, SR = speech recognition score, RS = retrospective study, CI = compared with cochlear implantation, CC = case-control study, WRS = Word Recognition Score, DSW = Disyllable Word Testing, MSW = Monosyllable Word Testing, SDS = Speech Discrimination Score, SEN = Sentence Recognition Testing.*

Patients of our department included in this meta-analysis

Five patients with FAO were included in this study and treated by stapedotomy. All patients were affected bilaterally and, at the moment of writing, a second contralateral stapedotomy was performed in two patients (patient 1 and 4; Table II), resulting in a total of seven stapedotomies in five patients. Stapedotomy was performed with a skeeter drill and all patients received a titanium piston prosthesis (Kurz, Dusslingen, Germany). Table II shows the patients characteristics and the audiologic outcomes. After stapedotomy, a powerful hearing aid was fitted and audiological testing was performed in the best aided condition using monosyllable CVC-words presented in free field at 65 dB SPL. The mean preoperative speech recognition score was 6%, stapedotomy resulted in a mean speech recognition score of 72%. The mean pre- and postoperative PTA were 119 dB HL and 88 dB HL, respectively. One patient (patient 5; Table II) demonstrated no benefit of stapedotomy and therefore this patient received a CI which resulted in a satisfactory outcome (i.e., 68% speech recognition at 65dB SPL). The four patients which benefited from stapedotomy showed an excellent postoperative speech recognition score of 80% or more (Table II). Figure 1 illustrates a representative example of the pure-tone audiometry and speech recognition before- and after a successful stapedotomy (patient 1; Table II).

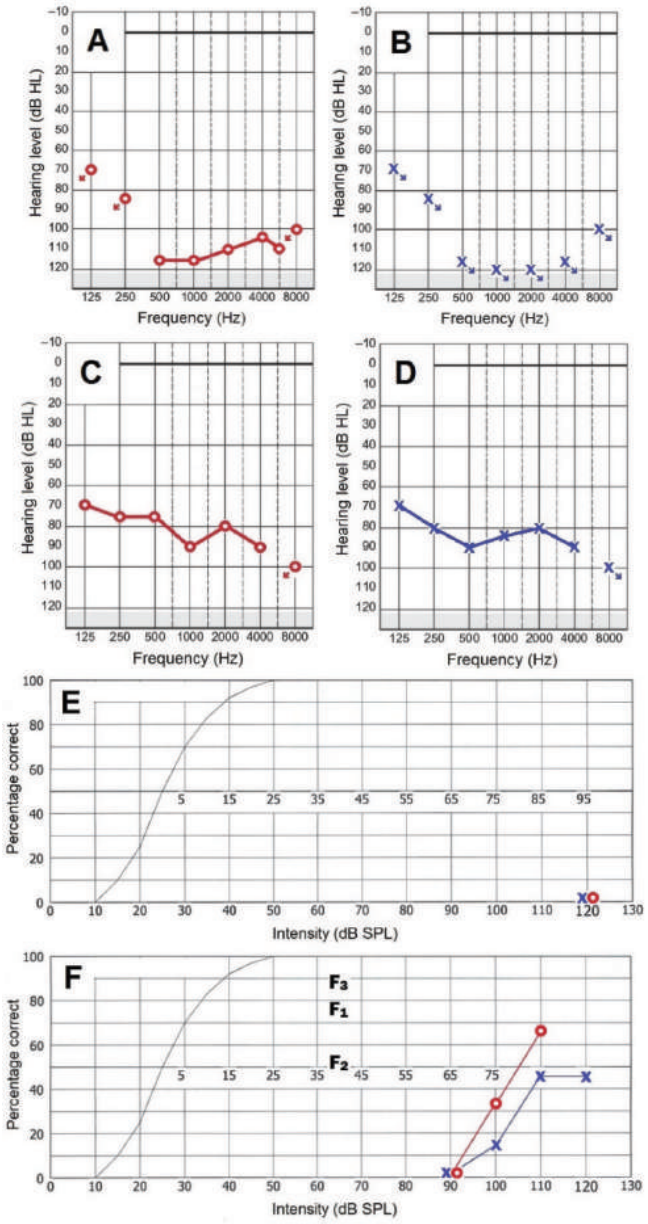


Figure 1: Pure-tone audiometry (PTA) and speech recognition outcomes of a patient with far-advanced otosclerosis treated by bilateral stapedotomy (Patient 1; Table 2). Preoperative PTA shows profound hearing loss of the right ear (A) and immeasurable air-conduction thresholds of the left ear (B). Unaided speech recognition at 120 dB SPL was 0% for both ears (E). Stapedotomy resulted in an improvement in air-conduction thresholds for both ears (C + D); corresponding speech recognition scores at 120 dB SPL were 68% (right ear, O) and 45% (left ear, X). Hearing aid fitting further increased the speech recognition to 76% (right ear, F_1) and 52% (left ear, F_2), measured at 65 dB SPL in free-field audiometry. Binaural speech recognition measurement demonstrates the benefit of binaural processing as the binaural speech recognition increased to 88% (F_3).

Table II: Characteristics and audiology of the VU Medical Center patients included in this meta-analysis

No	Sex	Age	CT*	Surgical procedure	Hearing aid	PTA (dB HL)		Speech recognition	
						Pre	Post	Pre (%)	Post (%)
1	F	64	2A	Right stapedotomy	Oticon Chili	111	82	0	76
			2A	Left stapedotomy	Oticon Chili	125	85	0	52
2	F	56	2A	Right stapedotomy	Resound Alera	112	78	25	88
3	F	62	1	Right stapedotomy	Oticon Sumo	125	73	0	97
4	M	41	2A	Left stapedotomy	Phonak Naida	110	93	20	94
			2A	Right stapedotomy	Phonak Naida	125	82	0	100
5	M	74	1	Right stapedotomy	-	125	125	0	0

*No = patient number, F = female, M = male, PTA = pure-tone average, Pre = before stapedotomy, Post = after stapedotomy, * = extent of otosclerosis on HRCT according to Rotteveel's classification, 1 = solely fenestral involvement, 2A = retrofenestral involvement with double ring. Speech recognition was tested with hearing aid in free-field audiometry at 65 dB SPL.*

Pure-tone thresholds after stapedotomy

PTA outcomes were available for 92/99 of the operated ears because the study of Calmels et al. only presented speech recognition scores and no PTAs[18]. The weighted mean PTA before stapedotomy was 112 dB HL (95% CI: 108-117 dB HL), the postoperative PTA was 80 dB HL (95% CI: 73-86 dB HL), resulting in a mean improvement in hearing threshold of 32 dB (Table III).

Table III: Pure-tone average before- and after stapedotomy

Author	Ears	Mean pure-tone threshold (dB)	Pre	Post	Impr
Berrettini et al. (2004)	9	130 120 110 100 90 80 70 60 50	110	92	18
Ghonim et al. (1996)	9		112	62	50
Glasscock et al. (1996)	15		117	89	29
Iurato et al. (1985)	18		102	71	31
Iurato et al. (1992)	4		125	94	32
Khalifa et al. (1998)	9		114	87	28
Lachance et al. (2013)	19		110	78	32
Wiet et al. (1987)	2		107	69	38
VUmc	7		119	88	31
Weighted mean	92		112	80	32

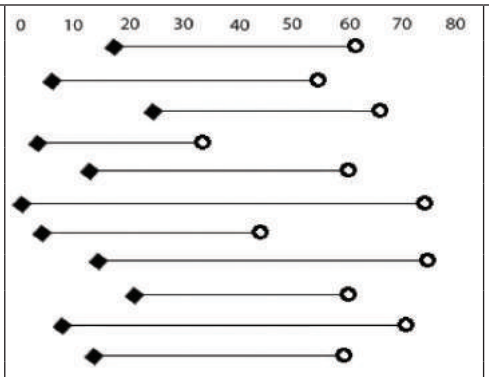
PTA = pure-tone average, Pre (◆) = mean PTA before stapedotomy (dB HL), Post (○) = mean PTA after stapedotomy (dB HL), Impr = the mean improvement in PTA after stapedotomy (dB). The weighted mean of all 92 ears was calculated with a random effects model.

Speech recognition after stapedotomy

Speech recognition scores were not available for eight ears due to the following reasons: language barrier (n=1)[6], or patients underwent bilateral stapedotomy and speech recognition

was only measured binaurally (n=7)[6,13]. Hence, the analysis was performed on 91/99 of the operated ears. Table IV shows the speech recognition scores for each study separately and provides a weighted mean of all studies combined. The mean preoperative speech recognition score was 11% (95% CI: 5-17%), the improvement in speech recognition was 48%, resulting in a mean postoperative speech recognition score of 59% (95% CI: 48-70%).

Table IV: Speech recognition before- and after stapedotomy

Author	Ears	Mean speech recognition (%)	Pre	Post	Impr
Berrettini et al. (2004)	6		18	61	43
Calmels et al. (2007)	7		6	54	49
Ghonim et al. (1996)	9		24	66	42
Glasscock et al. (1996)	15		3	33	30
Iurato et al. (1985)	18		12	60	48
Iurato et al. (1992)	4		0	73	73
Khalifa et al. (1998)	9		4	43	39
Lachance et al. (2013)	14		15	75	60
Wiet et al. (1987)	2		20	60	40
VUmc	7		6	72	66
Weighted mean	91		11	59	48

Pre (◆) = mean speech recognition score before stapedotomy (%), Post (○) = mean speech recognition score after stapedotomy (%), Impr = the mean improvement in speech recognition score after stapedotomy (%).The weighted mean of all 91 ears was calculated with a random effects model.

Speech recognition outcomes for individual patients

In the previous sections we analysed the improvement in speech recognition and PTA for each operated ear. However, some patients were operated bilaterally. In this section we will present the audiological performance per patient rather than looking at each operated ear separately. Figure 2 shows the speech recognition score before- and after stapedotomy for all 83 patients. The best performing ear was selected if patients were operated bilaterally. Ghonim et al. performed four bilateral stapedotomies but only presented the unilateral results separately and did not specify bilateral results per patient[11]. As a result, nine stapedotomies in five patients were analysed as nine separate unilateral stapedotomies.

Stapedotomy did not result in an increase in speech recognition score in 7/83 patients (8%). Stapedotomy resulted in over 30% increase in speech recognition in 59/83 patients (71%) and an increase of more than 50% was achieved 49/83 patients (59%). Moreover, 60/83 patients (72%) demonstrated a postoperative speech recognition score higher than 50% and were thus no longer CI candidates according to the Dutch criteria for CI. Stapedotomy resulted in an excellent speech recognition (higher than 80%) in 29/83 patients (35%).

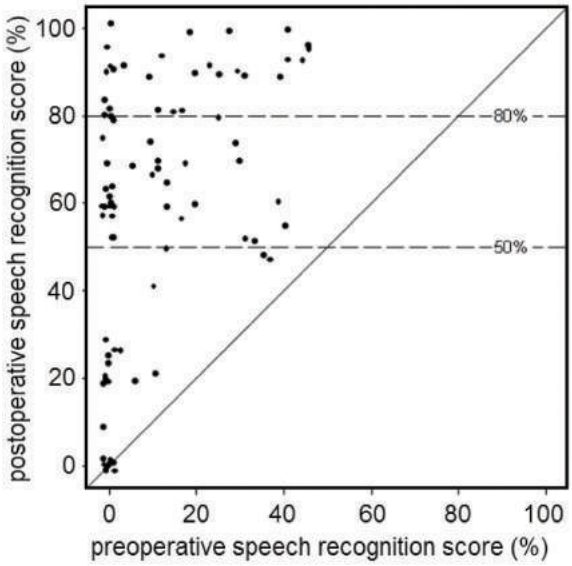


Figure 2: Speech recognition scores before and after stapedotomy in patients with FAO. Each dot represents one patient; the data were jittered to prevent overlap of data points. Stapedotomy yielded no benefit in seven of 83 patients. A speech recognition score higher than 50% was achieved in 60 of 83 of the patients, and 29 of 83 patients demonstrated a postoperative speech recognition score of more than 80%. A decrease in speech recognition scores after stapedotomy was not found.

DISCUSSION

Speech recognition outcomes after stapedotomy

This meta-analysis demonstrates that a stapedotomy can be a viable treatment option for CI candidates with FAO. Unilateral stapedotomy results in a mean speech recognition improvement of 48%. After stapedotomy, the majority (72%) of the patients were no longer CI-candidates. An excellent speech recognition score of 80% or more, was achieved in 35% of the operated patients.

It is very likely that these results represent an underestimation of the true potential of stapedotomy in this patient group. Otosclerosis occurs bilaterally in the majority of patients, especially if patients are affected by extensive otospongeotic lesions[1,2]. The majority of patients included in this meta-analysis however received a unilateral stapedotomy only (64/89 patients). As similar surgical outcomes and chances of improving speech recognition can be expected in the contralateral ear, bilateral stapedotomy would further increase the number of patients with good audiological performance [13]. Additionally, the postoperative

outcome in this analysis is often based on the best performing ear only. The best reflection of a patients' performance would be the binaural, aided free field measurement of speech recognition. Unfortunately, these measurements were only performed in the study of Berrettini et al. and in our own patients[13]. If all bilateral operated patients would have been measured binaurally, the speech recognition scores would have been higher as patients are able to benefit from binaural processing (Figure 1). In addition to the increase in speech recognition, binaural processing also results in better localisation abilities and better performance in the presence of background noise [21].

Differences across studies

Nine studies were included and combined with our own recent experience. All studies demonstrated that stapedotomy led to a significant increase in speech recognition scores; however the postoperative outcome was not consistent across studies. This heterogeneity can partially be explained by the method of speech recognition testing. Lachance et al. used an open-set sentence recognition test and reported the highest postoperative speech recognition score[6]. This positive finding might be an overestimation as compared to other studies because patients generally score better when tested with sentences instead of words[3,13]. All other studies used words for speech recognition testing, unfortunately the exact method of testing is often unclear. Even with comparable methods of testing, variations are present. Glasscock et al., Khalifa et al. and Calmels et al. described the poorest postoperative outcome with mean speech recognition of 33%, 43% and 54%, respectively[14,15,18]. A possible explanation for these poor results is the poor preoperative performance of the majority of patients in these studies (67-80% had immeasusurable speech recognition). Most of these patients did not use hearing aids and it is likely that their hearing loss was present for a long period of time, increasing the chance of a poor postoperative performance[15]. On the other hand, Iurato et al. also included patients with a mean preoperative speech recognition of less than 10%, yet they reported good postoperative speech recognition scores[12]. This might be explained by the study design, as they presented three individual patients in which stapedotomy was very successful instead of a group of patients, thereby possibly introducing selection bias. Nevertheless, our own experience also shows very promising results (postoperative speech recognition scores of 76% and higher) in 3/5 patients that preoperatively did not have any speech recognition abilities (patients 1, 3 and 4; Table II), indicating that poor preoperative speech recognition is an unreliable prognosticator for poor outcome after stapedotomy.

Comparison to CI

CI has become the treatment of choice for patients with profound SNHL. Over the last decades, numerous studies have evaluated CI as treatment for patients affected by FAO[3,7,8].

Patients with FAO demonstrate mean speech recognition scores of 54-75% after CI, lower than those of patients deafened by other etiologies[3,7,8]. The lower performance of CI in patients with FAO may be due to the extent of otosclerotic foci in- and around the cochlea which may lead to difficulties during cochlear implantation. Bone formation around the round window requires extra drilling and sometimes a scala vestibuli approach is necessary for electrode insertion. Intracochlear osteoneogenesis might result in a partial electrode insertion and pericochlear confluent otospongeotic lesions around the cochlea can cause electrode misplacement outside of the cochlear lumen.

Only two studies directly compared FAO patients treated with stapedotomy to patients receiving a CI. Both Berrettini et al. and Calmels et al. demonstrated that CI leads to statistically better mean speech recognition scores than stapedotomy when the whole group of CI patients was compared to the whole group of stapedotomy patients[13,18]. However, stapedotomy yielded excellent results in a considerable subgroup (in 4/6 and 4/7 of the patients). These successfully treated patients achieve mean postoperative speech recognition scores of 80 - 82%, which is comparable or even better than the performance after CI. As previously stated, these results are largely based on unilateral stapedotomies. In our opinion, a higher number of successfully rehabilitated patients, accompanied by a better audiological performance, may be expected from bilateral stapedotomies.

Clinical recommendation

Patients with FAO appear to be suffering from profound SNHL and are frequently treated by CI. However, as this meta-analysis shows, stapedotomy combined with hearing aid fitting can achieve a very satisfactory outcome in many of these patients. It is therefore important to identify otosclerosis as the causative pathology of hearing loss in patients that are referred for CI.

Stapedotomy has several important advantages over cochlear implantation. It is less expensive and the procedure is less complex. After stapedotomy, only hearing aid fitting is required whereas CI is followed by an intensive rehabilitation program. The quality of sound is more natural after stapedotomy, and consequently the appreciation of music is likely to be better preserved. Stapedotomy can easily be performed bilaterally and can restore binaural hearing, thereby improving directional hearing and speech in noise recognition. Stapedotomy can also be performed under local anesthesia, making stapedotomy especially applicable for the elderly and patients with comorbidities.

The standard criterion for measuring the success of stapedotomy; closure of the air-bone gap to 10 dB or less, is not relevant in patients with FAO because bone-conduction levels are often immeasurable even postoperatively[18,21,22]. Likewise, the commonly used Belfast Rule of

Thumb (stating that patients are likely to benefit from stapedotomy if the hearing threshold in the operated ear is brought to 30 dB HL or better or within 15 dB of contralateral ear) does not seem to be applicable for estimating the effect of stapedotomy in patients with FAO[23]. Patients with FAO never achieve a postoperative air-conduction threshold of less than 30 dB HL. Even the best performing patients in this meta-analysis demonstrated a postoperative PTA of more than 50dB HL. Similarly, an interaural difference of more than 15dB was almost always present after (bilateral) stapedotomy. Since these conventional paradigms do not seem valid, we believe that the best indicator of success of stapedotomy in patients with FAO is the postoperative aided speech recognition measured in free-field as these actually represent a patient's performance and impairment in daily life.

It is important to realize that the observed effects of stapedotomy are predominantly based on a single postoperative measurement as most included studies lack long term follow-up. Although stapedotomy in otosclerosis can achieve a stable long-term hearing improvement[24], patients with otosclerosis may demonstrate a further progression of SNHL that cannot be explained by age alone[2,25]. To date, the exact rate of this progression remains unclear, emphasizing the need to for studies with longer follow-up after stapedotomy in patients with FAO.

Currently, there are no reliable prognosticators for the performance after stapedotomy in FAO patients. Age, gender, preoperative PTA and preoperative speech recognition scores do not predict the outcome after stapedotomy. The pericochlear extent of otospongeotic foci as seen on HRCT also seems not correlated to the audiological performance[18]. We therefore feel that a stapedotomy should be attempted before considering CI in all patients with FAO. If unilateral stapedotomy does not result in a satisfactory outcome, a contralateral stapedotomy can be performed as the chance of success in the contralateral ear is not influenced by the previous stapedotomy. If the first stapedotomy was successful, a consecutive contralateral stapedotomy can offer patients the benefits of binaural processing[13]. When (bilateral) stapedotomy does not yield a satisfactory result, the option of cochlear implantation is still open, as a previous ipsilateral stapedotomy will not affect the outcome or performance of CI[3,7,8]. Conversely, patients with bilateral FAO who previously have received a unilateral CI, may still benefit from a contralateral stapedotomy, as this can restore binaural hearing by means of bimodal stimulation[26].

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Chapter 6

The role of MRI in the evaluation of patients with sensorineural hearing loss caused by meningitis

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ABSTRACT

Objectives*:* To determine the role of MRI in the evaluation of patients with sensorineural hearing loss (SNHL) caused by meningitis. Gadolinium enhanced T1-weighted MRI (GdMRI) and 3D heavily weighted T2-weighted MRI (T2MRI) were associated with the occurrence of SNHL and the peroperative surgical findings during cochlear implantation, respectively.

Study design*:* Retrospective cohort study.

Setting*:* Tertiary referral otology and cochlear implant center.

Patients*:* Seventeen patients who developed SNHL after bacterial meningitis were evaluated with MRI. Twenty-one cochlear implantations were performed in eleven patients with severe bilateral SNHL. Six patients developed unilateral SNHL and did not receive a CI.

Interventions*:* MRI scans were independently scored by three observers. Sensitivity, specificity, positive predictive value, negative predictive value and interobserver reproducibility were calculated.

Results*:* Cochlea enhancement on GdMRI was present in 87% of the ears affected by SNHL. In patients with unilateral SNHL, a non-enhancing cochlea predicted the preservation of hearing on the ipsilateral side. In all cases with an incomplete electrode insertion (6/21), loss of cochlear patency was already seen on T2MRI. However, loss of fluid was also found in 29% of the cases in which full electrode insertion was achieved.

Conclusion*:* MRI is crucial for decision making in patients with SNHL following meningitis. Diminished cochlear patency, as seen on T2MRI, is related to electrode insertion difficulty but does not always preclude full electrode insertion in cochlear implantation. Cochlear enhancement on GdMRI is associated with the occurrence of SNHL.

Keywords*:* Magnetic resonance imaging, meningitis, cochlear implantation, sensorineural hearing loss, neuro-radiology.

INTRODUCTION

Sensorineural hearing loss (SNHL) is a serious complication after meningitis and is the most common cause of acquired SNHL in children[1-3]. Approximately 5% to 36% of all patients with bacterial meningitis will develop SNHL[2-4], and severe bilateral SNHL will occur in 3% to 9% of the postmeningitic patients[3,4]. Postmeningitic SNHL can be caused by inflammation of the cochlea because of spread of the infection from the subarachnoid spaces to the inner ear[5,6]. Alternatively, SNHL and meningitis may be caused by otitis, spreading through the cochlea and aqueduct system to the subarachnoid spaces[7]. This inflammation takes place at an early stage of meningitis, SNHL can be present as soon as two days after onset of meningitis[8-10]. Cochlear inflammation can lead to obliteration of the cochlear lumen, caused by fibrosis or ossification[1,5,6,8,11-13]. If obliteration occurs, it usually starts within the first weeks after onset of the meningitis[1,8,11], ossification of the cochlear lumen can be complete within months after meningitis[5,6,8,12]. Nowadays, cochlear implantation (CI) is the treatment of choice for postmeningitic patients with severe bilateral SNHL. However, postmeningitic fibrosis or ossification can block the cochlear lumen and hamper electrode insertion. Patients should preferably be implanted before obliteration occurs, and the timing is crucial to achieve a successful electrode insertion with optimal audiologic performance[5,14,15]. Magnetic resonance imaging (MRI) is an essential diagnostic tool for the follow-up of patients in the direct postmeningitic phase. 3D heavily T2-weighted MRI (T2MRI) allows for detailed imaging of the inner ear anatomy[16]. T2MRI visualizes fluid distributions within the cochlea and can therefore detect narrowing or obliteration of the cochlear lumen caused by ossification as well as fibrosis[12,13,17]. Hence, T2MRI can reveal fibrotic depositions that are not yet calcified. The sensitivity of T2MRI for predicting cochlear obliteration as encountered during surgery is 92% to 100%[1,12], much higher than the 60% to 73% sensitivity of high resolution computed tomography (HRCT), which only detects ossification[5,8,12]. Remarkably, the role of gadolinium enhanced T1- weighted MRI (GdMRI) in the follow-up of meningitis patients is scarcely reported in literature. GdMRI can reveal increased perfusion of the stria vascularis, an indication of active inflammation within the cochlea[9,13]. There is some evidence that cochlear enhancement on GdMRI is related to the occurrence of SNHL[9]. Moreover, cochlear inflammation can be followed by obliteration[11,13,17], accentuating the necessity for rapid cochlear implantation. The aim of this study is to evaluate the predictive value of MRI for the development of sensorineural hearing loss after meningitis by comparing the cochlear enhancement on GdMRI with the degree of hearing impairment at audiologic evaluation. Furthermore, the patency of the cochlear lumen on T2MRI will be compared with the degree of cochlear obliteration encountered during surgery. Also, images of the vestibular system will be investigated; as in some articles, an association with the degree of cochlear inflammation is suggested[1,12,13].

MATERIALS AND METHODS

Study design

Retrospective cohort study.

Dutch Cochlear Implant Group Consensus protocol on postmeningitic hearing evaluation

All eight cochlear implant centers in the Netherlands have agreed on a protocolized follow-up of patients surviving a bacterial meningitis to increase the chance of early detection of SNHL[14]. The Dutch Cochlear Implant Group Consensus Protocol recommends audiological evaluation for all (post)meningitis patients as soon as the clinical condition of the patient allows[14]. If hearing impairment is present, patients are referred to an audiological- or cochlear implant center for further hearing evaluation and imaging of the cochlea. According to the protocol, both a gadolinium enhanced T1-weighted MRI (GdMRI) and a 3D heavily T2-weighted MRI (T2MRI) of the inner ear are performed[14].

Table I: Patient details, clinical presentation and treatment

No.	Age at diagnosis	Sex	Pathogen	Other symptoms	Duration of AB treatment (days)
1	20 mo	M	Pneumococcus	none	16
2	7 mo	M	Pneumococcus	ES, RI	19
3	6 mo	M	Pneumococcus	ES, RI	12
4	4 mo	M	Pneumococcus	ES	13
5	2 yr	M	Pneumococcus	none	9
6	56 yr	F	Unknown	ES, RI, ENC, CEI	14
7	11 yr	M	Pneumococcus	none	10
8	77 yr	F	Pneumococcus	ES, RI, ATA, BLI	69
9	4 yr	M	Unknown	none	10
10	3 mo	M	Pneumococcus	ES, RI, CEI	14
11	51 yr	M	Pneumococcus	HEM	8
12	1 yr	M	Pneumococcus	ES, RI	16
13	5 yr	F	Pneumococcus	none	8
14	7 yr	F	Pneumococcus	none	8
15	5 mo	M	Pneumococcus	ES, RI	11
16	5 mo	M	Pneumococcus	ES, RI	14
17	9 mo	M	Pneumococcus	HEM	10

No. = patient number, AB = antibiotic, M = male, , F = female, ATA = ataxia, BLI = blindness, CEI = cerebral infarction, ENC = encephalitis, ES = epileptic seizures, HEM = hemiparesis, RI = respiratory insufficiency.

Patients

We reviewed the charts of patients with SNHL caused by meningitis who were referred to the VU University Audiological and Cochlear Implant Center in Amsterdam between December 2005 and December 2010. Meningitis was present if patients met at least one of the following criteria: bacteria growth in cerebrospinal fluid (CSF) or increased leukocytes present in CSF. SNHL was defined as greater than 30 dB hearing loss in one or both ears. Seventeen patients (14 children and 3 adults) met our criteria and were included in this study. Eleven patients had severe bilateral hearing loss and were cochlear implant candidates; 6 patients were affected by unilateral hearing impairment only. Table 1 shows the characteristics, clinical presentation, and treatment of patients included in this study. The median age was 2.0 years (range, 3 months to 77 years). The causative pathogen was identified as S. pneumoniae in 15 of 17 patients; the pathogen remained unknown in two patients. Patients were treated with ceftriaxone or benzylpenicillin for a mean period of 15.3 days (range, 8-69 days). Intravenous corticosteroid (dexamethasone) therapy was administered to all patients and started before antibiotic treatment.

MRI evaluation

GdMRI scans were acquired immediately after the admission of a gadolinium containing contrast agent on a Siemens Sonata 1.5 Tesla MRI scanner. Depending on the date of scanning, 0.2 to 0.4 ml/kg of either Gadovist (Bayer Healthcare Pharmaceuticals, West Haven, CT, USA), Magnevist (Bayer Healthcare Pharmaceuticals, West Haven, CT, USA), or Dotarem (Gueret, Aulnay-sous-Bois, Seine-Saint-Denis, France) was used. All gadolinium-enhanced magnetic resonance images had a section thickness of 3.3 mm, except 2 sequences with a slice thickness of 3.0 or 4.0 mm. A simple 3-stage scoring system was applied to grade the enhancement of the cochlea and labyrinth on GdMRI: (0) no enhancement, (1) moderate enhancement, and (2) severe enhancement. Figure 1 shows the GdMRI characteristics for the different outcome categories of cochlear enhancement. T2MRI scans with a slice thickness of 0.7 mm were obtained from a Siemens Sonata 1.5 Tesla MRI scanner. Constructive interference in steady-state sequence was used to provide more detailed imaging of the inner ear[16]. A simple scoring system was applied to grade the patency of the cochlea and labyrinth: (0) normal hyperintensity or no loss of fluid, (1) moderate hypointensity or partial loss of fluid (<50%), and (2) severe hypointensity or severe loss of fluid (>50%). Figure 2 shows the T2MR images, illustrative for the different categories for loss of cochlear fluid. For statistical analysis purposes, the cochlear lumen was defined as being patent if T2MRI was scored as 0 or 1; cochlear obstruction was present if T2MRI was scored as 2. All MRI scans were reviewed and scored by two blinded ENT surgeons (EF. Hensen and and P. Merkus) and 1 blinded neuroradiologist (B. de Foer). GdMR images were compared with the extent of sensorineural hearing loss; T2MR images were compared with the observations during

cochlear implantation. Multiple MRI scans were available for 1 patient (Patient 11), the first GdMRI (11A) was used for the comparison with the occurrence of SNHL, and the most recent preoperative T2MRI (11B) was compared with the peroperative findings.

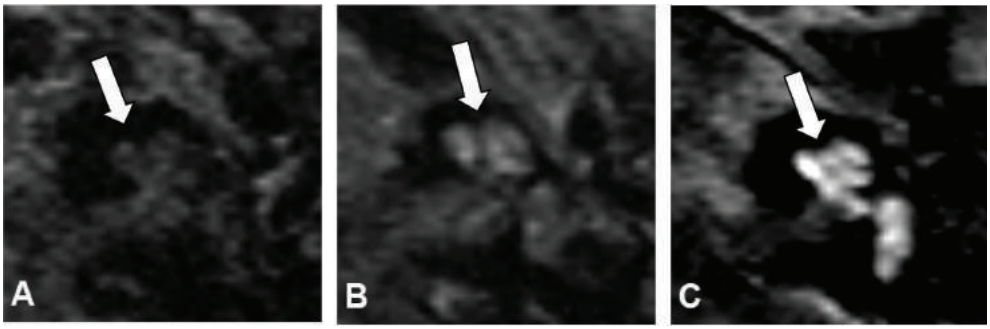

Figure 1: Grading of cochlear enhancement. Axial gadolinium enhanced T1-weighted MRI showing different grades of cochlear enhancement after contrast admission (arrows). A, Grade 0: no enhancement of the cochlea (Patient 14), B, Grade 1: moderate enhancement (Patient 9), C, Grade 2: severe cochlear enhancement (Patient 13).

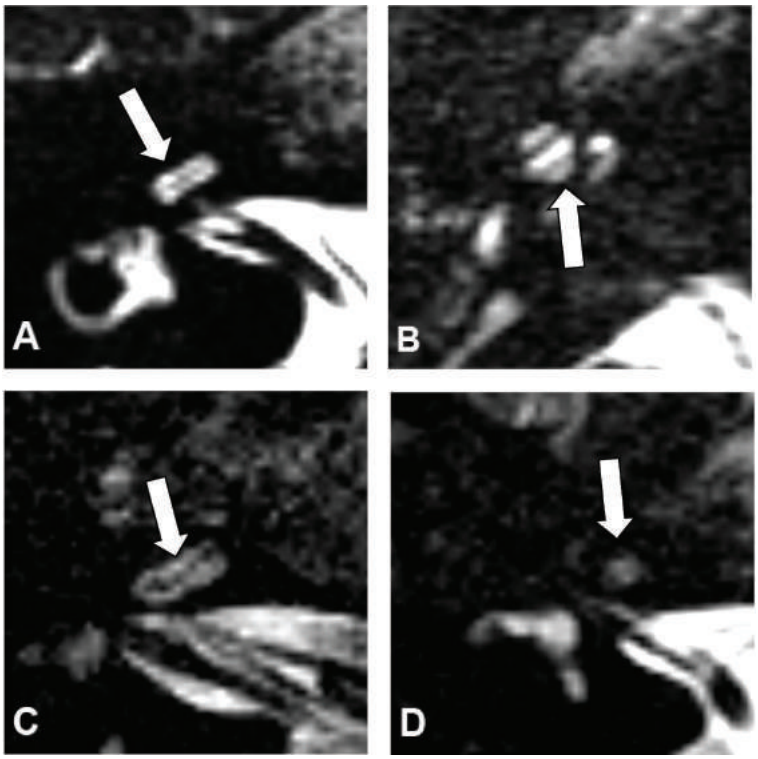

Figure 2: Grading of cochlear patency. Axial 3D heavily T2-weighted MRI images showing different grades of intensity or fluid distribution within the cochlea (arrows). A, Grade 0: hyperintens or no loss of fluid (Patient 12), B, Grade 1: partial and irregular loss of fluid (Patient 2), C, Grade 1: moderate hypointensity (Patient 9), D, Grade 2: severe hypointensity or severe loss of fluid (>50%) (Patient 13).

Audiometric data evaluation

Audiologic testing was performed by a certified audiologist using age-appropriate testing, which included pure tone audiometry (PTA), free-field audiometry (FFA), otoacoustic emissions (OAE), or brainstem evoked response audiometry (BERA). The severity of SNHL was graded by dividing the hearing of each ear in one of the 4 following outcome categories: (A) no hearing impairment (hearing threshold: <25 dB), (B) slight hearing loss (hearing threshold: 26-40 dB), (C) moderate hearing loss (hearing threshold: 41-60 dB) and (D) severe or profound hearing loss (hearing threshold >61 dB). These categories correspond with the commonly used classification of the World Health Organization[18].

Peroperative surgical findings

Only patients who had severe-to-profound bilateral SNHL were operated and received a cochlear implant (n = 11). The surgical records of these patients were reviewed in detail; observations of the surgeon during cochlear implantation were scored on a 4-point scale. Points were assigned to the presence of cochlear obliteration and the procedure of electrode insertion: (0) patent cochlear lumen, full electrode insertion; (1) partial obliteration, full electrode insertion; (2) partial obliteration, partial electrode insertion; and (3) extensive obliteration, standard CI impossible. For statistical analysis purposes, outcome categories 2 or 3 were defined as a complicated electrode insertion.

Statistical analysis

MRI scans were scored by three observers independently. Enhancement on GdMRI (scan scored as 1 or 2) was compared with the occurrence of moderate-to-profound hearing loss (outcome category C or D). The patency of the cochlear lumen on T2MRI was compared with the method of electrode insertion during cochlear implantation. Definitions of the scoring system of the cochlear cochlear patency on T2MRI and the surgical outcome are addressed in the previous paragraphs. The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for both MRI settings were estimated for all observers combined using generalized estimating equations. Repeated measures for each ear (subject) were defined as the scores of the three different observers, and an exchangeable structure was chosen for the correlation matrix. The logit-function was used as link function between the outcome (MRI results for sensitivity and specificity, hearing loss or presence of cochlear obliteration for PPV and NPV) and the predictor (hearing loss or presence of cochlear obliteration for sensitivity and specificity, MRI results for PPV and NPV). To provide an estimation of precision, 95% confidence intervals were calculated. Fleiss' kappa statistics was used to evaluate concordance of agreement between the observers.

RESULTS

Audiometry

Audiometric data were available for all 17 patients, Table 2 shows the outcome of audiometric evaluation. Eleven patients (Patients 1-11) had bilateral SNHL, five patients had unilateral SNHL (Patients 12-16). One patient (Patient 17) had no hearing loss on further evaluation; 25 of 34 ears had severe-to-profound SNHL (>61 dB); moderate SNHL was present in 2 of 34 ears, albeit borderline with a threshold shift of 60 dB (cut off point, >61 dB). Seven of 34 ears showed no hearing impairment. The audiometric data of two patients (Patients 3 and 8) were not used in our analysis because of the absence of a suitable GdMRI. Of the remaining patients, the median time interval between the diagnosis of meningitis and the performance of audiometry was 9 days (range, 2-48 days).

Table II: Audiometry outcome and surgical observations

No.	Audiometry		Men-Aud interval (d)	Men-MRI Interval(d)	Surgical findings				Men-CI interval	MRI-CI interval
	Right	Left			Right		Left			
1	D	D	14	24	O-	FE	O-	FE	30	6
2	D	D	26	33	O-	FE	O-	FE	41	8
3	D	D	26	36	O-	FE	O+	PE	57	21
4	D	C	48	68	O+	PE			84	16
5	D	D	10	56	O+	PE	O+	PE	62	6
6	D	D	32	32	O-	FE	O-	FE	37	5
7	D	C	2	9	O-	FE	O-	FE	15	6
8	D	D	285	294	O+	DA	O+	DA	349	55
9	D	D	9	15	O-	FE	O-	FE	32	17
10	D	D	11	13	O+	FE	O+	FE	34	21
11A	D	D	4	3	O-	FE	O-	FE	52	49
11B	D	D	4	51	O-	FE	O-	FE	52	1
12	A	D	9	10						
13	A	D	9	18						
14	D	A	7	23						
15	A	D	14	19						
16	D	A	5	20						
17	A	A	8	4						

Aud = audiometric assessment, Men = meningitis symptom onset and start with antibiotic treatment, MRI = magnetic resonance imaging, CI = cochlear implantation, A = no hearing impairment (hearing threshold of 0-25 dB), B = slight hearing loss (hearing threshold of 26-40 dB), C = moderate hearing loss (hearing threshold of 41-60), D = severe or profound hearing loss (hearing threshold of 961 dB), O- = no obliteration, O+ = obliteration present, FE = full electrode insertion, PE = partial electrode insertion, DA = double array placement.

Enhancement on gadolinium enhanced T1-weighted MRI and the occurrence of SNHL

A GdMRI with satisfactory quality was available for 15 of 17 patients (30/34 cochleae) (Table 2). Proper MRI evaluation was impossible because of artifacts in one patient (Patient 3), and in one patient (Patient 8), only a T2MRI was available because of a delayed referral to our hospital (99 months). GdMR imaging was performed at a median of 19 days (range, 3-68 d) after the start of antibiotic treatment.

A significant ($p < 0.01$) association between the enhancement of the cochlea on GdMRI and the occurrence of hearing impairment (hearing threshold, 60 dB) was found. The calculated sensitivity and specificity for enhancement on GdMRI in predicting SNHL were 87% and 90%, respectively (Table 3). Cochlear enhancement had a positive predictive value (PPV) of 96%, and the negative predictive value (NPV) was 64%. A Fleiss' kappa score of 0.89 was calculated for the interobserver agreement; this falls into the category of ''almost perfect agreement'' between the three observers (Table 3). Hence, it can be stated that scoring GdMRI scans on a three-point scale is consistent and reproducible. Enhancement of the labyrinth was also significantly associated to the occurrence of hearing loss; analysis showed a sensitivity of 62% and a specificity of 90% ($p < 0.01$).

Table III : Cochlear enhancement on GdMRI associated with the occurrence of hearing loss

Variable	Outcome	95% CI
Sensitivity	87%	69%-95%
Specificity	90%	56%-99%
PPV	96%	75%-99%
NPV	64%	34%-86%
Kappa	0.89	0.70-0.96

Association between enhancement on GdMRI and the occurrence of hearing loss is significant ($p < 0.01$). CI = confidence interval; PPV = positive predictive value; NPV = negative predictive value.

Patency on 3D heavily T2-weighted MRI and peroperative surgical findings

Only Patients 1 to 11 had bilateral SNHL and were implanted with a cochlear implant. One patient (Patient 4) was implanted unilaterally because the contralateral ear repeatedly showed responses at 60 dB in the high frequencies. In this patient, the ear with residual hearing was fitted with a hearing aid. All other patients were implanted bilaterally, resulting in a total of 21 cochlear implantations in 11 patients. Table 2 presents the surgical observations during cochlear implantation. Cochlear implantation was performed at a median of 12 days (range, 1-55 d) after T2MRI and 47 days (range, 15-349 d) after the start with antibiotic treatment for meningitis. A full electrode insertion was achieved in 15 of 21 cochleae. A partial electrode insertion because of obliteration occurred in 4 of 21 cochleae

(Patients 3Y5). One patient (Patient 8) required a bilateral double array placement because of severe obliteration of the cochlear lumen.

Diminished cochlear patency on T2MRI was significantly associated with surgical complications ($p < 0.01$); the calculated sensitivity and specificity were 100% and 71%, respectively (Table 4). Loss of fluid on T2MRI had a positive predictive value (PPV) of 55%, and the negative predictive value (NPV) was 100%. A Fleiss' kappa score of 0.66 was calculated, which falls in the category of ''substantial interobserver agreement'' (Table 4). The patency of the labyrinth on T2MRI had a sensitivity 83% and a specificity 76% for predicting peroperative complications; however, this association was not significant ($p = 0.87$).

Table IV: Loss of cochlear fluid on T2MRI associated with peroperative surgical findings

Variable	Outcome	95% CI
Sensitivity	100%	54%-100%
Specificity	71%	46%-88%
PPV	55%	27%-80%
NPV	100%	69%-100%
Kappa	0.66	0.48-0.83

Association between enhancement on GdMRI and the occurrence of hearing loss is significant ($p < 0.01$). CI = confidence interval; PPV = positive predictive value; NPV = negative predictive value.

DISCUSSION

Cochlear enhancement on gadolinium enhanced T1-weighted MRI

GdMRI, performed in patients within 2 months after the onset of bacterial meningitis, was significantly associated with the development of SNHL ($p < 0.01$). Only 2 patients, which developed SNHL showed no cochlear enhancement on GdMRI. A plausible explanation might be the timing of MRI in relation to the acute inflammatory phase. In the first patient (Patient 11), GdMRI was made as soon as three days after the onset of symptoms of meningitis, the shortest time interval of all patients. The inflammatory process was starting to develop, and cochlear enhancement was not yet visible on GdMRI in this patient. A second GdMRI was made seven weeks later and showed bilateral severe cochlear enhancement (Figure 3). In the second patient (Patient 6), MRI was performed 32 days after the onset of symptoms, and the acute inflammatory phase was probably finished. Although other patients still showed enhancement on GdMRI at longer time intervals, it seems therefore that the inflammatory process varies in its duration; it can continue to be present after 68 days but can be undetectable as soon as 32 days after the meningitis. Based on this observation, we

recommend that GdMRI should be performed within the first month after meningitis. No correlation between cochlear enhancement and central nervous system findings (increased intracranial pressures and evidence of CNS inflammation) could be determined.

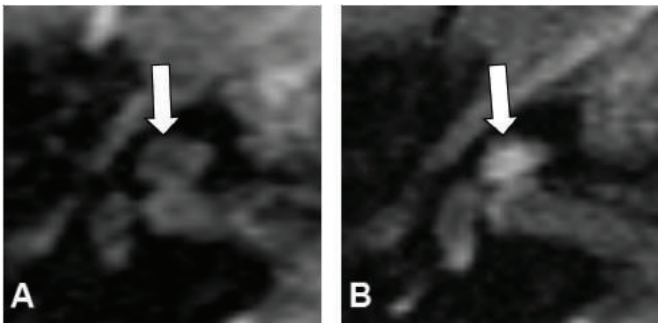

Figure 3: Variable cochlear enhancement at different postmeningitic time intervals. Axial gadolinium enhanced T1-weighted MRI of same patient (Patient 11). A, after 3 days, B, after 51 days.

Previously, two other studies investigated the diagnostic value of GdMRI in (post) meningitic patients. Beijen et al.[13] compared cochlear enhancement on GdMRI with surgical observations of the cochlear lumen. Unfortunately, the mean period between meningitis and GdMRI was between 0 to 11 months, making it plausible that the cochlear enhancement had disappeared at the time of imaging in some cases. Moreover, CI took place more than 3 months after imaging in 23 of 45 of the patients. This long delay hampers the comparison of magnetic resonance findings and the surgical findings. Cochlear obliteration is an ongoing process and might continue to develop in the months between imaging and surgery. Our findings concur with Kopelovich et al.[9] who reported that GdMRI had a sensitivity of 87% and a specificity of 100% for predicting the occurrence of SNHL. Kopelovich et al.[9] studied all magnetic resonance scans of meningitis patients, whether hearing loss occurred, resulting in less patients with actual SNHL (8/23 patients). Even so, Kopelovich et al.[9] demonstrated that cochlear enhancement, accompanied by SNHL, can be present as soon as one day after the first symptoms of meningitis. On the other hand, they also presented a case with SNHL with no enhancement on MRI 3 days after meningitis onset.

Clinical applicability of gadolinium enhanced T1-weighted MRI

The additional value of GdMRI in patients with severe bilateral SNHL is limited because these patients are already cochlear implant candidates. However, in patients with bilateral SNHL accompanied by residual hearing, the findings on GdMRI can support the decision not to perform bilateral cochlear implantation. For instance, one of the study patients with bilateral SNHL (Patient 4) showed enhancement of the entire cochlea and profound ipsilateral SNHL on the right side, whereas on the left side mild enhancement was seen at the basal turn only; the apical turn showed no enhancement (Figure 4). The ABR responses

of this left ear showed repeatedly a hearing threshold of 60 dB in the high frequencies. It was decided to perform unilateral cochlear implantation on the right, deaf ear and hearing aid fitting and hearing follow-up of the contralateral ear. Until now, the patient has a stable residual hearing of 55 dB in the low frequencies on the left side and shows age appropriate language development.

Also in patients affected by unilateral hearing loss, GdMRI can play a crucial role in decision making. In these patients, a non-enhancing cochlea on the contralateral side (Figure 5) seems to predict the preservation of hearing in this ear. None of our patients with unilateral cochlear enhancement on MRI (Patients 12-16) showed hearing deterioration of the contralateral ear during a follow-up of up to 28 months and thus did not become CI candidates. As the prospect of impending bilateral loss of hearing after meningitis can be very stressful, a non-enhancing cochlea on GdMRI may serve as a reassurance for these patient and parents.

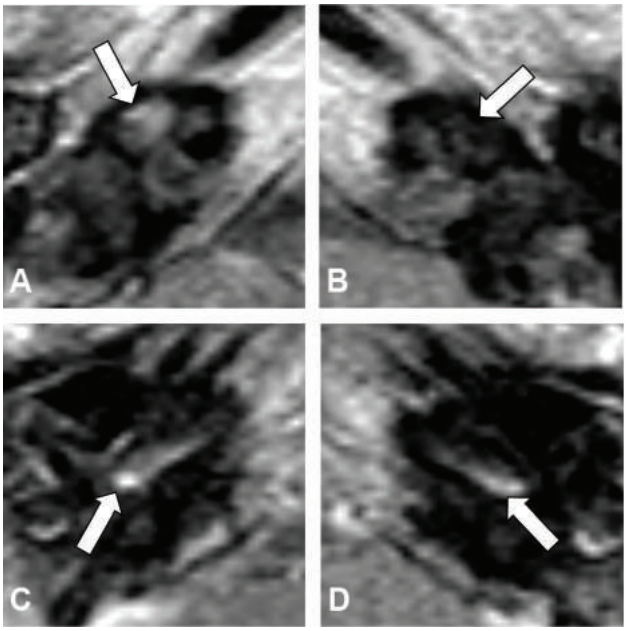

Figure 4: Case with partial cochlear enhancement of the basal turn (Patient 4). Axial gadolinium enhanced T1-weighted MRI which shows slight cochlear enhancement of the right apical turn (A), the left apical turn showed no enhancement (B). Enhancement of the basal turn was present on both the right side (C) and the left side (D). The ABR responses of the left ear showed repeatedly a hearing threshold of 60dB in the high frequencies. Therefore it was decided only to perform cochlear implantation on the right side; the contralateral left side was treated with a hearing aid hearing follow-up. In the non-enhancing part of the cochlea, hearing remained stable.

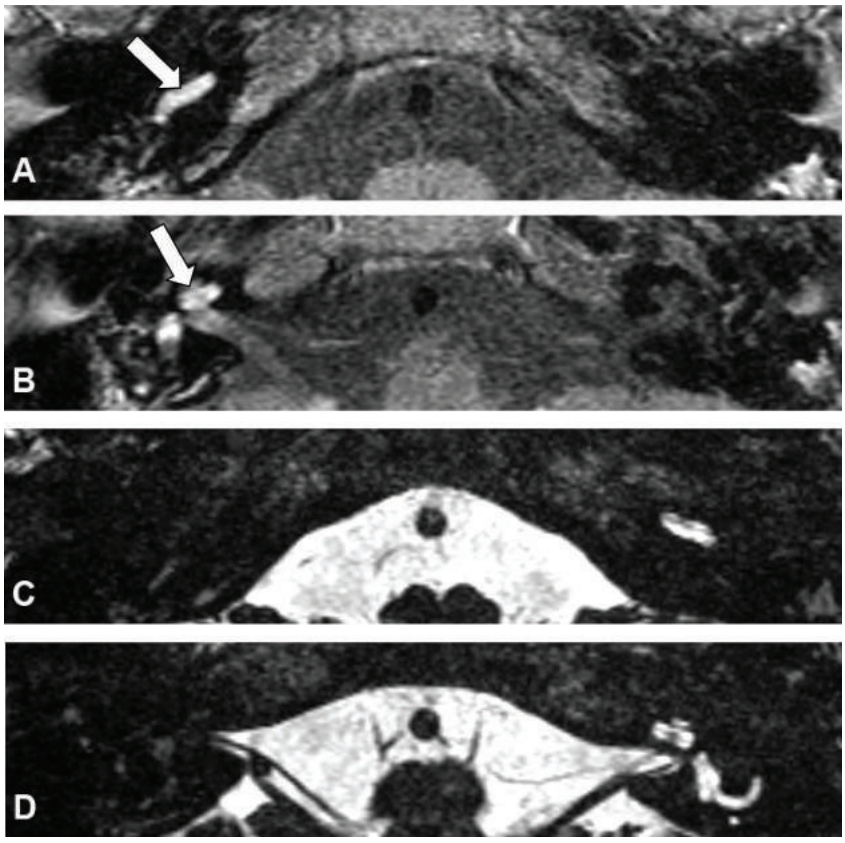

Figure 5: Unilateral cochlear inflammation and obliteration. Gadolinium enhanced T1-weigthed MRI shows enhancement of the right-sided cochlea (A = basal turn, B = apical). 3D heavily T2-weighted MRI shows unilateral loss of fluid of the right-sided cochlea (C = basal turn, D = apical) (Patient 14). A non-enhancing cochlea on the contralateral side seems to predict the preservation of hearing in this ear. The patient was not implanted and good hearing remained.

Cochlear patency on T2-weighted MRI and surgical observations

Full electrode insertions were achieved in all patients with an open cochlea on T2MRI (NPV 100%). In 71% of the cochleae with a loss of fluid on T2MRI, the information given by MRI is associated with a complicated electrode insertion. Moreover, all six cochleae in which a complicated electrode insertion occurred (partial insertion or double array placement) showed a reduced cochlear patency on T2MRI (Table 4). This observation concurs with Chan et al.[12] and Isaacson et al.[1], who also showed a strong association between a complicated electrode insertion and loss of fluid on T2MRI (sensitivity of 92% and 100%, respectively). Not surprisingly, the four patients (Patient 3, 4, 5, and 8) of this study with complicated electrode insertions were the 4 patients with the longest time interval between the onset of meningitis and cochlear implantation (57, 84, 62, and 349 d, respectively). All other cochlear

implantations were performed within the first eight weeks after meningitis, resulting in a full electrode insertion in all of these patients. This accentuates the need for rapid audiologic assessment, decision making, and (possible) cochlear implantation in postmeningitic patients. On the other hand, a full electrode insertion was still possible in 45% of the cochleae, which showed a loss of fluid on T2MRI (PPV, 55%). This can be explained by the fact that the displacement cochlear perilymph as detected by MRI can be caused by multiple conditions ranging from fibrosis to end-stage ossification. These conditions do not hamper cochlear implantation equally; a full electrode insertion might still be achieved in a fibrotic cochlea. HRCT can reveal ossification of the cochlear lumen, but the absence of ossification on HRCT is not always associated with a true patent cochlea because obliteration caused by fibrosis is not visible on HRCT. The combination of MRI and HRCT is required to optimize the surgeon's preoperative knowledge regarding cochlear patency.

Model for postmeningitic cochlear inflammation on MRI

Based on the enhancement on GdMRI and the fluid distribution on T2MRI of patients in this study, we suggest a model, which describes the different phases of postmeningitic cochlear inflammation as seen on MRI (Figure 6). The acute phase (approximately the first 7 weeks) is characterized by cochlear enhancement on GdMRI in the absence of abnormalities on T2MRI. In the second phase, the intermediate phase (around weeks 2-10), cochlear enhancement is still present but is accompanied by a loss of fluid of the cochlear lumen on T2MRI. Important is the end of this phase, suggesting that acute inflammatory enhancement will diminish approximately 10 weeks after the onset of meningitis. The final stage (which can start after approximately four weeks) is a condition in which the acute inflammatory phase has finished, characterized by the absence of enhancement on GdMRI. T2MRI shows loss of fluid of the cochlear lumen caused by either fibrosis or ossification. The combination of MRI and HRCT is needed to distinguish between these conditions. Figure 7 shows an example of a patient in which both cochlea showed a severe loss of fluid on T2MRI. Corresponding HRCT (performed on the same day) shows extensive calcifications on the right side, whereas the left cochlea displays no calcifications. Nonetheless, a normal electrode insertion could not be achieved on either side, and both cochleae required a double array cochlear implant placement.

There are several limitations of this study. As we could evaluate an unaffected contralateral ear only in patients with unilateral SNHL, only 7 of 34 unaffected ears were included in our control group, affecting primarily the negative predictive value of GdMRI. Second, a delay in both hearing assessment and MRI occurred in the majority of patients because they were referred by peripheral hospitals. This delay in reference makes it impossible to determine the exact moment of onset of the cochlear inflammation in these patients. Therefore, the relation between cochlear enhancement and the occurrence of hearing loss in the first days

remains unknown. This precludes a more exact recommendation for the ideal timing of MRI after the onset of bacterial meningitis. Furthermore, as contrast enhancement of the cochlea on GdMRI did not always indicate a total loss of hearing, GdMRI should always be used in addition to formal hearing assessment, and MRI cannot substitute audiometric evaluation. It is known that a recovery of hearing can occur in postmeningitic patients with partial hearing loss. Our study population consisted predominantly of patients affected by severe hearing loss, and an improvement in hearing was not observed. Moreover, in our study population, pneumococcus was the only identified pathogen, whereas hearing recovery is only described in other causative pathogens[20].

In conclusion, MRI plays a crucial role for decision making in the postmeningitic patient. If diminished cochlear patency on T2MRI is present in patients with bilateral hearing loss, rapid cochlear implantation should be considered to minimize the risk of a complicated electrode insertion because of cochlear obliteration. Cochlear enhancement on GdMRI can be seen from the first days up till 2 months after the start of the meningitis and is highly associated with the occurrence of SNHL. In patients with residual hearing, the presence of partial cochlear enhancement warrants the surgeon toward a stringent follow-up policy. Moreover, in patients with unilateral SNHL, a non-enhancing cochlea on the contralateral side is highly indicative of hearing preservation over time.

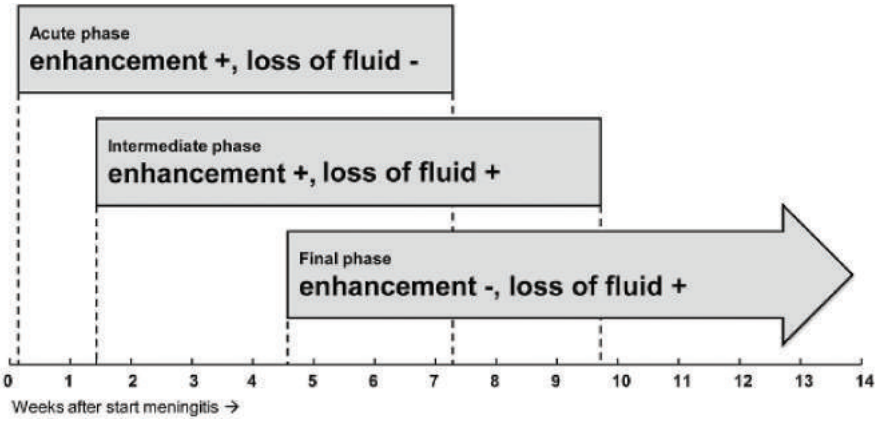

Figure 6: Different phases of postmeningitic cochlear inflammation as seen on MRI. In the acute phase, MRI can show enhancement of the cochlea from the first day after meningitis [data validated on our series and Kopelovich et al. (9)]. Enhancement can last until 68 days (end intermediate phase). Loss of fluid is seen in our series as early as 10 days after start of the meningitis (start intermediate phase) and will most likely be permanent. Loss of fluid can be caused by fibrosis which, over a period, can partly or completely be transformed into ossification. Ossification can be seen on CT as early as 14 to 30 days after start of the meningitis[11,19].

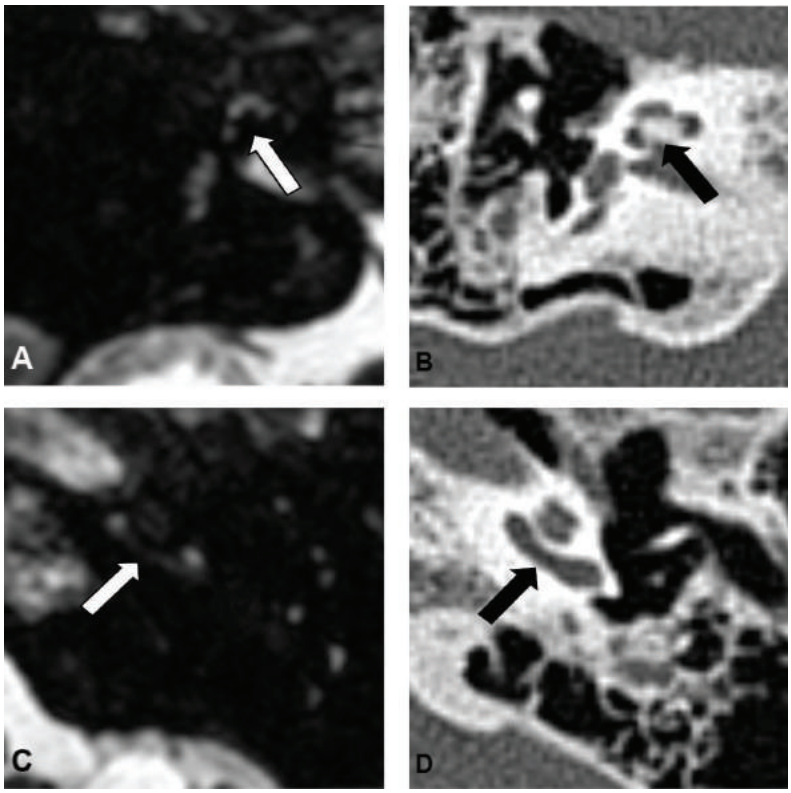

Figure 7 A-D: MRI corresponds better with the surgical findings than CT. Axial 3D heavily T2-weighted MRI and HRCT through the modiolus of the right cochlea (A and B) and through the basal turn of the left cochlea (C and D). T2MRI shows a severe loss of both sides (white arrows, image A+C). Corresponding HRCT shows however extensive calcifications round the modiolus of the right cochlea (black arrow, image B), whereas the basal turn of the left cochlea displays no calcification (black arrow, image D). HRCT can be misleading as this cochlea was full of fibrosis during surgery and only a double array placement was possible (Patient 8).

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Chapter 7

Cochlear implantation after bacterial meningitis in infants younger than 9 months

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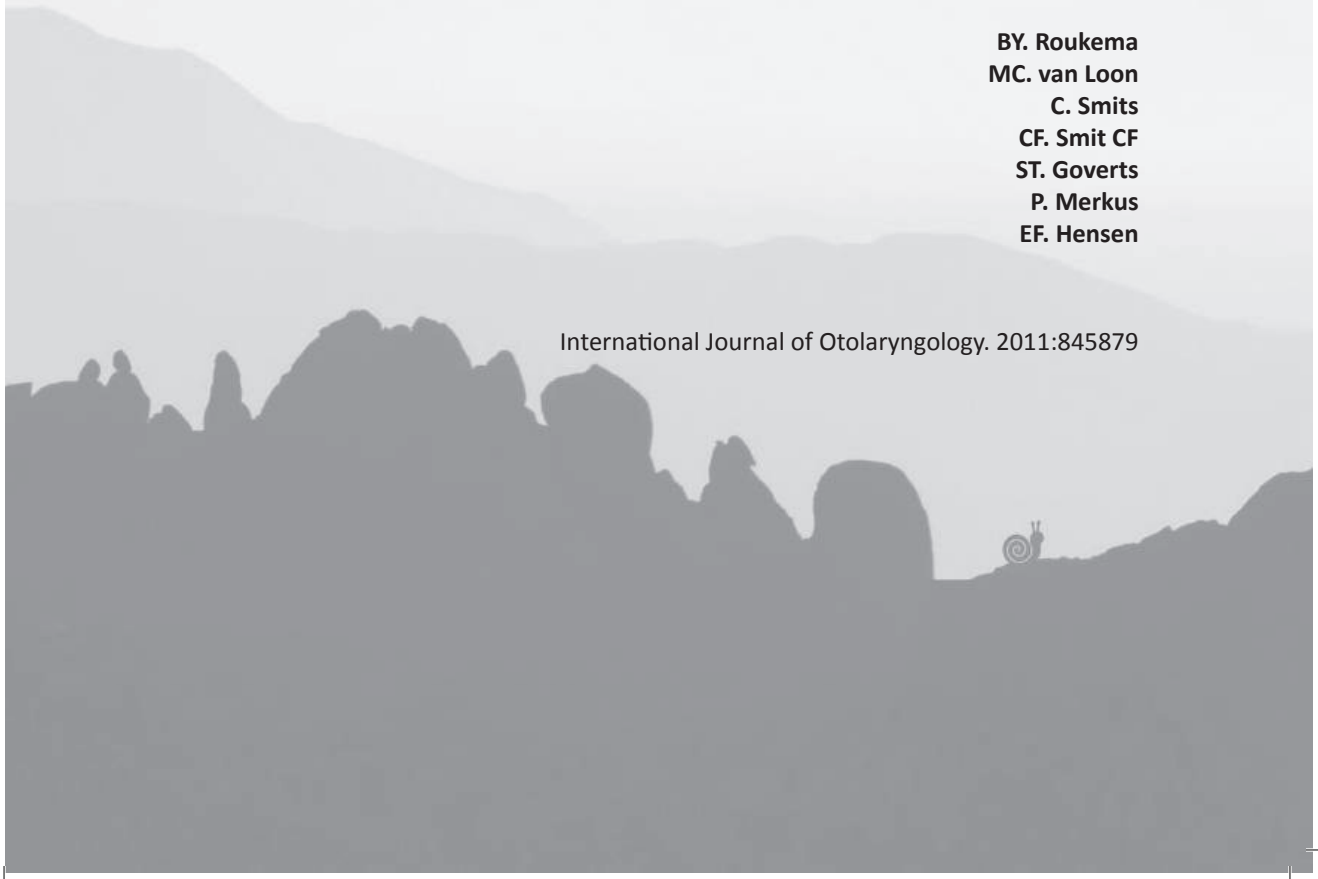

ABSTRACT

Objective: To describe the audiological, anesthesiological, and surgical key points of cochlear implantation after bacterial meningitis in very young infants.

Material and Method:. Between 2005 and 2010, 4 patients received 7 cochlear implants before the age of 9 months (range 4–8 months) because of profound hearing loss after pneumococcal meningitis.

Results: Full electrode insertions were achieved in all operated ears. The audiological and linguistic outcome varied considerably, with categories of auditory performance (CAP) scores between 3 and 6, and speech intelligibility rating (SIR) scores between 0 and 5. The audiological, anesthesiological, and surgical issues that apply in this patient group are discussed.

Conclusion: Cochlear implantation in very young postmeningitic infants is challenging due to their young age, sequelae of meningitis, and the risk of cochlear obliteration. A swift diagnostic workup is essential, specific audiological, anesthesiological, and surgical considerations apply, and the outcome is variable even in successful implantations.

Key Words: cochlear implant, meningitis, children, audiology, surgery, anesthesia.

INTRODUCTION

Current standards for cochlear implantation in infants with severe congenital sensorineural hearing loss (SNHL) advocate an age at implantation between 9 and 12 months. On the one hand, a growing body of evidence indicates that hearing rehabilitation is more effective when the patient is implanted at a young age[1-4]. On the other hand, a certain period of time is needed to determine a reliable hearing threshold, to allow for improvement of hearing due to maturation of the auditory system after birth, and to test the performance of the patient with hearing aids[5]. Furthermore, the benefits of cochlear implantation before the age of 9 months should be weighed against the higher risk of anesthesia at this young age[5].

In case of sensorineural hearing loss caused by acute bacterial meningitis, different considerations apply. A swift diagnostic workup is imperative because of the risk of cochlear fibrosis and subsequent obliteration of the cochlear lumen, which may occur within weeks after the onset of meningitis, especially if the meningitis is caused by pneumococci[6,7]. This diagnostic workup should include a thorough evaluation of the hearing as well as adequate imaging of the cochlea in order to assess the need and feasibility of cochlear implantation. In infants that suffer from postmeningitic SNHL, this may lead to an indication for cochlear implantation at an age younger than 9 months. If so, this patient group presents the cochlear implant (CI) team with a very specific set of challenges due to the young age of the patient, the additional sequelae of meningitis, and limitations to the time interval between the onset of meningitis and cochlear implantation.

In order to illustrate these issues and discuss possible solutions and outcome, we describe our experience with patients that underwent cochlear implantation before the age of 9 months because of postmeningitic profound hearing loss. Furthermore, the specific diagnostic, anesthesiological, and surgical issues that have to be taken into consideration when performing cochlear implantations in very young postmeningitic patients are discussed.

MATERIAL & METHODS

We evaluated the patients younger than 9 months, who were selected for CI because of profound postmeningitic SNHL in the period from February, 2005 till March, 2010 at the VU University Medical Center, Amsterdam, the Netherlands.

All patients had participated in the Dutch youth health care programme. This programme is offered to all newborn children in The Netherlands and comprises of regular checkups (at the age of 2, 4, 8, 12, 16, 24, 30, and 48 weeks within the first year of age) by specialized physicians and youth health care workers, evaluating the physical health, immunology status, motor skills, speech functions, and the social, emotional, and psychological development of the infant. In the course of this programme, all four patients had received vaccines against Streptococcus Pneumoniae, Haemophilus Influenzae and Neisseria meningitidis. All patients had shown a normal development prior to the onset of meningitis.

In all patients, a full neurological and otolaryngological evaluation was performed. The causative microorganism was determined by culture of the cerebrospinal fluid. The audiological evaluation consisted of auditory brainstem response audiometry (ABR) and otoacoustic emissions (OAE) if possible in combination with visual reinforcement audiometry (VRA) or behavioral observation audiometry (BOA). In addition, all patients underwent a radiological evaluation consisting of high-resolution computed tomography (HRCT) of the middle ear and mastoid, and magnetic resonance imaging (MRI) of the brain and inner ear, including contrast-enhanced T1 weighted images and T2 weighted constructive interference steady state (CISS) images of the cochlea.

All patients were implanted with a Nucleus Freedom with Contour Advance electrode (C124RE (CA), Cochlear limited, Australia). The auditory and linguistic performance was evaluated 1 year after cochlear implantation. Parts of this evaluation are presented in Table 1, the Dutch version of the categories of auditory performance (CAP-NL) and the Speech Intelligibility rating (SIR) are presented in Tables 2 and 3, respectively[9,10].

Table 1: Clinical characteristics and outcome of infants receiving cochlear implantation because of postmeningitic profound sensorineural hearing loss before the age of 9 months

No.	Age at onset meningitis	ABR results	T1+ contrast cochlear MRI image	T2 weighted cochlear MRI image	Age at cochlear implantation	Side of implantation	Surgical findings	Result of implantation	Categories of Auditory Performance	Speech Intelligibility Rating	Other sequelea
1	3 months	>85dB L+R	enhancement cochlea L+R	normal hyperintense	4 months	L+R	cochlear fibrosis	full insertions	4	0	epilepsy
2	5 months	>85dB R 60dB L	enhancement cochlea L+R	unilateral hypointensity	7 months	R	cochlear fibrosis	full insertion	5-6	5	none
3	6 months	>85dB L+R	enhancement cochlea L+R	hypointensity and artifacts	7 months	L+R	cochlear fibrosis	full insertions	3-4	1	epilepsy, DD, areflexia, ataxia
4	7 months	>85dB L+R	enhancement cochlea L+R	severe hypointense	8 months	L+R	cochlear fibrosis	full insertions	3	5	AD, hemiparesis of tongue

No. = patient number, ABR = auditory brainstem response audiometry, MRI = magnetic resonance imaging, , L = left, R = right, DD = developmental delay, AD = attention defecit

Table 2: The Dutch Categories of Auditory Performance (CAP-NL)

Categories of Auditory Performance (CAP-NL)	Score
Use of telephone with known speaker	7
Understanding of conversation	6
Understanding common phrases without lip-reading	5
Discrimination of speech sounds without lip-reading	4
Identification of environmental sounds	3
Response to speech sounds	2
Awareness of environmental sounds	1
No awareness of environmental sounds or voice	0
Use of telephone with known speaker	7

Table 3: Speech Intelligibility Rating (SIR) criteria

Speech Intelligibility Rating (SIR)	Score
Connected speech is intelligible to all listeners. Child is understood easily in everyday context.	7
Connected speech is intelligible to a listener who has little experience of a deaf person's speech.	6
Connected speech is intelligible to a listener who concentrates and lip-reads.	5
Connected speech is unintelligible. Intelligible speech is developing in single words when context and lip-reading cues are available.	4
Connected speech is unintelligible. Prerecognizable words in spoken language, primary mode of communication may be manual.	3

RESULTS

Between 2005 and 2010, a total of 55 children were fitted with CI at our institution, 4 of which received the CI before 9 months of age because of bilateral severe SNHL caused by bacterial meningitis. All 4 patients were male. The youngest patient, aged 4 months at the time of implantation, was born prematurely at 33 weeks and 5 days gestation. He developed meningitis when he was 3 months of age and the other patients contracted meningitis at 5, 6, and 7 months of age (Table 1). Evaluation with ABR showed bilateral thresholds exceeding 85 dB in all patients but one. In this patient (case 2), ABR showed a hearing threshold exceeding 85 dB on the right side and a medium sloping SNHL (60 dB at 3 kHz) on the left (Table 1).

In all four cases, the meningitis was caused by Streptococcus pneumoniae even though they had all received a pneumococcal 7-valent vaccine (Prevenar, Pfizer) before the age of 5 months. All patients had a normal physical and psychological development at the time of the onset of meningitis. In accordance with the Dutch Consensus Protocol on Postmeningitic

Hearing Evaluation, MR imaging was performed within 14 days after the identification of severe SNHL by ABR[7]. All cases showed enhancement of the cochlea on contrast enhanced T1 images, indicating active inflammation of the cochlea (Table 1). In the patient with asymmetric hearing loss (case 2), the best hearing ear (left side) showed enhancement of the scala tympani close to the round window in the basal turn only and no enhancement of the apical turn (Figure 1). T2 weighted images displayed a variety of outcomes in this patient group, varying from a hyperintense image indicating a normal fluid-filled cochlea, to a severe hypointense image, correlating with the formation of fibrous tissue or ossification within the cochlea (Table 1 and Figure 1)[11].

Three patients received bilateral cochlear implants; one patient (case 2) with residual hearing at the left ear received a cochlear implant in the right ear and a hearing aid on the left side. The mean age at implantation was 6.5 months (range 4–8 months) (Table 1). All patients were implanted within a month of the diagnosis of SNHL (range 15–31 days). Peroperative findings included thickened perilymphe and minimal cochlear fibrosis in case 1 to more extensive cochlear fibrosis in cases 2, 3, and 4. We encountered no cochlear ossification, and full insertions were achieved in all operated ears (n = 7). There were no complications related to the surgery or CI activation. The key points of the anesthetical and surgical technique that have to be considered in this patient group are discussed below. The specific surgical issues are summarized in Table 4.

Table 4: Problem solving during cochlear implantation in postmeningitic infants

Problem	When	Suggested technique
Superficial course of facial nerve	At incision	Less pressure on the knife and more superior incision.
Bilateral 'symmetrical' position of the implant	At incision	Drawing of the position of the implant on a blueprint and copy at the contralateral side (figure 3).
Profuse bleeding because of bone marrow filled mastoid	During mastoidectomy	Use diamond burrs and close off the mastoid cells with bone wax.
'Thick' implant and thin skull cortex	During creation of the implant bed	Create a bony island over the dura (figure 4).
Round window in a more horizontal plane	Before cochleostomy	Make the posterior tympanotomy as wide as possible, drill towards stapes to find round window.
Ossification of the cochlea	At cochleostomy and electrode insertion	Drill-out of basal turn of the cochlea, partial electrode insertion, scala vestibuli insertion, or split electrode insertion.
Hematoma at the first implanted ear	At closure of first side	Place surgical drain superficial of the musculoperiostal flap, remove after head bandage.
Electrode can dislocate out of the cochlea	During development of the mastoid process	Position and fixation of the electrode lead in the round window, posterior tympanotomy, but not in the mastoid tip region. Ensure there is enough lead on electrode to allow for development of temporal bone.

The auditory and linguistic outcome after cochlear implantation is summarized in Table 1. One year after implantation, we found considerable variation of the auditory performance within our patient group although all patients seem to benefit from the CI. The patient with the best performance (case 2), who had open set speech perception, was able to understand conversations without the aid of lip reading, and his speech was intelligible to all. The patient with the least favorable outcome (case 3) received bilateral implants at the age of 7 months and recognized sounds 1 year after implantation but was not able to understand words and had no intelligible speech. While in case 2, there appear to be no other meningitis-related sequelae beside the loss of hearing, case 3 also developed epilepsy, areflexia, cerebellar ataxia, and a developmental delay in cognitive and motor skills (Table 1).

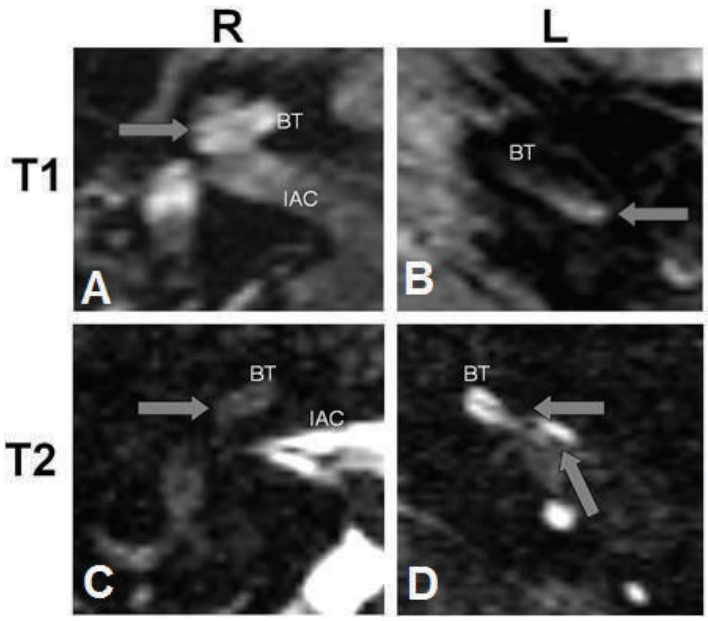

Figure 1: MR images of the right (R) and left (L) inner ears of a patient (case 2) after pneumococcal meningitis. Depicted are the axial T1 weighted MR images with contrast enhancement (T1, top row) and the T2 weighted MR images (T2, bottom row). The patient, a boy aged 7 months, suffered from asymmetric hearing loss after pneumococcal meningitis. Auditory brain stem response (ABR) audiometry showed a deaf ear on the right side and a sloping hearing loss (60 dB at 3 KHz) on the left side. Arrows show contrast enhancement in the cochlea on the T1 weighted images of both ears ((a) and (b)). The contrast enhancement involves the whole cochlea and vestibulum on the right side, but it is limited to the basal turn (BT) on the left. Arrows show loss of fluid in the cochlea on the T2 weighted images on both sides ((c) and (d)). Whereas on the right side, the loss of fluid involves the complete cochlea and the basal turn is barely visible, the loss of fluid only partially involves the basal turn of the left cochlea. IAC: internal auditory canal.

DISCUSSION

The young infant with profound SNHL due to bacterial meningitis presents specific challenges to the cochlear implant team. First, the time frame in this patient group is very different from congenitally deaf infants. In the latter, the currently reported optimal age at implantation is between 9 and 12 months of age, leaving ample time for extensive assessment of hearing, evaluation of possible improvement of hearing thresholds due to neuronal development after birth, a trial with hearing aids, cochlear imaging and the comprehensive counseling of parents. In postmeningitic profound SNHL, the risk of impending cochlear fibrosis and ossification resulting in increased surgical difficulty and risk of partial electrode insertion requires a swift audiological and radiological assessment and may necessitate cochlear implantation in infants younger than 9 months of age.

Sensorineural Hearing Loss after Bacterial Meningitis

Bacterial meningitis is the most common etiology for acquired hearing loss in children[12,13]. Five to 35% of the patients with bacterial meningitis will develop permanent SNHL, which is profound and bilateral in up to 4%[14,15]. Almost all bacteria species causing meningitis have been associated with permanent postmeningitic hearing loss, but this complication is most frequently found in S. pneumoniae, N. meningitides, and H. Influenza infections[6,15,16]. The prevalence of meningitis caused by these bacteria has decreased after the implementation of vaccination programmes in western countries[15,17,18]. The patients described in the current study also received vaccines against S. pneumoniae, N. meningitides, and H. Influenza. Even so, they all developed pneumococcal meningitis. Since 2006, all infants in The Netherlands are offered a pneumococcal 7-valent vaccine (Prevenar, Pfizer). Although this has led to a reduction in severe pneumococcal infections of approximately 50%, meningitis due to Streptococcus pneumoniae continues to occur (source:http://www.rivm.nl/). In The Netherlands, a new 10-valent vaccine (Synflorix, GSK) will replace the currently used 7-valent vaccine in 2011 because of the improved serotype immunization.

A loss of hearing caused by meningitis is not always readily apparent, especially in young infants due to their inability to communicate the problem and the possible cognitive effects of the infection. If SNHL remains undetected for a long period of time, it may critically affect the auditory and linguistic development[12,15,19,20]. A formal audiological assessment is therefore mandatory in order to adequately identify the children at risk and prevent developmental delay due to missed SNHL[7]. The audiological evaluation should ideally be performed as soon as the medical condition of the patient allows, because cochlear ossification, resulting in increased risk of partial insertion of the CI electrode and a less favorable outcome, may occur as early as 3-4 weeks after the onset of meningitis[6,7,21-26]. Cochlear ossification is a

known complication of S. pneumoniae, N. meningitides, and H. influenza infections, but pneumococci present the highest risk[6,27].

Radiology and Decision Making

Profound SNHL after meningitis warrants a radiological evaluation of the temporal bone and cochlea ideally within 2 weeks of audiological assessment because of the risk of cochlear fibrosis and ossification (as discussed above)[7]. HRCT is an excellent tool for the evaluation of the temporal bone anatomy, but it is not suitable for the detection of cochlear fibrosis and its sensitivity for the detection of cochlear ossification is poor (40%)[6]. T2 weighted MR images (especially those with steady state sequence protocols such as CISS or FIESTA) are superior in the evaluation of the cochlear patency. Loss of fluid, seen as loss of the hyperintense signal in the cochlea, is evidence of fibrosis or ossification (Figure 1). T1 weighted contrast-enhanced MR images are useful in the identification of active cochlear inflammation, which is seen as contrast-enhancement within the cochlea. There is evidence that abnormalities on T1 contrast enhanced images precede loss of cochlear patency as seen on T2 images and that positive contrast enhancement is correlated with the occurrence of SNHL, accurately predicting a deterioration of sensorineural hearing after meningitis[28]. In line with this observation, we found contrast enhancement in all patients, but T2 abnormalities were only seen in case 2 (unilateral), 3 (bilateral), and 4 (bilateral). In case 2, the patent contralateral cochlea did show contrast-enhancement limited to the basal turn on T1 weighted images. The hearing in this ear was only partially affected and remained stable (a hearing threshold of 60 dB at 3000 Hz). We consider patients with bilateral profound hearing loss in combination with loss of cochlear patency as seen on T2 weighted MR images and/or active cochlear inflammation as identified on contrast enhanced T1 weighted MR images definite candidates for CI and would schedule the cochlear implantation as soon as their medical condition allows. In patients with unilateral hearing loss, MRI abnormalities in the best hearing ear warrant intensive audiological followup and cochlear implantation as soon as the hearing decreases.

Audiological Assessment and Counseling

The preoperative audiological evaluation and workup of young children with profound hearing loss after meningitis differs from other hearing impaired children, mainly because of the short time interval between assessing loss of hearing and cochlear implantation. Even so, thorough audiological assessment is essential in order to avoid unnecessary implantations. Ideally, a combination of objective measurements (ABR and OAE) and observational audiometry (BOA or VRA) should be performed[29]. However, in infants younger than six months, behavioral measurements cannot be used to reliably obtain hearing thresholds. Furthermore, the medical condition of the patient or the sequelae of meningitis

may hamper behavioral observations. In addition, a trial with hearing aids, considered a standard procedure in most cochlear implant centers, is omitted if the MR imaging of the inner ear shows abnormalities indicative of inflammation or obliteration of the cochlear lumen following meningitis. The methods used for the hearing evaluation in very young postmeningitic CI-candidates therefore depend on the developmental age of the infant and its ability to cooperate. The audiological evaluation should at least include multiple objective measurements. Auditory brainstem response audiometry (ABR) is a well-established method to predict the hearing threshold around 2 to 4 kHz although the ABR response is not fully matured in infants younger than 6 months of age[30]. In some cases, more frequency-specific information is needed. For instance, children with moderate-to-severe hearing losses in the lower and middle frequencies and hearing loss exceeding 100 dB in the higher frequencies may show an absent click-ABR[31]. These children could greatly benefit from hearing aids and are not cochlear implant candidates per se. Other objective measurements like auditory steady state responses (ASSR), tone burst ABR, and electrocochleography may provide better frequency-specific information[32,33].

In the short and often stressful period between the onset of meningitis, the recognition of profound SNHL and cochlear implantation, the parents need to be counseled, both on the fact that hearing loss has occurred as a complication of meningitis as well as on the benefits and risk of cochlear implantation. It is important that parents fully realize the fact that the hearing loss is profound and almost always permanent. In this process, behavioral observation audiometry may be helpful. As the expectations of cochlear implantation may be lower in postmeningitic CI candidates (see below), discussing realistic expectations is essential.

Anesthesiological Technique

Patients younger than 9 months of age have specific physiological characteristics that increase the risk of general anesthesia, and complications of meningitis may confer an even higher anesthetic risk. Specialized pediatric anesthesiologists are therefore an indispensable part of the pediatric cochlear implant team[5,34]. Key points in the anesthesiological technique include the parental presence at induction, which significantly reduces separation anxiety and distress in the infant[35]. Gaseous or intravenous induction are both suitable, and the choice of anesthetic agent should be based on minimizing postoperative nausea and vomiting and minimizing the intraoperative bleeding. The use of facial nerve monitoring is strongly recommended but precludes the use of long-acting muscle relaxants. Special care must be taken with the positioning of the child. Because of the length of the procedure, wiring under the child or folds in clothes and draping can cause skin injury. It is important to minimize heat loss, as infants are particularly vulnerable to hypothermia because of a

large body-surface-to-weight ratio[5]. The operation theatre should therefore be preheated, and a temperature control blanket should be applied. Conversely, prolonged surgery in a small surgical field using draping that covers a large surface area could increase the body temperature, and the body temperature should thus be monitored during the procedure[5]. If bilateral implantations are performed, the alternating position of the head should be anticipated. Furthermore, the pediatric trachea is of a shorter length, which makes the infant patient more prone to accidental extubation with head movement. Infants have higher relative oxygen consumption, and respiratory insufficiency due to suboptimal ventilation may rapidly escalate into a critical situation. Because of this, the tube should always be secured, preferably manually while positioning the head, and the anesthetist should be an expert in pediatric airway management[5].

Due to the small circulating blood volume, young infants are vulnerable to cardiovascular compromise, and meticulous hemostasis is of utmost importance. Hypovolemic effects can occur when blood loss exceeds 10% of the total blood volume[36]. This equals 65 mL of blood loss in a baby of 6 months (with an approximate weight of 8 kg)[5,36]. The margin of safety in an infant of 4 months is obviously lower.

Surgical Technique

The specific surgical considerations in cochlear implantation in very young postmeningitic patients are summarized in Table 4. We perform a retroauricular S shape incision (“lazy S”), which allows for adequate exposure of the mastoid. It should not be extended downwards over the mastoid tip as far as in adults, because the undeveloped mastoid tip at this age does not yet cover the facial nerve, which is situated more superficial to the skin (Figure 2). When performing a bilateral implantation, symmetry must be observed in the placement of the implant. This can be achieved by creating a paper blueprint, marking the place of the implant relative to the ear, and using it to determine the correct position of the implant on the contralateral side (Figure 3). In order to avoid formation of a subcutaneous hematoma during bilateral surgery, a drain is placed lateral to the closed musculoperiosteal layer at the side of the first implanted ear. It can be taken out once the head bandage is in place.

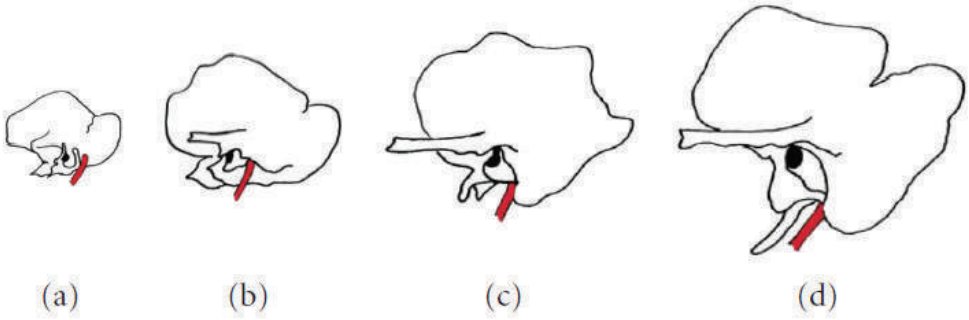

Figure 2: Development of the mastoid process. Schematic representations of the development of the temporal bone from infancy to adulthood (from left to right). In the young infant, the mastoid is small, and the facial nerve, marked in red, is not yet covered by the mastoid process.

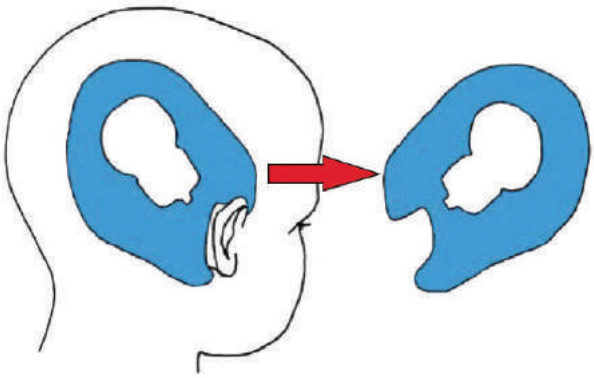

Figure 3: Drawing of a paper blueprint of the position of the implant relative to the ear in order to determine the correct, symmetrical position of the contralateral implant in bilateral implantation. The position of the implant at the first operated ear is marked on a paper sheet and transposed on to the contralateral side.

Mastoid cells in very young children are relatively poorly pneumatized and contain bone marrow, causing profuse bleeding when performing the mastoidectomy[5,37]. Hemostasis is important for an adequate surgical view but also because the small circulating blood volume of the infant does not allow for extensive blood loss[4]. As bipolar cauterization is often not helpful in this situation, hemostasis can be achieved by using diamond burrs and bone wax to obliterate the bleeding mastoid cells. Although the infant mastoid is small and sometimes consists of only the antrum, there is enough space for an adequate mastoidectomy and posterior tympanotomy[37]. The view through the posterior tympanotomy can be limited, however, due to the undeveloped mastoid and the restrictions in the angle looking through the posterior tympanotomy. In addition, the round window is often located in a more horizontal plane, parallel to the surgeons view.

Performing a cochleostomy can be a challenge in postmeningitic cases because of ossification of the cochlea. Even in cases with limited ossification, identification of the proper lumen is sometimes only possible after drilling out sections of the basal turn of the cochlea[25,38]. Cochlear fibrosis or ossification may prevent full electrode insertions[6,39,40]. In some cases, a scala tympani insertion is impossible, and the electrode can only be placed in the scala vestibuli[41,42]. Another solution may be a split electrode insertion[38-40]. In our patients, we did not encounter cochlear ossification, probably due to the short time interval that had elapsed between the onset of meningitis and cochlear implantation. We did, however, find cochlear fibrosis in case 2, 3, and 4, which could be overcome by gently removing it from the basal turn and subsequently inserting the electrode.

When creating the bone bed for the cochlear implant, the thin cortex of the skull has to be taken into account. We perform a "bony island" construction, as it fixes the implant and minimizes the force on the skin and dura (Figure 4)[5,37]. Alternatively, one may create a subperiosteal pocket only and avoid drilling a cortical well; however, this may affect the fixation of the implant in its position on the infant skull unless additional tie-down ligatures are placed[37].

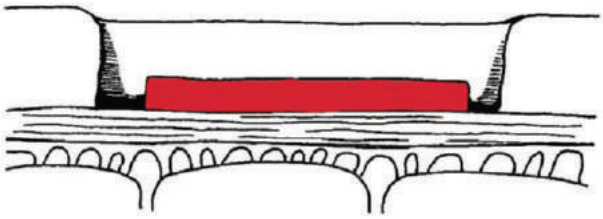

Figure 4: Schematic drawing of the construction of a bony island. The cortical bone is thinned in the middle of the CI-shaped well, and the dura is completely uncovered at the borders of this well, creating an "island" of cortical bone (red) protecting the dura.

Finally, when fixing the electrode within the mastoid cavity, the altering dimensions of the developing temporal bone have to be taken into account. In contrast to the cochlea, the mastoid process is not fully developed at birth, and it expands during childhood (Figure 2). In the review of the growth pattern of the temporal bone by Dahm et al., it is demonstrated that whereas the distance between the round window and the fossa incudis does not increase after birth, the distance between the round window and the sinodural angle as well as the distance between the fossa incudis and the mastoid tip increase considerably during the first 18 years of life (Figures 2 and 5)[8]. Fixation of the lead on the electrode in the caudal part of the mastoid is therefore not advisable, as the development of the mastoid tip could cause dislocation of the electrode. In addition, there has to be enough lead (about 20–25 mm) on the electrode to allow for the increase in distance between the round

window and the implant fixed to the skull. Fixation of the electrode at the round window or cochleostomy and of the electrode lead within the posterior tympanotomy is safe and will support a proper electrode position during childhood. If these surgical considerations are taken into account, cochlear implantation in very young children is not associated with an increased risk of surgical complications[37,39].

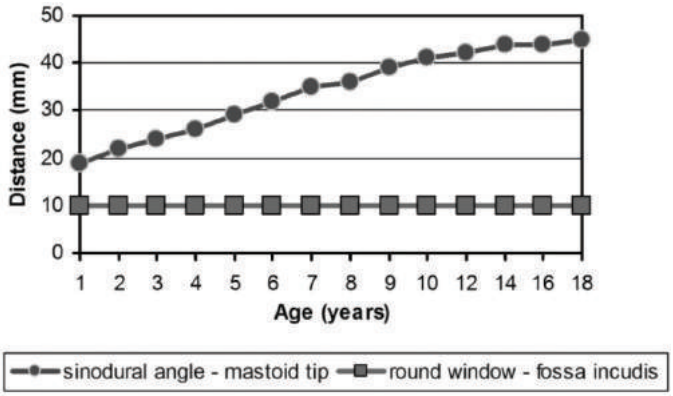

Figure 5: Growth of the middle ear versus mastoid: the mastoid tip develops, whereas the middle ear dimensions remain the same. The distance of the round window to the fossa incudis and facial recess does not change over time, but the mastoid process increases in size. When the electrode is fixed to the mastoid tip, the increasing distance from round window to mastoid tip could cause a possible displacement of the electrode out of the cochlea. Adapted from Dahm et al.[8].

Outcome

The outcome of cochlear implantation in postmeningitic infants is less predictable than the outcome in congenitally deaf children[6,39]. It is not only dependent on the proper CI placement and the depth of electrode insertion, which can be compromised in these patients due to obliteration of the cochlear lumen, but also on the type and severity of additional sequelae of meningitis if present. Bacterial meningitis may cause damage to the cochlear spiral ganglia, which may result in failure of the neuronal response even in cases with full electrode insertions[43,44]. Moreover, the outcome of cochlear implantation also depends on the cognitive and linguistic abilities of the recipient, which is of special significance in patients with profound SNHL due to meningitis, as this condition may affect these factors as well. This is also reflected in the considerable variation in audiological performances of our patient group, ranging from open set speech perception to the identification of sounds only (Table 1). Not surprisingly, the best performing patient (case 2) had no other complaints besides hearing loss, whereas the patient with the worst performance (case 3) suffered from severe neurological sequelae (Table 1). Importantly, postmeningitic children seem to benefit from CI even in case of incomplete insertions or comorbidity associated with meningitis[42].

CONCLUSION

Cochlear implantation is indicated in infants younger than 9 months if postponing surgery would decrease the chances of successful implantation. This is the case in profound SNHL and impending obliteration of the cochlear lumen due to fibrosis or ossification caused by meningitis. In postmeningitic patients younger than 9 months, cochlear implantation is feasible, but specific diagnostic, anesthesiological, and surgical considerations related to the early age at implantation and the possible sequelae of bacterial meningitis apply. Furthermore, the outcome of CI in postmeningitic infants is variable even in technically successful implantations. A multidisciplinary CI team, consisting of pediatric audiology, anesthesia, speech therapy, and otology specialists is therefore essential in the successful management of this challenging patient group.

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Chapter 8

General discussion and future perspectives

Cochlear implantation has proven its effectiveness over the last decades and the number of people who received a CI was estimated to be approximately 324.000 in 2012[1]. Currently 65.0000 CIs are implanted worldwide each year and the number of shipped CIs is expected to hit 96.000 by 2020 (Figure 1)[2]. The substantial increase of the number of people that receive cochlear implants can in part be attributed to the expected increase of the worldwide geriatric population, resulting in an increased prevalence of acquired SNHL. Other contributing factors include a high growth potential in emerging economies and the expansion of the indications for CI, which make cochlear implantation the hearing revalidation option of choice for an increasing proportion of the patients suffering from hearing loss. In the beginning of the CI era only adult patients with bilateral profound hearing loss were eligible for CI. Nowadays patients with residual hearing, selected cases of prelingual deafened adults and children with genetic or acquired SNHL are also being indicated for CI[3-5].

Figure 1: Chart demonstrating the expected number of shipped cochlear implants till 2020. A compound annual growth rate of 13.60 – 14.09% would result in 96.000 shipped cochlear implants in 2020. *Image adapted from https://www.technavio.com.*

Although the international criteria for cochlear implantation have broadened, rather rigid audiometric cut off points determine whether CI is reimbursed or not. As a result, patients borderlining the criteria might be deprived of the optimal rehabilitation strategy for their hearing loss. On the other hand, patients who meet the audiometric criteria for CI might be better off with an alternative treatment option. The general aim of this thesis was to elucidate aspects of the diagnostic work-up and treatment specifically pertaining to patients with asymmetric hearing loss, patients with far-advanced otosclerosis and patients with deafness caused by bacterial meningitis.

ASYMMETRIC HEARING LOSS

Asymmetric sensorineural hearing loss

Two studies in this thesis address individuals with asymmetric hearing. The first subgroup consists of patients with severe asymmetric SNHL, i.e. unaidable hearing on one side in addition to suboptimal hearing on the contralateral side. This specific group of patients does not meet the current standard criteria for cochlear implantation and often must wait until their speech recognition deteriorates further to meet the criteria for CI. The study in Chapter 2 addresses the outcome of CI in patients with asymmetric SNHL. The inclusion criteria for this study are defined as less than 30% aided speech recognition in the worst hearing ear and an aided speech recognition between 60% and 85% for the best hearing ear. We demonstrated that CI in these patients significantly increases the patients' hearing performance, especially in challenging listening conditions.

An important drawback of the current guidelines is that patients' speech recognition scores are measured in quiet. This method determines the maximum performance in optimal listening conditions. Whereas speech recognition in quiet can seem to be relatively good, the speech recognition may become poor in the presence of background noise. Also in Chapter 2, we evaluate a group of unilateral hearing-aid users with an average speech recognition score in quiet of 74%. When the signal was mixed with disturbing noise and presented in front of the listener, patients scored a mediocre SRT score of +2.6. Adversely, normal hearing listeners, evaluated in Chapter 3, performed substantially better with an SRT score of -9.4dB in the same test condition. The differences in performance become even more apparent when speech and noise are spatially segregated. The latter demonstrates that, although patients sometimes seem to perform fairly good in quiet, their actual limitations are better reflected by testing speech recognition in challenging conditions. A more appropriate method to select patients would thus be to include bilateral speech recognition abilities in noise as this better reflects the actual performance in daily life.

Unilateral cochlear implant recipients

The second subgroup of patients with asymmetric hearing abilities that is evaluated in this thesis comprises unilateral CI-users with unaidable hearing on the contralateral side. Because a second CI is currently not reimbursed for this group of adult patients, an alternative would be helpful. The addition of a second satellite microphone (CI-CROS) could potentially be a cost-effective alternative to bilateral CI. However, our observations indicate that CI-CROS is an inadequate method to further rehabilitate unilateral CI users, as reported in Chapter 3. The advantages in specific spatial listening conditions are cancelled out by disadvantages

in opposite listening conditions. Moreover, CI-CROS users are not able to perform as well as unilateral CI-users, because the elimination of the head shadow effect prevents patients to acquire an optimal listening position to block interfering noise. A direct comparison with bilateral CI-users favors bilateral implantation with regard to improved spatial speech recognition and the ability to benefit from binaural input. Expansion of the guidelines in order to allow bilateral CI, and not CI-CROS, should be considered to further improve the performance unilateral CI-users with unaidable contralateral hearing.

Bilateral implantation

Over the last years several systematic reviews recommended bilateral cochlear implantation in adults. Gaylor et al. (2013) reported in their meta-analysis that "bilateral implantation showed improvement in communication-related outcomes compared with unilateral implantation"[6]. Van Schoonhoven et al. (2013)[7] provided in their meta-analysis additional evidence in favor of bilateral cochlear implantation, even in complex listening situations. Finally, Crathorne et al. (2012)[8] mentioned that "all studies reported improvements in bilateral cochlear implantation for improved hearing and speech perception". Based on these recent insights, a second CI is currently reimbursed in an increasing number of countries[9]. In the Netherlands, bilateral cochlear implantation is only reimbursed for children and not for adults, precluding them from using binaural processing to perform better in challenging listening conditions. Dutch insurance companies decided that reimbursement of a second CI cannot be justified due to the low level of evidence and an incomplete assessment of cost-effectiveness. Hence, Smulders et al. (2016)[10] recently initiated the first randomized controlled trial which compared bilateral CI with unilateral CI. Patients who underwent bilateral cochlear implantation had significantly better hearing results in everyday listening situations and were able to localize sounds[10,11]. Moreover, bilateral cochlear implantation seemed a cost-effective treatment for patients with a life expectation of 5-10 years or longer[12]. Based on the findings presented above, the current criteria for a second CI in adults seem too restrictive and revision is warranted.

The benefit of binaural input over monaural hearing has been analyzed also in this thesis. Chapter 2 demonstrates that bimodal stimulation in patients with asymmetric SNHL results in significant better speech recognition (in quiet, noise and spatial), better localization abilities and an improvement in quality of life. Additionally, Chapter 3 showed that bilateral CI-users performed better with both implants than with one CI with respect to speech recognition in noise and spatial speech recognition. The advantages of binaural hearing are further elucidated in Chapter 5 where the binaural benefit after bilateral stapedotomy is demonstrated.

FAR-ADVANCED OTOSCLEROSIS

The term far-advanced otosclerosis is defined as an air conduction threshold of more than 85dB HL and an immeasurable bone conduction threshold[13]. Patients with far-advanced otosclerosis (FAO) may demonstrate unmeasurable bone- and air conduction thresholds at audiometry. A blank audiogram with no response to any frequency does however not necessarily mean absence of hearing as it only indicates that the hearing thresholds are beyond the limits of the audiometer. For bone conduction the limit of the audiometer lies around 60dB HL whereas air conduction is, depending on the frequency, measured up to 120dB HL. For instance, a patient with a bone conduction level at 65dB HL and a 60dB HL air-bone gap would hence seem to be suffering from profound SNHL. Even after fitting a powerful hearing aid, the patient may still be severely impaired and will demonstrate very poor speech recognition abilities, meeting the criteria for cochlear implantation in most countries. However, full closure of the air bone gap by a successful stapedotomy would result in a rather good aidable 65dB HL air conduction threshold. Figure 2 illustrates the air conduction thresholds and (bilateral) speech recognition scores before- and after a successful stapedotomy of one of the patients included in the meta-analysis of Chapter 5. This example underlines the potential of stapedotomy combined with hearing aid fitting as an alternative to CI in patients with FAO.

Imaging in far-advanced otosclerosis

HRCT is the modality of choice for the evaluation of the temporal bone anatomy and pathology and is also considered to be the imaging technique of choice in patients with otosclerosis. In addition to assisting in the diagnosis, HRCT can also be used to determine the extent of the cochlear involvement, preparing the surgeon for the challenges he or she might encounter during cochlear implantation. For instance, obliteration or a double ring effect can be readily seen on HRCT, alerting the surgeon to the risk of partial electrode insertion or misplacement. Although not significant, the extent of otosclerotic lesions on HRCT tends to be greater in patients with a problematic insertion of a cochlear electrode array[14,15].

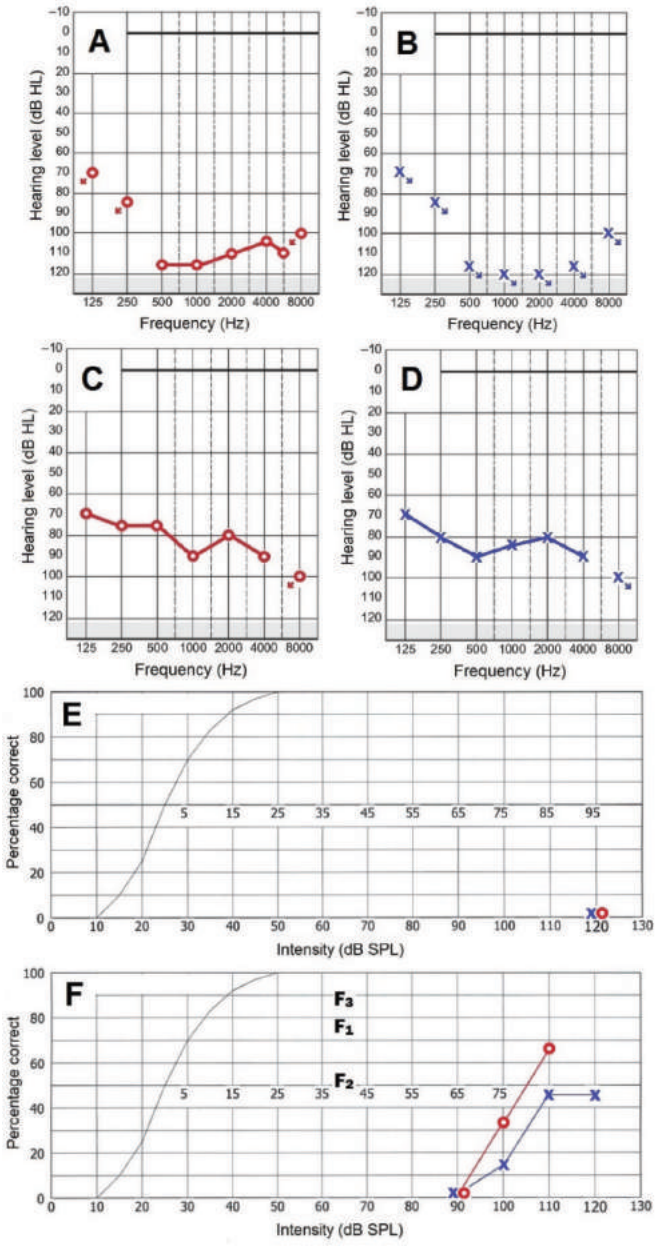

Figure 2: Pure-tone audiometry (PTA) and speech recognition outcomes of a patient with far-advanced otosclerosis treated by bilateral stapedotomy. Preoperative PTA shows profound hearing loss of the right ear (A) and immeasurable air conduction thresholds of the left ear (B). Unaided speech recognition at 120dB HL was 0% for both ears (E). Stapedotomy resulted in an improvement in air conduction thresholds for both ears (C+D), corresponding unaided speech recognition scores at 120dB HL were 68% (right ear, O) and 45% (left ear, X). Hearing aid fitting further increased the speech recognition to 76% (right ear, F_1) and 52% (left ear, F_2). The binaural aided speech recognition reached 88% (F_3). Bone conduction threshold were unmeasurable before and after stapedotomy.

Stapedotomy in far-advanced otosclerosis

The meta-analyses in Chapter 5 shows that stapedotomy combined with hearing aid fitting can achieve a very satisfactory outcome in a substantial percentage of the patients with FAO. Stapedotomy has several important advantages over cochlear implantation. It is less expensive and the procedure is less complex. After stapedotomy, only hearing aid fitting is required whereas cochlear implantation is followed by an intensive rehabilitation period. Moreover, the quality of sound is more natural after stapedotomy restores unaidable hearing to aidable 'natural' hearing, which also contributes to the detection of sounds when the hearing aid is not worn. Although patients with FAO are eligible for cochlear implantation according to the current guidelines, we recommend that a stapedotomy should be attempted first in patients with FAO. If a unilateral stapedotomy does not result in a satisfactory hearing, a contralateral stapedotomy can be performed. When the first stapedotomy was successful, a consecutive contralateral stapedotomy should be offered as this can restore binaural hearing and offer patients the benefits of binaural processing.

The standard criterion for measuring the success of stapedotomy, i.e. closure of the air-bone gap to 10dB or less, is not suitable for patients with FAO because bone-conduction levels are often immeasurable even postoperatively. Likewise, the commonly used Belfast Rule of Thumb (stating that patients are likely to benefit from middle ear reconstructive surgery if the hearing threshold in the operated ear was less than 30dB HL or if the interaural difference in reduced to less than 15dB) HL[16] is not suitable for estimating the effect of stapedotomy in patients with FAO. Patients with FAO never achieve a postoperative air-conduction threshold of less than 30dB HL. Additionally, an interaural difference of more than 15dB HL is almost always present after (bilateral) stapedotomy. Since these conventional paradigms do not seem valid, we believe that the best indicator of success of stapedotomy in patients with FAO is the postoperative (bilateral) aided speech recognition as this better reflects a patients' performance in daily life.

Patients with FAO who underwent (bilateral) stapedotomy can roughly be subdivided in three groups according to the outcome: good performers (more than 80% aided speech recognition), mediocre performers (an aided speech recognition between 50% and 80%) and poor performers (less than 50% aided speech recognition). The good performers achieve a satisfactory outcome after stapedotomy which is comparable, or even better than the average performance after cochlear implantation[17-22]. For the mediocre and poor performers, the option of cochlear implantation is still open, as a previous stapedotomy does not affect the technical feasibility or performance of (ipsilateral) CI[19,23].

Cochlear implantation in far-advanced otosclerosis

Extensive otosclerotic foci of the otic capsule pose surgical challenges that have to be taken into account when performing cochlear implantation in patients with FAO. Substantial fenestral involvement or narrowing of the basal turn of the cochlea might require extra drilling in order to identify the scala tympani[17,20]. Otosclerosis can also lead to obliteration at the apical regions of the cochlea hampering a complete electrode insertion. Furthermore, confluent otospongiotic lesions can surround the cochlea, resulting in an electrode misplacement in this false lumen[14,15]. An additional problem associated with CI in otosclerosis is postoperative electrical stimulation of the facial nerve. Facial nerve stimulation (FNS) is thought to be caused by decreased impedance of otospongiotic foci in combination with the rather high current levels that are required to achieve thresholds in otospongiotic bone. FNS is managed by reducing stimulus levels or by deactivating the causative electrodes. Fewer active electrodes, due to partial electrode insertion or deactivation of electrodes in FNS, is associated with a less favourable outcome. Even so, patients with otosclerosis have been shown to perform as well as matched non-otosclerotic CI recipients[19,22].

Although not significant, the extent of otosclerotic lesions on HRCT tends to be greater in patients with a problematic insertion of the electrode array[14,15]. Hence, one could hypothesize that it might be favorable to perform cochlear implantation and not stapedotomy in patients with retrofenestral otospongiosis, as in theory, proliferation of the cochlear otospongiotic foci after stapedotomy might complicate cochlear electrode insertion in future. To date however, no reliable prediction can be made regarding the progression of SNHL nor the rate of proliferation of the otospongiotic foci in FAO patients. We therefore recommend that a stapedotomy should be attempted first in patients with FAO, because of the advantages of stapedotomy listed above. The site and extent of otosclerotic foci do not seem to predict the outcome of a stapedotomy[18]. Within weeks after a stapedotomy it is clear whether stapedotomy yields a satisfactory outcome, or if cochlear implantation should be considered.

POSTMENINGITIC HEARING LOSS

One of the severe possible sequelae of bacterial meningitis is the occurrence of profound (bilateral) SNHL. The risk of postmeningitic SNHL differs for the various causative pathogens. It is most common in S. Pneumoniae (31-36%), followed by N. Meningitidis (8-11%) and H. Influenzae (6-11%)[24,25]. The introduction of vaccination programs in the Netherlands have led to a dramatic decrease in the incidence of bacterial meningitis. Since vaccination against H. Influenzae type b (HiB) in 1993, HiB meningitis has virtually disappeared and now has a stable incidence of 0.12:100.000[25]. Vaccination against N. Meningitidis serogroup C started

from 2002 and led to a seventeen fold decrease in incidence to 0.18:100.000[25]. The incidence of S. Pneumoniae meningitis halved to 0.84:100 since vaccination against S. Pneumoniae introduced in 2006[25]. Nowadays, S. Pneumoniae is the most common causative pathogen of meningitis accounting for approximately 50% of the bacterial meningitis cases. Despite the decrease in incidence, bacterial meningitis is still an important cause of acquired deafness[26-28]. Approximately 6-36% of all patients with bacterial meningitis will develop SNHL, and severe bilateral SNHL will occur in 3-9% of the postmeningitic patients[27,28].

SNHL after meningitis

The occurrence of postmeningitic SNHL is caused by spread of bacteria and endotoxins from the subarachnoidal space to the cochlea resulting in inflammatory reaction within the cochlea[29]. The cochlear aqueduct is the most likely pathway, but other possible routes have been speculated[30]. Alternatively, SNHL and meningitis may be caused by otitis, spreading through the cochlea and aqueduct system to the subarachnoid spaces[31]. As demonstrated in Chapter 6, both cochlear inflammation and profound SNHL can be present within days after the first onset of the symptoms of meningitis. In a proportion of patients with severe-to-profound SNHL after meningitis, cochlear inflammation progresses to obliteration of the cochlear lumen caused by fibrosis, calcification or ossification[32]. The sequence of events, which starts with an inflammation and progresses to fibrosis and ultimately ossification, may commence directly after the onset of meningitis and ossification of the cochlear lumen may be present within weeks[24,33]. Figure 3 illustrates the different radiologic phases of postmeningitic inflammation (on GdMRI, T2MRI and HRCT) ranging from cochlear enhancement to near total ossification of the cochlear lumen.

Cochlear implantation after meningitis

Cochlear implantation is the treatment of choice for rehabilitation patients with severe bilateral SNHL after meningitis. Since postmeningitic fibrosis or ossification can block the cochlear lumen and hamper electrode insertion, patients should preferably be implanted before obliteration occurs as the number of active intracochlear electrodes is a significant parameter for the auditory performance after cochlear implantation[21,34]. It is therefore essential to identify patients with postmeningitic SNHL as early as possible. Unfortunately, postmeningitic SNHL is not always noticed directly, particularly in critically ill patients. As a result, hearing loss sometimes remains undetected. In order to prevent delayed diagnosis of postmeningitic SNHL, the CI centers in the Netherlands have agreed on a protocol for the audiometric follow-up of patients after bacterial meningitis. This protocol advocates the first audiologic assessment as soon as possible after the meningitis has resolved, a prolonged audiologic follow-up, and swift referral to a CI center in case of SNHL[35].

Imaging after meningitis

Current T2MRI sequences, including CISS (Constructive Interference In Steady State) and FIESTA (Fast Imaging Employing Steady-state Acquisition), allow for thin slice thickness and detailed fluid imaging, resulting in more precise imaging of the inner ear anatomy[36]. T2MRI visualizes fluid distributions within the labyrinth and can detect loss of fluid in the cochlear lumen, the semicircular canals and the vestibulum. This loss of fluid may be caused by any type of intraluminal mass, but in postmeningitic patients is most likely the result of post-inflammatory fibrosis or calcification[24,37,38]. The study in Chapter 6 demonstrates that diminished cochlear patency on T2MRI is significantly associated with a complicated electrode insertion. Hence, loss of fluid on T2MRI should guide the surgeon towards rapid cochlear implantation as progression from cochlear fibrosis to labyrinthitis ossificans most likely hampers electrode insertion in the (near) future. In contrast to T2MRI, HRCT can only detect calcification or bony alterations of the cochlea, but cannot identify the preceding stage of fibrosis[39]. HRCT is still considered an essential imaging technique prior to cochlear implantation because it allows a more detailed imaging of the temporal bone. Moreover, distinguishing between fibrosis and ossification is only possible with a combination of T2MRI and HRCT (Figure 3).

Gadolinium enhanced T1-weighted MRI (GdMRI) can reveal increased perfusion of the cochlea, which can be an indication of active inflammation[24,31]. The study of Chapter 6 demonstrated that enhancement on GdMRI was significantly associated with the development of SNHL (96% positive predictive value). As cochlear enhancement on GdMRI is suggestive of cochlear inflammation, it also indicates a risk of fibrosis and ossification of the cochlear lumen. In bilateral postmeningitic profound SNHL and postmeningitic enhancement on GdMRI, we therefore recommend bilateral CI as soon as possible to minimize the risk of a complicated electrode insertion, especially when diminished cochlear patency on T2MRI is already present. In the clinical setting, this means that the decision for CI is sometimes made before all standard requirements are met. Measuring speech recognition and pure-tone audiometry for instance, may be difficult, due to the young age or to the rehabilitation of the sequelae of meningitis. Moreover, a test period with hearing aids, which is part of the normal preoperative evaluation, could take up valuable time increasing the risk of cochlear obliteration and a suboptimal CI outcome.

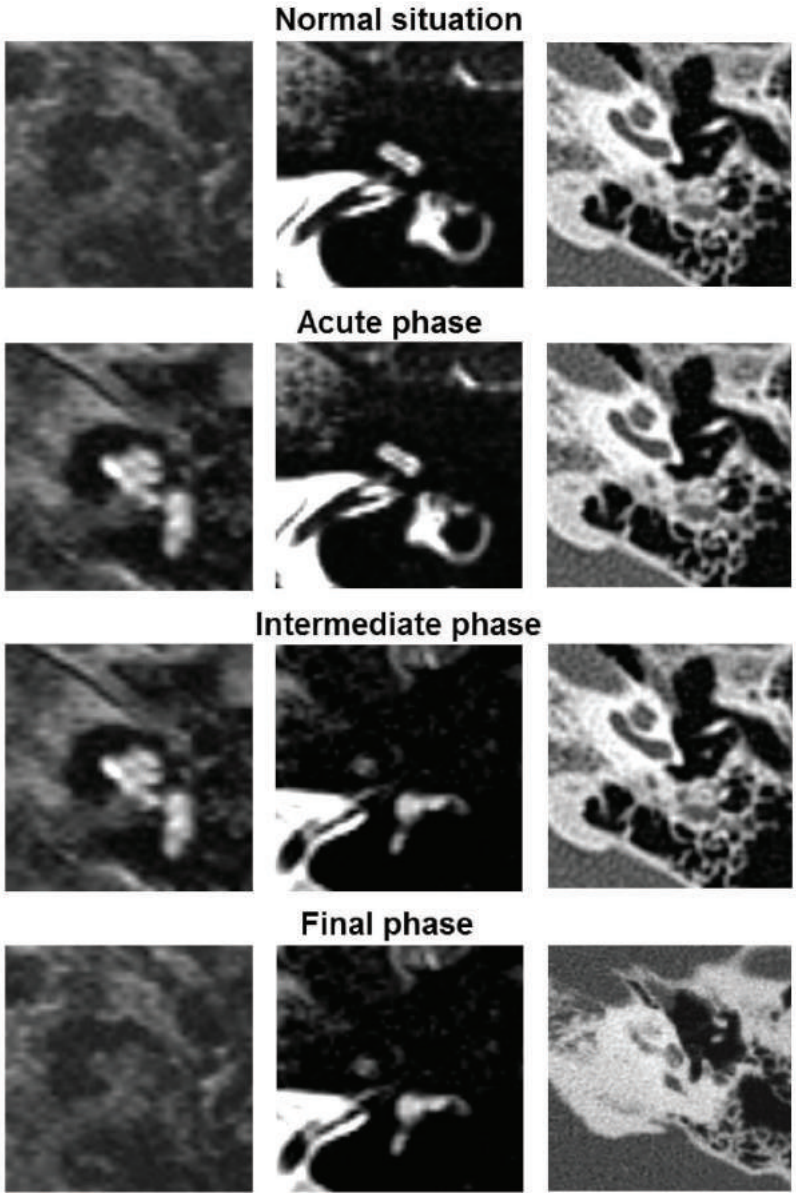

Figure 3: Illustration of the different phases of postmeningitic cochlear inflammation, fibrosis and ossification as seen on MRI and HRCT. Shown in the first column are the contrast enhanced T1MR images (GdMRI), in the second column are T2MR images, and in the third column are HRCT images. The top row illustrates the normal aspect of the cochlea on MRI and HRCT. The second row shows the acute phase characterized by cochlear inflammation on GdMRI (white arrow) with no loss of fluid on T2MRI. The third row shows the intermediate phase with cochlear enhancement on GdMRI accompanied by loss of fluid on T2MRI (open arrow), but without ossification of the cochlear lumen on HRCT. The bottom row shows the final phase in which the cochlear enhancement on GdMRI has disappeared and diminished cochlear patency on T2MRI is present caused by cochlear ossification (black arrow) as identified on HRCT.

One might state that the additional value of GdMRI is limited since hearing loss, rather than enhancement on GdMRI, should determine whether patients are suitable candidates for CI. But for patients with unilateral postmeningitic SNHL and ipsilateral enhancement on GdMRI, the absence of contralateral enhancement seems to predict postmeningitic hearing preservation on that side. This finding may assist in the decision not to perform cochlear implantation and can serve as a reassurance for patients and/or parents, as the prospect of impending bilateral loss of hearing can be very stressful. The data of the study of Chapter 6 indicate that MRI is important in the follow-up of patients with SNHL after meningitis. Although the outcome of postmeningitic audiometry is the dominant factor, MRI assists in selecting patients for cochlear implantation and choosing between uni- or bilateral implantation. Moreover, MRI is essential in the timing of the procedure and in predicting peroperative challenges.

FUTURE PERSPECTIVES

This thesis focuses on the potential of cochlear implantation for patients with challenging indications like asymmetric sensorineural hearing loss, far-advanced otosclerosis and postmeningitic deafness. One of the main challenges is to implement the recommendations made in this thesis to optimally rehabilitate these specific groups of patients. Future guidelines for CI candidacy should allow patients with asymmetric SNHL, who insufficiently benefit from hearing aid amplification, to benefit from a CI in the functional deaf ear. Cochlear implantation could also improve the performance of already unilateral implanted patients as sequential bilateral cochlear implantation will to some degree restore binaural hearing in these patients. The present thesis does not include cost-effectiveness, however this topic should not be ignored in future policy.

Optimizing the methodology for selecting candidates suitable for cochlear implantation is a leading thread of this thesis. We advise to include (bilateral) speech recognition abilities in noise in the audiologic test battery as this better reflects the actual performance in daily life than speech recognition in quiet. Future research is necessary to determine a criterion for CI candidacy based on speech recognition in noise.

Although patients with FAO are eligible for cochlear implantation according to the current guidelines, we recommend that a stapedotomy should be attempted first, because of the arguments listed above (see paragraph ‘far-advanced otosclerosis, this chapter). However, as of yet it is unclear whether the improvement in hearing after stapedotomy is sustained over a long period of time. Progressive deterioration of hearing thresholds may ultimately

exceed the limits of hearing aid amplification even after stapedotomy. As demonstrated by Topsakal et al. (2006), the progression of the sensorineural hearing loss component in patients with otosclerosis seems to be more pronounced than the normal age-related progression of SNHL[41]. The long term results of stapedotomy in FAO should therefore be evaluated to assess whether the initial choice for a stapedotomy over a CI is an adequate strategy to rehabilitate hearing in an enduring way.

HRCT has proven to be a valuable tool in assessing the severity of the cochlear involvement in patients with FAO. Extensive cochlear involvement on HRCT seems more prevalent in patients with a complicated electrode insertion, although this association is not statistically significant[14,15]. One can hypothesize that it might be better to perform CI and not stapedotomy in patients with extensive cochlear involvement on HRCT, because progression of the disease could influence the feasibility of cochlear implantation in the future, should CI become necessary. To date, the growth rate of cochlear otosclerotic foci remains unclear. Larger prospective studies with longer follow-up of FAO patients are needed to determine: (1) the expansion rate of otosclerotic foci, (2) the correlation between otosclerotic changes on HRCT and hearing loss, (3) the association between the extent of the cochlear otosclerosis and peroperative complications, both after cochlear implantation and stapedotomy. Performing large prospective studies in this patient group is rather difficult as FAO cases with severe or extensive otospongeotic lesions are rare. A multicenter approach is needed to gather sufficient data to answer these important questions.

Cochlear implantation has proven its effectiveness over the last decades and is nowadays widely accepted as an effective way to rehabilitate patients with profound sensorineural hearing loss. The studies in this thesis provide new insights, challenging the indications of cochlear implantation candidacy, especially for non-standard cases borderlining the current criteria. Continuous assessment of the potential of cochlear implantation, as well as alternative interventions, should result in ongoing evidence-based revisions of the guidelines for cochlear implantation in order to optimally rehabilitate future patients with severe-to-profound hearing loss.

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Chapter 9

English summary

ENGLISH SUMMARY

Chapter 1 provides a brief introduction regarding the physiology of hearing and the principals of binaural hearing. The development of cochlear implants is described starting with the first electrical stimulation of the inner ear. Additionally, the functionality is described of current cochlear implants. Several limitations of the current international criteria for cochlear implantation candidacy are elucidated and finally the outline of this thesis is presented.

Chapter 2 consists of a prospective study on the outcome of cochlear implantation in patients with asymmetric sensorineural hearing loss. These patients are often not eligible for cochlear implantation due to the remaining hearing abilities of the best hearing ear. Because of monaural input, these patients lack the ability to benefit from binaural processing. Seven postlingually deafened adults received a cochlear implant in their worst hearing ear. Bimodal stimulation, through unilateral cochlear implantation and contralateral hearing aid use, resulted in significant better speech recognition in quiet as compared to stimulation with only hearing aid or only CI. Speech recognition in noise, spatial hearing and localization abilities all significantly improved, indicating that these patients were able to successfully integrate electrical stimulation with contralateral acoustic amplification and thereby benefit from binaural hearing. We therefore conclude that cochlear implantation should be considered for patients with asymmetric SNHL, even in the presence of substantial residual hearing on the contralateral side.

Chapter 3 comprises of a study on unilateral CI users with profound hearing loss on the contralateral side. These patients are often not eligible for a second cochlear implant, the addition of a second contralateral microphone (CI-CROS) has the potential to improve spatial hearing. The performance of ten CI-CROS users was compared to five bilateral CI users and a control group of twelve normal hearing individuals. The main effect of a CROS microphone was the elimination of the head shadow effect by mixing the signal originating from both sides and presenting the signal to one single CI. CI-CROS resulted in better performance when speech was presented to the CROS microphone but yielded a disadvantage when disturbing noise was presented to the CROS microphone. Patients using CI-CROS lost the ability to block interfering noise using the head shadow and could therefore not acquire the optimal listening position to benefit from the spatial separation of speech and noise. As a result, CI-CROS users were in some listening conditions not able to perform as well as unilateral CI users. CI-CROS was therefore not advised to rehabilitate unilateral CI users with bilateral severe to profound SNHL. Bilateral cochlear implantation would be a better option to rehabilitate unilateral CI users with unaidable contralateral hearing.

Chapter 4 is a review of the literature regarding the outcome of stapedotomy and cochlear implantation in patients with far-advanced otosclerosis. The review yielded 24 studies from which 135 cochlear implantations and 331 stapedotomies in patients with far-advanced otosclerosis were extracted. An algorithm is proposed, based on speech performance, the extent of (peri-) cochlear otosclerotic alterations as seen on HRCT and the extent of the air-bone gap. This algorithm aims to assist the clinician to decide between cochlear implantation and stapedotomy combined with hearing aid fitting as the optimal strategy for hearing rehabilitation.

Chapter 5 consists of a meta-analysis of the literature aimed at evaluating the potential of stapedotomy in patients with far-advanced otosclerosis that meet the criteria for cochlear implantation. Individual audiologic measurements of 83 patients with far-advanced otosclerosis who underwent a stapedotomy were extracted and included in the meta-analysis. Stapedotomy resulted in a mean improvement of the aided speech recognition of 48%. After stapedotomy, the majority of the patients (72%) achieved a speech recognition of more than 50% and were no longer candidates for cochlear implantation. An excellent speech recognition score of 80% or more, was achieved in 35% of the operated patients. We conclude with the recommendation that a stapedotomy should be attempted before considering cochlear implantation in patients with far-advanced otosclerosis. If a (bilateral) stapedotomy does not yield a satisfactory result, patients can still be treated by cochlear implantation, because a previous stapedotomy does not affect the technical feasibility nor the performance of a cochlear implant.

Chapter 6 presents a retrospective study evaluating the role of MRI in the decision and timing of cochlear implantation in patients suffering from SNHL after meningitis. Gadolinium enhanced T1-weighted MRI (GdMRI) and T2-weighted MRI (T2MRI) were associated with the occurrence of SNHL and the peroperative findings during cochlear implantation, respectively. A significant association between the enhancement of the cochlea on GdMRI and the occurrence of hearing loss was found. Additionally, loss of cochlear fluid on T2MRI was significantly associated with a complicated electrode insertion. If diminished cochlear patency on T2MRI is present in patients with bilateral hearing loss, urgent cochlear implantation should be considered to minimize the risk of a complicated electrode insertion. In patients with unilateral SNHL, a non-enhancing cochlea on the contralateral side was highly indicative of hearing preservation over time. The different phases of postmeningitic inflammation are described based on the findings on GdMRI, T2MRI and HRCT.

Chapter 7 describes our experience in performing cochlear implantation in four very young patients with SNHL after meningitis. Because of the risk of postmeningitic cochlear fibrosis or subsequent ossification of the cochlear lumen, cochlear implantation is sometimes

necessary before the advocated optimal age of nine to twelve months. The audiological assessment in these patients can be challenging due to the young age and the possible sequelae after meningitis. Moreover, a young age at implantation poses several surgical challenges with regard to the incision, the mastoidectomy, embedding of the implant in the skull, creating the cochleostomy and fixation of the electrode. If these aspects are taken into account, CI is feasible even in very young patients.

Chapter 10

Nederlandse samenvatting

NEDERLANDSE SAMENVATTING

Hoofdstuk 1 betreft een algemene introductie over de fysiologie van het gehoor en de principes van binauraal horen. De ontwikkeling en de werking van cochleaire implantaten wordt beschreven, beginnend met de eerste elektrische stimulatie van het binnenoor. Vervolgens wordt de werking uitgelegd van de cochleaire implantaten die momenteel worden gebruikt. De beperkingen van de huidige internationale criteria voor cochleaire implantatie worden verhelderd en er wordt afgesloten met een beschrijving van de opzet van dit proefschrift.

In **Hoofdstuk 2** wordt een studie beschreven naar de uitkomst van cochleaire implantatie bij patiënten met asymmetrisch perceptief gehoorverlies. Deze patiënten komen vaak niet in aanmerking voor cochleaire implantatie vanwege het restgehoor van het best horende oor. Vanwege de monaurale input kunnen deze patiënten geen voordeel halen uit binaurale verwerking. Zeven volwassenen met postlinguaal ontstane doofheid ontvingen een cochleair implantaat in het slechtst horende oor. Bimodale stimulatie, door middel van een unilateraal cochleair implantaat en een contralateraal hoortoestel, resulteerde in een significant verbeterd spraakverstaan in stilte in vergelijking met de situatie waar alleen het hoortoestel of alleen het CI werd gedragen. Spraakverstaan in stilte, ruimtelijk spraakverstaan en de mogelijkheid tot het lokaliseren van geluid verbeterden allen significant, wat illustreert dat deze patiënten in staat zijn om elektrische stimulatie succesvol te integreren met contralaterale akoestische versterking en daarmee kunnen profiteren van binauraal horen. Er wordt afgesloten met de aanbeveling dat cochleaire implantatie overwogen dient te worden voor patiënten met asymmetrisch perceptief gehoorverlies, zelfs in de aanwezigheid van substantieel restgehoor aan de contralaterale zijde.

Hoofdstuk 3 betreft een studie naar unilaterale CI gebruikers met ernstig gehoorverlies aan de contralaterale zijde. Deze patiënten komen vaak niet in aanmerking voor vergoeding van een tweede CI, en daarom zou een alternatief hiervoor welkom zijn. Dit alternatief zou het toevoegen van een tweede contralaterale microfoon (CI-CROS) kunnen zijn. In theorie herstelt een CI-CROS de bilaterale input, hetgeen zou kunnen resulteren in een beter ruimtelijk spraakverstaan. Het functioneren van tien CI-CROS patiënten werd vergeleken met vijf bilaterale CI gebruikers en een controlegroep bestaande uit twaalf normaalhorenden. Het belangrijkste effect van de CROS microfoon was de eliminatie van de hoofdschaduw doordat het geluid afkomstig van beide zijden werd gemixt en aangeboden werd aan één CI. CI-CROS resulteerde in een beter functioneren wanneer het geluid werd aangeboden aan de CROS microfoon maar een in gelijke mate minder functioneren werd geobserveerd wanneer verstorende ruis werd aangeboden aan de CROS microfoon. Patiënten met CI-CROS

verloren de mogelijkheid om gebruik te maken van de hoofdschaduw om verstorende ruis te blokkeren en hierdoor konden zij niet de optimale luisterpositie aannemen om voordeel te hebben van de ruimtelijke verdeling tussen spraak en ruis. Dit had tot gevolg dat CI-CROS gebruikers in sommige luistercondities niet in staat waren om even goed te functioneren als unilaterale CI gebruikers. Hierdoor wordt CI-CROS niet geadviseerd voor de rehabilitatie van unilaterale CI gebruikers met bilateraal ernstig perceptief gehoorverlies. Bilaterale cochleaire implantatie lijkt een betere mogelijkheid te zijn om unilaterale CI gebruikers te revalideren.

Hoofdstuk 4 beslaat een review van de literatuur over de uitkomst van stapedotomie en cochleaire implantatie bij patiënten met vergevorderde otosclerose. Een systematische zoekvraag leverde 24 bruikbare studies op waarin 135 cochleaire implantaties en 331 stapedotomieën bij patiënten met vergevorderde otosclerose werden beschreven. Er wordt algoritme voorgesteld, gebaseerd op spraakverstaan, (peri-) cochleaire otosclerotische veranderingen op CT scan en de grootte van het geleidingsverlies. Dit algoritme heeft als doel om de operateur te assisteren bij het bepalen van de optimale behandelmogelijkheid: cochleaire implantatie, of een stapedotomie in combinatie met het aanmeten van een hoortoestel.

Hoofdstuk 5 beschrijft een meta-analyse van de literatuur met als doel om het potentieel van stapedotomie te onderzoeken bij patiënten met vergevorderde otosclerose die zo ernstig slechthorend zijn dat zij voldoen aan de criteria voor cochleaire implantatie. De indivuduele audiologische metingne van 83 patiënten met vergevorderde otosclerose, die behandeld zijn middels een stapedotomie, werden geïncludeerd in de meta-analyse. Stapedotomie resulteerde in een gemiddelde toename in het spraakverstaan van 48%. Een groot deel van de patiënten (72%) bereikte een spraakverstaan van meer dan 50% en was daardoor geen kandidaat meer voor cochleaire implantatie. Een uitstekend spraakverstaan van meer dan 80% werd bereikt bij 35% van de geopereerde patiënten. We concluderen met de aanbeveling een stapedotomie te verrichten alvorens cochleaire implantatie te overwegen bij patiënten met vergevorderde otosclerose. Als een (bilaterale) stapedotomie niet het gewenste resultaat oplevert, kunnen patiënten nog steeds behandeld worden middels cochleaire implantatie aangezien een eerdere stapedotomie geen effect heeft op de technische mogelijkheid tot, of het functioneren van een cochleair implantaat.

Hoofdstuk 6 beschrijft een retrospectieve studie naar de waarde van MRI bij patiënten met perceptief gehoorverlies na meningitis. Het doel van deze studie was het evalueren van de associatie van T1-gewogen MRI met gadolinium (GdMRI) en T2-gewogen MRI (T2MRI) met het ontstaan van perceptief gehoorverlies en de peroperatieve bevindingen tijdens cochleaire implantatie. Een significante associatie tussen de aankleuring op GdMRI en

het optreden van perceptief gehoorverlies werd aangetoond. Daarnaast was verlies van cochleair vocht op T2MRI significant geassocieerd met een gecompliceerde elektrode insertie. Wanneer bij patiënten met bilateraal perceptief verlies er een verminderde cochleaire vochthoudendheid wordt gezien op MRI, dient snelle cochleaire implantatie overwogen worden om het risico op een onvolledige of gecompliceerde elektrode insertie te minimaliseren. Bij patiënten met unilateraal perceptief verlies bleek een niet-aankleurende contralaterale cochlea een indicatie te zijn voor het behoud van het gehoor in de toekomst. De verschillende fasen van postmeningitis inflammatie worden beschreven, gebaseerd op de bevindingen op GdMRI, T2MRI en HRCT.

Hoofdstuk 7 beschrijft onze ervaring met cochleaire implantatie bij vier zeer jonge patiënten met perceptief verliesverlies na meningitis. Door het risico op cochleaire fibrose of ossificatie van het cochleaire lumen, is cochleaire implantatie soms noodzakelijk vóór de aanbevolen leeftijd van negen tot twaalf maanden. De audiologische metingen kunnen uitdagend zijn vanwege de jonge leeftijd en de mogelijke restverschijnselen van de meningitis. Daarnaast resulteert de jonge leeftijd tijdens implantatie in enkele specifieke chirurgische uitdagingen met betrekking tot de incisie, de mastoïdectomie, de plaatsing van het implantaat in de schedel, het creëren van de cochleostomie en de fixatie van de elektrode. Als rekening wordt gehouden met deze factoren is cochleaire implantatie mogelijk, ook bij zeer jonge patiënten.

Chapter 11

Dankwoord

Curriculum Vitae

List of publications

DANKWOORD

Nu op pagina 162 ben ik dan eindelijk aangekomen bij het meest gelezen onderdeel van ieder proefschrift: het dankwoord. Helaas is dit kleine hoofdstukje soms ook het enige deel van het proefschrift dat wordt gelezen. Degenen die niet in staat waren om het gehele boekje door te lezen, verwijs ik graag naar de Summary op pagina 154 waarin in een aantal paragrafen het werk van de afgelopen jaren wordt samengevat. Er is ook een Nederlandse samenvatting beschikbaar op pagina 158 zodat een ieder op de hoogte kan zijn van de conclusies van dit proefschrift.

Allereerst wil ik mijn waardering uitspreken voor de patiënten die hebben deelgenomen aan de studies die in dit proefschrift zijn beschreven. Ik wil hen bedanken voor hun bereidheid om belangeloos te participeren aan de diverse onderzoeken, zonder hun investering was deze promotie niet mogelijk was geweest. Tijdens de talloze meetmomenten ontdekte ik een van de voordelen van onderzoek naar het gehoor, en naar cochleaire implantatie in het bijzonder: het resultaat is vaak direct zichtbaar, zowel voor de patiënt als voor de onderzoeker. Hierdoor was tijdens de dataverzameling al duidelijk wanneer patiënten profijt hadden bij een bepaalde interventie, een belangrijke tussentijdse motivator die lang niet voor iedere promovendus is weggelegd. De uitgebreide metingen op verschillende tijdsintervallen en in verschillende luistercondities, de diverse vragenlijsten en de statistische analyse, hadden vaak slechts het doel om iets te bevestigen dat ik en de patiënt allang hadden waargenomen.

Daarnaast wil ik een aantal mensen in het bijzonder bedanken:

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Dr. Merkus, beste Paul, inmiddels acht jaar geleden kwam ik via-via bij jou terecht met het verzoek onderzoek te doen binnen de KNO. Na de eerste publicatie werd er een constructie gecreëerd waardoor ik kon promoveren met jou als een van de twee co-promotoren. Ik ben je erg dankbaar voor het gestelde vertrouwen in mij en de moeite die je hebt gedaan om dit promotietraject mogelijk te maken. De laagdrempelige en gelijkwaardige samenwerking heb ik altijd enorm gewaardeerd en ik kijk dan ook uit naar mijn laatste differentiatiejaar waarin de otologie centraal zal staan. Ik zie het als een voorrecht dat ik de eerste otologische promovendus van het VUmc heb mogen zijn!

Dr. Hensen, beste Erik, als tweede co-promotor heb je een grote rol gespeeld in alle onderzoeken uit dit proefschrift. Daarnaast ben je cruciaal geweest bij het uitzetten van

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De leden van de leescommissie, Prof. Dr. S.E. Kramer, Prof. Dr. Ir. J.H.M. Frijns, Prof. Dr. E.A.M. Mylanus, Prof. Dr. A.M. Tutu van Furth, Dr. M.M.L. De Win, Dr. G.A. Van Zanten, wil ik bedanken voor hun bereidheid om dit manuscript te beoordelen en dank voor het plaatsnemen in de promotiecommissie.

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Het is volbracht, het is af: opluchting, blijdschap en trots!
De voldoening is oneindig...

CURRICULUM VITAE

Maarten Caspar van Loon was born on the 31th of August 1985 in Geldrop, the Netherlands. He attended the Strabrecht College in Geldrop, where he received his athenaeum diploma in 2003. In the same year he started his study in medicine at the University of Utrecht. During the final year of his study, he studied the morphologic degeneration of spiral ganglion cells after deafening and the effects of neurotropic treatment, supervised by Dr. H. Versnel and Prof. Dr. W. Grolman. After obtaining his medical degree in 2010 he started his first research project at the VU University Medical Center in Amsterdam. This research regarded patients with far advanced otosclerosis and is also included as a chapter in this thesis. Between 2010 and 2012 he worked as resident surgery at the Diakonessenhuis in Utrecht and as an independent medical examiner. Since 2012 he started working as a research-resident at the department of Otorhinolaryngology and Head and Neck Surgery of the VU University Medical Center of Amsterdam, supervised by Prof. Dr. C.R. Leemans and co-supervised by Dr. P. Merkus and Dr. E.F. Hensen. During this period, several chapters of this thesis have been presented in national and international conferences. Parallel to his Ph.D. research, he worked as a tutor for medical students at the faculty of medicine at the VU University in Amsterdam. In 2014 he commenced his training as resident otorhinolaryngology at the VU University Medical Center of Amsterdam under supervision of Prof. Dr. Leemans and Dr. Merkus, consecutively. During his residency he worked at the Diakonessenhuis in Utrecht and at the Westfries Gasthuis in Hoorn, under supervision of Dr. J.J. Quak and Dr. L.J.J.M. Bauwens, respectively. Currently, Maarten is in his last year of his specialization in the field of otorhinolaryngology.

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