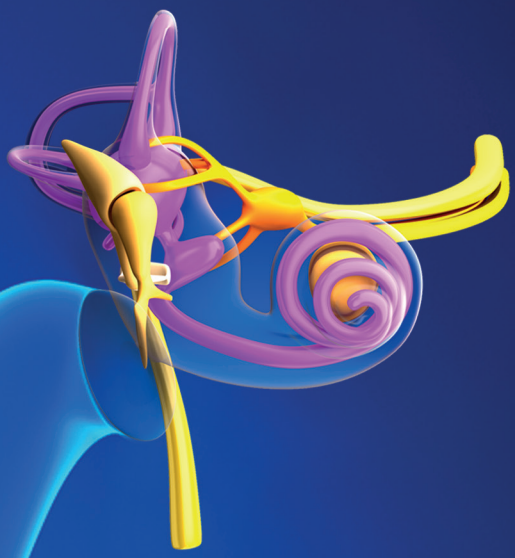
AUDITORY IMPLANTS IN OTOLOGY

active middle ear implants and
direct acoustic cochlear stimulation:
indications and outcome



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active middle ear implants and direct acoustic cochlear stimulation: indications and outcome

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Aan mijn gezin en mijn familie

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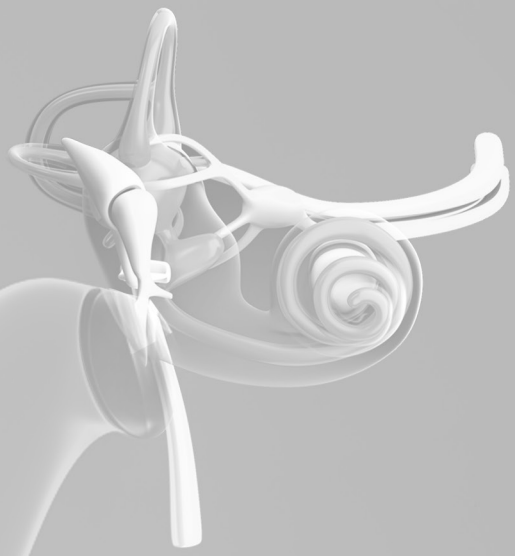

1.1.

General Introduction

General introduction

Hearing is one of man's most important senses. Not only can we interact with our surroundings by sound, but most of human communication is based on the production and recognition of sound and speech. An intact function of the hearing organ is one of the key elements in the development of speech and language. Loss of hearing can cause an important disability in the development of language in children or in the communicational skills in adults and therefore it strongly influences learning capabilities and school development. Furthermore, hearing is of great importance for our physical safety, since it can protect us from harm by other persons, animals or objects. Multiple causes are known for both congenital as acquired and inherited hearing loss.

Anatomy and physiology of the hearing organ

The human ear is divided into three main parts (**figure 1**). Firstly, the outer ear, which contains the auricle or pinna and the outer ear canal. The ear canal is made up of skin, cartilage and bone, from the pinna up to the eardrum. The function of the outer ear is to collect sound and guide it towards the middle ear. It slightly enhances the sounds

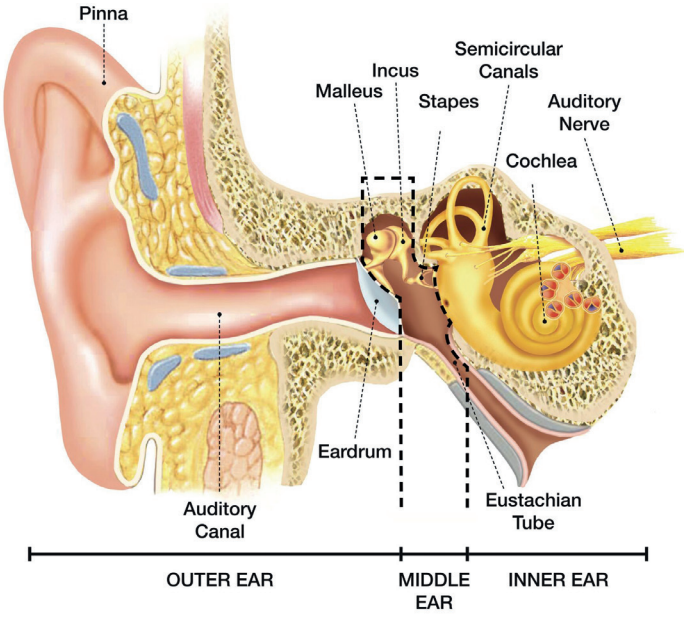

Figure 1 Anatomy of the ear.

Courtesy unknown.

between 2000 to 3000 Hertz (Hz). Furthermore the pinna has a function in directional hearing by picking up various cues in sound that can be interpreted by the brain (e.g. frequency, time and pitch differences) (1).
The second part is the middle ear which consists of the ear drum, the auditory ossicles (malleus, incus and stapes), their connecting ligaments, tendons and muscles and the Eustachian tube. The function of the ear drum and the ossicles is to transfer and enhance the vibrations of sound in air effectively to the fluid of the inner ear (called transformation). It has an amplification function, due to the surface proportion between de ear drum and the oval window, which connects the ossicular chain to the inner ear fluid. Thereby it compensates for the loss of amplitude (or sound loudness) by the transfer of air vibration to the fluid vibration in the inner ear. The muscles connected to the ossicles (tensor tympani and stapedial muscle) are able to stiffen the ossicular chain during loud sounds and large pressure shifts. The function of this stiffening remains uncertain (2). They can contract, thereby stiffening the connection between the ear drum and the inner ear and decreasing the amplitude of the vibration. The Eustachian tube functions as an access to the middle ear to equalize the air pressure with the surrounding environment. Moreover, it has a function in the clearance and protection of the middle ear. It is the connection between middle ear and nasopharynx and is made up by cartilage and partly by bone (1, 3).
The inner ear contains the labyrinth, which consists of the vestibule and semicircular canals (balance organ) and the cochlea, which is the actual hearing organ itself. It is made up by three canals, separated by membranes (see **figure 2**). The most important of the membranes, the basilar membrane, contains the organ of Corti (**figure 3**). This organ is made up of specific hair cells, containing stereocilia, which are capable of creating an

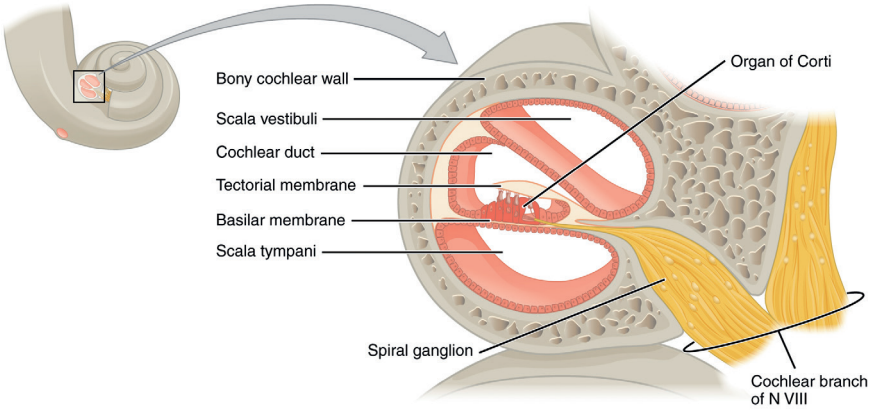

Figure 2 Anatomy of the cochlea.

Courtesy of Wikimedia user OpenStax.

action potential when they are displaced. This action potential initiates a signal through the cochlear nerve to the brain. Displacement of the hair cells occurs when the vibrations of sound, transferred by the ossicles to the inner ear fluid through the oval window, induces fluid vibrations in the cochlea. These vibrations are transferred over the basilar membrane. High pitched frequencies only reach the base of the membrane and low pitched frequencies are conducted up to the apical part of the membrane. The round window membrane ensures that the amplitude of the pressure fluctuations in the cochlea is kept as small as possible. Since complex sound is made up of multiple combined frequencies, the transfer of the vibration into fluid waves along the basilar membrane causes multiple hair cells to be displaced at the same time. This enables the cochlea to send multiple combined action potentials to the brain, thereby sensing the complete complexity of sound, e.g. music or speech in noise. The human spectrum of sound perception reaches from 20 to 20.000 Hz between 0 and 110 decibels (dBHL) (1, 3).

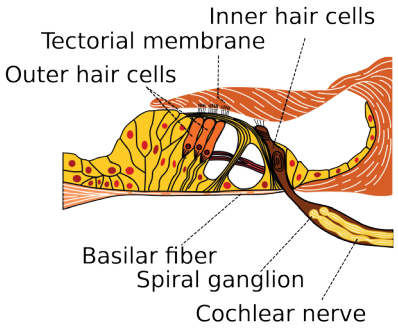

Figure 3 Organ of Corti.

Courtesy of Wikimedia user Madhero[88].

Hearing loss

Sensorineural hearing loss

A decrease in hearing is defined as hearing loss and it can be divided into three groups. Sensorineural hearing loss (SNHL) in general is caused by a deficit in the sensory hearing organ in the cochlea or in the neural pathway to the brain. It can be congenital or acquired or a combination of both. Hearing loss can either present as high frequency hearing loss, e.g. presbyacusis or due to ototoxicity, or a flat hearing loss on all frequencies. Middle and low frequency hearing loss are mostly associated with inherited sensorineural cochlear damage or due to advanced meniere's disease and mostly progressive. According to the world health organization, the severity of hearing loss is expressed in mild hearing loss (25-40 dBHL), moderate (40-60 dBHL), severe (60-80 dBHL) and profound (>80 dBHL)(4). See **figure 4** for an example of various sound levels.

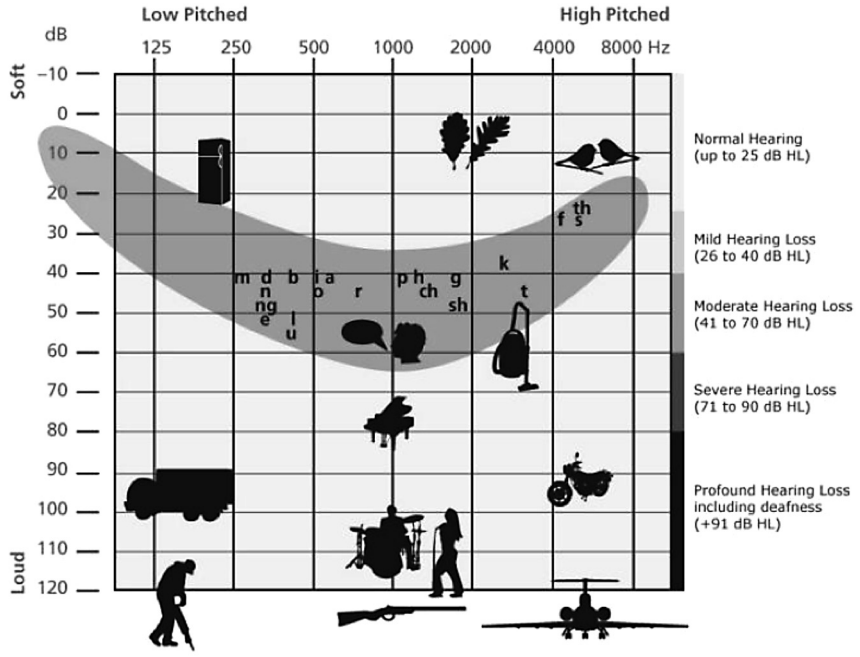

Figure 4 Audiogram of familiar sounds.

Courtesy of Phonak.

Conductive hearing loss

Another form of decrease in hearing is conductive hearing loss (CHL). In this form, regular hearing is present in a normal functioning cochlea, but the sounds do not pass the external ear and/or the middle ear correctly or the sound transfer is ineffective. Therefore, a so called air-bone gap is present in pure tone audiometry, which is the difference between the air conduction hearing loss thresholds and the function of the inner ear measured by bone conduction thresholds. The hearing loss may be temporary, e.g. due to secretory fluids in the middle ear, or permanent and even progressive. The severity of CHL is determined by the type of pathology. In absence of the external ear canal a maximum CHL of 60 dBHL may be present.

Mixed hearing loss

At last, mixed hearing loss (MHL) may be present with a combination of pathologies. For example, a tympanic membrane perforation may be present in a patient with an age related sensorineural hearing loss, or otosclerosis may have affected the oval window as well as the cochlear function. Revalidation of hearing may be challenging in MHL, since

the sounds need to be enhanced loud enough to overcome the CHL at first and secondly to compensate for the remaining SNHL component. In certain situations, this may add up to severe hearing loss.

Pathology of the ear

Apart from aging of the cochlea, many diseases of the ear can affect the hearing function, both temporarily and permanent and varying from slight hearing loss to total deafness. The causes can be divided per location and consist of infections, inflammation, malformation or destruction of vital structures by (benign or malignant) tumors or by trauma.

Outer ear pathology

At birth, some illness that influences hearing can be present. Congenital malformations of the pinna (called microtia), the ear canal or even middle ear structures can lead to various forms of uni- or bilateral conductive hearing loss. Microtia occurs mostly isolated, but it may occur in conjunction with other anomalies, such as hemifacial microsomia or as a syndrome like Goldenhar, DiGeorge or Treacher-Collins syndrome (5).

When a defect to the outer ear canal is present, a partial or complete obstruction may occur. In congenital cases the complete outer ear canal may be absent. In acquired cases, mostly due to recurrent infections, narrowing of the ear canal or an acquired atresia causes a inadequate transfer of the sound vibrations through the ear canal, leading to hearing loss. External otitis is an infection of the skin in the outer ear canal. In most cases this is of short duration due to pathologic causes such as bacteria or fungi. For other patients, the skin in the outer ear canal may suffer from seborrheic eczema. Another cause may be due to poor ventilation because of a narrow entrance to the ear canal. Therefore, the condition in the ear canal changes and chronic recurrent infections may occur. Another cause of poor ventilation may occur due to wearing blocking ear molds of hearing aids in the ear canal.

When the tympanic membrane is (partly) absent, an open connection to the middle ear is present. This may cause recurrent infections, especially when the middle ear is exposed to water. Furthermore, a perforation of the tympanic membrane will cause conductive hearing loss, as the sound transfer function of the membrane is diminished.

Middle ear pathology

Various causes of middle ear pathology can cause hearing loss. In most cases the ossicular chain is involved, either when a congenital absence or malformation is present or due to acquired interruptions. In children, the most common cause of hearing loss is chronic serous otitis media. This causes an accumulation of mucus in the middle ear that alters the transfer function of sound and causes a conductive hearing loss. The etiology of this disease is caused by a malfunction of the ventilation of the middle ear by the eustachian tube. It can lead to chronic recurring middle ear infections or a permanent decrease in middle ear pressure that may alter the tympanic membrane. When the tympanic

membrane gets retracted into the middle ear, it may cause arrosion of the ossicular chain, in most cases located at the long process of the incus. The membrane may even completely retract against the medial wall of the middle ear cavity, creating a so called atelectasis. When the tympanic membrane gets retracted even further in the superior and posterior quadrant, it may cause retraction pockets that may lead to cholesteatoma. In limited disease this may only damage the tympanic membrane or the ossicles. In extensive disease, the mastoid may be involved.

Another well known cause of conductive and mixed hearing loss is otosclerosis. Due to a disturbed balance between bone resorption and formation, the stapes may form otospongiosis that will fixate the stapes footplate in the oval window. Because of this fixation, the vibrations of the tympanic membrane and ossicular chain will not reach the cochlear fluid properly. Typically, during audiometry a so-called 'Carhart's notch' is visible and a conductive hearing loss in the lower and higher frequencies with a pseudo sensorineural hearing loss around 2-4 kHz (6). In advanced cases of otosclerosis, the bone surrounding the cochlea may also be involved in the spongiotic process. It may even distort the cochlear lumen (7). Then sensorineural hearing loss is found in these patients. It has been argued that some of the released enzymes and toxins may damage the inner ear hair cells (8).

Besides the more frequent causes mentioned, some disease of the middle ear are less common but can also be responsible for hearing loss. This concerns benign lesions like paraganglioma or schwannoma. These causes are outside the scope of this thesis.

Middle ear surgery

For several middle ear diseases, ear surgery to restore hearing is an option for treatment, i.e. in otosclerosis, tympanosclerosis, ossicular chain disruptions, tympanic membrane perforations or chronic otitis media. On the other hand, for cholesteatoma, surgery is imminent as the disease will progress when untreated and further damage to the middle ear structures can thereby be prevented. So for some indications the hearing loss itself may be the indication for surgical treatment, whereas the result in hearing will be secondary in cholesteatoma surgery.

In cases of otosclerosis or osteogenesis imperfecta, a stapedotomy can be performed, replacing the fixed stapes by a small prosthesis, also called a piston, connected to the intact incus. For serous otitis media, grommet insertion through the tympanic membrane is an easy solution to temporarily resolve the accumulation of mucus in the middle ear and provide improvement of aeration of the middle ear. In situations where the ossicular chain is damaged, either due to retraction of the tympanic membrane or due to cholesteatoma, the incus and/or the stapes may be replaced by a so called partial or total ossicular replacement prosthesis or by using autogeneous material like remnants of the incus. In small defects cement or hydroxyapatite can be applied. In all these procedures the goal is to (partially) resolve the conductive hearing loss. In some cases, this cannot be completely

achieved and a remaining conductive or mixed hearing loss may still be present after the intervention.

Inner ear pathology

For inner ear hearing loss, numerous causes are known. Congenital causes are either genetic abnormalities in the anatomy of the inner ear or congenital infections, e.g. Rubella or Cytomegalovirus. Genetic defects may occur in various forms or in combination with other deformations or diseases in syndromic hearing loss. The severity and age of onset can vary widely from mild hearing loss at later age to severe hearing loss or deafness at birth.
Acquired causes can be very various. It ranges from trauma, prematurity and infections (either of the middle ear, the cochlea or the cochleovestibular nerve) to ototoxicity by drugs such as aminoglycosides, loop diuretics and chemotherapeutics. For example, cisplatin and carboplatin cause damage to the cochlear hair cells. In most cases it starts with a high frequency hearing loss, but with severe cases all frequencies can be affected (9).
Presbycusis is also known as the aging process of the inner ear. It mostly starts of as a measurable increase of hearing thresholds in the high frequencies in the sixth decade of age. The general idea is that the organ of Corti and the stria vascularis in the cochlea increasingly degenerate. During the years the thresholds increases even further, leading to a hearing loss in the mid- and lower frequencies and rehabilitation will be required.
Another form of inner ear pathology is noise induced hearing loss (NIHL). It can be divided in two basic types: acoustic trauma or gradually developing NIHL. The first can be the result of an acute exposure to an excessive sound pressure, i.e. from explosions, firecrackers or gunfire. It is mostly accompanied by tinnitus. Sound over 120 dBSPL may cause inner ear damage to the outer and/or inner hair cells. For gradually developing NIHL, long term exposure to sound over 85 dBSPL for longer than 8 hours per day is harmful. In many cases the exposure is due to occupational noise, such as loud music or due to operating machines. In some cases a predisposition is found for patient with certain genetic variations (10). The chronic repeated long term activation of the outer hair cells causes a continuous metabolic activity that may alter some of the proteins in the ear. Furthermore, it may cause the formation of free radicals of oxygen molecules, which may damage the organ of Corti (11). The frequency range of NIHL starts around 4 kHz and may gradually increase to the higher frequencies at first and the lower frequencies later on.

Retrocochlear pathology

Besides the inner ear, pathology of the vestibulocochlear nerve, the brainstem and cerebrum might also be causative for sensorineural hearing loss. Especially vestibular schwannoma is more common as a cause for damage to the cochlear part of the eighth cranial nerve due to pressure. Even though the cochlea functions properly and the hair cells within it are not damaged, when the nerve itself cannot properly conduct the hearing information through the pathway to the central parts of the brain, the sounds will not be

properly perceived. Other causes are of cerebrovascular or neurological origin. These diseases are outside the scope of this thesis as no revalidation can be achieved by hearing aids.

Functional hearing tests

Pure tone audiometry

As hearing is a function of sound perception, the levels in hearing can be tested by determining the exact sound level per frequency that a person can perceive. These thresholds are expressed in frequency specific relative hearing decibels, called dBHL. The test is conducted in a standard soundproof environment. In a regular pure tone audiogram 6 thresholds are determined in the frequency range of 250 to 8000 Hz in octave steps. In certain situations, the intermediate frequencies of 0.75, 1.5, 3 and 6 kHz will also be determined. This can be graphically presented as exemplified in figure 4. For speech understanding the frequency range from 0.5 to 4 kHz is specifically important. In the Netherlands, the averaged thresholds of 0.5, 1 and 2 kHz are referred to as the fletcher-index, whereas the averaged thresholds of 1, 2 and 4 kHz are referred to as the fletcher-high-index. In English literature, the most common used value is the pure tone average (PTA) for the average of 0.5, 1 and 2 kHz (in common with the fletcher index) or the pure tone average of 0.5, 1, 2 and 4 kHz, referred to as PTA4.
In the audiometry test, tones are presented with a headphone (air conduction thresholds), but these test tones can also be presented by a speaker in the soundproof audiometric booth. In this way, hearing can also be tested while using hearing aids (so called free field aided condition). Furthermore, by applying the sound directly as vibrations to the skull, these are directly transferred to the cochlea by bone conduction. By comparing the bone conduction thresholds with the air conduction thresholds (by using the headphone), different types of hearing loss can be determined.

Speech testing

To have an idea of the capacity of a person to understand speech, this can be tested by a word recognition test. During the test, words at varying sound level intensity are produced and the test-subject has to reproduce the words. Each word is scored for correctness of the phonemes, the various sounds in monosyllabic words. The outcome is noted as the percentage of correctness per sound level, although the speech reception threshold (SRT) is the most relevant parameter. This threshold is determined as the presentation level in dBHL for which the subject was able to reproduce 50% of the phonemes correctly.

Speech testing in noise

An even more important function of hearing is to understand speech in noisy conditions and to distinguish the spoken words of one person from the other. On average, a normal hearing person is able to understand speech correctly in conditions where the noise will be 5 dB louder than the spoken words. For patients suffering from hearing loss, this ability

will be diminished and thereby speech understanding will be strongly compromised. This is especially due to hearing loss in the higher frequencies. An example of an adaptive sentence in noise test is a so-called Plomp test (12). During this test, a spoken sentence is played in varying conditions of noise loudness. Thereby the actual speech in noise (SIN), or signal to noise ratio can be determined in decibels.

Rehabilitation of hearing loss

Conventional hearing aids

When a person suffers from hearing loss, rehabilitation can be achieved in various ways. In the Dutch healthcare system, funding is granted for conventional hearing aids (CHA) if the hearing loss exceeds 35 dBHL or more at 1, 2 and 4 kHz. The types of hearing aids may vary from devices in the ear canal to devices behind the auricle in varying sizes.

If the level of hearing loss increases, more powerful hearing aids are required. CHA are capable to provide a maximum loudness up to the uncomfortable loudness level of a patient. To provide more powerful sound, the hearing aid will in general need to be larger in size. It also is more important that the ear canal is properly closed off by an ear mould in order to prevent the escape of energy of the sound. Unfortunately, this causes feedback and re-amplification of sounds produced by the hearing aid.

Conventional hearing aids come with some disadvantages and limitations. Firstly, the ear mould may cause medical complaints of chronic external otitis due to blocking of the ear canal. Another complaint of this blocking is the distortion of the sound of the patient's own voice, called the occlusion effect. In patients with a tympanic membrane perforation or radical cavity, the closing of the ear canal may cause or aggravate infections of the middle ear or cavity. Secondly, hearing aids are associated with social stigma. The problems described above may give rise to a contraindication for the use of conventional hearing aids. A patient with hearing loss faced with these problems is dependable on alternative solutions.

Acoustic implants

For several decades various acoustic implants have been developed and applied as an alternative to conventional hearing aids. The drive of the development has been a result of the medical problems rising with conventional hearing aids. They are based on different kinds of sound amplification or stimulation of the cochlea. Each device has its own advantages and disadvantages that need to be considered. Acoustic devices require a surgical procedure and risks need to be taken into consideration. In general, the costs of acoustic implants are higher than the costs for conventional hearing aids.

Bone conduction implants

Since the 1950s and 1960s bone conduction devices have been available. These devices are based on a technique that applies vibrations to the skull, thereby directly stimulating

the inner ear. The mechanism is based on conduction of the sounds on the skull to the external ear canal, the ossicles and the cochlea itself. Firstly, these devices were bodily worn against the skull or built into spectacles. From 1977, a percutaneous solution was developed and the vibrations were directly applied by a vibrating sound processing device coupled to an implanted skin penetrating coupler into the skull. This technique increased the effectiveness of the transfer of the vibrations and reduced the issues involved with the pressure on the skin. The device was called a bone-anchored hearing aid or Baha. Because of the appearance of several types of bone conduction implants since the development of the BAHA, more general terms for the percutaneous titanium implant like bone anchored hearing implant (BAHI) or bone implant (BI) are more appropriate nowadays (13, 14). See **figure 5** for the components of the Baha system.

The indication for a BI was primarily conductive hearing loss, either uni- or bilateral. Following the percutaneous application and the availability of newer devices with a higher output, BI were also indicated for mixed hearing loss (15-17). The indication range is set for a maximum level of sensorineural hearing loss up to 55 dBHL. Another application is for single sided deafness, where the device can be implanted on the deaf side to use it for contralateral stimulation (18).
Currently two percutaneous bone conduction implants are commercially available, namely the Baha system (Cochlear BAS, Gothenburg, Sweden) and the Ponto system (Oticon Medical, Copenhagen, Denmark). More recently transcutaneous bone conduction

Figure 5 The three components of the Baha system: the implant, the percutaneous abutment, and the vibrating sound processor.

Courtesy of Cochlear.

implants have been introduced. These devices consist of an implanted magnet coupled to the skull underneath the skin. Onto the magnet, an external sound processor is coupled that transfers the vibrations through the skin. This technique has been applied in the Otomag system (Sophono, Boulder, CO, USA) (19) and the Baha Attract system (Cochlear BAS, Gothenburg, Sweden) (20). Another option is an implanted vibrating stimulator into the skull behind the ear and an externally worn audio processor that communicates by radio frequency signals through the skin, as applied in the Bonebridge system (Med-El, Innsbruck, Austria) (21-24).

Active middle ear implants

Active middle ear implants or AMEI have been around for almost two decades (25, 26). This type of implant consists of an active transducer and an implantable processor (**figure 6**). It can be either semi or fully implantable. If the microphone is also implanted, the fully implantable device will be invisibly hidden under the skin. In the semi implantable device, an externally worn sound processor magnetically couples to the implant and communicates with the internal part to send the audiometric information as well as the energy provision

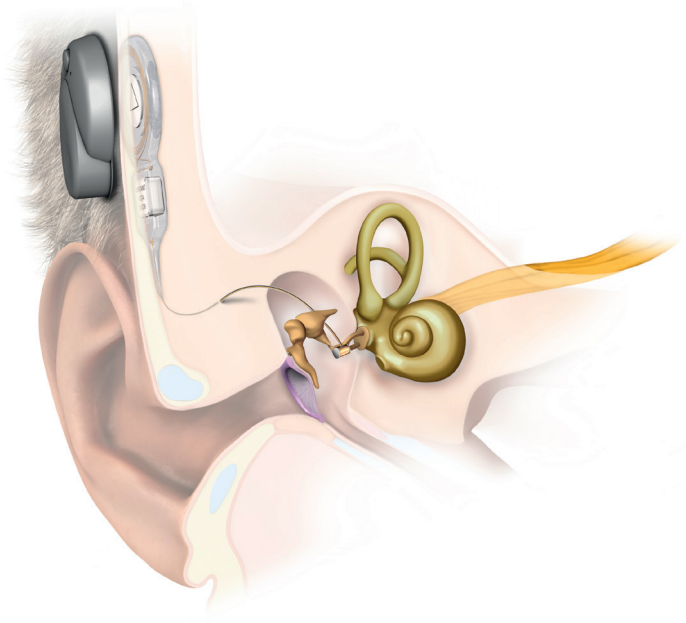

Figure 6 Detailed image of the Vibrant Soundbridge.

Courtesy of Med-el.

for the implant. The active transducer is coupled to any part of the ossicular chain to mechanically drive the ossicles to vibrate, which consequently drives the inner ear fluids. In general the upper limit of hearing loss for the devices is set at 65 – 70 dBHL (27).
AMEI have initially been developed for sensorineural hearing loss as an alternative for conventional hearing aids. Especially in patients with therapy resistant external otitis, the implants are ideal since they avoid and prevent blocking of the external ear canal. Esthetical arguments have also been decisive for many patients. Since about a decade, surgical techniques for AMEI have been adapted to also suit patients with mixed hearing loss due to ossicular and middle ear pathology. Several couplers have been developed to couple the AMEI directly to the round window or stapes supra structure or footplate. (28-30)
Currently three AMEI are commercially available, viz. the Envoy Esteem (St. Croix Medical, Minneapolis, MN, USA) (31), the Middle Ear Transducer and Carina (Cochlear, Sydney, Australia) (**figure 7**) and the Vibrant Soundbridge or VSB (Med-El, Innsbruck, Austria). The latter two devices are the major topic of this thesis and will be additionally described further on.

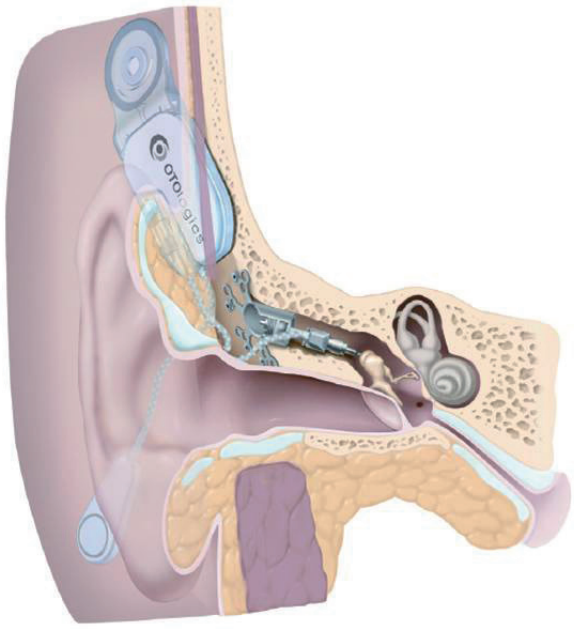

Figure 7 Detailed image of Otologics / Cochlear middle ear transducer (MET).

Courtesy of Otologics / Cochlear.

Direct acoustic cochlear implants

The technique of direct acoustic cochlear stimulation (DACS) was introducted by Häusler in 2008 (32). It is indicated for severe combined hearing loss in advanced otosclerosis. It comprises of an implantable hearing aid that combines the application of a regular stapedotomy piston with the surgical placement of an actuator with a so called artificial incus (**figure 8**). The magnet in the actuator drives the artificial incus and directly transduces the inner ear fluid through the coupled stapes piston. An experimental device based on this technique was constructed under the name of Codacs investigational device by Cochlear (Cochlear Benelux, Mechelen, Belgium). The clinical results of this implant will be discussed in this thesis.

Cochlear implants

For severe to profound sensorineural hearing loss and complete deafness, CHA are no longer effective. Cochlear implants have been available since the 1980's. By introducing an electrode array into the scala tympani of the cochlea, electric stimuli can be delivered to the dendritic and ganglion cells of the cochlear nerve. This artificial method of delivering electrical pulses in the cochlea provided a new method of hearing. The results have been well established both in pre- and postlingually deaf subjects. For postlingual deaf adults, the majority is able to reach good levels of speech recognition in quiet and the ability to use the telephone (33, 34). In prelingual deafness in children, good results have been found for both the outcome in hearing as well as speech and language development (33, 35). Because of these impressive results and adequate cost-effectiveness on societal level, the eligibility criteria for cochlear implantation are still expanding.

Figure 8 Codacs direct acoustic cochlear stimulator.

Courtesy of Cochlear.

General scope of this thesis

For almost 3 decades, research in the field of otology in Nijmegen has been focused on finding the best solutions for previously unresolved severe hearing problems. As such, the application of cochlear implants, bone-conduction implants and active middle ear implants has been addressed as 'last-resort' solutions. Defining the application criteria and evaluating these treatments is still ongoing. In the mid-nineties, based on this research, cochlear implants and bone conduction implants were accepted as regular treatment options in the Dutch healthcare system; cochlear implants for patients with profound hearing loss and bone-conduction implants (Baha) for patients with chronic running ears and for patients with aural atresia. In 2006, active middle ear implants were also accepted as regular healthcare, namely for patients with sensorineural hearing loss in combination with chronic external otitis due to intolerance of ear moulds of conventional hearing aids. Through the years, these implantable hearing devices have been improved by the introduction of better sound processing algorithms and improved coupling options, including direct stimulation of the cochlea.

The aim of this thesis is to present ongoing research regarding long-term stability, device usage and satisfaction of middle ear implantation, and to introduce a model that compares amplification options for patients with mixed hearing loss. In these patients, middle ear implants (including implants that directly stimulate the cochlea) can be applied as well as bone-conduction implants. A synopsis and scope of the thesis' chapters are described below.

Scope per chapter

The indications for the various acoustic implants are overlapping, as has been described by Verhaegen in her doctorate thesis on active implants in 2012 (36). It is important to conduct more studies to provide evidence on long term stability of the implants and on patient satisfaction. Furthermore, the development of new acoustic implants will broaden the indication range and bring more competition to this field of hearing loss rehabilitation. This thesis provides the results of several studies on the surgical and functional outcome of some specific acoustic implants and on the comparison between the systems.

Part 2 describes two studies on the long term use of active middle ear implants Vibrant Soundbridge (VSB) and Otologics MET (oMET). **Chapter 2.1** presents a study on the long term evaluation of patient satisfaction in active middle ear implantation for patient with severe external otitis. Since the beginning of middle ear implantation surgery in Nijmegen in 1996 the patient satisfaction has been evaluated using different patient questionnaires. A short term study on the results of patient satisfaction had already been published (Snik 2006 & 2007). The recent study reevaluates the outcome after an average postoperative period of 7.5 years and describes the patient satisfaction and quality of life compared to the preoperative measurements, with conventional hearing aids, and the short term results after 6 and 12 months with the AMEI.

Chapter 2.2 focuses on the surgical complications in the implantation process of the VSB for patients with sensorineural hearing loss and external otitis by an experimental approach through the ear canal. This so called transcanal approach was developed to simplify the implantation procedure and avoid the need to drill the mastoid. The study compares the audiometric evaluations to the regular surgical approach and describes the encountered surgical complications.

Chapter 2.3 focuses on the clinical long term outcome in active middle ear implantation. The complete cohort of patients with an AMEI was evaluated for technical and medical complications and the implant survival was studied.

Part 3 focuses on a new technique in acoustic implants called direct acoustic cochlear stimulation.

In **chapter 3.1** the multicenter phase I study is described which evaluates the experimental Codacs investigational device (Codacs ID). This device is one of the first so-called direct acoustic cochlear implants or DACI and was applied in patients with severe sensorineural hearing loss due to otosclerosis. The chapter provides an extensive device description and pre- and post-operative hearing thresholds were evaluated in aided and unaided situations, as well as the surgical procedure, complications and patient satisfaction.

In **chapter 3.2** the results of a long term evaluation of the Codacs ID device are presented. This study has reevaluated the aided and unaided hearing thresholds, daily usage and patient satisfaction after an average postoperative period of 40 months to determine the stability of the outcome for the device.

Part 4 of this thesis serves a comparison between the various acoustic implants. We performed two studies to evaluate the audiological characteristics of the devices VSB, MET, various BCD and Codacs.

Chapter 4.1 presents the results of a study in which patients with sensorineural hearing loss after implantation with a VSB, MET and Codacs were tested by so-called input-output measurements. In this way, we could analyze an averaged maximum output per implant and determine the available dynamic range for the amplification of sound. Furthermore, the average gain per device was determined. We developed a method to present the gain independent from any air-bone gap that would possibly remain after implantation. The study provides insights for the clinical considerations when determining which device will provide the best benefit for the patients' current and future needs.

In **chapter 4.2** a second study is presented which compares different acoustic devices for mixed hearing loss. New input-output measurements were conducted on the patients with a Codacs, as well as determining gain and maximum output. In another group of patients, the VSB middle ear implant had been directly coupled to the round and oval window of the cochlea. These patients were also evaluated. All results were compared to the available capabilities of three types of bone conduction implants to present an overview of the audiological aspects for the clinical options in the treatment of mixed hearing loss.

Finally, in **part 5** a general discussion and conclusion on this thesis is presented in **chapter 5.1,** followed by a summary of this thesis in English and Dutch.

References

1. Guyton A, Hall J. The sense of hearing. Textbook of medical physiology2006. p. 651-62.
2. Puria S, Fay R, Popper A. The middle ear, science otosurgery and technology. New York: Springer; 2013.
3. Merchant S, Rosowski J. Acoustics and mechanics of the middle ear. In: Gulya A, editor. Glasscock-Shambaugh - Surgery of the Ear2010. p. 49-55.
4. http://www.who.int/pbd/deafness/hearing_impairment_grades/en/.
5. Yellon R, Denoyelle F. Evaluation and management of congenital aural atresia. In: Lesperance M, editor. Cummings Pediatric Otolaryngology2015. p. 196.
6. Carhart R, Hayes C. Clinical reliability of bone conduction audiometry. The Laryngoscope. 1949;59(10):1084-101.
7. Rotteveel LJ, Proops DW, Ramsden RT, Saeed SR, van Olphen AF, Mylanus EA. Cochlear implantation in 53 patients with otosclerosis: demographics, computed tomographic scanning, surgery, and complications. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 2004;25(6):943-52.
8. Cureoglu S, Baylan MY, Paparella MM. Cochlear otosclerosis. Current opinion in otolaryngology & head and neck surgery. 2010;18(5):357-62.
9. Langer T, am Zehnhoff-Dinnesen A, Radtke S, Meitert J, Zolk O. Understanding platinum-induced ototoxicity. Trends in pharmacological sciences. 2013;34(8):458-69.
10. Konings A, Van Laer L, Michel S, Pawelczyk M, Carlsson PI, Bondeson ML, et al. Variations in HSP70 genes associated with noise-induced hearing loss in two independent populations. European journal of human genetics : EJHG. 2009;17(3):329-35.
11. Henderson D, Bielefeld EC, Harris KC, Hu BH. The role of oxidative stress in noise-induced hearing loss. Ear and hearing. 2006;27(1):1-19.
12. Plomp R, Mimpen AM. Speech-reception threshold for sentences as a function of age and noise level. The Journal of the Acoustical Society of America. 1979;66(5):1333-42.
13. Tjellstrom A, Lindstrom J, Hallen O, Albrektsson T, Branemark PI. Osseointegrated titanium implants in the temporal bone. A clinical study on bone-anchored hearing aids. The American journal of otology. 1981;2(4):304-10.
14. Hakansson B, Tjellstrom A, Rosenhall U. Hearing thresholds with direct bone conduction versus conventional bone conduction. Scandinavian audiology. 1984;13(1):3-13.
15. Flynn MC, Sadeghi A, Halvarsson G. Baha solutions for patients with severe mixed hearing loss. Cochlear implants international. 2009;10 Suppl 1:43-7.
16. Bosman AJ, Snik AF, Mylanus EA, Cremers CW. Fitting range of the BAHA Cordelle. International journal of audiology. 2006;45(8):429-37.
17. Snik AF, Mylanus EA, Proops DW, Wolfaardt JF, Hodgetts WE, Somers T, et al. Consensus statements on the BAHA system: where do we stand at present? The Annals of otology, rhinology & laryngology Supplement. 2005;195:2-12.
18. Hol MK, Bosman AJ, Snik AF, Mylanus EA, Cremers CW. Bone-anchored hearing aids in unilateral inner ear deafness: an evaluation of audiometric and patient outcome measurements. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 2005;26(5):999-1006.
19. Siegert R. Partially implantable bone conduction hearing aids without a percutaneous abutment (Otomag): technique and preliminary clinical results. Advances in oto-rhino-laryngology. 2011;71:41-6.
20. Clamp PJ, Briggs RJ. The Cochlear Baha 4 Attract System - design concepts, surgical technique and early clinical results. Expert review of medical devices. 2015;12(3):223-30.
21. Mertens G, Desmet J, Snik AF, Van de Heyning P. An experimental objective method to determine maximum output and dynamic range of an active bone conduction implant: the Bonebridge. Otology & neurotology : official publication of the American Otological Society, American Neurotology Society [and] European Academy of Otology and Neurotology. 2014;35(7):1126-30.
22. Hassepass F, Bulla S, Aschendorff A, Maier W, Traser L, Steinmetz C, et al. The bonebridge as a transcutaneous bone conduction hearing system: preliminary surgical and audiological results in children and adolescents. European archives of oto-rhino-laryngology: official journal of the European Federation of Oto-Rhino-Laryngological Societies. 2015;272(9):2235-41.

23. Riss D, Arnoldner C, Baumgartner WD, Blineder M, Flak S, Bachner A, et al. Indication criteria and outcomes with the Bonebridge transcutaneous bone-conduction implant. The Laryngoscope. 2014;124(12):2802-6.
24. Zernotti ME, Sarasty AB. Active Bone Conduction Prosthesis: Bonebridge(TM). International archives of otorhinolaryngology. 2015;19(4):343-8.
25. Snik AF, Cremers CW. First audiometric results with the Vibrant soundbridge, a semi-implantable hearing device for sensorineural hearing loss. Audiology : official organ of the International Society of Audiology. 1999;38(6):335-8.
26. Snik AF, Mylanus EA, Cremers CW, Dillier N, Fisch U, Gnadeberg D, et al. Multicenter audiometric results with the Vibrant Soundbridge, a semi-implantable hearing device for sensorineural hearing impairment. Otolaryngologic clinics of North America. 2001;34(2):373-88.
27. Verhaegen VJ, Mylanus EA, Cremers CW, Snik AF. Audiological application criteria for implantable hearing aid devices: a clinical experience at the Nijmegen ORL clinic. The Laryngoscope. 2008;118(9):1645-9.
28. Colletti V, Soli SD, Carner M, Colletti L. Treatment of mixed hearing losses via implantation of a vibratory transducer on the round window. International journal of audiology. 2006;45(10):600-8.
29. Kiefer J, Arnold W, Staudenmaier R. Round window stimulation with an implantable hearing aid (Soundbridge) combined with autogenous reconstruction of the auricle - a new approach. ORL; journal for oto-rhino-laryngology and its related specialties. 2006;68(6):378-85.
30. Venail F, Lavieille JP, Meller R, Deveze A, Tardivet L, Magnan J. New perspectives for middle ear implants: first results in otosclerosis with mixed hearing loss. The Laryngoscope. 2007;117(3):552-5.
31. Marzo SJ, Sappington JM, Shohet JA. The Envoy Esteem implantable hearing system. Otolaryngologic clinics of North America. 2014;47(6):941-52.
32. Hausler R, Stieger C, Bernhard H, Kompis M. A novel implantable hearing system with direct acoustic cochlear stimulation. Audiology & neuro-otology. 2008;13(4):247-56.
33. Bond M, Wyatt K, Lloyd J, Welch K, Taylor R. Systematic review of the effectiveness and cost-effectiveness of weight management schemes for the under fives: a short report. Health technology assessment. 2009;13(61):1-75, iii.
34. Peterson NR, Pisoni DB, Miyamoto RT. Cochlear implants and spoken language processing abilities: review and assessment of the literature. Restorative neurology and neuroscience. 2010;28(2):237-50.
35. Rubinstein JT. Paediatric cochlear implantation: prosthetic hearing and language development. Lancet. 2002;360(9331):483-5.
36. Verhaegen VJO. Active implants in Otology - overlapping indications. Nijmegen2012.

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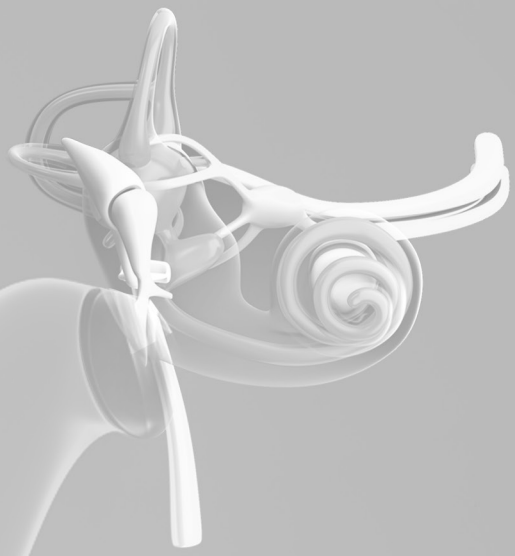
Active middle ear implants



2.1.

Vibrant Soundbridge surgery in patients with severe external otitis: complications of a transcanal approach

Published as

Vibrant Soundbridge surgery in patients with severe external otitis: complications of a transcanal approach

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Abstract

Objective: To evaluate the transcanal surgical implantation of the semi-implantable Vibrant Soundbridge device in patients with severe external otitis.

Patient and Methods: Long-term postoperative complications and postoperative hearing thresholds were evaluated in 13 adults with bilateral sensorineural hearing loss (average of between 40 dB and 55 dB HL) and therapy-resistant external otitis after implantation of the Vibrant Soundbridge by a transcanal surgical method.

Results: Postoperative audiometry findings were comparable with those reported after the transmastoidal posterior tympanotomy approach. In two patients the chorda tympani was intentionally sacrificed to maximize the size of the facial recess. Seven postoperative complications occurred in six patients (46%) during a mean follow-up period of 51 months: extrusion of the conducting wire into the ear canal (5), collapse of the cartilaginous part of the ear canal (1) and tympanic membrane perforation (1). In the revision surgeries that added additional layers of fascia for the patients with wire extrusions, repeated extrusion occurred in three of four cases.

Conclusions: The transcanal approach for implantation of the Vibrant Soundbridge has led to postoperative complications different from those reported after the transmastoidal posterior tympanotomy approach. External otitis should be considered as a contraindication for VSB surgery by the transcanal approach.

Introduction

In September 1996, a European multicenter trial was started to evaluate the safety and effectiveness of the semi-implantable Vibrant Soundbridge hearing device (Symphonix Devices Inc., San Jose, California, USA and, later, Med-El, Innsbruck, Austria) (1, 2). Since then, both EU and FDA approval have been granted for the device. In 2003, the application of the Vibrant Soundbridge for use as a part of regular medical health care was approved in the Netherlands for hearing-impaired subjects with an extra medical indication, such as therapy-resistant external otitis that occurs spontaneous or that is due to an occluded ear canal.

The European study group that initially guided the phase III Vibrant Soundbridge clinical trial opted to introduce the transducer of the Vibrant Soundbridge (called the floating mass transducer or FMT) into the middle ear using a transmastoidal posterior tympanotomy approach (1). A transcanal approach that included widening of the external bony ear canal was considered to be an alternative approach. For reasons of uniformity, however, only one surgical technique was permitted.

The results of the initial Nijmegen Vibrant Soundbridge series that formed part of this European trial have been published (2-4). One of the six patients that had the implantation in the primary trial had insufficient aeration of the middle ear postoperatively as a result of chronic underpressure, which led to an air-bone gap of approximately 20 dB (3). In two other patients who were re-implanted, full mastoid cavity obliteration by connective tissue ensued, probably as a reaction to the silicon wire in the mastoid. It was assumed that obliteration of the mastoid cavity might lead to permanent aeration problems in ears that were poorly ventilated before implantation. In view of this presumed disadvantage of the transmastoidal posterior tympanotomy approach, we decided, after completion of the European trial, to perform an additional study to implant the FMT by a transcanal approach. In addition to providing a possible solution to mastoid aeration problems, our study offers an opportunity to examine the advantages and disadvantages of the transcanal approach in patients with therapy-resistant external otitis. The purpose of this study is to report the long-term outcome of patients whose FMT was implanted by means of the transcanal approach from 2003 to 2005.

Patients and methods

In the initial consecutive series from September 1996 to September 2003, 22 patients underwent Vibrant Soundbridge implantation using the transmastoidal posterior tympanotomy approach. From September 2003 to October 2005, 13 consecutive patients were implanted using the transcanal approach. An overview of these patients and their outcomes is presented in **Table 1**.

Table 1 Overview of patients.

No	Sex	Side	Age (year)	Follow up (month)	PTA (dB) operated	PTA (dB) unoperated	Follow-up	Active use of implant
1	F	AD	78	49	37	33	Uncomplicated, primary coverage of the groove with fascia	Deceased
2	M	AS	62	57	45	48	Stricture of the EAC, meatoplasty. Reimplantation by mastoidectomy	Yes
3	M	AD	56	50	40	43	Sacrifice of chorda tympani, further uncomplicated FU	Non-user
4	F	AS	46	73	48	35	Uncomplicated	Yes
5	F	AS	79	55	42	45	Perforation of the TM and wire extrusion, repeated extrusion after revision surgery	Yes
6	M	AS	45	68	42	40	Wire extrusion, repeated extrusion after revision surgery	Yes
7	F	AD	44	50	35	45	Uncomplicated FU, explantation after otosclerosis	Explanted
8	F	AS	61	49	53	53	Wire extrusion in the EAC	Yes
9	M	AD	46	66	53	45	Uncomplicated	Yes
10	M	AD	69	30	45	47	Wire extrusion, repeated extrusion after revision surgery. Seborrhoeic eczema of the EAC. Explantation	Explanted
11	M	AD	64	40	57	60	Sacrifice of chorda tympani, further uncomplicated FU	Yes
12	F	AD	64	26	42	45	Uncomplicated FU, many complaints of pain	Yes
13	M	AS	57	51	47	37	Wire extrusion in the EAC	Yes
Mean			59	51	45	44		

Age is at the date of implantation. PTA = pure tone average,
EAC = external auditory canal, FU = follow up, TM = tympanic membrane.

A recent inquiry showed that nine of the thirteen patients implanted by the transcanal approach are currently using their VSB on a daily basis and are benefiting from it. Two of the four non-users were explanted as is stated in the results. One patient is a non-user as result of device-failure and one patient has deceased. The actual use of the implant is displayed in **Table 1**.

Preoperative sensorineural hearing loss of the patients (seven men and six women) at 0.5, 1 and 2 kHz varied between 38 dB HL and 57 dB HL in the operated ear (with a mean of 45 dB HL) and between 33 dB HL and 60 dB HL in the non-implanted ear (with a mean of 44 dB HL). The age of the patients at implantation ranged from 44 to 79 years with a mean of 59 years. All of the patients were suffering from therapy-resistant external otitis.

Outcomes of this study include postoperative hearing thresholds and follow-up period complications. Changes in hearing thresholds were studied in both the implanted ear and, for reference purposes, the non-implanted ear. Pure-tone and bone conduction thresholds were measured using standard audiometric equipment.

Surgical technique

In the transcanal approach applied in our study, the retro-auricular skin and periosteum were incised, followed by the careful lateral to medial separation of the skin of the EAC (external auditory canal) from the posterior wall and by the widening of the posterior bony wall up to the level of the annulus. A groove with a width of approximately 1 mm was drilled postero-inferior laterally to postero-inferior medially to accommodate the silicon-coated conducting wire. The titanium clip of the FMT was manually bent 45 degrees to enable placement over the lateral surface of the distal part of the long process of the incus, as described by Truy et al. in 2006 (5). The postero-inferior location of the groove combined with widening of the bony ear canal provided sufficient space to manipulate the FMT in the middle ear and attach it to the incus as prescribed, parallel to the stapes crura. The bony groove was covered and filled by bone-pâté and fibrin glue until the conducting wire could no longer be seen. However, the length of the silicon-coated wire was too long for direct placement. To solve this problem, an extra loop in the wire was placed over the lateral surface of the mastoid cortex. A bony well was drilled in the mastoid cortex postero-superior to the external bony ear canal to facilitate the receiver of the device. Fixation of the implant was obtained by suturing in the conventional manner.

In case of revision surgery, the transcanal operating technique was modified with either an emphasis on achieving a more complete seal with the fascia of the temporal muscle or on the drilling of an even deeper bony groove, or both.

Results

Postoperative hearing thresholds

The mean preoperative and postoperative hearing thresholds of the patients' implanted and non-implanted ears were evaluated. The threshold values were obtained relatively soon after implantation (mean 2.7 months, range 0.9 to 7.5 months). **Figure 1** shows the mean normalised changes as a function of frequency. The different values were normalised using the measurements from the non-implanted ear. For reference purposes, we also present data from the initial European trial, which used the posterior tympanotomy approach (1), and from the results of Schmuziger et al. (6). The presented data were calculated from the original figures of pre- and postoperative thresholds in the implanted and non-implanted ears. Standard deviations of our data (not indicated) varied between 8.5 and 17.8 dB.

The postoperative normalised hearing thresholds were slightly deteriorated with a mean decrease at 0.5, 1 and 2 kHz of 5.5 dB (standard deviation ± 7.6 dB). Four of the thirteen patients had a clinical significant decrease of hearing thresholds at 0.5, 1 and 2 kHz with a range from 11.7 to 18.3 dB.

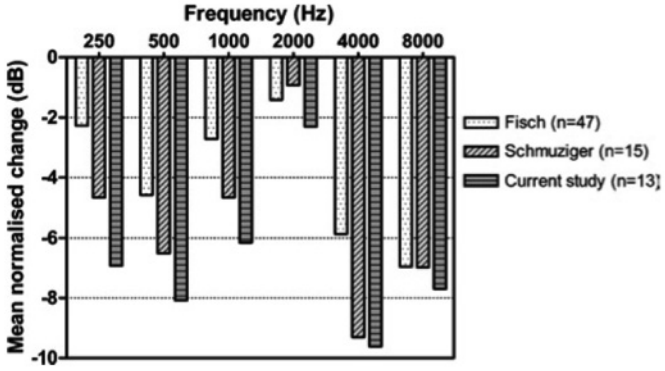

Figure 1 Mean normalized change in hearing thresholds (pre-operative minus postoperative thresholds) as a function of frequency. To correct for any changes related to measurement conditions, the change in hearing threshold also was determined in the nonimplanted ear. Subtraction of that change was used to normalize the change in hearing threshold in the implanted ear. Present data are compared with those reported by Fisch et al. (1) and Schmuziger et al. (6).

Complications of surgery

The mean duration of the follow-up period ranged from 26 to 73 months with a mean of 51 months. An overview of the complications is presented in **Table 2.** No injury of the facial nerve was observed, although in two patients (15%), the chorda tympani was intentionally sacrificed during surgery to maximize the size of the facial recess. In one patient, lacerations of the skin of the posterior bony canal occurred where the posterior bony canal obstructed the view of the tympanic ridge. The surgeon (C.C.) observed that the skin of the EAC was thin and much more vulnerable to damage in our group of patients, presumably as a result of skin changes caused by the persistent external otitis. Immediate postoperative healing of the skin of the external ear canal was nevertheless uneventful in all the patients.

Table 2 Overview of reported complications.

Complication	No.	(%)
Tympanic membrane perforation	1	8
EAC collapse	1	8
Wire extrusion	5	38
Chorda tympani sacrificed	2	15

Percentage of the complete study group. EAC = external auditory canal.

In one patient, the external cartilaginous meatus became narrowed 8 weeks postoperatively as a result of the retro-auricular skin and periosteal incisions. In this case, the pre-existent external otitis was therefore aggravated by the obstruction of the ear canal. The collapse of the ear canal occurred three months after surgery, and additional meatoplasty was performed with success (follow-up since meatoplasty: 36 months).
In five patients (38%), the silicon-coated wire extruded through the skin of the EAC. The wire extrusion was noticed at a mean postoperative period of 25 months (range 4 to 41 months). Revision surgery was performed on four of the patients. Although the revision surgery was uneventful, this procedure represented a risk of damage to the conducting wire because of its protrusion from the posterior edge of the external bony ear canal. Despite coverage of the silicon-coated wire with fascia, repeated extrusion through the skin of the EAC occurred in three of the four patients who underwent revision surgery. One of these three patients suffered from therapy-resistant seborrhoeic eczema of the external ear canal, and therefore explantation of the Vibrant Soundbridge became ultimately inevitable. Despite the extrusion of the wire in the EAC, the patients are still actively using their VSB. No clinical signs of infection of the conducting wire have been noticed during regular visits.

Perforation of the tympanic membrane occurred in the eldest patient in the study group four months after implantation. Gradual widening of the perforation produced an air-bone gap that ultimately became 30 dB (average at 0.5, 1, 2 kHz) in contrast to the absence of decrease in hearing thresholds directly postoperative. Bone-conduction thresholds were not affected. As time progressed, deterioration occurred in the aided sound field thresholds and the aided speech score. The patient's monosyllable phoneme score at 65 dB SPL presentation level changed from 85% to 68% to 32% at present. Because of an increase of the perforation and extrusion of the wire in the EAC, a myringoplasty with cartilage tissue was performed in combination with reconstruction of the skin of the EAC four years after implantation. Unfortunately, extrusion of the wire reoccurred post-operatively within five months.

In another patient, an air-bone gap was detected 25 months after implantation, which gradually increased to 25 dB (average at 0.5, 1 and 2 kHz). The direct postoperative hearing thresholds had been unchanged. Repeated otoscopy showed a narrow ear canal that was repeatedly obstructed with earwax. However, removal of the wax did not lead to the expected improvement in air conduction thresholds. Therefore, the air-bone gap remained unexplained. In addition, there was slight deterioration (10 dB) in the bone conduction thresholds in the implanted ear. No cause was found for this hearing loss, but it has been noted in similar studies. These changes in hearing did not affect the aided hearing thresholds or the aided speech recognition score. Because of the lack of change in hearing capacity, revision surgery was not considered.

Discussion

In the primary European clinical trial, placement of the FMT by means of the transmastoidal posterior tympanotomy approach led to chronic underpressure in the middle ear in certain patients who suffered preoperatively from inadequate middle ear aeration (3). To address this problem, a clinical study was initiated to evaluate implantation using a transcanal approach. In addition to the problems of aeration of the middle ear, the mastoidectomy and especially the posterior tympanotomy technique bring an additional risk of damage to the facial nerve and the chorda tympani. Although no facial palsies have been reported after VSB surgery in the literature, this phenomenon has been described in cochlear implantation, varying from 0.14% (7) to 0.7% (8) and, more recently, 2.3% (9). Damage to the chorda tympani has been described in VSB surgery varying from 2 to 15% (1, 6, 10).

To avoid the complications of the transmastoidal posterior tympanotomy approach, several transcanal methods have been proposed in Vibrant Soundbridge and cochlear implant surgery. Truy et al. (5) have described two different methods to allow the FMT to pass into the middle ear: the EAC-cutting approach and the EAC tunnel approach. Both

methods consist of a small mastoidectomy in combination with separation of the skin of the posterior wall of the EAC, a tympanomeatal flap and atticotomy. Next, a bony groove is drilled in the inferior part of the EAC. In the EAC tunnel approach, a tunnel is drilled from the mastoid cavity to the EAC above the emergence of the chorda tympani to facilitate the passing of the FMT. The article describes of two clinical cases in which the VSB was implanted by the EAC-cutting approach and the conducting wire covered by bone pâté and fibrin glue. Although the duration of follow-up was rather short, no postoperative complications were observed. Truy et al. concluded that their transcanal approach simplified the procedure and shortened the duration of surgery.

A more recent publication by Bruschini et al. (11) presented the clinical results of a transcanal implantation method. The applied surgical technique consisted of a small cortical mastoidectomy, separation of the skin of the EAC from the posterior wall and a minimal superior atticotomy.

The small superficial mastoidectomy was drilled in order to facilitate the extra length of conducting wire of the VSB. The groove that was drilled measured 1.5 mm in diameter and extended from the annulus to the outer border of the EAC. The groove and wire were covered by bone pate and tissucol. During a mean follow-up period of 21 months, no postoperative complications were reported, and no decrease in postoperative hearing thresholds was observed.

In cochlear implantation surgery a suprameatal approach (SMA) was developed in 2000 by Kronenberg (12). In this method, a tunnel is drilled supraposteriorly to the suprameatal spine towards the EAC in combination with a subperiostal tunnel to facilitate the conducting wire. The SMA was recently compared with the classic approach by Postelmans et al. (13, 14). No facial nerve paralysis was reported in the SMA approach, whereas the classic approach led to two facial nerve injuries during the posterior tympanotomy. Another transcanal approach in cochlear implantation, called the transmeatal approach (TMA), has recently been described by Taibah (15). In this open-tunnel approach, the drilling of a groove that is comparable with that of our approach is combined with the drilling of a parallel tunnel towards the middle ear. In Taibah's series of 131 patients, no extrusion of the wire was reported during a follow-up period of 2 to 46 months. In five of the cases (3.8%), a tympanic membrane perforation was reported. The method of drilling a bony groove with an overhanging roof in CI implantation has also been described by Slavutsky (16). After 3 to 18 months of follow-up, no wire extrusions were reported.

In this article, we present the results of VSB surgery by a transcanal approach in 13 patients suffering from therapy-resistant external otitis. During the two years of this trial, the actual implantation of the VSB by the transcanal approach was successful in all operated patients. In two patients, the chorda tympani was sacrificed to maximize the size of the facial recess. No other perioperative complications were reported. The mean normalised postoperative air-conduction thresholds deteriorated slightly (5.5 dB). This deterioration was comparable with the presented outcome after implantation by transmastoidal posterior tympanotomy

approach (1, 6). **Figure 1** suggests minor differences among the data of the three compared studies. In a recent publication by Bruschini et al. (11) in which a transcanal approach was evaluated, no differences in pre- and postoperative thresholds were reported. Nevertheless, in our study, 4 of the 13 patients had a larger decrease at 0.5, 1 and 2 kHz with a range from 12 to 18 dB, namely patients 3, 7, 11 and 12 (see **Table 1**). No correlation between the deterioration in hearing thresholds and the presented complications was found. However, the mean hearing threshold deterioration of 5.5 dB at 0.5, 1 and 2 kHz in the entire group of patients suggests that the new approach does not involve significantly more risk to postoperative hearing thresholds than the traditional approach.

Apart from two per operative sacrificed chorda tympani, seven postoperative complications were observed in this study in six patients (46%) during a mean follow-up period of 51 months. As shown in **Table 2**, these complications consisted of collapse of the EAC (1), the extrusion of the conducting wire (5) and perforation of the tympanic membrane (1). No further postoperative complications occurred during the follow-up period. No post-operative complications were observed for seven patients (54%) in this study.

In our opinion the high rate of postoperative complications in the transcanal approach can be traced to the presence of therapy-resistant external otitis. All of the patients in our study group were suffering from this condition because the combination of sensorineural hearing loss and therapy-resistant external otitis is the primary indication for VSB implantation in our clinic. Even though no results of studies of VSB surgery on a large group have been published, virtually no conducting wire extrusions have been recorded in large studies on the transcanal or transmeatal approaches in cochlear implant surgery (15, 16). In the publications concerning VSB implantation by Truy et al. (5) (n=2) and Bruschini (11) (n=12), no surgical complications were reported. No patients in either of these studies concerning VSB or cochlear implantation were suffering from external otitis. In treatment of patients with pre-existing external otitis, we considered the skin on the medial wall of the posterior bony ear canal to be fragile. Thus, modification of the surgical method to prevent the complication of conducting wire extrusion is required. The tunnelling technique proposed by Taibah (15) and Slavutsky (16) might be applied. The posterior and inferior bony ear canal provides sufficient space to do so without interfering with the diameter of the ear canal. However, in our series, a deepening of the bony groove and better coverage of the wire did not guarantee that repeated extrusion of the wire would be prevented. Because revision surgery was unsuccessful in four of five patients, we conclude that the transcanal approach for VSB implantation is unfavourable in patients suffering from therapy-resistant external otitis.

Conclusion

We consider it of great importance to define the optimal clinical conditions and the indications for the application of this innovative device. In the interests of this definition, we have introduced the extra inclusion criterion of therapy-resistant external otitis in our clinic. For treatment of this group of hearing-impaired patients, it is essential to have an alternative for the conventional hearing aid. Although the results of transcanal implantation of the Vibrant Soundbridge and cochlear implantation seem promising in general, the described approach in this article showed a high number of postoperative complications. This indicates that the condition of the skin of the external auditory canal in otitis externa is not suitable for covering of the conducting wire of the FMT. Despite the fact that the implanted patients do benefit from their VSB, we have not applied this method of implantation in our clinic since the end of the study period in 2005. The authors suggest that therapy-resistant external otitis should be considered as a contraindication for a transcanal approach in the implantation of the Vibrant Soundbridge.

References

1. Fisch U, Cremers CW, Lenarz T, et al. Clinical experience with the Vibrant Soundbridge implant device. *Otol Neurotol.* 2001; 22: 962-972.
2. Snik AF, Mylanus EA, Cremers CW, et al. Multicenter audiometric results with the Vibrant Soundbridge, a semi-implantable hearing device for sensorineural hearing impairment. *Otolaryngol Clin North Am.* 2001; 34: 373-388.
3. Snik AFM, Cremers CWR. The effect of the "floating mass transducer" in the middle ear on hearing sensitivity. *Am J Otol.* 2000; 21: 42-48.
4. Snik AF, Cremers CW. Vibrant semi-implantable hearing device with digital sound processing: effective gain and speech perception. *Arch Otolaryngol Head Neck Surg.* 2001; 127: 1433-1437.
5. Truy E, Eshraghi AA, Balkany TJ, Telishi FF, Van De Water TR, Lavieille JP. Vibrant soundbridge surgery: evaluation of transcanal surgical approaches. *Otol Neurotol.* 2006; 27: 887-895.
6. Schmuziger N, Schimmann F, aWengen D, Patscheke J, Probst R. Long-term assessment after implantation of the Vibrant Soundbridge device. *Otol Neurotol.* 2006; 27: 183-188.
7. Kim CS, Oh SH, Chang SO, Kim HM, Hur DG. Management of complications in cochlear implantation. *Acta Otolaryngol.* 2008; 128: 408-414.
8. Fayad JN, Wanna GB, Micheletto JN, Parisier SC. Facial nerve paralysis following cochlear implant surgery. *Laryngoscope.* 2003; 113: 1344-1346.
9. Loundon N, Blanchard M, Roger G, Denoyelle F, Garabedian EN. Medical and surgical complications in pediatric cochlear implantation. *Arch Otolaryngol Head Neck Surg.* 136: 12-15.
10. Sterkers O, Boucarra D, Labassi S, et al. A middle ear implant, the Symphonix Vibrant Soundbridge: retrospective study of the first 125 patients implanted in France. *Otol Neurotol.* 2003; 24: 427-436.
11. Bruschini L, Forli F, Giannarelli M, Bruschini P, Berrettini S. Exclusive Transcanal Surgical Approach for Vibrant Soundbridge Implantation: Surgical and Functional Results. *Otol Neurotol.* 2009;
12. Kronenberg J, Baumgartner W, Migirov L, Dagan T, Hildesheimer M. The suprameatal approach: an alternative surgical approach to cochlear implantation. *Otol Neurotol.* 2004; 25: 41-44; discussion 44-45.
13. Postelmans JT, Grolman W, Tange RA, Stokroos RJ. Comparison of two approaches to the surgical management of cochlear implantation. *Laryngoscope.* 2009; 119: 1571-1578.
14. Postelmans JT, Tange RA, Stokroos RJ, Grolman W. The suprameatal approach: a safe alternative surgical technique for cochlear implantation. *Otol Neurotol.* 2010; 31: 196-203.
15. Taibah K. The transmeatal approach: a new technique in cochlear and middle ear implants. *Cochlear Implants Int.* 2009; 10: 218-228.
16. Slavutsky V, Nicenboim L. Preliminary results in cochlear implant surgery without antromastoidectomy and with atraumatic electrode insertion: the endomeatal approach. *Eur Arch Otorhinolaryngol.* 2009; 266: 481-488.

2.2.

Active middle ear implantation for patients with sensorineural hearing loss and external otitis: long-term outcome in patient satisfaction

Published as

Active middle ear implantation for patients with sensorineural hearing loss and external otitis: long-term outcome in patient satisfaction

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Abstract

Objective: To study long-term subjective benefit of patients with sensorineural hearing loss and chronic external otitis who use active middle ear implants.
Design: Single-subject repeated measures in a pre- and post-intervention design with multiple post intervention measurements (questionnaires).

Patients and methods: Moderate to severe sensorineural hearing loss (n=56) with severe chronic external otitis who use the Vibrant Soundbridge (VSB) or Otologics MET middle ear implant systems. The main outcome measures were: changes in hearing disability and handicap as evaluated using the Abbreviated Profile of Hearing Aid Benefit (APHAB), the Nijmegen Cochlear Implant Questionnaire (NCIQ) and the Glasgow Benefit Inventory (GBI).

Results: Data of 33 patients (mean post-operative duration of 7.5 years) were available. No difference in subjective results was found between the VSB and Otologics MET patient groups. Total percentage of non-use was 13%. Long-term APHAB results show a significant decrease in disability for 43% of the patients compared to 54% at 1-year postoperative. NCIQ results show a significant benefit for all sub domains with a negative trend over time. The GBI results show a significant long-term increase in quality of life with positive scores for 82% of the assessed patients.

Conclusions: Long-term post-operative patient satisfaction and quality of life results show a significant difference compared to pre-operative measurements, with conventional hearing aids. A negative trend over time is found on all questionnaires, which might reflect patient aging (increase of hearing loss) or habituation to a situation with fewer concerns regarding a patient's external otitis.

Introduction

Some patients with hearing loss decline to use acoustic hearing aids because of cosmetic reasons or complaints about poor sound quality (1-3). For other patients, application of acoustic devices might be troublesome because of therapy-resistant chronic external otitis. Although ventilated or specially coated ear moulds might be beneficial for the latter patient group, many patients cease to use the hearing device due to pain or itching (4). For such patients, an active middle ear implant (AMEI) has been advocated.

An AMEI comprises an externally worn audio processor and an implanted signal processor and output transducer. The transducer is a specially developed implantable magnetic actuator that is in contact with the middle ear ossicles. The audio processor is magnetically connected to the implant and communicates with it through the skin by means of radiofrequency signals. AMEI are generally believed to be more attractive from a cosmetic point of view as the audioprocessor is easily hidden by hair. Furthermore, better sound quality has been claimed over conventional hearing aids (1-3) and, as the device bypasses the external ear canal, it might be the solution for patients with chronic external otitis (5).

In 1996, we started implanting the semi-implantable Otologics MET (MET) device (Otologics LLC, Boulder, CO, USA) and the Vibrant Soundbridge (VSB) middle ear implant (Med-El, Innsbruck, Austria) in patients with sensorineural hearing loss who also had severe, therapy-resistant external otitis, thereby avoiding the use of ear moulds.

To evaluate the subjective benefit of AMEI we sent questionnaires to all patients before implantation and at 6 and 12 months after middle ear implantation. The short-term results of this study have been published (5). In short, from a disability point of view, middle ear implants were not more positively appreciated than conventional devices. With regards to (disease-specific) quality of life, patients experienced a significant improvement in quality of life which the authors ascribed to the use of this ear mould-free hearing device that could be worn all day without pain or itching (6).

To assess patient long-term subjective benefit, we recently performed an additional cross-sectional evaluation. All patients with at least two years of postoperative follow-up were selected. This group comprised 56 middle ear implant users. Since 2000, we used a standardized protocol to assess subjective benefit (5). In short, to assess the (remaining) disability, the Abbreviated Profile of Hearing Aid Benefit (APHAB) is administered (7). This questionnaire quantifies hearing difficulties in various everyday listening situations. In addition, we used the disease-specific quality of life questionnaires, namely the Nijmegen Cochlear Implant Questionnaire (NCIQ) and Glasgow Benefit Inventory (GBI). We evaluated daily use by a specific questionnaire, which is addressed as 'daily use questionnaire'. To assess generic quality of life, we used the SF-36 questionnaire (6). However, as it became clear that this questionnaire is rather insensitive to problems with communication (6,8), we discontinued its use in 2006.

Long-term studies of subjective benefit in middle ear implant users are scarce; we identified only three studies in our review of the literature (9-11). These studies mainly comprised patients who were implanted with an active middle ear implant because they disliked their conventional hearing aid(s).
Our present study might present a different outcome as our patients were not dissatisfied with their previous conventional devices, rather, the patients couldn't wear these devices because of complaints of external otitis. In a recent systematic review on AMEI, Tysome et al. (12) conclude that the overall quality of the studies concerning AMEI is moderate to poor because of a lack of comparisons with conventional hearing aids. Unlike the included long-term implant studies in their systematic review, our research design is a prospective study with validated outcome measures.
In summary, the aim of the study was to evaluate long-term gain in subjective benefit of AMEI implantation in a group of hearing impaired subjects with chronic external otitis.

Materials and methods

Study design

To assess the patient's subjective benefit over time, longitudinal data were collected. We used the same prospective, single-subject repeated-measures protocol as in the previous study (5). After being selected for middle ear implantation, patients filled in the APHAB and NCIQ questionnaires. The same questionnaires were also filled in 6 and 12 months after the middle ear implant audioprocessor had been fitted. These questionnaires were recently repeated by patients with a variable follow-up time of at least 24 months (referred to as the long term evaluation moment). The retrospective GBI questionnaire was completed at the 12-month follow-up and in the recent long term evaluation assessment. All the questionnaires were sent to the patients by mail. Concerning the recent survey, patients who had not returned the questionnaire were telephoned to enquire about their daily usage of the AMEI. With respect to audiology, follow-up comprised audiometric measurements and regular refitting during the first year of device use and at subsequent 5-year intervals in cases of stable results.

Study population

The study population comprised 56 middle ear implant users who had been implanted between February 1997 and May 2010 at our department with a semi-implantable device. Because of the Dutch inclusion criteria for reimbursement of the AMEI, only patients with severe therapy resistant external otitis are eligible to be implanted. Fifteen patients were excluded from the long-term evaluation. Patients with known complications did not receive questionnaires and patients who did not meet the postoperative duration of two years. The exclusion criteria are presented in **table 1**.

Table 1 Overview of the total study population of the long term evaluation.

Middle ear implant patients (n=56)			
Excluded		**Included**	
1. Deceased	4	Assessment completed	33
2. Complications	4	Non use (3)	
Incus necrosis (3)			
TM perforation (1)		Assessment not completed	8
3. Postoperative duration <2y	7	Non use (2)	
		Deceased (1)	
		Not interested (4)	
		No contact (1)	
	15		**41**

TM = tympanic membrane.

Altogether, 41 patients were included in the recent survey: the MET device was used by 8 patients (19%) and the VSB was used unilateral by 29 patients (71%) and bilateral by 4 patients (10%). All patients had symmetrical sensorineural hearing loss within 10 dB (at 0.5, 1 and 2 kHz) with a mean hearing loss (at 0.5, 1 and 2 kHz) from 32 dB HL to 77 dB HL. All patients used conventional hearing aids before implantation; however, this was mostly on an irregular basis owing to external otitis. Baseline measurements were gathered pre-implantation and, as such, measurements reflect the aided condition with conventional hearing aids. The mean age of the study population was 60 years (range 28 to 76 years) and 24 patients (58.5%) were female. The number of questionnaires available for analysis at baseline, 6-month and 12-month evaluation moments were 42, 28 and 26, respectively.

Questionnaires

APHAB questionnaire

To assess the (remaining) disability, the APHAB was used. This questionnaire quantifies hearing difficulties in various everyday listening situations (7) and contains four subscales: ease of communication (EC), listening in reverberate situations (RV), listening in background noise (BN) and aversiveness to sounds (AV). This fourth subscale measures negative reactions to environmental sounds. The results of each subscale are presented as percentages of difficulty with listening in that specific situation on a score from 0 to 100%. The APHAB questionnaire has been used in several studies on active middle ear implantation (1,2) as well as studies on conventional hearing devices (7).

Nijmegen Cochlear Implant Questionnaire

The NCIQ assesses disease-related quality of life. It was initially developed to evaluate how cochlear implantation affects health status (13,14). The NCIQ comprises three sub domains: the general physical domain focuses on hearing and speech problems, the psychological domain assesses mainly self-esteem and the social domain addresses activity limitations and social interactions. Scores can range from 0 (extremely poor) to 100 (excellent). The NCIQ is reliable, robust and sensitive to clinical changes (13,15,16). Nowadays, the NCIQ is widely used within the field of cochlear implantation (17) and is also used to evaluate patients with conventional hearing devices (18) and patients with bone-anchored hearing aids (16). We have adapted the NCIQ to the use in the evaluation of middle ear implantation by excluding six of the questions that concern complete deafness or the use of sign language, namely, questions 8, 15, 33, 39, 56 and 57 (13).

GBI questionnaire

The GBI is a quality of life questionnaire developed to retrospectively assess the outcome of otorhinolaryngology interventions (19). Change in patient health status after the intervention is evaluated with respect to psychological and social functioning and physical well-being (19). The benefit score can range from –100 (extreme deterioration) to +100 (excellent improvement). Since the GBI is a retrospective questionnaire, recall bias might play a part in long-term evaluations. The GBI has been used to evaluate the benefit of cochlear implants, middle ear implants and bone-anchored hearing aids, as reviewed by Snik et al. (17).

The 'daily use' questionnaire

This questionnaire is an adapted version of the questionnaire used by de Wolf et al (16) to evaluate use of the bone-anchored hearing aid. This questionnaire focuses on the per day duration of device use, the ease of controlling the device and the general appreciation of the device and the produced sounds. This questionnaire was only used in the recent long-term evaluation

Statistics

Differences between mean baseline and mean aided scores were analysed using ANOVAs and Student's t-tests. For patients with a complete data set, paired t-tests were performed. All statistical tests were performed with SPSS (version 16). Significance level was set at $p=0.05$. Normal distribution was tested using the Shapiro-Wilk test of normality.

Individual differences in APHAB scores over time (baseline minus aided data; short-term compared to long-term data) were checked for significance using the guidelines formulated by Cox and Alexander (7). Alexander and Cox reported the 95% critical difference on the APHAB subscales EC, RV and BN to be 22%; any change exceeding 22% is therefore considered significant (20). In the joint evaluation of the subscales EC, RV and BN, they considered a difference of 10% or more for each of the three subscales as significant ($p < 0.02$).

Results

Thirty-three patients (80%) returned the recent questionnaires. **Table 1** lists the reasons why the remaining eight patients (20%) did not return the questionnaires. Three of the patients who returned the questionnaires had recently ceased using their devices but answered the questionnaire according to their situation before they stopped using their device. The mean postoperative duration of device use was 7.5 years (SD ± 3.4 years). **Table 2** lists an overview of the patient characteristics and the results per sub domain of the APHAB and NCIQ questionnaire per evaluation. In **Table 3** the results of the so-called "daily use questionnaire" are listed. A one-way ANOVA (data not presented) indicated no significant differences ($p < 0.05$) for the total scores of all outcome parameters between the Otologics MET and VSB devices (either unilateral or bilateral).

Table 2 Overview of available data, patient characteristics of the returned lists and questionnaire scores per evaluation moment.

Evaluation moment	Baseline	6-months	12-months	Long term
Included	56	52	52	41
Excluded	0	4[A]	4[A]	15[B]
Returned list	42 (75%)	28 (54%)	26 (50%)	33 (80%)
Male : Female	15 : 27	11 : 17	11 : 15	11 : 22
Mean age (range)	56 (18-80)	56 (19-79)	56 (19-79)	60 (28-76)
MET : VSB uni : VSB bil	8 : 30 : 4	7 : 17 : 4	5 : 17 : 4	5 : 25 : 3
NCIQ (mean, ± SD)	n=17	n=22	n=23	n=31
Physical	49.9 ± 10.5	68.3 ± 13.9[E]	62.3 ± 15.6[D]	60.4 ± 14.2[D]
Physiological	52.5 ± 22.3	70.6 ± 15.6[D]	66.7 ± 19.3[C]	58.9 ± 17.3
Social	46.6 ± 23.5	66.9 ± 13.0[D]	62.0 ± 17.8[C]	64.1 ± 17.7[D]
Total	49.7 ± 16.4	68.6 ± 11.6[E]	63.7 ± 15.5[D]	61.1 ± 13.7[C]
APHAB (mean, ± SD)	n=42	n=28	n=24	n=32
EC	53.2 ± 20.9	26.9 ± 18.9[E]	33.3 ± 22.8[D]	42.4 ± 21.3[C]
BN	70.7 ± 17.3	54.9 ± 17.2[E]	58.9 ± 17.2[D]	65.3 ± 19.6
RV	66.0 ± 15.9	49.0 ± 12.5[E]	47.7 ± 17.6[E]	59.4 ± 16.9
AV	36.7 ± 26.6	42.9 ± 26.2	47.0 ± 29.0	41.9 ± 27.7
Global	63.3 ± 14.8	43.6 ± 12.6[E]	46.6 ± 16.2[E]	55.6 ± 16.6[C]

MET: Otologics MET; VSB uni: Vibrant Soundbridge unilateral; VSB bil: Vibrant Soundbridge bilateral.
[A] Patients with known complications were excluded.
[B] See table 1 for exclusion criteria.
[C] Unpaired t-test versus baseline: [C] $p < 0.05$; [D] $p < 0.01$; [E] $p < 0.001$

Table 3 Results of *The "daily use" questionnaire*

Question	Response	n (%)
Are you still using your MEI?	Yes	30 (91)
	No	3 (9)
How many hours per day have you been using the MEI on a regular basis?	Not worn	3 (9)
	1-4 hours a day	2 (6)
	4-8 hours a day	5 (16)
	> 8 hours a day	22 (69)
In general, is your MEI worth the effort?	No	1 (3)
	A little	4 (13)
	Moderately	4 (13)
	Much	8 (26)
	Very Much	14 (45)
Do you have difficulties placing your MEI?	Yes	1 (3)
	No	29 (97)
Can you handle the controls of your MEI well?	Yes	27 (93)
	No	2 (7)
How do you judge the sound of the MEI?	Very Good	3 (9)
	Good	18 (56)
	Reasonable	7 (22)
	Bad	4 (13)
	Very bad	0 (-)
Would you recommend a MEI to a friend with the same hearing loss as yours?	Yes	27 (84)
	No	5 (16)
How much would you be willing to pay for you MEI yourself?	Nothing	3 (11)
	€ 500	5 (19)
	€ 1000	11 (41)
	€ 2500	3 (11)
	€ 5000	5 (18)
Would you, based on your experience with your MEI, choose your MEI again?	Yes	25 (83)
	No	5 (17)

APHAB

Figure 1 displays the mean data of the APHAB sub-domains and total score (mean score for EC, BN and RV) as a function of follow-up. Statistical analysis of the post-intervention data compared to baseline data is presented in the figure and in **table 2**. Significant changes were found in the APHAB total domain ($p< 0.05$) for all evaluation moments

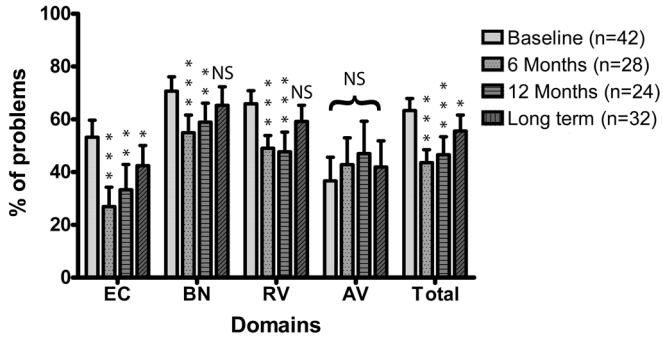

Figure 1 Mean APHAB scores per evaluation moment. A lower value indicates a better result. AV indicates aversiveness; BN background noise; EC ease of communication; RV reverberation. Note: results of unpaired t-test versus baseline. *p < 0.05, ** p < 0.01, *** p < 0.001, NS = not statistically significant.

although the difference with the baseline and the last evaluation moment is small. For the AV subscale, the increase in problems found at all evaluation moments was not significant. Over time, the benefit in APHAB scores seems to drops. The long-term evaluation shows a significant difference with the baseline data for the EC domain and the total score.
Next, an analysis was performed with a subgroup of the patients, viz. those with paired data. **Table 4** lists the outcomes. Compared to baseline the number of patients with significant improvement was 19 (68%), 13 (54%) and 10 (43%) at the 6-month, 12-month and long-term evaluation moments, respectively.

NCIQ

Figure 2 displays the NCIQ questionnaire results per domain by evaluation moment. The 6-month and 12-month evaluations show a significant difference with the baseline data for all sub domains, whereas the long-term evaluation is non-significant in the physiological subdomain. In **table 2**, the results are listed per sub domain. A significant difference in the long-term results is found for the physical ($p < 0.01$), social ($p < 0.01$) and total ($p < 0.05$) scores when analyzed with unpaired t-tests. When the results were analyzed with paired t-tests, the long-term benefit is significant for all general domains, including the total result ($p < 0.01$, n=9). At the 6-month evaluation moment, the difference with the baseline is significant for all subdomains (n=8). This is in contrast to the 12-month evaluation moment in which only the social subdomain difference is significant (n=8). Unfortunately, only few questionnaires were available for the paired analysis. The results are listed in **Table 5**.

Table 4 Outcome of the APHAB results per subscale displayed per evaluation moment.

APHAB Subscale	# (%) significant ***BENEFIT*** versus baseline		
	6 months (n=28)	**12 months (n=24)**	**Long term (n=23)**
Ease of Communication	16 (57%)	11 (46%)	7 (30%)
Reverberation	11 (39%)	9 (38%)	3 (13%)
Background Noise	9 (32%)	7 (29%)	5 (22%)
Aversiveness	0 (-)	0 (-)	2 (9%)
Global APHAB (EC, RV, BN)	16 (57%)	12 (50%)	9 (39%)
Significant improvement*	19 (68%)	13 (54%)	10 (43%)

APHAB Subscale	# (%) significant ***DETERIORATION*** versus baseline		
	6 months (n=28)	**12 months (n=24)**	**Long term (n=23)**
Ease of Communication	0 (-)	1 (4%)	2 (9%)
Reverberation	1 (4%)	1 (4%)	0 (-)
Background Noise	0 (-)	0 (-)	2 (9%)
Aversiveness	0 (-)	0 (-)	6 (26%)
Global APHAB (EC, RV, BN)	1 (4%)	0 (-)	1 (4%)
Significant improvement*	-	-	-

* significant improvement if more than 22% benefit in 1 subscale or more than 10% benefit in EC, RV and BN subscales. (Cox et al. 1997)

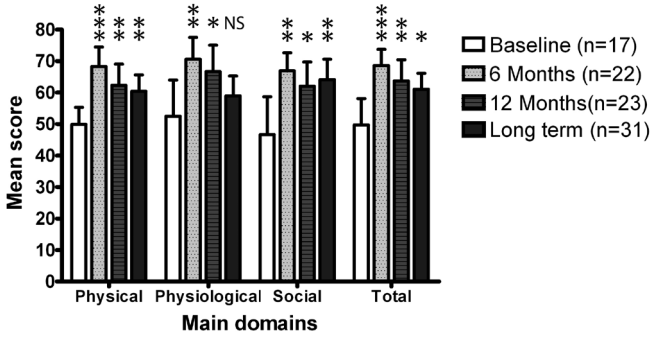

Figure 2 Mean NCIQ scores per evaluation moment. A higher value indicates a better result. The error bars represent the 95% confidence interval. Note: results of unpaired t test versus baseline *p < 0.05, ** p < 0.01, *** p < 0.001, NS = not statistically significant.

GBI

Of the 33 patients at the long-term evaluation moment, 27 (82%) had a positive total GBI scores (mean score +26.5, SD ± 17.5), 3 (9%) had no change in total GBI scores and 3 (9%) had a negative change in total GBI scores (mean score -5.9, SD ± 2.9) (**Table 5)**. The overall mean score was +21.2 (SD ± 19.6). These results are lower compared to the 12-month results in which 23 patients (92%) had a positive GBI score (mean +22.6, SD ± 13.7), 1 patient (4%) had no change and 1 patient (4%) had a negative change (-17.6). At this evaluation moment the overall mean score was +20.1 (SD ± 16.0). No significant difference in benefit between the evaluation moments was found in a paired t-test analysis (n=19 patients; $p > 0.05$).

Table 5 Overview of individual benefit values per evaluation moment, compared with baseline.

Evaluation moment	6-months	12-months	Long term
NCIQ benefit (mean, ± SD)	n=8	n=8	n=9
Physical, benefit	21.5 ± 12.2[B]	6.5 ± 10.7	18.6 ± 12.6[B]
Physiological, benefit	28.3 ± 20.7[B]	13.2 ± 18.7	12.7 ± 12.6[A]
Social, benefit	36.3 ± 20.6[B]	14.2 ± 16.6[A]	22.6 ± 20.8[A]
Total, benefit	28.7 ± 14.4[B]	11.3 ± 13.7	18.0 ± 12.4[B]
GBI, benefit in aided condition (mean, ± SD)		n=25	n=33
Total		20.1 ± 16.0	21.2 ± 19.6
General		24.6 ± 18.2	25.0 ± 20.8
Social		14.0 ± 21.9	13.6 ± 22.6
Physical		9.3 ± 32.0	13.6 ± 34.0

[A] Paired t-test $p < 0.05$; [B] $p < 0.01$

Discussion

This study evaluates the long-term subjective benefit in middle ear implantation for patients with therapy-resistant chronic external otitis. We compared data collected with the APHAB, NCIQ and GBI questionnaires and evaluated device use and device satisfaction as reported by AMEI users. Of the 56 patients who provided baseline data, at long-term follow-up 5 patients were deceased, 5 patients had become device non-users and 4 patients had known complications and were excluded from the study (see **Table 1**). At the long-term evaluation moment, 5 of the 39 patients reported being device non-users, meaning that the total percentage of non-user was 13%. Main reasons for non-use were insufficient

benefit and device problems. Mosnier et al. reported a comparable percentage of device non-users (15%) in their paper on long-term effects of active middle ear implantation (9). Schmuziger et al. (2006) also published long-term data on a group of 20 middle ear implant users. Although these authors reported no device non-use, their data was gathered only after 3.5 months of device use (11). In 2010, Rameh et al. published the long term postoperative results of their AMEI users. In general, patients were satisfied with their implants although great variation was found between the devices. The audiologic gain was adequate, but not spectacular. Especially, the daily life audiologic gain was poor in relation to patient satisfaction. Many patients considered their contralateral conventional hearing aids more satisfying (10).

In the long run, the majority of patients in our study are content with their AMEI: 71% of the patients report that the AMEI is worth the effort and 85% report wearing the device more than 4 hours a day (see **Table 3**). This result is comparable to the short-term results reported by Sterkers et al (3) and published long-term patient satisfaction results (9,10). The patients in our study consider the devices easy to use and the sound is judged positively by 87%. More than 80% would choose this device again or would recommend the device to others. These results are comparable with those published by Mosnier (77% satisfaction and 72% would repeat the surgery) (9). The respondents also reported being willing to pay an average price of up to 1750 Euros for their device, which is comparable to the average price of high-end conventional hearing aids in the Netherlands.

The results from our study are better than the outcome presented by Rameh et al. (10). In their study, 42% of the VSB users were more satisfied with the implant than with the contralateral behind the ear (BTE) hearing aid, whereas only 29% of the MET users were more satisfied with it. Only 67% of the patients with a VSB and 55% of patients with a MET reported they would undergo the surgery again. We believe that these differences are best explained by differences in study inclusion criteria, such as cosmetic considerations because of visibility issues with regular hearing aids (10). Besides this, the results in our study are based on data of patients who are using the device and only 3 of the 5 non-users (total 13%).

The results of the APHAB questionnaire (**Figure 1**) suggest that patients experience a significant decrease in problems after AMEI implantation (compared to the pre-implant situation, viz. using conventional devices). Nevertheless, the results show a negative long-term trend. This leads to a decreasing level of statistical significance at each follow-up evaluation moment and even results in a non-significant difference at the long-term evaluation moment for the BN and RV subdomains. We found that the questionnaire scores dropped by approximately 10 points over the evaluation period of 7 years. Few results have been published on the long-term stability of perceived benefit and satisfaction of any type of hearing aid fitting. Similar to our study, Takahashi et al. found that the APHAB scores deteriorated over time at a similar rate in patients who used conventional hearing aids (21). This suggests deterioration in APHAB scores is not device

specific, but rather it is a general trend in long-term evaluation by means of questionnaires. In the paired-data analysis by Cox and Alexander (**Table 4**), this decline in benefit is visible as a decrease in number of patients with significant benefit (68% versus 43%) (20). The deterioration over time might be ascribed to advancing hearing loss (similar to presbyacusis) or the patient becoming accustomed to a new hearing situation without adverse effects of external otitis.

Another method to evaluate hearing impairment disability is by using the NCIQ questionnaire. We previously applied this method to evaluate the short-term result of middle ear implantation (6). From the results displayed in **Figure 2** and listed in **Tables 2 and 5**, we can conclude that middle ear implantation has a significant positive effect on NCIQ scores at all evaluation moments. The long-term total score of 61.3 proves to be comparable with the results after application of a BAHA or a cochlear implant (range 59-73) (13,15,16,18). Comparing the long-term and short-term evaluation moments, a decline in benefit over time is found for the APHAB results. In the unpaired data, this decline reaches 7.5 points.

The results of the GBI QoL analysis show a significant difference of +21.2. Although we had expected improvements in the physical aspects domain as the patients all had complaints of external otitis, the benefit is almost completely accredited to the general domain. A large variation was found between individual patients. A disadvantage of the GBI is the retrospective character of the questionnaire, and as such, a recall bias might be present in the GBI scores. This is not apparent in the NCIQ and APHAB questionnaires, as a baseline measurement is available. The GBI scores in our study are slightly higher than those reported by Schmuziger et al (+14.7) and Mosnier et al. (+17.8) (9,11).

Conclusions

Although a negative trend is found over time, the Vibrant Soundbridge and Otologics active middle ear implants provide significant long-term benefit in disability and quality of life. No difference in subjective results was found between the two devices. The percentage of device non-users was 13% and patient satisfaction scores and daily usage percentage were over 80%. Overall, active middle ear implants provide a good option for hearing rehabilitation in patients with sensorineural hearing loss and recurrent external otitis.

References

1. Jenkins HA, Niparko JK, Slattery WH, Neely JG, Fredrickson JM. Otologics Middle Ear Transducer Ossicular Stimulator: performance results with varying degrees of sensorineural hearing loss. *Acta oto-laryngologica* 2004;124:391-4.
2. Luetje CM, Brackman D, Balkany TJ, et al. Phase III clinical trial results with the Vibrant Soundbridge implantable middle ear hearing device: a prospective controlled multicenter study. *Otolaryngol Head Neck Surg* 2002;126: 97-107.
3. Sterkers O, Boucarra D, Labassi S, et al. A middle ear implant, the Symphonix Vibrant Soundbridge: retrospective study of the first 125 patients implanted in France. *Otology & Neurotology* 2003;24:427-36.
4. Boeheim K, Pok SM, Schloegel M, Filzmoser P. Active middle ear implant compared with open-fit hearing aid in sloping high-frequency sensorineural hearing loss. *Otology & Neurotology* 2010;31:424-9.
5. Snik AF, van Duijnhoven NT, Mulder JJ, Cremers CW. Evaluation of the subjective effect of middle ear implantation in hearing-impaired patients with severe external otitis. *Journal of the American Academy of Audiology* 2007;18:496-503.
6. Snik AF, van Duijnhoven NT, Mylanus EA, Cremers CW. Estimated cost-effectiveness of active middle-ear implantation in hearing-impaired patients with severe external otitis. *Archives of otolaryngology--head & neck surgery* 2006;132:1210-5.
7. Cox RM, Alexander GC. The abbreviated profile of hearing aid benefit. *Ear and hearing* 1995;16:176-86.
8. Barton GR, Bankart J, Davis AC, Summerfield QA. Comparing utility scores before and after hearing-aid provision : results according to the EQ-5D, HUI3 and SF-6D. *Applied health economics and health policy* 2004;3:103-5.
9. Mosnier I, Sterkers O, Bouccara D, et al. Benefit of the Vibrant Soundbridge device in patients implanted for 5 to 8 years. *Ear and hearing* 2008;29:281-4.
10. Rameh C, Meller R, Lavieille JP, Deveze A, Magnan J. Long-Term Patient Satisfaction With Different Middle Ear Hearing Implants in Sensorineural Hearing Loss. *Otology & Neurotology* 2010;31:883-92.
11. Schmuziger N, Schimmann F, aWengen D, Patscheke J, Probst R. Long-term assessment after implantation of the Vibrant Soundbridge device. *Otology & Neurotology* 2006;27:183-8.
12. Tysome JR, Moorthy R, Lee A, Jiang D, O'Connor AF. Systematic review of middle ear implants: do they improve hearing as much as conventional hearing aids? *Otology & Neurotology* 2010;31:1369-75.
13. Hinderink JB, Krabbe PF, Van Den Broek P. Development and application of a health-related quality-of-life instrument for adults with cochlear implants: the Nijmegen cochlear implant questionnaire. *Otolaryngol Head Neck Surg* 2000;123:756-65.
14. Krabbe PF, Hinderink JB, van den Broek P. The effect of cochlear implant use in postlingually deaf adults. *International journal of technology assessment in health care* 2000;16:864-73.
15. Damen GW, Beynon AJ, Krabbe PF, Mulder JJ, Mylanus EA. Cochlear implantation and quality of life in postlingually deaf adults: long-term follow-up. *Otolaryngol Head Neck Surg* 2007;136:597-604.
16. de Wolf MJ, Shival ML, Hol MK, Mylanus EA, Cremers CW, Snik AF. Benefit and quality of life in older bone-anchored hearing aid users. *Otology & Neurotology* 2010;31:766-72.
17. Snik A, Verhaegen V, Mulder J, Cremers C. Cost-effectiveness of implantable middle ear hearing devices. *Advances in oto-rhino-laryngology* 2010;69:14-9.
18. Klop WM, Boermans PP, Ferrier MB, van den Hout WB, Stiggelbout AM, Frijns JH. Clinical relevance of quality of life outcome in cochlear implantation in postlingually deafened adults. *Otology & Neurotology* 2008;29:615-21.
19. Robinson K, Gatehouse S, Browning GG. Measuring patient benefit from otorhinolaryngological surgery and therapy. *The Annals of otology, rhinology, and laryngology* 1996;105:415-22.
20. Cox RM. Administration and application of the APHAB. *Hearing journal* 1997;50:32-48.
21. Takahashi G, Martinez CD, Beamer S, et al. Subjective measures of hearing aid benefit and satisfaction in the NIDCD/VA follow-up study. *Journal of the American Academy of Audiology* 2007;18:323-49.

2.3.

Active middle ear implantation: long-term medical and technical follow-up, implant survival and complications

Published as

Active middle ear implantation: long-term medical and technical follow-up, implant survival and complications.

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Abstract

Objective: To evaluate the long-term medical and technical results, implant survival and complications of the semi-implantable Vibrant Soundbridge (VSB), Otologics Middle ear Transducer (MET), and the Otologics fully Implantable Ossicular Stimulator (FIMOS)

Patients and methods: a retrospective cohort study was conducted in tertiary referral center for patients with chronic external otitis and either moderate to severe sensorineural or conductive/mixed hearing loss who were implanted with the VSB, MET or FIMOS. Main outcome measures: medical complications, number of re-implantations and explantations.

Results: 94 patients were implanted, 12 patients with a round window or stapes application. 28 patients were lost to follow up. The average follow-up duration was 4.4 years (range 1 month to 15 years). 128 devices were evaluated: (92 VSB, 32 MET, 4 FIMOS). 36 devices (28%) have been explanted or replaced (18 VSB, 14 MET, 4 FIMOS). Device failure was 7% for VSB, 28% for MET and 100% for FIMOS. In 16 patients (17%) revision surgery (n=20) was performed. Twenty patients (21%) suffered any medical complication.

Conclusion: medical and technical complications as well as device failures have mostly occurred in the initial period of AMEI implementation and during clinical trials or experimental procedures. All four FIMOS had technical difficulties. An important decrease in the occurrence of both medical and technical complications was observed. Application in more recent years did not show any complications and the recent device failure rates are acceptable. MRI incompatibility should be taken into account when indicating AMEI.

Introduction

Active middle ear implants (AMEI) have been used in otologic surgery for more than two decades. The most frequently applied AMEI systems in the Netherlands are the Vibrant Soundbridge or VSB (Symphonix, San Jose, CA, USA and later Med-El, Innsbruck, Austria) and the Middle Ear Transducer or MET (Otologics LLC, Boulder, CO, USA and recently Cochlear Ltd, Sydney, NSW, Australia). The devices generally consist of an implanted actuator and an externally worn sound processor. The actuator is coupled to either the ossicular chain or to the round or oval window of the cochlea. The sound processor with battery is coupled by a magnet to an implanted receiver to enable communication with the internal part by radio frequency. The receiver is connected to the actuator. We also applied the Fully Implantable Middle ear Ossicular Stimulator (FIMOS) devices (Otologics; later called the Carina device). The internal battery has to be charged daily by the use of an external charging device. The microphone is also implanted, under the skin behind the ear.

Indications

The indication for an AMEI varies from (pure) sensorineural hearing loss (1-4) to mixed hearing loss (5-10) and even pure conductive hearing loss (i.e. in case of a bony atresia of the external ear canal) (11,12). In the Netherlands, AMEIs are reimbursed for patients with sensorineural hearing loss, if they suffer from therapy resistant chronic external otitis that inhibits the use of a conventional hearing aid with any ear mould in the external ear canal. This limitation was proposed by our centre and became a requirement by the health authorities for the patient to be eligible for reimbursement of both the device and the treatment.

As part of the European phase 1 trial, the initial patients in our centre were among the first to be implanted with a VSB in 1996 (3). In consequence, our center got also involved in the introduction of the MET and FIMOS. Several experimental surgical techniques involving the implantation of the VSB have been studied, e.g. the transcanal approach and the use of additional cement to fixate the floating mass transducer (FMT) onto the long process of the incus. These applications will be discussed later on.

After the first introduction to apply the VSB to the oval or round window in mixed hearing loss by Colletti et al., we started to apply this method in our clinic (13)**.** The FMT was either coupled to the remains of the stapes or the stapes footplate. In other patients, the FMT was placed in the round window niche, mostly in patients with subtotal petrosectomy after chronic middle ear disease.

In the last years, a number of studies have been published about the applications of AMEI, focusing on both surgical as audiological outcome. These studies have mainly focused on the short and long term benefits in terms of amplification, stability and quality of life outcome. Some authors have published on the expanding indication range for the

application of AMEI, both for sensorineural hearing loss, mixed hearing loss and, specifically, in otosclerosis (14,15). Few publications discussed device explantation in the long run, either due to medical or technical problems, including the need for MRI diagnostics. In this study, we provide such long-term data on implant stability and complications to improve evidence based decision making for the indication of active middle ear implants.

Materials and methods

A retrospective cohort study was conducted at a tertiary academic medical centre. This centre was among the first to initiate and evaluate the application of AMEI in patients who experienced problems with conventional hearing aid revalidation. For this study we included the complete cohort of patients who received an AMEI. The implantations were carried out between October 1996 and February 2014. All patient charts were checked for complications during implantation and during the follow-up period. Furthermore, all re-implantations, explantations and other surgical procedures were evaluated. We adapted a previously described database for the analysis of complications in cochlear implantation, which was developed at our centre and is freely available online (16).
The first outcome parameter for the study was the number of explantations and re-implantations per type of AMEI. Implant survival was calculated as the duration of follow-up until device explantation, either due to a technical implant failure or due to any medical indication. The second outcome parameter was the number of revision surgeries owing to medical or technical complications. The third outcome parameter was the total number of complications.

Surgical procedure

For the surgical procedure, we refer to previous publications concerning the introduction of the implants. The standard surgical procedure was used for both the VSB and the MET as mentioned by Fisch et al and Jenkins et al (1,4). Although the devices have been developed for use in patients with pure sensorineural hearing loss, several patients have been implanted with mixed hearing loss, following the procedure described by Colleti et al (13). From September 2003 to October 2005, thirteen consecutive patients were implanted with a VSB using a transcanal approach. This surgical procedure has been described previously. In short, a bony canal or groove was drilled in the external ear canal to avoid a mastoidectomy by providing an access for the electronic wire of the VSB device. The groove was covered with bone dust (17).

Statistical analysis

For the calculations and graphs we have used Microsoft Excel (Microsoft, Redmond, WA, USA), SPSS (SPSS Inc., Chicago, IL, USA) and Graphpad Prism (GraphPad Software Inc., La Jolla, CA, USA).

Results

Patient characteristics

In total, 94 patients have been implanted. The group consisted of 39 men and 55 women, with a mean age at implantation of 55 years (range 18 to 79 years). In the final situation at the time of analysis (2014), bilateral VSB implantation was indicated in 8 patients and 2 patients were implanted with a VSB and MET (**figure 1**). The follow-up period was 4.4 years on average (range of 1 month to 15 years) with an average of 4.8 years for VSB (range 1-180 months), 3.6 years for MET (range 1-153 months) and 5 months for the FIMOS (range 2-16 months). During the follow-up period 28 patients were considered lost to follow up; 7 patients had deceased, 12 patients were explanted and 6 patients were lost to follow up appointments. Three patients could not use their AMEI due to increased hearing loss. One patient switched to a conventional hearing aid, another one changed to a bone conduction device due to deterioration in mixed hearing loss and one patient received a cochlear implant. All non-users were included in the follow-up analysis.

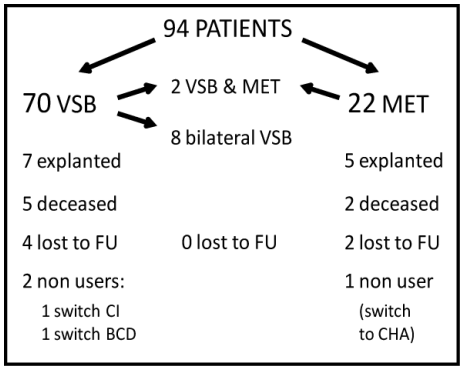


Figure 1 Patient overview of the situation at the end of the study period and result of follow up.

FU = follow up. CI = cochlear implant. BCD = bone conduction device. CHA = conventional hearing aid

Mixed hearing loss

For 12 of the 94 patients, mixed hearing loss was the indication for primary or revision implantation. One of these patients was bilaterally implanted. All these patients were implanted with the VSB, either coupled to the stapes (n=10), or directly onto the round window niche (n=3). The coupling details are displayed in **table 1**. Some of the patients had mixed hearing loss as a result of a previous AMEI implantation that lead to incus necrosis (see complications). The audiometric results of the first five patients have been previously described by Verhaegen et al (8).

Table 1 Connection details of implantation in patients with mixed and conductive hearing loss.

Connection type	n	Remarks
Stapes coupling after incus necrosis	2	One patient implanted with a CI
Stapes head coupling in subtotal petrosectomy	4	
RW coupling in subtotal petrosectomy	2	
Stapes VORP to tympanic membrane	2	One explanted because of chronic pain
Stapes head coupling in aural atresia	1	Re-implantation; technical defect
RW coupling in mastoidectomy	1	
Stapes remains coupling in mastoidectomy	1	
Total	13	10 stapes and 3 round window

RW = round window. VORP = vibrating ossicular replacement prosthesis. CI = cochlear implant.

Surgical results

In total, 161 surgical procedures were evaluated, which were conducted between October 1996 and February 2014. For the 94 patients, 104 primary implantations were registered, 79 VSB (8 bilateral), 23 MET (2 bilateral) and 2 FIMOS. All patient characteristics per implant type can be found online in the **table 2**. The 4 recently implanted MET devices in 2014 were obtained from Cochlear and will be addressed as cMET.

For 15 patients a revision implantation was performed (10 VSB, 3 MET and both FIMOS implants). Of these 15 patients, 6 patients needed a secondary revision implantation (3 VSB and 3 MET). Unfortunately, one patient with a MET implant needed 3 more revision implantations (on a total number of 6 MET implants). He has recently been implanted with a cMET. For the FIMOS device, technical problems with charging of the internal battery and pain complaints lead to replacement of both devices with another.

Some of the devices were explanted without reimplantation, both for medical as well as technical reasons. For the VSB, 12 devices were explanted because of medical indications,

Table 2 Patient characteristics per implant type.

	VSB	MET	FIMOS
Number	79 (8 bilateral)	23	2
Mean age (Y)	57	52	48 ; 58
Gender	44 F ; 27 M	12 F ; 11 M	2 M

F = female, M = male.

which are presented in **table 3**. For the MET device, 5 patients were definitively explanted, 4 because of medical complaints (pain complaints, a skin problem, decrease in audiological benefit and 1 unsatisfied patient) and 1 because of a technical defect, without the desire for revised implantation. So far, none of the recent cMET devices has had any technical problem. Concerning the 2 revised FIMOS implants, both devices were explanted again because of technical defects, leading to a total of 100% technical failure of these devices. No further FIMOS implantations were performed and both revision implants were replaced by a VSB.

Table 3 Device explantations and indications.

Device	VSB	n	MET	n	FIMOS	n	Total n
Medical indications	Incus arrosion	1	Skin defects	2			
	Pain complaints	3	Ossification	1			
	MRI indication	3	Dissatisfied patient	1			
	CI implantation	1	Incus fracture	1			
	Wire problems	4					17
Technical indications	Technical defects	6	Technical defects	9	Technical defects	4	19
Total		18		14		4	36

Revision surgery

For 16 patients (17%) revision surgery, other than re-implantation or explantation of the device was performed. In total, 20 surgical procedures were conducted, varying in severity (**table 4**). Three revisions were indicated because of wire extrusions and skin defects in de external ear canal, as a result of the specific surgical method of implantation, the transcanal approach in patients with a therapy resistant external otitis. The evaluation of this method

has been described in detail previously (17). Middle ear inspection was indicated for 8 VSB implants because of a presumed decrease in fixation of the FMT onto the incus. Some revision or replacement of the magnet of the MET receiver was necessary in 4 patients, as well as revision of the position of the MET transducer onto the incus in 2 patients. One patient needed a myringoplasty because of a tympanic membrane perforation, which occurred after implantation. The other minor revisions were surgical corrections of the place of the implant or the magnet, a revision of the skin of the temporal bone and surgical correction of some bony overgrowth.

Table 4 Description of revision surgery, excluding explantations.

Type of surgery	n	Implant
Middle ear inspection with crimping of FMT	8	VSB
Revision of implant or magnet	4	MET
EAC skin dehiscence revision (wire problems)	3	VSB
Correction of skin defect temporal skull	1	MET
Myringoplasty	1	VSB
Revision MET-incus coupling	2	MET
Revision of bone overgrowth	1	MET
Total	20	

FMT = floating mass transducer. EAC = external auditory canal.

Implants

During the study period a total of 128 implants were implanted: 92 VSB devices, 32 MET (of which 4 cMET) and 4 FIMOS devices. In total, 36 devices were replaced or explanted, 18 VSB (20%), 14 MET (44%) and 4 FIMOS (100%). Most implants (75%) were replaced or explanted within the first 5 years and about one third (36%) even within the first 18 months after implantation. **Figure 2** shows that for the MET most implants were lost within the first 4 years of follow-up, whereas for VSB this was spread over the total 12 years of follow up. As can be seen in **table 3**, the reasons for the device replacement or explantation varied between medical issues (n=17; 47%), i.e. wire extrusions, incus erosion or strict MRI indication, and technical failures of the device itself (n=19; 53%). In total, the device failure rate due to technical defects was 7% for VSB, 28% for MET and 100% for FIMOS.

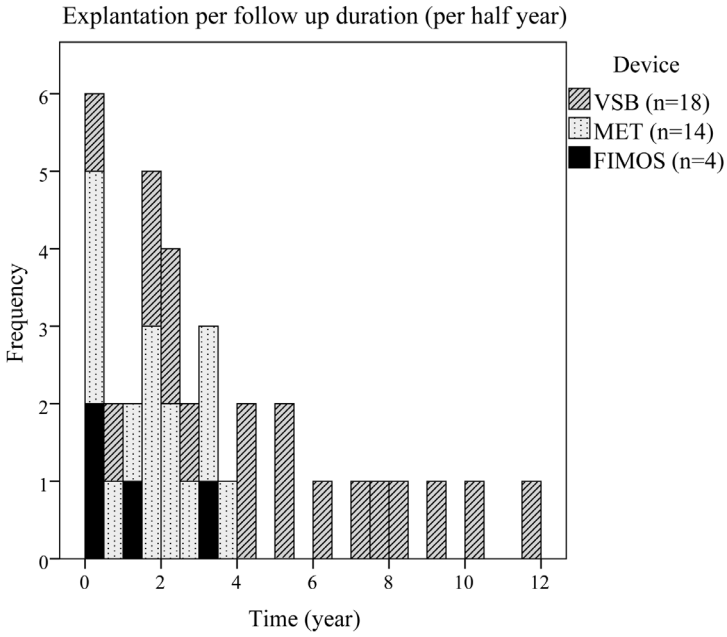


Figure 2 Explantations during follow up period per half year.

Implant survival

Survival analysis was studied by summing all individual follow-up data. A subdivision was applied for the medical and technical failures. Non-users were not considered as lost to follow up in this analysis. **Figure 3** shows the Kaplan Meier graph of the result per implant. For the VSB, it shows a steadily decreasing survival rate. The majority is explained by the explantations for the various medical indications. Some technical failures did occur for the VSB, mainly within the first years after implantation. On the other hand, for the MET device, the device explantation is mostly explained by technical failures.

To calculate the average number of implant loss per follow up year for technical defects we added up the total duration of follow up per device. Non usage was not considered as device loss. The results can be found in **table 5.** In short, the calculated implant loss for VSB is 1 per 74 years of follow up and for MET 1 per 13 years of follow-up. For cMET, no complications were registered. All 4 FIMOS implants were lost within a summed total of 27 months of follow up.

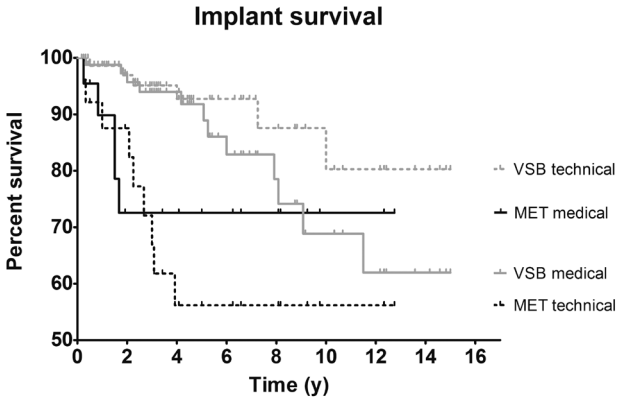


Figure 3 Explantations during follow up period per half year.

Table 5 Device failure rate, revision rate and follow up duration

Implant type	No. of implants	Technical defects (n)	Device failure rate (%)	No. of revisions and explantations
VSB	92	6	7	33
MET	32	9	28	22
FIMOS	4	4	100	4

Implant type	Total sum of follow up (year)	Follow up mean (y) and range (month)	Device failure rate (1/year)	Revision rate (1/year)
VSB	445	4.4 y (1-180)	1 / 74 y	1 / 13 y
MET	115	3.6 y (1-153)	1 / 13 y	1 / 5y
FIMOS	2.3	0.4 y (2-16)	1.7 / 1 y	1.7 / 1 y

Medical complications

During the study period, 20 patients (21%) had a minor or more serious medical complication. **Table 6** presents all the complications. Some of the complications are to be expected in AMEI implantation, especially the sacrifice of the chorda tympani nerve since the posterior tympanotomy needs to be large enough to pass the FMT of the VSB.

The wire extrusion complications all occurred in patients where the transcanal method was used. Some wire extrusions were revised and covered with temporal muscle fascia,

Table 6 Complications.

More serious	n	Implant	Minor	n	Implant	
Incus erosion	4	VSB	Insufficient coupling FMT	1	VSB	
Wire extrusions in the ear canal	5	VSB	Insufficient contact to incus	1	MET	
Laceration of the chorda tympani	4	VSB	Pain complaints due to ossification	1	MET	
Skin dehiscence	1	MET				
Infection	3	both				
Totals	17			3		20

FMT = floating mass transducer.

but in most cases the wire repeatedly extruded in the ear canal. These patients underwent revision surgery by the classical transmastoid approach.

In four patients the long process of the incus was eroded at the location of the attachment of the clip of the FMT of the VSB device. In eleven cases Serenocem (Corinthian Medical Ltd, Nottingham, UK) was experimentally applied to strengthen the fixation of the clip of the FMT onto the long process of the incus. As a result of the erosion, 2 patients ended up with a mixed hearing loss. In these cases, the FMT was coupled to the stapes (see Verhaegen et al) (8).

In general, the frequency of complications has decreased with the years as is presented in **figure 4**. The complication rate increased during 2003-2005, mostly because of the previously mentioned experimental transcanal approach technique. In the last 6 years of the evaluation period, hardly any complications have occurred during or after the implantation of the AMEI.

Mixed hearing loss

For the 12 patients with mixed hearing loss, the mean duration of follow is 28 months (range 8-61 months). In 3 patients the device has been explanted. One patient the level of sensorineural hearing loss progressed and he was implanted with a cochlear implant. In another patient pain complaints occurred over the area of the skull surrounding the implant and ultimately no other option than explantation was available. The third explantation was because of a technical failure. One of the 12 patients (8%) is a non-user, since the audiological gain was insufficient. In this patient the round window application technique was performed as part of a subtotal petrosectomy and the patient refused revision surgery.

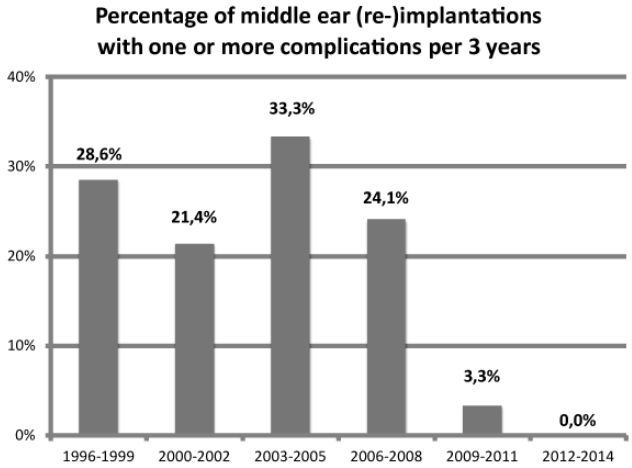


Figure 4 Complication rate during follow up period.

Discussion

This article provides a comprehensive description of a complete cohort of patients, implanted with an active middle ear implant. It presents the issues involved with the start-up and introduction of new devices: technical, as well as medical and surgical issues. We have focused this study on the outcome in implant survival and daily usage and the medical complications that occur during the surgery and thereafter.

Previous publications have mainly focused on long term outcome of audiological results, patient satisfactions and daily usage by the patients. Sterkers et al. have published short term results of 125 VSB devices. During their follow-up of 17 months, 5 device failures had occurred. No serious events had occurred (18). Schmuziger et al. published results of 20 VSB users with an average follow-up of 3.5 years. Complaints related to the chorda tympani had occurred in 3 of the 20 patients. In three patients revision surgery was necessary. They reported one device failure (5%) (19). In the article by Vincent et al, the authors report on the long term audiological results of 39 VSB users. No outcome results for device failure or complications were mentioned (20). Mosnier et al. have reported their results with an average follow up 6 years in 77 patients with a VSB. During this period, 7 patients (9%) were explanted, 3 because of device failure, 1 because of a switch to a cochlear implant, 2 because of poor audiological benefit and 1 because of psychological problems. For 7 other patients (9%) re-implantation was necessary because of device failure. They reported 8 patients as non-users (10%). Five patients (6%) needed revision surgery, mainly due to problems with the coupling of the FMT onto the incus, magnet problems and fibrous

tissue in the middle ear. Chorda tympani complaints occurred in 8% of the patients and 27% complained of aural fullness (21). In 2010, Rameh et al have reported their results on MET (n=19; 5.1 years), Carina (n=10; 1.9 years) and VSB (n=45; 3.3 years) implantations. Revision surgery due to implant dysfunction was needed in 16% of the MET implants and 9% of the VSB implants. Non-use and complications are not mentioned (22). In another publication, Debeaupte et al. describe their experience with the successive generations of FIMOS devices. As in our series, all first generation devices in their series have been explanted. The most recent devices with at least a follow up of 22 months had survival rates of 100% (23).

Since cochlear implants have been applied for over 30 years in greater numbers than AMEI, more knowledge of the reliability of these devices is available over the longer term. In 2010, a consensus statement was published on the international classification of CI reliability, which states guidelines on the report of device failures (24). In the current article we have tried to report according to this guideline. Considering the reports on technical device failure in literature, the revision rates are varying between 1.2% and 15.1% as presented by Wang et al. in 2014. The mean calculated device failure rate was 5.1%, ranging from 0.5% to 14.7% (25). In a recent, not included publication, Theunisse et al have published the results of over 1000 CIs in our clinic and reported a device failure rate of 2.4% (16).

In short, we can state that the failure rate of the VSB (7%) is acceptable within the range of the results of cochlear implants. Especially if we take into consideration that our series for VSB include the phase I primary clinical trial results as well. Moreover, we have observed a decrease in hardware failures (see **figure 4**). At present, the incidence of revision surgery or medical problems with the VSB is low. A similar decrease in implant failures and revision surgeries was observed for the MET. The overall rate of hardware failures was considered high (28%), which can be explained by technical failures of the early generation implants. Considering the increasing availability of high-field MRI scanners, some technical and medical challenges may arise in patients with an AMEI, as well as other otologic implants. In a large US report in 2012 an increase in MRI usage between 1996 and 2010 is presented. The authors report an increase from 1.7% to 6.5% of the enrolled patients and 10 percent increase per year (26).

In an extensive publication in 2011, Wagner et al have described a review on the results of all published in vivo en ex vivo experiments with the VSB and MRI scanning (27). They state that MRI up to 1.5 Tesla can be performed at calculated risk, although the possible side effects of loud hearing sensations and possible dislocation of the FMT should be weighed against the necessity of the imaging. Since 2014, the Med-El company has introduced the newest version of the VSB implant and states a MRI-compatibility up to 1.5 Tesla (Med-El company information). The Cochlear MET has not been granted a MRI safety approval. However, experiments to assess the effects of MRI scanning on the present device are ongoing.

Conclusion

The early introduction of the VSB, MET and FIMOS active middle ear implants at our centre has lead to this long term retrospective study of clinical follow-up outcome. During the years, both the technical and medical issues in implantation have drastically improved for the VSB and the MET, with few medical complications in the last few years. The technical challenges have been overcome by the industry, with a decreasing need for re-implantation and explantation rates.

From a surgical point of view, we consider the VSB a reliable AMEI for the use in sensorineural and mixed hearing loss with an acceptable implant survival period and limited explantation rate. The MET has had a low reliability in the early days, which has strongly increased more recently. Compared to the VSB, the MET is applicable in relatively more extensive sensorineural hearing loss, since it provides a higher output as we have published previously (28,29). Therefore, we consider the MET an important alternative option. As the four experimental FIMOS devices that we applied all have been explanted within 2 years, we have not continued the application in our clinic, although Debeaupte et al. recently showed that the current Carina version has become more stable over time (23).

We believe that candidacy for an active middle ear implant should be well considered, both audiological and medical. Possible complications concerning the surgical procedure and the follow-up period should be counseled. MRI compatibility will remain a challenge with an increasing frequency in MRI-diagnostics and possible increase in field strength.

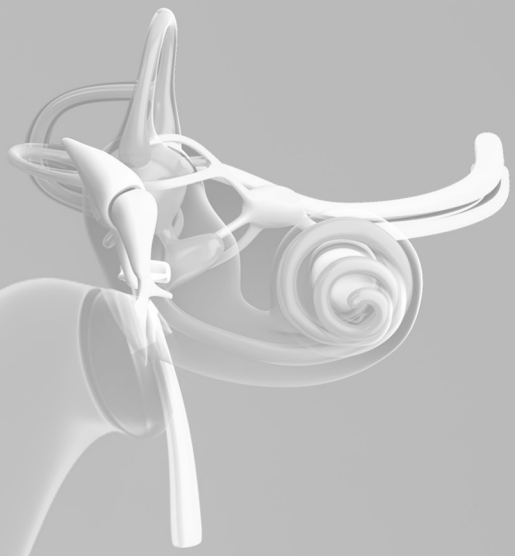
References

1. Fisch U, Uziel AS, Cremers CW, et al. Clinical experience with the Vibrant Soundbridge implant device. *Otol Neurotol* 2001;22:962-72.
2. Snik AF, Cremers CW. Vibrant semi-implantable hearing device with digital sound processing: effective gain and speech perception. *Arch Otolaryngol Head Neck Surg* 2001;127:1433-7.
3. Snik AF, Cremers CW, Snik FM, et al. First Audiometric Results with the Vibrant ® Soundbridge, a Semi-implantable Hearing Device for Sensorineural Hearing Loss. *Int. J. Audiol* 1999;38:335-8.
4. Jenkins HA, Niparko JK, Slattery WH, et al. Otologics Middle Ear Transducer (TM) ossicular stimulator: Performance results with varying degrees of sensorineural hearing loss. *Acta Otolaryngol* 2004;124:391-4.
5. Beltrame AM. Coupling the Vibrant Soundbridge to Cochlea Round Window: Auditory Results in Patients With Mixed Hearing Loss. *Design* 2009:194-201.
6. Gunduz B, Atas A, Bayazıt Ya, et al. Functional outcomes of Vibrant Soundbridge applied on the middle ear windows in comparison with conventional hearing aids. *Acta Otolaryngol* 2012;132:1306-10.
7. Marino R, Linton N, Eikelboom RH, et al. A comparative study of hearing aids and round window application of the vibrant sound bridge (VSB) for patients with mixed or conductive hearing loss. *Int. J. Audiol* 2013;52:209-18.
8. Verhaegen VJO, Mulder JJS, Cremers CWRJ, et al. Application of active middle ear implants in patients with severe mixed hearing loss. *Otol Neurotol* 2012;33:297-301.
9. Verhaert N, Desloovere C, Wouters J. Acoustic hearing implants for mixed hearing loss: a systematic review. *Otol Neurotol* 2013;34:1201-9.
10. Verhaert N, Mojallal H, Schwab B. Indications and outcome of subtotal petrosectomy for active middle ear implants. *Eur Arch Otorhinolaryngol* 2013;270:1243-8.
11. Frenzel H, Hanke F, Beltrame M, et al. Application of the Vibrant Soundbridge to unilateral osseous atresia cases. *Laryngoscope* 2009;119:67-74.
12. Verhaert N, Fuchsmann C, Tringali S, et al. Strategies of active middle ear implants for hearing rehabilitation in congenital aural atresia. *Otol Neurotol* 2011;32:639-45.
13. Colletti V, Soli SD, Carner M, et al. Treatment of mixed hearing losses via implantation of a vibratory transducer on the round window. *Int J Audiol* 2006;45:600-8.
14. Dumon T. Vibrant Soundbridge middle ear implant in otosclerosis *Adv Otorhinolaryngol*, 2007:320-2.
15. Venail F, Lavieille JP, Meller R, et al. New perspectives for middle ear implants: first results in otosclerosis with mixed hearing loss. *Laryngoscope* 2007;117:552-5.
16. Theunisse HJ, Mulder JJ, Pennings RJE, et al. A database system for the registration of complications and failures in cochlear implant surgery applied to over 1000 implantations performed in Nijmegen, The Netherlands. *J Laryngol Otol* 2014;128:952-7.
17. Zwartenkot JW, Mulder JJS, Snik AFM, et al. Vibrant Soundbridge surgery in patients with severe external otitis: complications of a transcanal approach. *Otol Neurotol* 2011;32:398-402.
18. Sterkers O, Boucarra D, Labassi S, et al. A middle ear implant, the Symphonix Vibrant Soundbridge: retrospective study of the first 125 patients implanted in France. *Otol Neurotol* 2003;24:427-36.
19. Schimmann F, Probst R, Schmuziger N, et al. Long-term assessment after implantation of the Vibrant Soundbridge device. *Otol Neurotol* 2006;27:183-8.
20. Vincent C, Fraysse B, Lavieille JP, et al. A longitudinal study on postoperative hearing thresholds with the Vibrant Soundbridge device. *Eur Arch Otorhinolaryngol* 2004;261:493-6.
21. Mosnier I, Sterkers O, Bouccara D, et al. Benefit of the Vibrant Soundbridge device in patients implanted for 5 to 8 years. *Ear Hear* 2008;29:281-4.
22. Rameh C, Meller R, Lavieille J-P, et al. Long-Term Patient Satisfaction With Different Middle Ear Hearing Implants in Sensorineural Hearing Loss. *Otol Neurotol* 2010;31:883-92.
23. Debeaupte M, Decullier E, Tringali S, et al. Evolution of the reliability of the fully implantable middle ear transducer over successive generations. *Otol Neurotol* 2015;36:625-30.
24. Battmer R-D, Backous DD, Balkany TJ, et al. International classification of reliability for implanted cochlear implant receiver stimulators. *Otol Neurotol* 2010;31:1190-3.
25. Wang JT, Wang AY, Psarros C, et al. Rates of revision and device failure in cochlear implant surgery: a 30-year experience. *Laryngoscope* 2014;124:2393-9.

26. Smith-Bindman R, Miglioretti DL, Johnson E, et al. Use of diagnostic imaging studies and associated radiation exposure for patients enrolled in large integrated health care systems, 1996-2010. *JAMA* 2012;307:2400-9.
27. Wagner JH, Ernst A, Todt I. Magnet resonance imaging safety of the Vibrant Soundbridge system: a review. *Otol Neurotol* 2011;32:1040-6.
28. Zwartenkot JW, Snik AFM, Kompis M, et al. Gain and maximum output of implantable hearing devices in patients with moderate to severe sensorineural hearing loss. *Journal of hearing science* 2012;2:35-40.
29. Zwartenkot JW, Snik AF, Mylanus EA, et al. Amplification options for patients with mixed hearing loss. *Otol Neurotol* 2014;35:221-6.

3.

Direct acoustic cochlear stimulation



3.1.

Multicenter study with a direct acoustic cochlear implant

Published as

Multicenter Study With a Direct Acoustic Cochlear Implant.
Lenarz Th, Zwartenkot JW, Stieger C, Schwab B, Mylanus EAM, Caversaccio M, D'hondt C and Mojallal H.
Otology & Neurotology Sep 2013; 34:1215-1225

Abstract

Objective: To confirm the clinical efficacy and safety of a Direct Acoustic Cochlear Implant.

Patients and methods: A prospective multi-center study was performed at three University Hospitals in Europe (Germany, The Netherlands and Switzerland). Fifteen patients with severe to profound mixed hearing loss due to otosclerosis or prior failed stapes surgery implanted with a Codacs™ Direct Acoustic Cochlear Implant investigational device (ID) (Cochlear Ltd., Sydney) combined with a stapedotomy with a conventional stapes prosthesis. The pre- and post-operative (3 months after activation of the investigational Direct Acoustic Cochlear Implant) audiometric evaluation measured conventional pure tone and speech audiometry, tympanometry, aided thresholds in sound field and hearing difficulty by the APHAB-questionnaire.

Results: The pre- and post-operative air and bone conduction thresholds did not change significantly by the implantation with the investigational Direct Acoustic Cochlear Implant. The mean sound field thresholds (0.25 to 8 kHz) improved significantly by 48 dB. The word recognition scores (WRS) at 50, 65 and 80 dB SPL improved significantly by 30.4, 75 and 78.2% respectively after implantation with the investigational Direct Acoustic Cochlear Implant compared to the pre-operative unaided condition. The difficulty in hearing, measured by the APHAB, decreased by 27% after implantation with the investigational Direct Acoustic Cochlear Implant.

Conclusion: Patients suffering moderate to severe mixed hearing loss due to otosclerosis can benefit substantially using the Codacs investigational device.

Introduction

Acoustic implants can be divided in 3 categories: middle ear implants (MEI), bone conduction implants (BCI) and direct acoustic cochlear implants (DACI). The transducers of MEI are coupled to the ossicular chain and make use of the ossicles to transmit the amplified vibration to the cochlea. They were originally developed for pure sensorineural hearing losses, but have been indicated to be beneficial in mixed hearing loss when coupled to the round or oval window. BCI couple to the skull and make use of the cranial bone to transmit vibrational energy to the cochlea, thereby circumventing the outer and middle ear and directly stimulating the cochlea. Their main indication is pure conductive and mixed hearing loss. The strongest BCI transducers are able to partially compensate for the sensorineural component of the hearing loss as well (overclosure of the air-bone gap). DACI directly couple to the inner ear, i.e. via the oval or round window or via a surgically created window. They were developed to compensate for severe to profound mixed hearing losses.

Mixed hearing loss combines sensorineural and conductive hearing loss and can possibly cause high hearing thresholds. Hearing devices that make use of the natural sound transmission structures of the ear (i.e. the external and middle ear), such as acoustic hearing aids or MEI, must provide a correspondingly high power output to compensate for the conductive hearing loss component and must still be able to provide a sufficiently amplified broad band signal to the cochlea to compensate for the sensorineural hearing loss. The coupling of MEI to the inner ear is also an important issue for effectiveness

A more efficient approach might be to bypass the natural sound transmission structures of the ear and directly provide an amplified signal to the cochlea. In this approach, conductive losses no longer have to be compensated by increased output power, and the required amplification is determined by the sensorineural hearing loss only. This can be done with a BCI or a DACI. The BCI available today have limited power, and can therefore compensate for the sensorineural component of the hearing loss to a limited level. A DACI provides its power directly to the inner ear by vibrating the perilymph. However, a good coupling of the DACI to the perilymph is essential. In 2008, Häusler et al. (1) presented a new DACI, an implantable hearing system which included a newly developed transducer, the Direct Acoustic Cochlear Stimulator (DACS). This transducer coupled directly to the perilymph via a conventional stapes prosthesis. The device consisted of the transducer, a fixation system and a percutaneous plug, to which an externally worn sound processor was connected. It was implanted in four patients with severe to profound mixed hearing loss during a clinical trial. The trial proved the concept and showed that the hearing and speech intelligibility of those patients improved substantially after implantation with the DACS compared to the pre-operative unaided condition.

Since the initial clinical trial with the DACS system, Cochlear has further developed the device to improve upon important aspects of the design and functionality. These development steps have included the development of custom implantable electronics, an electronics packaging, and a transcutaneous communication and power link with the external sound processor. In addition, surgical tools to aid the surgeon to place the implant have been developed together with a modified fixation system, which allows more degrees of freedom. A Cochlear Nucleus Freedom sound processor (Cochlear Ltd., Sydney) was adapted to deliver acoustical information to the implantable electronics by using custom firmware. Finally, custom fitting rules have been developed together with investigational software to optimize treatment results. All these efforts resulted in the new Codacs™ direct acoustic cochlear implant. Cochlear's Codacs investigational device (ID) is depicted in **Figure 1**.

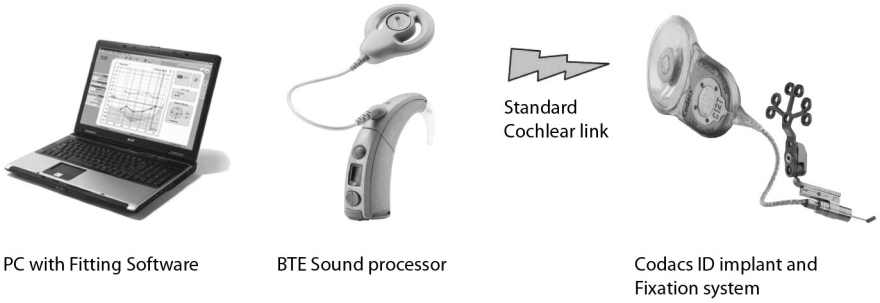


Figure 1 Codacs investigational device.

Between November 2009 and May 2011, the Codacs investigational device has been successfully implanted in 15 patients during a European multi-center trial. This publication presents the results of the clinical trial.

Methods

Device description

The concept of DACS was introduced by Häusler et al. (1). As the concept of the Codacs is the same, it will only be shortly illustrated again. The Codacs investigational device consists of an externally worn behind-the-ear sound processor with radio frequency (RF) coil. The implantable part consists of a receiver coil, the implant electronics and the electro-magnetic transducer (2). The sound processor is Cochlear's Freedom sound processor with a modified firmware to allow for acoustic signal processing. Sound is picked up by

the sound processor's directional microphone and converted into a digital signal. The signal is then broken down into its constituent frequency components (20 bands), amplified and re-synthesized. The whole path from analysis to synthesis runs at a sampling rate of 19.6 kHz. The re-synthesized audio is then streamed over the RF-link into the implant. The RF link encoding and power transmission is copied from the Nucleus Freedom implant (Cochlear Ltd., Sydney) high-rate protocol. The implant decodes the incoming RF, and sends a stimulating current to the electro-magnetic transducer. The transducer (**Figure 2**) vibrates the off-the-shelf stapes prosthesis, thereby mechanically stimulating the perilymph in the inner ear and leading to sound perception. The actuator design was described in Häusler et al. (1) and Bernhard et al. (2) and has not been changed from its earlier design.

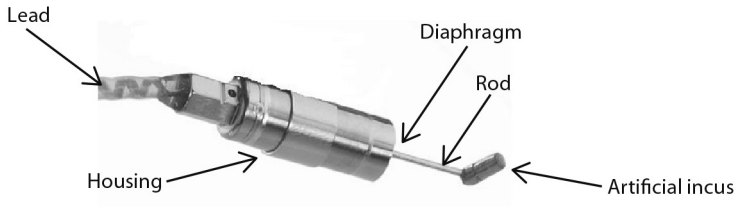


Figure 2 Codacs ID actuator.

The fixation system that keeps the transducer firmly in place within the mastoid cavity has been optimized to allow greater flexibility for the placement of the device (**Figure 3**). It consists of a bone plate, a ball joint and a clamping mechanism, which hold the actuator. During implantation, the bone plate is fixed to the temporal bone with bone screws. The ball joint allows a precise positioning of the clamping mechanism, and like this the actuator, in the mastoid. The ball joint and the clamping mechanism can be manipulated with the help of two torque limiting screwdrivers.

Surgical procedure

The surgical procedure to implant the DACI investigational device was based on the retromeatal approach taken during the clinical trial with the percutaneous DACS described by Häusler (1).

In a first step, the location of the implant and the sound processor were marked on the skin using the surgical templates. After a postauricular incision, the underlying periosteum and lower portion of the temporalis muscle were incised and a flap was formed. A mastoidectomy in the shape of a kidney was performed and the bone of the posterior external ear canal was thinned. A bony bed for the implant body and a bony canal were

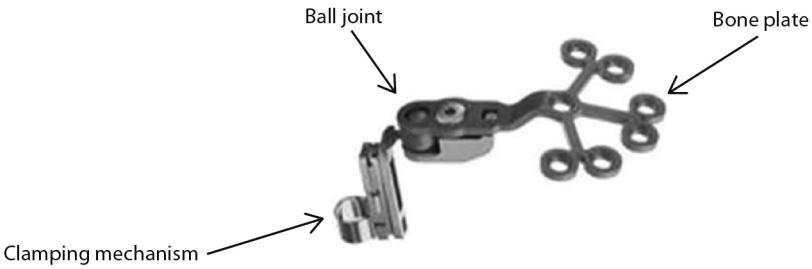


Figure 3 Codacs ID fixation system.

drilled. A tympanomeatal flap was created, after which the middle ear structures could be assessed and otosclerosis could be confirmed. In order to have a direct view on the whole footplate, a segment of the posterior canal wall was removed. A large posterior tympanotomy was performed to expose the middle ear. The ossicular chain was disrupted and the suprastructure of the stapes was removed using a laser. A small canal for the ball joint of the fixation system was drilled in the mastoid and the fixation system was placed and fixed with bone screws. A template of the actuator was used to find a good position of the fixation system.

The ball joint was fastened with a screwdriver. A perforation of the stapes footplate was performed by laser or by drill. The implant body was placed in the bony bed and the actuator was positioned using the applicator. Once a good position for the actuator without contact to the surrounding structure was found, the actuator was fixed in its position. A conventional stapes prosthesis was inserted in the perforation of the stapes footplate and crimped to the artificial incus of the actuator via the ear canal. The actuator cable was protected by securing it in a bony canal and covered with bone paste and fibrin glue. Intra-operative testing was performed to check the functionality of the actuator and implant. The wound was closed subsequently.

The surgical approach is a transmastoid approach with an additional transcanal approach in some cases where the exposure of the stapes footplate is not adequate through the posterior tympanotomy. In 6 cases it was possible to perform the stapedotomy completely through the posterior tympanotomy after removal of the stapes suprastructure. In those cases, the elevation of a tympanomeatal flap and the partial removal of parts of the superior and posterior outer ear canal bone could be avoided and no reconstruction of the posterior ear canal wall with cartilage was necessary, that is, there was less manual work, less bone dust in the middle ear cavity, and less risk of infection. However, the advantages of the combined approach (transmastoid and transmeatal) are a better view on the stapes footplate and no need to expose the facial nerve. The transmastoid approach is described by Lenarz et al. (3).

Study Protocol

The Codacs ID Clinical Trial was designed as a prospective, multicenter study in up to 15 patients. Study centers were the Hannover Medical School (MHH) in Hannover/Germany, the Radboud University Nijmegen Medical Centre (RUNMC) in Nijmegen/The Netherlands and the Inselspital at the University of Bern/Switzerland. The study protocol was submitted to and approved by the responsible ethics commissions and competent authorities. The presented results concern all fifteen included patients. No patients were withdrawn or lost to follow up.

Adult subjects with otosclerosis and a severe to profound mixed hearing loss and subjects with a failed stapes surgery were considered for inclusion in the clinical trial. The bone conduction thresholds had to be at least 30 dB in the audiometric frequencies 0.5 kHz, 1 kHz, 2 kHz, 3 kHz and 4 kHz and had to be measurable at those frequencies. The air-bone-gap had to be at least 30 dB in three of those five frequencies.

All patients were informed about alternative treatments. For some patients, stapes surgery and wearing a hearing aid would have been the best alternative treatment; for others, a cochlear implantation would have been the only alternative solution. All patients who took part in the clinical trial chose to have a DACI investigational device implanted, as they would have needed surgery anyway and the DACI ID combines stapes surgery and acoustic amplification.

All subjects needed to complete 5 study visits and were followed up to three months after initial activation of the DACI investigational device. Pre- and post-operatively medical and audiological evaluations were performed. These included a physical examination, a tympanometry, measurements of the air conduction (AC) and bone conduction (BC) thresholds at standard audiometric frequencies and a measurement of the unaided sound field thresholds using warble tones. Pre-operatively, the uncomfortable loudness levels were measured and a CT scan was performed to verify a sufficient mastoid size. Aided thresholds in sound field were measured pre-operatively using warble tones if the patient was wearing a hearing aid, and post-operatively with the DACI investigational device. The unaided and aided speech reception thresholds (SRTs) and word recognition scores (WRS) were obtained pre-operatively and post-operatively in the sound field using recorded speech. The SRT was measured at the lowest intensity level at which the subject could correctly repeat 50% of the speech. The WRS were measured at 50, 65, 80 and 95 dB SPL, if the uncomfortable loudness level was not reached at those levels. In Germany and Switzerland, the WRS were measured with the Freiburger word lists. In the Netherlands, the WRS were measured with the NVA word lists (word list from the Dutch Society for Audiology).

The speech reception thresholds in noise were established pre-operatively and post-operatively in sound field using the Oldenburg Sentence test (OLSA, developed by Wagener et al. (4) in Germany and Switzerland, and the Plomp test (developed by Plomp et al. (5) in The Netherlands. The signal to noise ratios at which 50% correct scores could be achieved

were assessed via an adaptive test procedure. The stimuli were presented at 0° azimuth and the noise level was fixed at 65dB. For all tests the contra-lateral ear was masked when necessary. A positive signal to noise ratio means that the speech had to be louder than the noise for the patients to be able to understand 50% of the speech. A negative signal to noise ratio means that the speech could be softer than the noise for the patient to be able to understand 50% of the speech. Normal hearing subjects can understand 50% of the speech at a signal to noise ratios of -7.1 dB or -5.5 dB SNR for the OLSA and Plomp respectively (4, 5).

The Abbreviated Profile of Hearing Aid Benefit (APHAB) (6) was completed by all study subjects pre-operatively and at the three months follow-up visit. The benefit was calculated by comparing the patient's reported difficulty in the pre-op condition with their amount of difficulty when using amplification (with the DACI investigational device). The APHAB produces scores of 4 subscales: ease of communications (EC), reverberation (RV), background noise (BN) and aversiveness (AV). The global score can be calculated by averaging those four subscales. Intra-operatively the functionality of the implant was measured with a laser Doppler vibrometer and a free movement of the artificial incus was confirmed. A surgical questionnaire had to be completed by the surgeon after each implantation to give feedback on the surgical procedure.

The DACI investigational device was fitted initially approximately 6 weeks after implantation. Part of the fitting process included an in-situ audiogram using implant stimuli. The fitting parameters were prescribed based on a fitting rule developed by Cochlear. At each study visit the subject was asked for adverse events that might have occurred.

Subjects

Fifteen subjects aged 47 to 79 (mean ± standard deviation (SD): 61 ± 9.4 years) were included in the clinical trial. Eight subjects were implanted at the Hannover Medical School, five patients at the Radboud University Nijmegen Medical Center and two patients at the Inselspital of the University of Bern. The surgeries were performed between November 2009 and May 2011. All study subjects, ten women and five men, had otosclerosis and a severe to profound mixed hearing loss. The duration of hearing impairment was between 10 and 55 years (mean ± SD: 24 ± 12.9 years). Eleven subjects had a hearing aid on the implanted ear pre-operatively, which they had used between 1.5 and 32 years (mean ± SD: 9.7 ± 9.4 years). On the contra-lateral ear, eleven subjects had a hearing aid, three patients had a cochlear implant and one patient didn't use any amplification. Six subjects had undergone a previous ear operation on the implanted ear (stapes surgery (3), tympanoplasty type III (1), ventilation tubes (1), middle ear inspection (1)). Each subject agreed to participate in the study by giving written informed consent. **Table 1** presents an overview of the patients' demographics.

Table 1 Patient's demographics.

No	Study number	Gender	Age	Duration of hearing impairment (years)	Implanted Ear	Duration of hearing aid use in implanted ear (years)	Previous ear operations in implanted ear	Contralateral ear
1	GE10-XEP-01	F	69	25	R	17	No	HA
2	GE10-XRK-02	F	56	55	L	4	No	/
3	GE10-XJH-03	M	47	13	R	2	No	CI (2008)
4	GE10-XAS-04	F	59	20	R	No hearing aid	No	CI (2009)
5	GE10-XJR-05	M	62	10	L	10	No	HA
6	GE10-XWH-06	M	73	22	R	5	No	HA
7	GE10-XRZ-07	F	56	30	R	No hearing aid	Yes	HA
8	GE10-XHS-08	F	65	15	L	No hearing aid	No	HA
9	NL06-GWK-01	F	57	32	R	32	No	HA
10	NL06-JPV-02	F	57	11	L	11	Yes	HA
11	NL06-XJH-03	M	71	15	L	No hearing aid	No	HA
12	NL06-JCJ-04	M	52	Unknown	R	14	No	HA
13	NL06-GHP-05	F	79	Unknown	L	unknown	No	HA
14	CH02-XSM-01	F	62	40	R		Yes	CI (2010)
15	CH02-XFL-02	F	48	25	R	1.5	Yes	HA

HA = hearing aid. CI = cochlear implant

Statistics

The statistical analysis was done with PASW 18.0 (SPSS Inc., Chicago, IL, USA) and included a normality test and a test on significant differences between pairs. Depending on the outcome of the normality test and the number of complete data sets, the paired Student's t-test (Student's t-test) or the Wilcoxon matched-pairs signed-rank test (Wilcoxon) was used to test statistical significance. The significance level was set to p= 0.05.

Results

Audiological outcome

All post-operative results shown and explained are the data from the 3 months follow-up visit i.e. three months after activation of the device.

Pre- and post-op audiometry

The mean pre- and post-operative air and bone conduction thresholds of all fifteen subjects are shown in **Figure 4**.

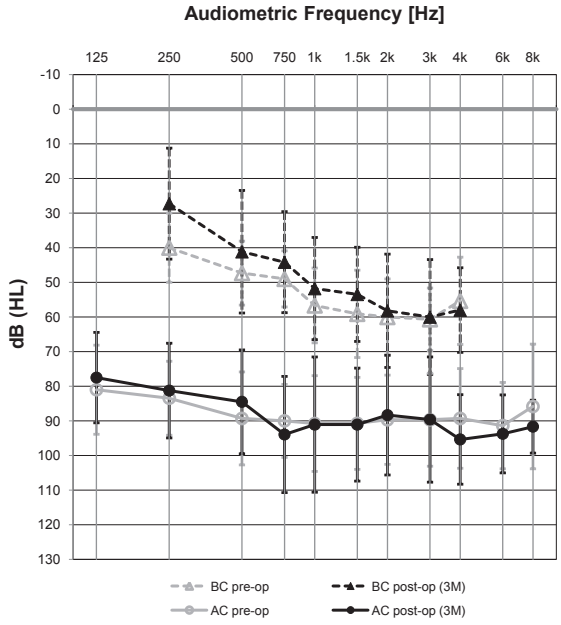


Figure 4 Mean (n = 15) preoperative and postoperative air and bone conduction thresholds. Error bars represent SD.

Pre-operatively, the patients, on average, had a severe to profound mixed hearing loss with a moderate sensorineural component and a mean air-bone gap of 46 dB. The pure tone average (PTA: average of air conduction thresholds at 0.5, 1 and 2 kHz) did not change significantly by the Codacs ID procedure (90 dB HL pre-op vs. 88 dB HL post-op; $p > 0.05$ in all frequencies). The bone conduction thresholds, however, improved significantly at 750 Hz (Wilcoxon, $p = 0.041$), 1 kHz (Student t-test, $p = 0.01$) and 1.5 kHz (Wilcoxon, $p = 0.016$) compared to the pre-operative bone conduction thresholds. The air-bone-gap increased significantly at one frequency only (500 Hz, Wilcoxon, $p = 0.044$).

Sound field Audiometry

Pre-operatively the sound field thresholds were measured monaurally unaided and aided with the subject's hearing aid (if the subject wore a hearing aid pre-operatively). Post-operatively, the sound field thresholds were measured monaurally in aided condition with the DACI ID. An overview of the results is shown in **Table 2**.

Table 2 Mean unaided and aided sound field thresholds and improvements by Codacs ID and HA.

Mean Sound Field Thresholds / Improvement	n = 15	n = 11
Pre-operative unaided [dB HL]	86	83
Pre-operative aided by HA [dB HL]		52
Post-operative aided by Codacs ID [dB HL]	38	37
Improvement by HA [dB HL]		31(*)
Improvement by Codacs ID [dB HL]	48*	46*
Codacs improvement compared to HA		15(*)

*indicate that there is a significant improvement in all (*) or most (*) frequencies

Figure 5 shows the mean sound field thresholds and standard deviations of all patients measured pre-operatively unaided and post-operatively aided with the DACI investigational device at the subject's three months' follow-up visit. The mean (250 Hz to 8 kHz) pre-operative unaided sound field threshold was 86 dB HL, whereas the mean post-operative aided sound field threshold was 38 dB HL. Thus, the mean improvement of the sound field thresholds by the DACI investigational device was 48 dB. The improvement is significant in all frequencies (Student's T-test or Wilcoxon, $p \leq 0.005$ in the frequencies up to 4 kHz, $p = 0.008$ for 6 kHz and $p = 0.043$ for 8 kHz).

Figure 6 shows the mean sound field thresholds and standard deviations of the eleven subjects who used a hearing aid (HA) pre-operatively. The sound field thresholds were

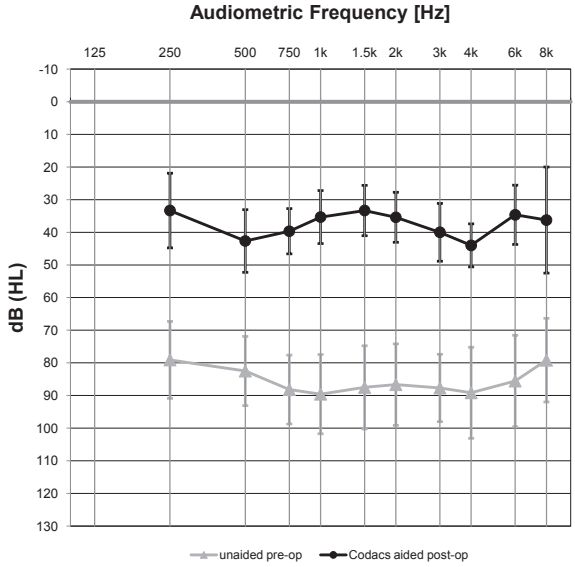


Figure 5 Mean (n = 15) unaided and Codacs ID aided sound field thresholds. Error bars indicate SD.

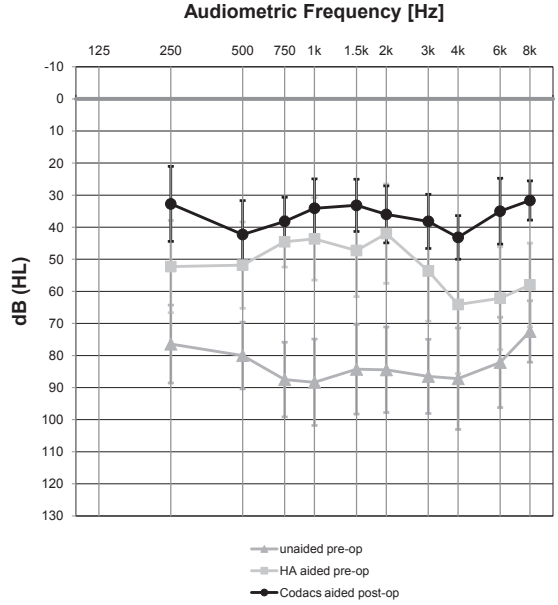


Figure 6 Mean (n = 11) preoperative and postoperative unaided and aided sound-field thresholds. Error bars indicate SD.

measured pre-operatively both unaided and aided with their hearing aid, and post-operatively aided with the DACI investigational device at the subject's three months follow-up visit. The mean (250 Hz to 8 kHz) pre-operative unaided sound field hearing threshold was 83 dB HL, the mean pre-operative HA aided sound field hearing threshold was 52 dB HL and the mean post-operative DACI investigational device aided sound field threshold was 37 dB HL. Thus, the mean improvement of the sound field thresholds by the hearing aid was 31 dB and by the DACI investigational device was 46 dB, i.e. an improvement of 15 dB compared to the hearing aid. The improvement with an acoustic hearing aid is significant in all frequencies (Wilcoxon, $p \leq 0.026$) except for 8 kHz. The improvement with the DACI investigational device is significant in all frequencies (Paired Student t-test or Wilcoxon, $p \leq 0.005$ in the frequencies 250 Hz to 4 kHz, $p = 0.008$ for 6 kHz and $p = 0.043$ for 8 kHz). The improvement of the DACI investigational device aided sound field thresholds post-operatively compared to the HA aided sound field thresholds pre-operatively is significant in all frequencies (Student t-test, $p \leq 0.028$) except at 2 and 8 kHz (Wilcoxon, $p > 0.05$). At 8 kHz, the number of pairs was only five, which might explain why the difference is not significant.

Figure 7 shows the effective gain that is delivered to the inner ear by the DACI investigational device. The effective gain is defined as the difference between the aided sound field thresholds and the bone conduction thresholds (here: pre-op bone conduction thresholds). It reflects the gain which the DACI investigational device delivers to the inner ear and which is accepted by the patient. The average gain over all subjects and frequencies (0.5 – 4 kHz) is 17.2 dB. The greatest gain is achieved at 1500 Hz, the smallest at 500 Hz.

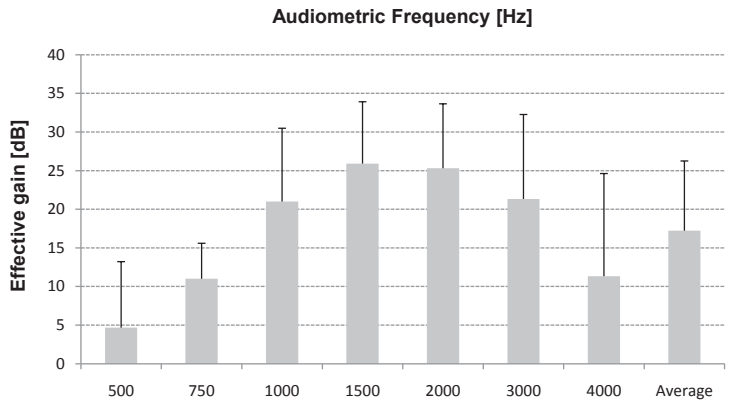


Figure 7 Mean (n = 15) gain delivered to the inner ear for the frequencies 0.5 to 4 kHz and the average of those frequencies. Error bars indicate SD.

Speech Audiometry

To evaluate the speech recognition with the DACI investigational device, the speech reception thresholds (SRT) and the word recognition scores (WRS) were measured using recorded speech (**Figure 8**).

The SRT improved significantly (Wilcoxon, p = 0.008) by 40.7 dB from 91.9 dB SPL pre-operatively to 51.2 dB SPL post-operatively, aided with DACI investigational device. Comparing the aided results from the subjects who wore a hearing aid pre-operatively, the SRT improved significantly (Wilcoxon, p = 0.044) by 12.2 dB, from 61.3 dB SPL pre-operatively aided to 49.1 dB SPL post-operatively aided.

The word recognition scores (WRS) were measured pre-operatively unaided and aided with the subject's hearing aid (if the subject wore a hearing aid pre-operatively, n=11) and post-operatively aided with the DACI investigational device. The mean (n=15) pre-operative unaided word recognition scores at 50, 65 and 80 dB SPL were 0%, 0% and 5.3% (SD: ±15.2 %) respectively. Post-operatively, the mean aided (with DACI investigational device) word recognition scores for all patients were 30.4% (SD: ±31.8%) at 50 dB SPL, 75 % (SD: ± 27.3 %) at 65 dB SPL and 85.5 % (SD: ± 25.3 %) at 80 dB SPL and improved significantly by 30.4%, 75% and 78.2% respectively compared to the pre-op unaided condition (Student's t-test, p = 0.002 for 50 dB, p < 0.001 for 65 and 80 dB).

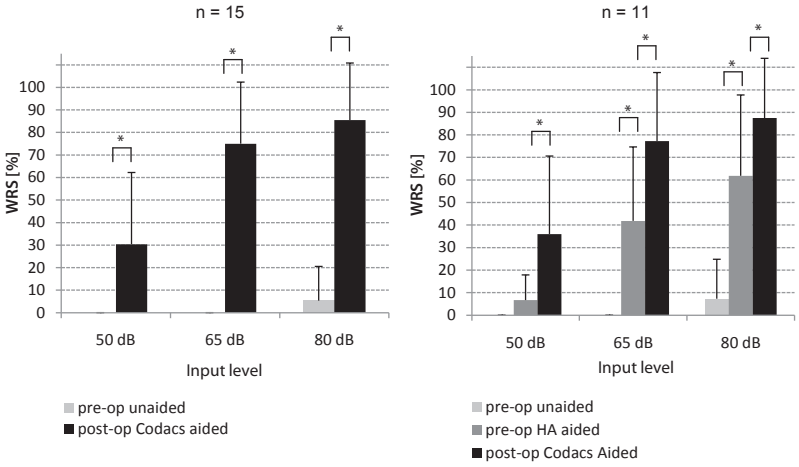


Figure 8 Mean word recognition scores (WRS in % correct) for presentation levels of 50, 65, and 80 dB SPL for the preoperative unaided condition (preop unaided), the preoperative aided condition with hearing aid (preop HA aided), and the postoperative aided condition with the Codacs ID at the 3 months follow-up visit (postop Codacs ID aided) for all patients (n = 15, left graph) and the 11 patients that used a hearing aid preop (right graph). Error bars indicate SD. * p ≤ 0.05.

For the patients that used a hearing aid pre-operatively, the mean (n=11) pre-operative unaided word recognition score at 50, 65 and 80 dB SPL were 0%, 0 % and 7.3 % (SD: ±17.5 %) respectively. The mean (n=11) pre-operative HA aided word recognition scores at 50, 65 and 80 dB SPL were 6.7% (SD: ± 11.2%), 41.8 % (SD: ± 32.8 %) and 61.8 % (SD: ± 35.9 %). The improvement was 6.7%, 41.8 % and 54.5 % respectively compared to the pre-op unaided condition. The mean (n=11) post-operative DACI investigational device aided word recognition scores were 36% (SD: ±34.6%) at 50 dB SPL, 77.3 % (SD: ± 30.4 %) at 65 dB SPL and 87.5 % (SD: ± 26.5 %) at 80 dB SPL, and improved by 36%, 77.3% and 80.2% respectively compared to the pre-op unaided condition, and 29.3%, 35.5% and 25.6% respectively compared to the pre-op aided condition. Post-operatively the mean (n=11) aided (with C-DACS ID) word recognition scores were 36% (SD: ± 34.6%) at 50 dB SPL, 77.3 % (SD: ± 30.4 %) at 65 dB SPL and 87.5 % (SD: ± 26.5 %) at 80 dB SPL and improved by 36 %, 77.3% and 80.2 % respectively compared to the pre-op unaided condition and 29.3 %, 35.5% and 25.7% respectively to the pre-op aided condition. The aided sound field thresholds improved significantly at all levels (50 dB: Wilcoxon, $p = 0.027$; 65 and 80 dB: Student's t-test: $p \leq 0.015$) compared to the pre-operative aided condition. An overview of the word recognition scores is shown in **Table 3**.

Table 3 Mean WRS scores.

	50 dB SPL	65 dB SPL	80 dB SPL
Unaided (n=15)	0%	0%	5.3 %
HA aided (n=11)	6.7 %	41.8 %	61.8 %
C-DACS ID aided (n=15)	30.4 %	75 %	85.5 %

HA = hearing aid.

The individual speech reception thresholds (SRT) in noise for the pre-operative condition (unaided or aided with HA) and the post-operative aided condition (with DACI investigational device) are shown in **figure 9**. If the OLSA or Plomp test was not measureable a value of +10 dB SNR was displayed with an arrow up, indicating that the real SRT was above +10 dB SNR. In 10 of 15 patients the SRT in noise improved, in two patients it was worse (patients 2 and 13) and in three patients it was not measurable pre- and post-op (patients 11, 14 and 15). Individual results show impressive improvements of the SRT in noise of around 7 to 8 dB (patients 1, 3 and 10) or even greater for those patients where the SRT was not measurable pre-op, but post-op (patients 4 - 8) by the Codacs ID implantation. The mean SRT in noise results for the OLSA and Plomp test apart are shown in **Table 4**.
The SRT in noise for the Oldenburg sentence test improved on average by 4.2 dB, from +3.9 dB SNR (SD: ± 3.3 dB SNR) pre-operatively to – 0.3 dB (SD: ± 3.7 dB SNR) post-

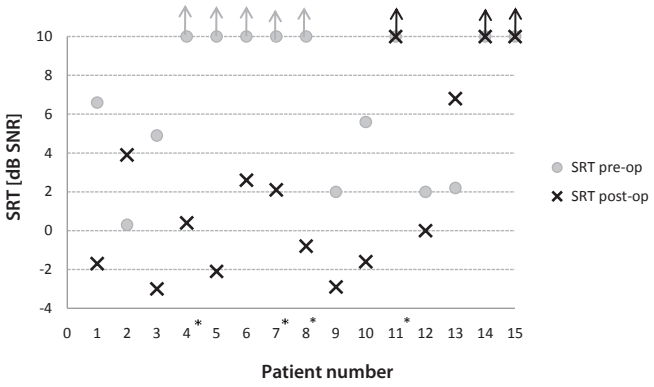


Figure 9 Individual preoperative and postoperative SRT in noise for all 15 patients. Preoperative SRT is measured with hearing aid except for patients indicated with a asterisk.

Table 4 Speech in noise test results.

	Mean SRT pre-op (dB SNR)	Mean SRT post-op (dB SNR)	Improvement SRT pre vs. post (dB SNR)	p-value
OLSA (n=3)	+3.9	-0.3	4.2	p > 0.05
Plomp (n=4)	+3.0	+0.6	2.4	p > 0.05

operatively, which is statistically not significant (Wilcoxon, p>0.05). However, the critical test-retest difference for the OLSA is 1.4 dB SNR and, therefore, a significant benefit is confirmed when the signal to noise ratio of the speech reception threshold decreases by this value [7].

The SRT for the Plomp test improved on average by 2.4 dB, from +3.0 dB SNR (SD: 1.8 dB SNR) pre-operatively to 0.6 dB SNR (SD: ± 4.3 dB SNR) post-operatively, which is statistically not significant either (Wilcoxon, p > 0.05). The standard deviation of the Plomp test is 1 dB and therefore a change of 2.4 dB can be seen as significant benefit.
It should be noted that the post-operative measurements were done without any pre-processing or noise suppression.

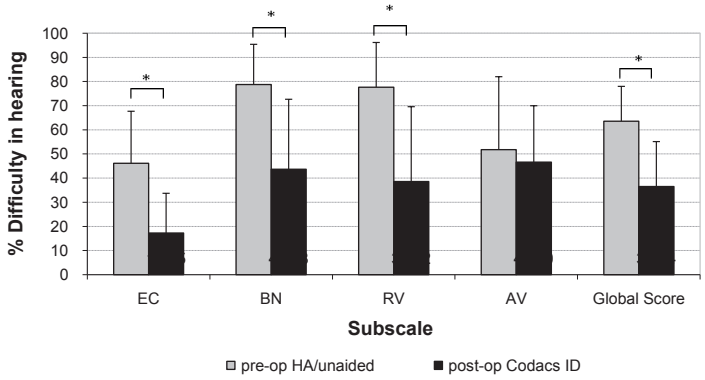


Figure 10 Mean (n = 15) difficulty in hearing shown for the 4 APHAB subscales and the global APAHB score. Error bars indicate SD.

Figure 10 shows the average APHAB subscale scores and the average APHAB total scores for all subjects (n=15) for their pre-operative and their post-operative condition. Please be aware that the APHAB questionnaire is a measurement of the daily condition i.e. with both ears. That means that the condition of the contra-lateral ear (e.g. aided with hearing aid or CI) has an influence on the measurement results. Three subscales (EC, BN, RV) and the global score show a significant benefit with the DACI investigational device compared to the pre-op condition (Student t-test, $p \leq 0.002$). On average the ease of communication improved by 29%, the communication in background noise and reverberation were, respectively, 35 % and 39 % less difficult and the aversiveness decreased by 5.2 %. This results in a total benefit/less difficulty in hearing of 27 % after implantation. The biggest benefit could be achieved for reverberation, the smallest for aversiveness. The aided APHAB scores are close to the median norm as presented by Cox and Alexander. (6)

Adverse Events

During the clinical study ten adverse events occurred. Five adverse events were rated as serious and were reported to the responsible competent authority. The serious adverse events are listed in **Table 5**, the adverse events in **Table 6**. In one patient there was a strange sound sensation after activation of system and hearing was rated as inferior to the preoperative hearing aid condition. This patient underwent revision surgery during which a potential contact of the artificial incus with the surrounding bone was found. After revision the hearing was clearer but still not satisfying. The patient had better results in speech understanding in quiet but not in noise.

Table 5 Serious adverse events.

No.	Patient	Serious adverse event	Procedure related?	Device related?	Outcome
1	GE10-XRK-02	Deterioration of bone conduction thresholds and tinnitus	No	No	Resolved
2	GE10-XJH-03	Facial palsy	Possibly	No	Resolved
3	GE10-XRK-02	Hearing of vibrating noise/feedback	Possibly	Yes	Resolved
4	GE10-XJH-03	Deterioration of bone conduction thresholds	No	No	Resolved
5	GE10-XJH-03	Heart attack	No	No	Resolved

Table 6 Adverse events.

No.	Patient	Adverse event	Procedure related?	Device related?	Outcome
1	NL06-JPV-02	Nausea and vomiting	No	No	Resolved
2	NL06-XJH-03	Bronchitis	No	No	Resolved
3	NL06-XJH-03	Deformed fixation system	No	Yes	Resolved
4	NL06-XJH-03	Deterioration of bone conduction thresholds	Possibly	Possibly	Ongoing
5	CH02-XFL-02	Sensation at receiver site	No	No	Resolved
6	CH02-XFL-02	Tinnitus in new frequency	Possibly	Possibly	Ongoing

Discussion

Audiological results

As presented in the results, no significant increase in averaged post-operative bone conduction thresholds was found. However, some increase of the bone conduction thresholds was found in three patients (12.5, 11 and 16 dB). An explanation may be that the averaged results are balanced by the increase in post-operative bone conduction thresholds in the other subjects. An improvement of BC thresholds has been described by Arnold et al. (8) and Perez et al. (9) in regular stapes surgery. It is indicated that the inner ear

function is, in fact, better than measured in the bone conduction testing caused by fixation of the stapes footplate in the oval window. After opening of the footplate and thereby relieving the fixation, better bone conduction thresholds were measured. (8)
No changes were found for the averaged air conduction thresholds, which indicates that the maximum conductive component – or air-bone gap – was reached already before the disruption of the ossicular chain.
The aided sound field measurements reveal interesting results. For all fifteen subjects a significant benefit is achieved when the device is switched on. But most interesting is the achieved gain in the higher frequency range. Compared to the pre-operative hearing aid gain (**Figure 6**, note n=11), a substantially increase is achieved with the DACI investigational device, which is even significant in most measured frequencies. The most plausible explanation is that the higher frequencies need to be tuned down in the acoustic hearing aid configuration to prevent feedback of amplified sounds. An acoustic hearing aid has to bridge the air-bone gap in case of mixed hearing loss. Due to the high gain the hearing aids have to deliver, they often work at their limit and, thus, the sound might be deteriorated. Also an impedance mismatch in the outer ear canal might be a reason for an irregular transfer of sound to the inner ear for the high frequencies. This is not the case with the DACI investigational device, since there is direct stimulation of the cochlea. Similar results were found in the study by Häusler et al., where the results of the DACS system were compared with acoustic hearing aid results after stapedotomy on the same ear. In that study, the hearing aid to which the DACS was compared featured the same signal processing capabilities and was fitted in the implanted ear (1). Not much has been published on MEI in otosclerosis. Venail et al. (10) presented data of 4 patients with otosclerosis using either the Vibrant Soundbridge (MED-EL, Innsbruck, Austria) or the Middle Ear Transducer (Otologics LLC, Boulder, Colorado, USA). From their figures it is clear that amplification in the high frequencies is poor, significantly poorer than in the mid frequencies (in contrast to the presented results with the DACI investigational device). Other authors reported on the implantation of middle ear implants in otosclerosis patients as well but mostly the aided sound field thresholds are not shown for 6 and 8 kHz or the average of a mixed group with various medical indications is shown (10-15). As the number of otosclerosis patients in those publications is low, there is insufficient data today to draw any firm conclusions yet.
As expected, the achieved WRS and SRT results in quiet with the DACI investigational device are significantly better than the unaided and aided pre-operative results. It is plausible that most of this increase in speech recognition is due to better hearing thresholds and, thus, due to increased audibility. In the literature, no data was found on speech recognition after stapedotomy in combination with regular hearing aid fitting in severe mixed hearing loss. With the percutaneous DACS clinical trial (1) a comparison was possible with an acoustic hearing aid since two stapes prostheses were implanted in the cochlea. (1) We believe that, in the current trial, a large component of the increase in

speech recognition can be ascribed to the direct coupling to the inner ear by the DACI investigational device device, surpassing the air-bone gap.
In contrast to SRT in quiet, which is directly related with audibility, the SRT in noise test is a measure of sound quality. The effects of the direct coupling to the inner ear are most clearly visible in the speech in noise test results. Although no significant difference was achieved because of a large preoperative as well as postoperative difference between the subjects, blunt evaluation of the data shows an impressive improvement of the SRT in the OLSA and Plomp tests. A reason for the improvement might be the better perception of high frequency sounds and/or the reduced sound distortion due to the flat frequency transfer function of the DACI investigational device (2). In three patients the SRT in noise could not be measured post-op. This can be related to the poor results those patients already have in their speech test in quiet post-operatively. At an input level of 65 dB SPL, these three patients did not reach a 50% score. The poor results in the speech tests of these three patients cannot be explained really but it might be that the cochlear reserve and the otosclerotic involvement of the cochlea might play a role. It could be that for those three patients a cochlear implant would be a better solution. Further research needs to be done to find the limits of the DACI investigational device system and to refine the inclusion criteria e.g. set a minimum pre-operative aided WRS score. We recommend to measure the pre-operative word recognition score via headphones up to 100 dB SPL to get an impression of the possible hearing gain by acoustical amplification. As was expected, evaluation of the subjective results by means of the APHAB questionnaire showed a significant improvement in the EC, BN and RV subscales, whilst no significant difference was experienced in the averseness of sounds (AV) subscale. The DACI investigational device aided scores were close to the norm of Cox and Alexander (6).
Concerning the patient who underwent revision surgery two points have to be mentioned. Firstly, the device has to be properly placed with some degree of freedom to prevent a potential contact with surrounding bone structures. Secondly this patient had very good speech recognition scores pre-operatively with her hearing aid so that the incremental improvement which could be achieved by the DACI investigational device was small. Indeed, this patient was initially not satisfied with the DACI investigational device and it took long until she got adjusted to the different type of hearing she had with the DACI investigational device. After two years of use she has accepted the sound and rated it as superior to her hearing with the hearing aid preoperatively. It shows us that in terms of the indications one should not implant patients who are still doing well with their hearing aid and reach monosyllabic word score which bring them close to values of normal hearing people.

Surgical results

The surgical procedure proved to be feasible. No adverse events occurred during the implantation procedure itself. As mentioned in the methods paragraph, two different

approaches were used by the surgeons. Some surgeons preferred the transmastoid approach with a posterior tympanotomy while others preferred the combined approach (transmastoid + transcanal) and set out to implant the DACI investigational device using the combined approach from the start of the operation. The transmastoid approach gave sufficient exposure of the stapes footplate in the six patients where it was used but it could happen that it is necessary to do the combined approach. The disadvantage of the combined approach is that parts of the posterior wall of the outer ear canal have to be removed to have a good view on the stapes footplate. To avoid contact between the tympanic membrane and the artificial incus it is necessary to reconstruct the ear canal with cartilage. The ossicular chain was not reconstructed in any case using a second stapes prosthesis as has been done in the preliminary trial in 4 patients (1).

During the surgery the most described notification was the shortage in length of the rod to which the artificial incus is attached (see **Figure 2**). In some cases, it was difficult to approach the stapes footplate close enough. Therefore, it was not possible in all cases to mount the actuator in the fixation system in the requested area of the actuator housing. The size of the mastoid and the bulging of the sigmoid sinus limited the freedom of rotation for the fixation bracket by the ball joint. No postoperative wound complications occurred. It is crucial to place the transducer with the artificial incus right over the footplate in a distance similar to that of the natural incus in order to be able to place the piston of the stapes prosthesis perpendicular to the stapes footplate. It is also necessary to avoid any contact of the transducer housing, the rod and the artificial incus with surrounding bone or other tissue in order to avoid damping or interference with the sound transfer through the eardrum.

The present implantation procedure took a considerable amount of time, namely an average of 4 hours and 52 minutes (SD: ± 1h26). Nevertheless, the operation time decreased during executive surgeries and the eighth surgery in Hannover could be done in 2 hours and 23 minutes. Time could be gained by the training effect, especially on finding a good position for the fixation system. An important phase is positioning the transducer in the mastoid towards the oval window, fixed in its bracket, avoiding any contact to the posterior bony canal wall. In relatively small mastoids this may be time consuming. Contact with the posterior canal wall will lead to an inadequate transmission of energy to the inner ear, possibly necessitating revision surgery.

Adverse events

In three patients a deterioration of the bone conduction thresholds (drop in PTA of 12.5 dB, 11 dB and 16 dB HL) was measured. In one patient this happened shortly after surgery, in the other two patients it happened after the DACI investigational device was switched on. In all these patients, surgery was uneventful, leaving no clear explanation for this phenomenon. These patients were treated with corticosteroids and in two of the three patients the bone conduction thresholds recovered. The sound processor fitting of the

patient where the bone conduction thresholds did not recover was adapted, and the patient reached the same word recognition scores as before the drop in bone conduction thresholds. Monitoring the sensorineural hearing loss component of the patients' mixed hearing loss is of importance to gather long term data, to evaluate the effect of direct mechanical stimulation of the inner ear.

Limitations

The study protocol implied strict indication criteria for the application of the DACI investigational device. Consequently, the patient group is very specific. Firstly, patients with otosclerosis and a mild sensorineural hearing loss will have no need for a DACI investigational device. They will have sufficient benefit of a stapedotomy, if necessary in combination with a hearing aid. In case of a small air bone gap and a moderate to severe sensorineural hearing loss it is questionable whether a high power hearing aid is indicated or whether a DACI investigational device will provide better results. This has to be investigated in future studies. The word recognition score under headphones measured up to 100 dB SPL might give a hint whether patients will benefit from a DACI investigational device or would rather get a cochlear implant using a hearing preservation procedure. For patients with severe to profound sensorineural hearing loss and limited speech discrimination, a CI might offer better revalidation options. Therefore, counseling is of great importance.

Secondly, the implantation of the present investigational DACI required a considerably otologic experience, as it was technically challenging. Although the fixation system offered three degrees of freedom for the positioning of the actuator, the margins were small. Changes in the system design will have to improve versatility and reduce surgery time.

Furthermore, a weakness of the present study is the lack of standardization in the procedure of the pre-operative acoustic hearing aids. Different types and models of hearing aids were used by the patients. Some of the patients used a cochlear implant contra lateral. This might have led to different fitting settings. However, we experienced that some of the users gave up using their hearing aid due to an unsatisfactory benefit. The other patients had a well selected hearing aid and could benefit from the acoustical amplification.

Further research

Half of the study patients would fulfill the indication criteria to get a cochlear implant. Three of them have a cochlear implant on the contra-lateral ear and prefer the sound of the DACI investigational device to the sound of their cochlear implant. Further research should have a closer look at this patient group and investigate quality of life, and maybe additional subjective measures like music perception, with DACI investigational device compared to cochlear implants. New coupling sites should also be investigated to be able to implant the DACI investigational device in patients with other medical indications like e.g. radical cavities, severe sensorineural hearing loss or other etiologies of mixed hearing loss.

Last, but not least, the long term effect of mechanical stimulation of the inner ear fluid is unknown at the moment and needs to be investigated further. Long-term data of the subjects implanted during this clinical trial need to be assessed and analyzed.

Conclusion

Patients with severe-to-profound mixed hearing loss because of otosclerosis can benefit substantially using the Codacs investigational device. The most important criterion for success is that they still have measurable bone conduction thresholds and some speech recognition (via headphones or, e.g., BAHA) in the ear to be implanted. Ideal candidates are patients who had unsuccessful previous stapes surgery. For this nonrandomized patient group, the averaged audiometric results show better hearing thresholds in sound field, as well as a better speech understanding in quiet and noise with the Codacs investigational device when com- pared with preoperative unaided and aided conditions using a state-of-the-art conventional hearing aid. All patients are satisfied with their device and use it daily. The results were gathered up to 3 months after the first device fitting. Although that is a short evaluation period, it should be noted that previous research with the first-generation DACS showed stable results over time (1).

References

1. Häusler R, Stieger C, Bernhard H, Kompis M. A novel implantable hearing system with direct acoustic cochlear stimulation. *Audiol Neurotol* 2008; 13:247-256
2. Bernhard H, Stieger C, Perriard Y: Design of a semi-implantable hearing device for direct acoustic cochlear stimulation. *IEEE Trans Biomed Eng.* 2011; 58:420-8
3. Lenarz T, Schwab B, Kludt E, Mojallal H: First surgical experiences with a transcutaneous Direct Acoustic Cochlear Implant. *Otol Neurotol.* 2013;34 1711-1718
4. Wagener K, Brand T, Kollmeier B. Entwicklung und Evaluation eines Satztests für die deutsche Sprache Teil III: Evaluation des Oldenburger Satztests; *Z Audiol* 1999; 38 (3) 86-95
5. Plomp R, Mimpen AM. Improving the reliability of testing the speech reception threshold for sentences. *Audiology* 1979; 18:43-52.
6. Cox RM, Alexander GC: The abbreviated profile of hearing aid benefit. *Ear Hear* 1995; 16:176-186
7. Brand T. Binaural speech intelligibility, Proceedings of the 49th International Congress of Hearing Aid Acousticians, Frankfurt am Main, 2004
8. Arnold A, Fawzy T, Steinhoff HJ, Kiefer J, Arnold W. Influence of a totally open oval window on bone conduction in otosclerosis. *Audiol Neurootol* 2011;16(1):23-8
9. Perez R, de Almeida J, Nedzelski JM, Chen JM. Variations in the "Carhart Notch" and overclosure after laser-assisted stapedotomy in otosclerosis, *Otol Neurotol* 2009; 30(8):1033-1036
10. Venail F, Lavieille JP, Meller R, Deveze A, Tardivet L, Magnan J. New perspectives for middle ear implants : first results in otosclerosis with mixed hearing loss. *Laryngoscope* 2007; 117(3):552-555
11. Baumgartner WD, Böheim K, Hagen R, et al. The Vibrant Soundbridge for conductive and mixed losses: European multicenter study results. *Adv Otorhinolaryngol* 2010; 69:38-50
12. Beltrame AM, Martini A, Prosser S, Giarbini N, Streitberger C. Coupling the Vibrant Soundbridge to cochlea round window: auditory results in patients with mixed hearing loss. *Otol Neurotol.* 2009; 30:194-201
13. Bernardeschi D, Hoffman C, Benchaa T, et al. Functional results of Vibrant Soundbridge middle ear implants in conductive and mixed hearing losses. *Audiol Neurotol.* 2011; 16:381-387
14. Dumon T. Vibrant Soundbridge middle ear implant in otosclerosis: technique – indication. *Adv Otorhinolaryngol.* 2007; 65:320-322
15. Dumon T, Gratacap B, Firmin F, et al. Vibrant Soundbridge middle ear implant in mixed hearing loss. Indications, techniques, results. *Rev Laryngol Otol Rhinol* 2009; 130:75-81
16. Martin C, Deveze A, Richard C, et al. European results with totally implantable Carina placed on the round window: 2-year follow-up. *Otol Neurotol.* 2009; 30:1196-203
17. Rajan GP, Lampacher P, Ambett R, et al. Impact of floating mass transducer coupling and positioning in round window vibroplasty. *Otol Neurotol.* 2011; 32:271-7

3.2.

Long term repeated outcome of an experimental direct acoustic cochlear implant

To be published as

Long term repeated audiometry outcome of an experimental direct acoustic cochlear implant.

Zwartenkot JW, Snik AFM, Noten J, Mulder JJS, Mylanus EAM (2016)

Abstract

Objective: To study the stability of audiometric, functional and subjective results for patients implanted with the Codacs™ ID Direct Acoustic Cochlear Implant (Cochlear Ltd., Sydney) for mixed hearing loss due to otosclerosis.

Patients and methods: A retrospective study was performed in a tertiary academic center in a pre- and post-intervention design with multiple post intervention hearing aid measurements and patient questionnaires. Five patients with severe to profound mixed hearing loss due to otosclerosis were implanted with the Codacs ID in the European phase 1 trial. The changes in hearing disability and handicap were evaluated using the Abbreviated Profile of Hearing Aid Benefit (APHAB) and a questionnaire on daily usage. Aided and unaided pure tone and speech audiometry, aided thresholds and speech in noise recognition were measured on three evaluation moments and compared to pre-operative results.

Results: The mean follow up periods were 19 and 40 months. One patient suffered from decrease in sensorineural hearing. The overall aided and unaided thresholds showed stable values compared with the short term results. Pure tone averaged results did not differ significantly from the pre-operative hearing aid results. The aided speech reception and speech in noise recognition values showed a significant improvement compared to the baseline. APHAB scores were equally improved from the pre-operative situation. All five patients used their implant on a daily basis and were content with the device. No device failure or complications occurred.

Conclusions*:* The Codacs ID provides stable improvements up to 40 months after implantation. A significant improvement of speech understanding and speech in noise was found compared to pre-operative hearing aid results. One patient suffered from sensorineural hearing loss and was a poor performer. No other changes in residual hearing were found and other technical or medical complications did not occur.

Introduction

For many years otosclerosis patients have been successfully treated for conductive and mixed hearing losses by regular stapes surgery. Fixation of the stapes footplate in otosclerosis, leading to a conductive hearing loss, was treated by improving the connection between the ossicular chain and the inner ear fluid with a prosthesis during stapedotomy or stapedectomy.
In case of mixed hearing loss due to a combination of stapes fixation and cochlear otosclerosis, the hearing loss is only partially solved by stapes surgery alone. The sensorineural part of the hearing loss will remain and is in most cases treated with regular hearing aid fitting. For advanced sensorineural hearing loss due to otosclerosis, cochlear implants have been introduced (1,2). After systematic reviewing, the results comparing cochlear implants to stapedotomy combined with hearing aids, this option should be reserved as a second choice (3,4).
More recently, middle ear implants have been successfully applied in patients with mixed hearing loss due to otosclerosis (5-8). Both the round window application of the Vibrant Soundbridge (Med-El, Innsbruck, Austria) as the power stapes or vibroplasty technique have been introduced for mixed hearing loss (9-18). The mechanically enhanced vibrational energy is transduced onto the oval or round window by the floating mass transducer (FMT) of the vibrant soundbridge. Despite the good audiological results, the maximum output varies between 65 and 85 dB HL, depending on the coupling effectiveness (19,20).
With the introduction of direct acoustic cochlear stimulation (DACS) by Häusler in 2008, a new treatment option became available (21). This technique combines the application of a regular stapedotomy piston with the surgical placement of an actuator with a so called artificial incus. The magnet in the actuator drives de incus and directly transduces the inner ear fluid through the coupled stapes piston. This device was further developed and tested in a phase 1 clinical study under the name of Codacs investigational device (Codacs ID) (Cochlear Ltd, Sydney, Australia). The application aims to aid patients with a mixed hearing loss as a results of otosclerosis with bone conduction thresholds worse than 30 dB HL (22).
This study presents a follow-up report of the Dutch cohort of the phase 1 clinical study. All measurements were repeated after approximately 1.5 year and 3 years to determine the patient satisfaction and stability of the audiological results.

Materials and methods

Device description and intervention

The Codacs ID has been previously described in the phase 1 European trial report. It is based on the principle of direct acoustic cochlear stimulation and exists of an internal implantable part with a magnetic receiver under the skin of the retroauricular skull that

connects to the actuator which is placed in a bracket that is mounted in the mastoid cavity. Regular stapedotomy surgery is performed and the piston is coupled to the artificial incus. For all surgical details and device specifications we refer to the clinical trial report (22).

Subjects

All five Dutch participants of the European trial (three women and 2 men) were included in the follow-up study. **Table 1** presents the patient characteristics. Mean age at the moment of measurement 1 postoperative was 64 years and the mean duration of follow-up was 20 and 40 months after implantation.

Table 1 Patient characteristics.

Subject	Gender	Side	Age (y)	FU (months)	FU (months)
NL06-GWK-01	F	R	59	22	43
NL06-JPV-02	F	L	55	20	41
NL06-XJH-03	M	L	71	20	39
NL06-JCJ-04	M	R	56	16	39
NL06-GHP-05	F	L	80	18	37
		Mean	64.2	19.2	39.8
		SD	10.9	2.3	2.5

Age at time of measurement and duration of follow up since implantation.
F = female, M = male. FU = follow up

Study design

In this study we have repeated the three months' measurements of the phase 1 clinical trial approximately one and a half and three years after implantation: unaided air conduction (AC) and bone conduction (BC) hearing thresholds, aided sound level thresholds, (un-)aided word recognition scores (WRS) and speech reception thresholds (SRT), as well as speech understanding in noise (Plomp testing, abbreviated to SIN). Patient satisfaction and subjective benefit in hearing disability was tested by the Abbreviated Profile of Hearing Aid Benefit (APHAB) (23). Daily use was tested with a specifically adapted questionnaire (**table 2**). The measurements at approximately 40 months was after fitting the new CP810 processor.

Table 2 Daily questionnaire outcome

Are you still using your Codacs?	Yes	5 (100)
	No	0 (0)
How many hours per day have you been using the Codacs on a regular basis?	Not worn	0 (0)
	1-4 hours a day	1 (20)
	4-8 hours a day	4 (80)
	> 8 hours a day	0 (0)
In general, is your Codacs worth the effort?	No	0 (0)
	A little	0 (0)
	Moderately	2 (40)
	Much	3 (60)
	Very Much	0 (0)
Do you have difficulties placing your Codacs?	Yes	0 (0)
	No	5 (100)
Can you handle the controls of your Codacs well?	Yes	5 (100)
	No	0 (0)
How do you judge the sound of the Codacs?	Very Good	3 (60)
	Good	0 (0)
	Reasonable	2 (40)
	Bad	0 (0)
	Very bad	0 (0)
Would you recommend a Codacs to a friend with the same hearing loss as yours?	Yes	4 (80)
	No	1 (20)
How much would you be willing to pay for you Codacs yourself?	Nothing	0 (0)
	€ 500	1 (20)
	€ 1000	1 (20)
	€ 2500	0 (0)
	€ 5000	3 (60)
Would you, based on your experience with your Codacs, choose your Codacs again?	Yes	3 (60)
	No	2 (40)

Statistics

The statistical analysis was done with IBM SPSS Statistics 20.0 (IBM Armonk, NY, USA) and included a normality test and a test on significant differences between pairs (Student's t-test or the Wilcoxon matched-pairs signed-rank test (Wilcoxon). The significance level was set to $p = 0.05$.

Results

General results

All five of the originally included patients participated in the follow up study. The mean follow-up duration was 19 and 40 months after implantation (**see table 1**). All patients were using their implant daily, although patient 3 was using it only for less than 4 hours (see **table 2**). The other patients used their device 4 to 8 hours per day. The device was considered moderately to much worth the effort and 80% would recommend the device to other patients, although only 60% would reconsider the device based on their current experience. On average, the patients would have been willing to pay approximately 3300 Euros for the device. No difficulties in placing or handling the device occurred and the quality of the sound was considered very good by 3 patients and reasonable by 2 patients, which was in accordance with the poorer outcome in audiological results for the latter two patients (specifically patient 3 and 5).

Residual hearing and benefit

Table 3 presents the results of all tone audiometry measurements. The mean bone conduction pure tone average for 0.5, 1, 2 and 4 kHz (PTA4) at baseline was 52 dB HL, although the patients varied strongly. During follow-up, the PTA4 mean results were 49 dB HL at 3 months, 51 dB HL at 19 months and 57 dB HL at 40 months (one missing value). The results of the mean PTA4 were analyzed using paired t-testing. For the follow-up results compared to the baseline, no significant differences ($p>0.05$) were found for the mean pre- and postoperative comparison of PTA4 thresholds for bone thresholds. Nevertheless, patient 3 suffered a decrease in residual hearing (10 decibels over all frequencies).

The mean air conduction PTA4 thresholds pre-operatively were 88 dB HL, resulting in a mean air-bone gap of 36 dB HL. After surgery, due to the disconnection of the stapedo-incudial joint, this air-bone gap remained and increased to 44 dB HL. The air conduction thresholds were 93 dB HL at 3 months, 95 dB HL at 19 months and 89 dB HL at 40 months (three missing values for the latter). For the 40-months results to few data was available for correct statistical analysis. For the 3 months and 19 months results, the comparison to the base line air conduction data shows no significant differences ($p>0.05$).

The free field audiometry PTA4 results were compared for the unaided pre-operative situation versus the postoperative aided situation. The mean unaided PTA4 was 83 dB HL and the long term aided results 35 dB HL for 3 months, 39 dB HL for 19 months and 41 dB HL for 40 months. Paired t-testing shows stable and significant results (all $p<0.001$). Compared to the aided pre-operative situation with a hearing aid (4 patients available, mean PTA 41 dB HL), no significant benefit could be determined ($p>0.05$). Because of this insignificance, we analyzed the results per frequency. As can be seen in the **figure 1**, the benefit between the aided conventional hearing aid and the Codacs ID is specifically

Table 3 Audiometry results of the implanted ear per patient.

Subject	Baseline				3 months			19 months			40 months		
	BC	AC	unaided	aided	BC	AC	aided	BC	AC	aided	BC	AC	aided
NL06-GWK-01	45	93	84	44	33	81	30	41	93	35	40	83	33
NL06-JPV-02	36	73	64	35	25	69	31	26	75	30	x	x	36
NL06-XJH-03	60	94	96	x	73	106	40	71	108	48	71	x	53
NL06-JCJ-04	60	84	81	43	55	105	34	45	100	40	55	95	40
NL06-GHP-05	59	98	90	41	60	105	39	69	100	41	60	x	45
mean	52	88	83	41	49	93	35	51	95	39	57	89	41
sdev	10.8	10.0	12.2	3.9	19.7	17.2	4.5	19.2	12.4	6.6	13.0	8.8	7.8
P vs unaided *					0.55	0.41	0.001	0.79	0.10	0.001	0.54	x	0.001
P vs aided ~							0.07			0.12			0.55

Mean values for 500, 1000, 2000 and 4000 Hz (PTA4) in dB HL for bone conduction (BC) thresholds, air conduction (AC) thresholds and free-field audiometry thresholds unaided and aided (conventional hearing aid pre-operative).

* P-value of paired t-test compared to baseline for BC and AC, compared to unaided baseline for free field audiometry.

~ P-value of paired t-test in free field audiometry compared to baseline aided conditions (n=4).

present in the frequencies from 4 kHz and higher. When separately comparing the paired t-test results for the 6 kHz (all FU moments) and 8 kHz frequencies (only available for 3 and 19 months) to the aided pre-operative situation, a significant benefit ($p<0.05$) is found.

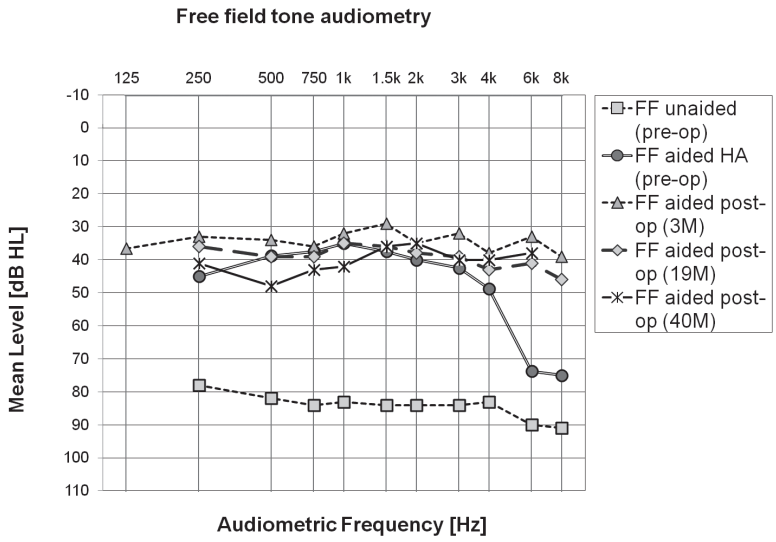


Figure 1 Free field audiometry (FF) results per evaluation moment.

Speech understanding and speech in noise

In **table 4** the results of the speech tests are presented. The mean pre-operative unaided SRT was 81 dB HL, with poor results for patient 3 and 5. Four patients, except patient 3, used hearing aids and were tested in pre-operative aided conditions with an average SRT of 42 dB HL, which is a benefit of 35.5 dB HL (see **figure 2**). At the 3 month measurements, all 5 patients had an improved SRT with a mean of 36.4 dB HL. Patient 3 was not able to score better than 60% correct word scores at 80 dB HL, which was in accordance with his pre-operative score of maximum 60% correct at 120 dB HL. For the 19 months' measurement his word score and SRT had worsened and for the 40 months' measurement, he was not able to score better than 40% at 80 dB HL. The results for the other 4 patients remained stable and significant compared to the unaided conditions ($p>0.01$) and also significantly better compared to aided pre-operative conditions ($p>0.05$) at 19 and 40 months, with an improved benefit compared to the preoperative hearing aids of 12.6 dB HL and 7.8 dB HL respectively (see **figure 2**).

Table 4 Audiometry results of speech reception thresholds (SRT) and speech in noise ratios (S/N) thresholds in dB HL.

Subject	Baseline			3 months		19 months		40 months	
	SRT unaided	SRT aided	S/N aided	SRT aided	S/N aided	SRT aided	S/N aided	SRT aided	S/N
NL06-GWK-01	73	40	2.0	20	-2.9	21	-1.9	26	x
NL06-JPV-02	54	34	5.6	20	-1.6	26	-2.6	30	x
NL06-XJH-03	95	x	nm	40	nm	60	nm	nm	x
NL06-JCJ-04	72	35	2.0	45	0	23	0.9	30	x
NL06-GHP-05	110	58	8.4	57	6.8	33	5	50	x
mean	80.8	41.8	4.5	36.4	0.6	32.6	0.4	34.0	x
sdev	21.9	11.1	3.1	16.2	4.3	16.0	3.4	10.8	x
P vs unaided		0.013		0.002		0.005		0.010	
P vs aided				0.421	0.059	0.024	0.068	0.041	

Measurements with the implanted ear activated and the unimplanted ear closed off. P-value of paired t-test; n=5 for unaided and n=4 for aided conditions.

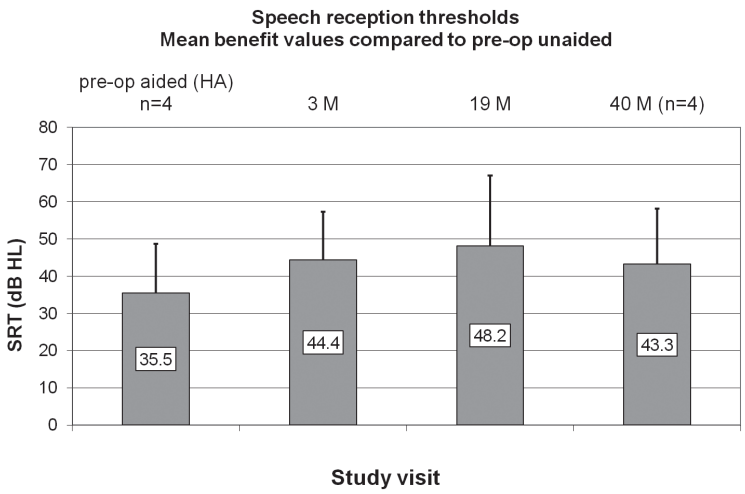


Figure 2 Benefit in speech reception thresholds compared to pre-operative unaided conditions.

HA = hearing aid. N = 4 patients, excluding patient 3.

For the analysis of the word recognition score (WRS) we have separated the results of patient 3 for the statistical analysis, see **figures 3a and 3b**. Due to poor WRS scores pre- and postoperatively and a decline in residual hearing, these results were considered as 'outliers'. The mean data for the other 4 patients is presented in **figure 3a**. Unfortunately, no test was taken from patient 2 during the 40 month evaluation. The mean pre-operative unaided scores were 0% for 50 and 65 dB HL and 16.5% for 80 dB HL. A significant benefit is achieved for the aided conditions postoperatively (not shown, $p>0.05$), except for the 50 dB HL results with the hearing aid pre-operatively and at 40 months. When comparing the aided conditions with Codacs ID compared to the hearing aid pre-operatively, the only significant difference is found for all three presentation levels at 3 months ($p>0.05$).
For the speech in noise (SIN) test, data was available at 3 and 19 months. Because of the poor speech results, patient 3 was not considered in the analysis. **Figure 4 and table 4** present the results. The mean speech-to-noise ratio (S/N) improved from 4.5 dB pre-operatively with hearing aids to 0.6 dB (3 months) and 0.4 dB (19 months).

Subjective results

For the comparison of the subjective benefit we analyzed the APHAB questionnaires before implantation and at the different follow-up moments (**figure 5**). For the 40 months' evaluation, the data for patient 4 was missing. Nevertheless, a significant improvement was found for the categories ease of communication, background noise and reverberation

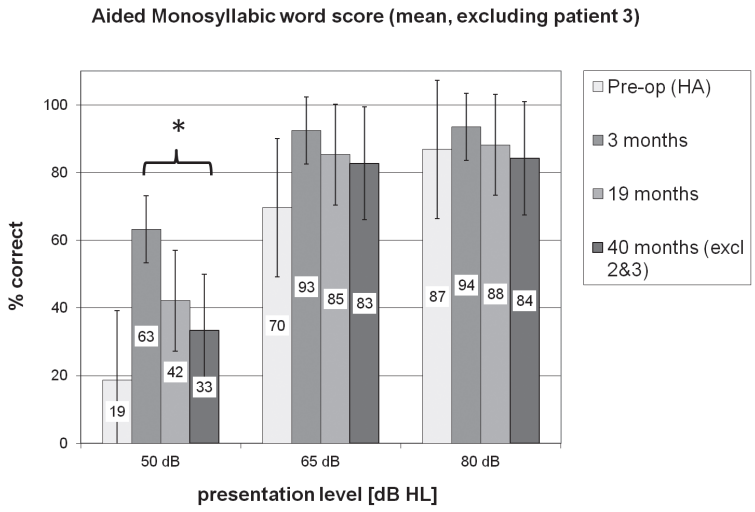


Figure 3a Aided monosyllabic word score.

Patient 3 was excluded. For 40 months results, missing values for patient 2. HA = hearing aid. * = significant benefit compared to pre-operative hearing aid ($p>0.05$).

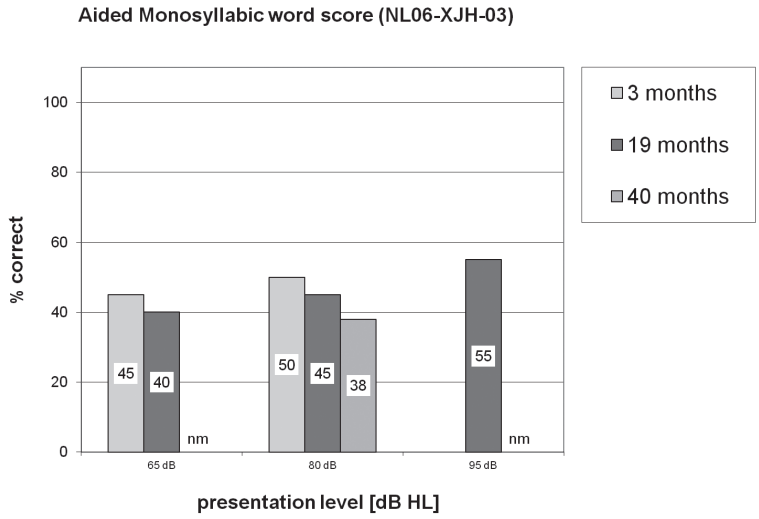


Figure 3b Aided monosyllabic word score for patient 3.

Nm = not measurable. Pre-operative scores not measurable for all frequencies.

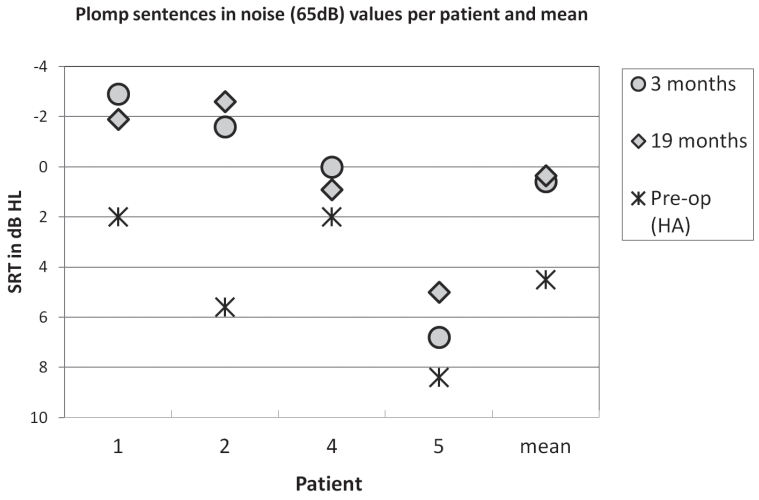


Figure 4 Speech in noise results per patient and mean results.

Patient 3 has missing data. HA = hearing aid. SRT = speech reception threshold.

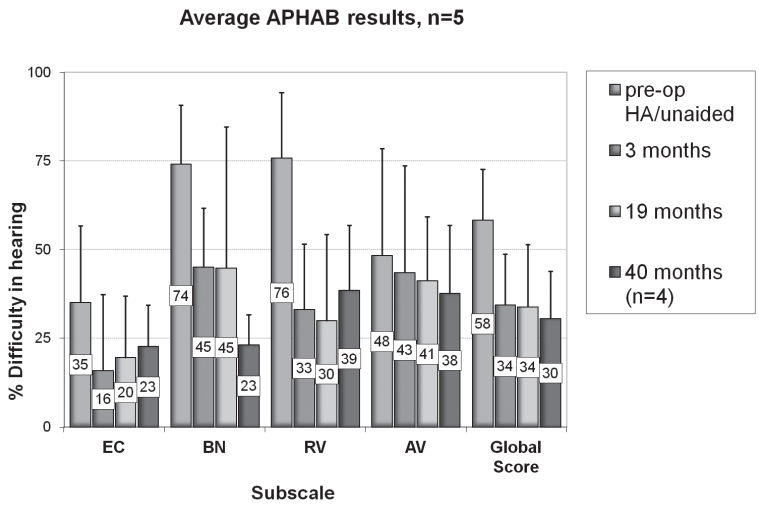


Figure 5 Results for APHAB questionnaire.

EC = ease of communication, BN = background noise, RV = reverberation, AV = aversiveness, HA = hearing aid.
* = significant benefit p > 0.05, compared to pre-operative with hearing aid. Missing data for patient 4 at 40 months.

($p<0.05$). The Codacs ID did not bring any improvement in the aversiveness category in any of the evaluation moments. In total, a significant global score improvement was found for all moments, almost halving the percentage of difficulty in hearing from 58% to 30%. When analyzing the data according to Cox and Alexander, all 5 patients meet the criteria of significant improvement (viz. 10% improvement on EC, BN and RV subscales or 22% in a single scale) for both the short term as the long term follow up results (24).

Complications

During the evaluation period no adverse events, complications or device failures have occurred.

Discussion

This article provides long term audiometric results on the Nijmegen cohort of the original phase 1 clinical trial patients for patients implanted with a Codacs ID direct acoustic cochlear implant. After three years a stable audiological outcome is found, with a significant improvement compared to the baseline measurements. Nevertheless, some findings are notable.

First of all, one patient (XJH-03) suffered a decrease in residual hearing of 10-15 dB HL and poor audiological outcome three months after surgery. He was treated with corticosteroids but only few of his residual hearing improved. His aided PTA4 was 35 dB HL before the event and did only improve to 40 dB HL after 6 weeks. At 1.5 years post-surgery the aided PTA4 was 47.5 dB HL and at 3 years 52.5 dB HL. His aided WRS was maximally 60% at 80 dB HL, both before and after the intervention with corticosteroids. On the long term he did not further improve with the Codacs ID and speech in noise measurements could not be completed. At the 40 months measurements his maximum speech understanding was 40% at 80 dB HL. His poor results are, beside the sudden loss in residual hearing, probably also explained by the 15 years duration of deafness and sound deprivation on the implanted ear.

For the other four patients, the long term results are more rewarding. The results in aided thresholds show a significant improvement over the pre-operative hearing aid in the 6 kHz and 8 kHz frequencies (**figure 1**), that is stable during the follow-up period. Nevertheless, the difference in SRT of 7.8 dB HL on the long term compared to pre-operative hearing aids did not show any significant statistical result ($p > 0.05$), see **figure 2**.

The aided monosyllabic WRS show a stable trend for the long term results (**figure 3a**). No difference was found compared to the pre-operative hearing aids for the louder sounds (80 dB HL). For the long term results at 65 dB HL a difference of 13% was found that did not prove to be significant. The softer sounds at 50 dB HL shows a decreasing trend compared to the baseline measurements. The long term improvement of 14% is still significant ($p < 0.05$). If we analyze the individual data (not presented), patients 1 and 4 show better improvements than patients 2 and 5 on the softer speech results (50 dB HL). For the presentation level at 65 and 80 dB HL, patients 1, 2 and 4 show equally well improved results, whereas patient 5 did only improve slightly. She also suffered from speech discrimination loss (maximum WRS result of 80% correct at 80 dB HL). This is probably as a result of presbyacusis at her age of 80 years.

Another notable result is the improvement in speech in noise. **Table 3b** and **figure 4** present the individual values for three evaluation moments. Especially patient 2 did improve impressively. Looking back, we believe that her pre-operative result with the hearing aid should probably be considered too poor. This might be explained due to conservative fitting of the hearing aid, since her aided pre-operative WRS at 65 dB HL was only 70 %. Analyzing the SRT results, we can calculate that the gain of the hearing aid was set at about 20 dB HL, as the unaided pre-operative free field SRT was 54 dB HL compared to 34 dB HL with the hearing aid switched on. Nevertheless, a stable result in the SIN tests with the Codacs ID is found for the other three patients, where the 19 months result of patient 5 even improved. No significance ($p>0.05$) was found for the mean benefit for the four patients of 4.1 dB HL signal to noise ratio. Considering the conservative fitting of patient 2, this benefit might be considered as too optimistic.

Benefit

We compared our results with the data by Busch et al. from another direct acoustic cochlear implant called DACS PI (Phonak Acoustic Implants SA, Lonay, Switzerland) which is no longer continued (25). This paper presents the results of 9 patients with otosclerosis, with the same hearing thresholds indication range. A comparable aided result is found with a mean PTA4 gain of 56 (±10 SD) dB HL with the DACS device, versus 53 (± 9.5 SD; n=4) dB HL in our study. The mean improvement in SRT at 6 months was about 10 dB, which is accordance with our study (16 dB at 19 months and 8 dB at 40 months). An improvement of the SNR was found of 3.5 dB versus hearing aids, which was 4.1 dB improvement in our study (19 months result). The aided WRS was comparable with our results (around 85% at 65 dB HL and around 90-95% at 80 dB HL). The APHAB results were globally assessed equally.

When comparing our data to the results of Lenarz & Verhaert et al. comparable results our found (26). In their study 19 patients were implanted with a Codacs ID, although 4 patients did not suffer from otosclerosis as a cause for their mixed hearing loss. A slightly smaller PTA4 gain improvement was found of 45.9 dB HL. An overclosure of the bone conduction thresholds was found in their study, which we could not establish in our data. The aided WRS outcome was comparable. The benefit in the APHAB score in their study was equal to our results (28% benefit), although the overall value was higher both before as after implantation.

Future options

Although the Codacs device has been developed to be applied in otosclerosis patients, some recent studies have presented alternative methods of applying DACI. As in the different coupling methods for the MET and Vibrant Soundbridge, the power of the implant does not necessarily have to be applied to the cochlear fluid by a stapes piston. Since the maximum output of the Codacs is almost unlimited, this would provide a very powerful alternative for the current middle ear implants, although these are much less expensive (20). As presented by Grossöhmichen et al., when connecting the DACI to an intact stapes supra-structure or mobile footplate, the energy could be transferred via a natural way to the cochlear fluid (27). Maier et al. have proven that round window stimulation seems to be an alternative option (28). Finally, Schwab et al. have proven that a DACI could be safely applied in subtotal petrosectomy surgery (29).

MRI incompatibility

When considering the use of acoustic implants, the MRI incompatibility of the devices should always be taken into account. Because of the magnet in the implant receiver, the device itself is not protected to any damage caused by the magnetic field of the MRI-scanner. Secondly, when imaging the head and specifically the brain, distortion will always remain a problem. Therefore, any revalidation option that would provide equal

results in the audiological and quality of life outcome needs to be balanced against the disadvantages or even the need to explant any acoustic implant (30).

Limitations

The conclusions in this article are based on small study groups and referred publications are based on non randomized controlled trials. The level of evidence is therefore poor.

Conclusion

The Codacs ID DACI provides stable results up to 40 months after implantation. A significant improvement of speech understanding and speech in noise was found compared to pre-operative hearing aid results, which was comparable to previous studies. Especially the high frequencies can be stimulated superior to the pre-operative hearing aid. One patient suffered from sensorineural hearing loss and was a poor performer. No other changes in residual hearing were found and other technical or medical complications did not occur. The results in quality of life questionnaires were stable and significant over time.

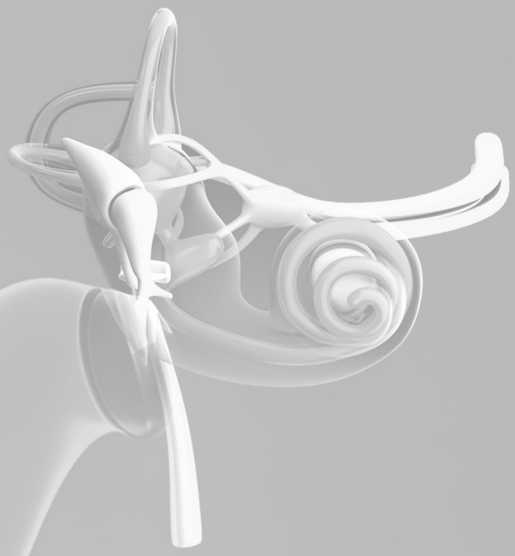
References

1. Ramsden R, Bance M, Giles E, et al. Cochlear implantation in otosclerosis: a unique positioning and programming problem. *J Laryngol Otol* 1997;111:262-5.
2. Rotteveel LJ, Snik AF, Cooper H, et al. Speech perception after cochlear implantation in 53 patients with otosclerosis: multicentre results. *Audiol Neurootol* 2010;15:128-36.
3. Kabbara B, Gauche C, Calmels MN, et al. Decisive criteria between stapedotomy and cochlear implantation in patients with far advanced otosclerosis. *Otol Neurotol* 2015;36:e73-8.
4. van Loon MC, Merkus P, Smit CF, et al. Stapedotomy in cochlear implant candidates with far advanced otosclerosis: a systematic review of the literature and meta-analysis. *Otol Neurotol* 2014;35:1707-14.
5. Colletti V, Soli SD, Carner M, et al. Treatment of mixed hearing losses via implantation of a vibratory transducer on the round window. *Int J Audiol* 2006;45:600-8.
6. Dumon T. Vibrant soundbridge middle ear implant in otosclerosis: technique - indication. *Adv Otorhinolaryngol.* 2007;65:320-2.
7. Venail F, Lavieille JP, Meller R, et al. New perspectives for middle ear implants: first results in otosclerosis with mixed hearing loss. *Laryngoscope* 2007;117:552-5.
8. Bernardeschi D, Hoffman C, Benchaa T, et al. Functional results of Vibrant Soundbridge middle ear implants in conductive and mixed hearing losses. *Audiol Neurootol* 2011;16:381-7.
9. Baumgartner WD, Boheim K, Hagen R, et al. The vibrant soundbridge for conductive and mixed hearing losses: European multicenter study results. *Adv Otorhinolaryngol* 2010;69:38-50.
10. Beleites T, Neudert M, Beutner D, et al. Experience with vibroplasty couplers at the stapes head and footplate. *Otol Neurotol* 2011;32:1468-72.
11. Beltrame AM, Martini A, Prosser S, et al. Coupling the Vibrant Soundbridge to cochlea round window: auditory results in patients with mixed hearing loss. *Otol Neurotol* 2009;30:194-201.
12. Böheim K, Mlynski R, Lenarz T, et al. Round window vibroplasty: long-term results. *Acta Otolaryngol* 2012;132:1042-8.
13. Dumon T, Gratacap B, Firmin F, et al. Vibrant Soundbridge middle ear implant in mixed hearing loss. Indications, techniques, results. *Rev Laryngol Otol Rhinol (Bord)* 2009;130:75-81.
14. Hüttenbrink K-B, Beutner D, Bornitz M, et al. Clip vibroplasty: experimental evaluation and first clinical results. *Otol Neurotol* 2011;32:650-3.
15. Kontorinis G, Lenarz T, Mojallal H, et al. Power stapes: an alternative method for treating hearing loss in osteogenesis imperfecta? *Otol Neurotol* 2011;32:589-95.
16. Mlynski R, Mueller J, Hagen R. Surgical approaches to position the Vibrant Soundbridge in conductive and mixed hearing loss. *Operative Techniques in Otolaryngology-Head and Neck Surgery* 2010;21:272-7.
17. Luers JC, Hüttenbrink K-B, Zahnert T, et al. Vibroplasty for mixed and conductive hearing loss. *Otol Neurotol* 2013;34:1005-12.
18. Beltrame AM, Todt I, Sprinzl G, et al. Consensus statement on round window vibroplasty. *Ann Otol Rhinol Laryngol* 2014;123:734-40.
19. Zwartenkot JW, Snik AFM, Kompis M, et al. Gain and maximum output of implantable hearing devices in patients with moderate to severe sensorineural hearing loss. *Journal of hearing science* 2012;2:35-40.
20. Zwartenkot JW, Snik AF, Mylanus EA, et al. Amplification options for patients with mixed hearing loss. *Otol Neurotol* 2014;35:221-6.
21. Hausler R, Stieger C, Bernhard H, et al. A novel implantable hearing system with direct acoustic cochlear stimulation. *Audiol Neurootol* 2008;13:247-56.
22. Lenarz T, Zwartenkot JW, Stieger C, et al. Multicenter study with a direct acoustic cochlear implant. *Otol Neurotol* 2013;34:1215-25.
23. Cox R. Administration and application of the APHAB. *The Hearing Journal* 1997;50:32-48.
24. Cox RM, Alexander GC. The abbreviated profile of hearing aid benefit. *Ear Hear* 1995;16:176-86.
25. Busch S, Kruck S, Spickers D, et al. First clinical experiences with a direct acoustic cochlear stimulator in comparison to preoperative fitted conventional hearing aids. *Otol Neurotol* 2013;34:1711-8.
26. Lenarz T, Verhaert N, Desloovere C, et al. A comparative study on speech in noise understanding with a direct acoustic cochlear implant in subjects with severe to profound mixed hearing loss. *Audiol Neurootol* 2014;19:164-74.

27. Grossohmichen M, Salcher R, Kreipe HH, et al. The Codacs direct acoustic cochlear implant actuator: exploring alternative stimulation sites and their stimulation efficiency. *PLoS One* 2015;10:e0119601.
28. Maier H, Salcher R, Schwab B, et al. The effect of static force on round window stimulation with the direct acoustic cochlea stimulator. *Hear Res* 2013;301:115-24.
29. Schwab B, Kludt E, Maier H, et al. Subtotal petrosectomy and Codacs: new possibilities in ears with chronic infection. *Eur Arch Otorhinolaryngol* 2015.
30. Wagner JH, Ernst A, Todt I. Magnet resonance imaging safety of the Vibrant Soundbridge system: a review. *Otol Neurotol* 2011;32:1040-6.

4.

Comparison of auditory implants



4.1.

Gain and maximum output of implantable hearing devices in patients with moderate to severe sensorineural hearing loss

Published as

Gain and maximum output of implantable hearing devices in patients with moderate to severe sensorineural hearing loss

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Abstract

Objective: To determine the dynamic range and the maximum output for 3 current middle ear implants and to discuss optimal candidacy in middle ear implantation.

Patients and methods: In a prospective multicenter clinical study we compared gain and output measurements for three types of middle ear implants: Otologics middle ear transducer (MET), Vibrant Soundbridge (VSB), and Direct Acoustic Cochlear Stimulator (DACS). The performance of these selected implants from users with severe, predominantly sensorineural, hearing loss (50-65 dB HL) was studied. Patients with chronic external otitis and sensorineural hearing loss used either a MET (n=9) or a VSB (n=9) implant. The patients with predominantly sensorineural hearing loss after surgically treated otosclerosis used a DACS (n=4). The patients were selected from two different implant teams but evaluated with the same protocol. The relative gain at threshold level was determined, viz. the bone-conduction threshold minus the aided sound-field threshold, divided by the bone-conduction threshold. Input-output measurements were performed with the devices in linear amplification mode and with unlimited output. In this latter data set, the maximum output and the input dynamic range of the devices were determined.

Results: The relative gain for each of the three implants was comparable; however, these values were slightly lower than the generally accepted target values. The input dynamic range of the devices varied, with the widest range for the DACS and Otologics devices.

Conclusion: The results from this study indicate that the first generation DACS device is a good option for patients with moderate/severe sensorineural hearing loss and surgically treated otosclerosis who require a hearing implant.

Background

Several types of implantable hearing systems, or active middle ear implants (AMEI), have been introduced over the last two decades. In 1996, the Vibrant Soundbridge (VSB, Med-El, Innsbruck, Austria) became available for clinical evaluation (1), and this was followed by the Otologics Middle Ear Transducer (MET, Otologics LLC, Boulder, CO, USA). These semi-implantable devices have been successfully applied in patients with sensorineural hearing loss (2-4). These devices typically consist of an actuator that is directly coupled to the ossicular chain and driven by an external audio processor (5). More recently, middle ear implants have also been used in patients with otosclerosis (6-9).

The Direct Acoustic Cochlear Stimulator (DACS) device, introduced in 2006, is a version of a semi-implantable middle ear implant that bypasses the outer and middle ear structures and directly stimulates the cochlea (10,11). The DACS has been used in a feasibility study of patients with moderate/severe sensorineural hearing loss due to otosclerosis.

The DACS system is a power-driven stapes prosthesis; an electromagnetic actuator is implanted in the mastoid cavity and connected to a conventional stapes prosthesis, which directly drives inner ear fluid movement. The external audio processor is connected to the actuator by a percutaneous plug. In the first DACS study, the ossicular chain was reconstructed during the implantation surgery by inserting an additional, passive stapes prosthesis (11). This surgery reduced the air-bone gap and a left a predominantly sensorineural hearing loss for the patients postoperatively.

Traditionally, to measure the gain and output of conventional hearing devices, artificial simulators are used. For middle ear implants, such simulators are not available; therefore, the basic amplification characteristics are typically measured in patients. For example, to measure gain, the functional gain (FG) can be determined by subtracting the aided sound field thresholds from the unaided sound field thresholds. However, measuring FG can be problematic when used for middle ear implant devices for three reasons. First, if an air-bone gap is present after the surgery, this proportionally raises the unaided threshold and will overestimate the FG. The measured FG will then be the sum of the pure device gain plus the post surgery air-bone gap. Second, noise-reduction algorithms, which are often present in current hearing devices including middle ear implants, can interpret test signals as noise and, consequently, reduce amplification. Finally, the middle ear implants studied here make use of adaptive, non-linear amplification. Therefore, sound field threshold measurements evaluate the (relatively high) gain for soft sounds and overestimate the gain for conversational speech levels (12).

An additional basic amplification characteristic is the saturation (SAT) level of the device, which is the loudest input sound that can be properly processed by the device. The input level at the point of saturation can be measured by studying the output behavior of the device. Previous research has shown that it is possible to measure output limitation characteristics objectively with a microphone placed in the ear canal. In the current study, we

have compared the basic capacities of three implantable hearing systems. The gain of the devices was compared in matched patient groups. In addition, the dynamic range and the maximum output of the three devices were determined, while the devices were programmed in linear amplification mode with unlimited output. The results of this study are used to discuss optimal candidacy for current middle ear implants.

Materials and methods

Patients

All data are acquired from patients who used a (unilateral) middle ear implant: 4 DACS users, the only patients with the first generation DACS as described by Hausler et al. (11), 9 VSB users and 9 MET users, who were selected from the Nijmegen database of 55 VSB users and 18 MET users. VSB and MET users were matched with the DACS users based on the degree of preoperative sensorineural hearing loss (criteria: bone-conduction thresholds between 30 and 60 dB HL at 500 Hz and between 50 and 75 dB HL at 4 kHz and a mean hearing loss between 50 and 65 dB HL at 0.5, 1, 2 and 4 kHz) and the length of device use (a minimum of one year).

Figure 1 shows the mean preoperative bone-conduction thresholds of the implanted ear in patients from each group. The VSB and MET users had been provided with implants due to therapy-resistant chronic external otitis. These patients had a predominantly sensorineural hearing loss, although an air-bone gap in the order of 5-10 dB was common. Prior to

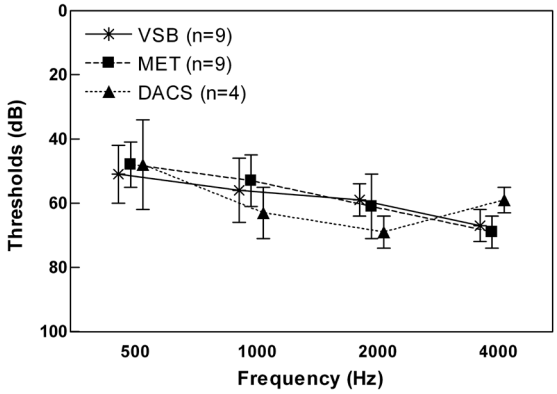

Figure 1 Mean bone-conduction thresholds plotted as a function of frequency for three groups of middle ear implant users: patients using the Vibrant Soundbridge (VSB), the Otologics MET (MET) or the DACS.

Vertical lines represent the standard deviations.

treatment, the DACS patients showed both sensorineural and conductive hearing loss caused by otosclerosis. At the DACS post-operative evaluation, the air-bone gap had been reduced because the fixed stapes had been replaced by a secondary, passive stapes prosthesis (11). A mean air-bone gap of 14 dB remained at 0.5, 1, 2 and 4 kHz (range 6 to 20 dB). The VSB users were fitted with the audio processor 404 (Med-El, Innsbruck, Austria), the MET users were fitted with the Button processor (Otologics LLC, Boulder, CO, USA) and the DACS users were fitted with the Savia 211 processor (Phonak, Staefa, Switzerland). All fittings were performed by experienced audiologists.

Parameters

The two parameters used in this study are a FG-based gain ratio (GR) and the input level at output saturation (ILOS). (13).

Gain ratio (GR)

The bone conduction, based on the functional gain at the threshold level, was defined as the difference between the bone-conduction threshold and the aided threshold. This value, divided by the bone-conduction threshold, was called the gain ratio (GR) and was calculated per frequency. The GR per frequency can be compared with target values, as produced by prescription rules. According to the commonly used NAL-NL prescription rule, for conversational levels, the GR should be 0.46; this indicates that the desired FG should be approximately 0.46 times the hearing threshold (at 1-4 kHz) (14). For softer sounds, ratios higher than 0.46 are prescribed (15). These reference ratios can be used to assess the adequacy of amplification provided by the middle ear implant. This ratio is independent of the patient's degree of hearing loss, unlike the FG. To determine the GR, noise-reduction algorithms were deactivated. All other settings were the patient's daily settings.

Input level at output saturation (ILOS)

To determine the input level at saturation for the three implant devices, the procedure described by Snik et al. was followed (13). Briefly, sound pressure levels were measured with the Aurical REM system in the ear canal of the aided ear (Madsen, Taastrup, Denmark). Measurements were conducted while the ear canal was occluded with an EARlink foam tip (Aearo Company, Indianapolis, IN, USA). After a foam tip was inserted, a probe tube microphone was pushed through the standard opening in the plug. In this manner, the sound pressure level could be measured in the occluded ear canal. Sound pressure levels were recorded as a function of frequency during the presentation of a calibrated frequency sweep produced in the sound field (sweep from 250 Hz to 8 kHz at 60 dB SPL, as standard on the Aurical REM system). The first measurement was carried out with the audio processor off (reference curve), and the measurement was repeated with the audio processor on. The difference curve was used for further analysis. Similar curves were obtained at 50, 70,

80 and 90 dB SPL. From the difference curves, the input level at which the device saturated was determined at 1 kHz and 2 kHz. Figure 3 shows representative data. Output limiting options were deactivated, and the device was programmed in the linear amplification mode.

To measure sound field thresholds, warble tones were presented via a loudspeaker placed 1 meter in front of the patient and calibrated according to Morgan et al. (16) Nine of the 22 patients participated in a special session to measure the output limitation of the devices (three MET users, four VSB users and two DACS users). These patients were randomly selected. The measurements were carried out in sound-proof double-walled rooms.

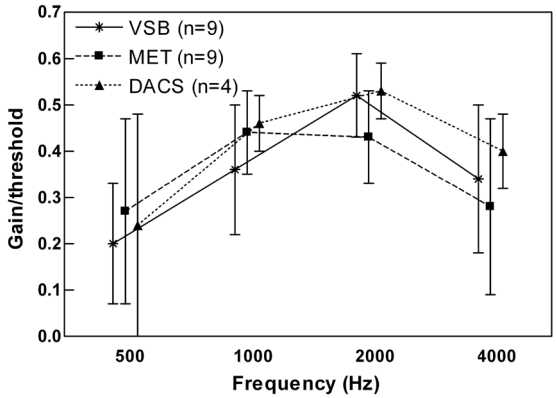

Figure 2 Functional gain at threshold level divided by bone-conduction threshold versus frequency for three groups of middle ear implant users: patients using the Vibrant Soundbridge (VSB), the Otologics MET (MET), or the DACS.

Mean values are displayed with standard deviations.

Results

The GR as a function of frequency is presented in **Figure 2**. The mean data are presented separately for the matched VSB, MET and DACS users. Vertical lines indicate the standard deviations.

A representative example of an input-output measurement, as derived from sound-pressure measurements in the occluded ear canal, is presented in **Figure 3**. After turning the device on, there was an increase of 15-20 dB SPL at 1 to 3 kHz in the ear canal. The data in **Figure 3** are from a patient using a DACS device. These data have a linear increase until the output levels off at an input level of 75 dB SPL at 1 kHz and 80 dB SPL at 2 kHz. In a

second patient with a DACS, the input level at saturation was above 80 dB SPL; this patient could not tolerate stimulation louder than 80 dB SPL. For the other two implant systems, the output saturated at lower input levels. **Figure 4** shows the maximum dynamic range

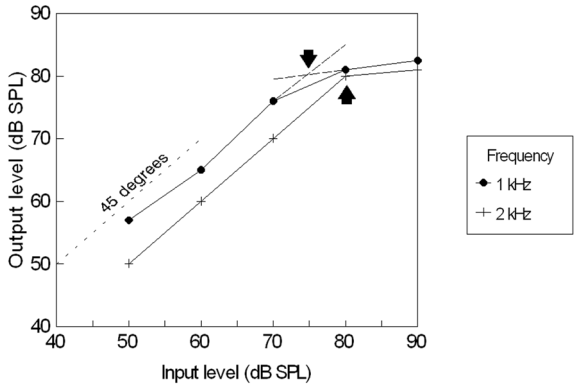

Figure 3 Input-output curves at 1 kHz and 2 kHz obtained from probe-tube microphone measurements in the ear canal of a patient with a DACS device.

The arrows indicate the point of device saturation.

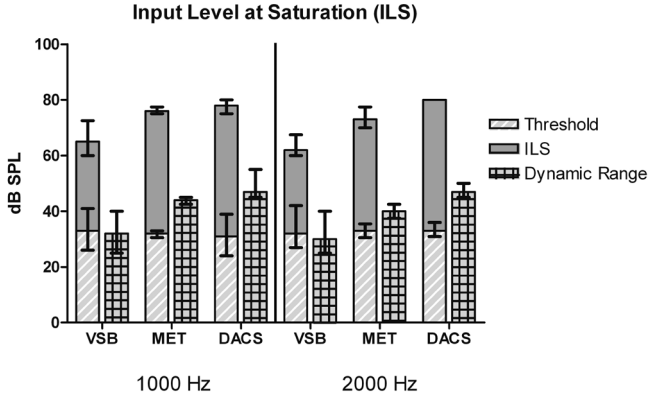

Figure 4 Hearing thresholds (striped), input level at saturation (ILS; grey) and the dynamic range (blocked) for the three groups of patients, as measured at 1 kHz (left columns) and 2 kHz (right columns).

The mean data with the range are presented. The audio processors were programmed in linear amplification mode and the maximum output was not limited.

of the three devices, which is defined as the difference between the input level at saturation and the aided thresholds, expressed in dB SPL, and obtained in the linear amplification mode.

Discussion

In contrast to studies that assess individual benefit and satisfaction levels, the measurements in the current study are device specific, not primarily patient specific dynamic range and maximum output, and are therefore helpful when comparing systems. While previous studies addressed benefit measures, such as speech perception and patient opinions, this study investigated the basic performance of three active, semi-implantable middle ear devices used in patients matched according to the extent of sensorineural hearing loss. Previously, it has been shown that the gain (amplification) and maximum output are important components in the evaluation of the basic function of implantable hearing systems (13,17).

Figure 2 shows the gain ratio (GR), a measure that is, in principle, hearing-loss independent and can, therefore, be averaged over patients. Significant differences between the three devices were not found (t-test, $p > 0.05$). This result is not surprising because the actual gain is determined by the user, either by adjusting the volume (MET and DACS), or, if volume control is absent, by adjustments made during the device fitting. The desired gain ratio, according to the NAL rule, should be at least 0.46 (at 1, 2, and 4 kHz). This GR was found at 1 kHz and 2 kHz for the DACS users and at 2 kHz for the VSB users; for MET users, the values at 1 kHz and 2 kHz approached this target value. A target ratio of 0.46, as prescribed by the NAL rule, was matched but not surpassed by the three systems (14,15).

As shown by Snik et al., the proper processing of loud sounds by the implant can be measured objectively with a probe microphone in the ear canal (13). The probe measures the vibrations produced by the actuator of the middle ear implant because these reach not only the cochlea but also the tympanic membrane. This probe thus measures the vibrations produced as a by-product. These vibrations are transmitted as acoustic signals into the ear canal and measured by a probe microphone. Although such measurements cannot be used to assess gain, they can be used to study the input-output behavior of middle ear implants (13). Measuring input-output behavior was possible with the VSB, the MET and the DACS (**Figure 3**). The input level at saturation was higher for the DACS than for the MET or VSB. As a consequence, the dynamic range was the widest for the DACS (see **Figure 4**). These data can be, in part, attributed to the percutaneous coupling between the actuator and audio processor, which may be more effective than the contact-free, radio-frequency coupling in the VSB and MET (18).

The individual (dynamic) hearing range of a patient can be determined from audiogram results as the difference between the hearing thresholds and the loudness discomfort

levels, or UCL (14). For patients with a sensorineural hearing loss of 50-65 dB HL, the dynamic hearing range is in the order of 50-60 dB (19). The DACS device best approaches this value (**Figure 4)**. When the dynamic range of a hearing device is less than the patient's hearing range, patients may choose to lower the gain to widen the dynamic range and prevent the distortion of loud sounds, such as their own voice, by the saturation of the device. This may explain why the amplification results for the VSB and MET are slightly, although not significantly, lower than those for the DACS (**Figure 2**).

Figure 4 shows that, for each device type, particularly for the VSB versus the DACS, the range of the input level at saturation minimally overlapped, suggesting that the differences between devices are important.

A restriction of the present study is the limited number of patients in the maximum output measurements. However, by the present protocol, these measurements are not patient specific but rather device specific, thereby fully minimizing subjective patient factors.

Compared to the implantation of the VSB and the MET, the DACS surgery is more invasive because the vestibulum is entered which can lead to damage. The risk of cochlear damage in the DACS surgical procedure is thought to be comparable to that of a classical stapedotomy, because a standard stapes prosthesis is used (11). Furthermore, the DACS system was developed and used only in patients with mixed hearing loss caused by otosclerosis.

Conclusion

The results of the present study suggest that the percutaneous DACS middle ear implant has a amplification capacity that outreaches the VSB and has a comparable or better capacity than the Otologics MET middle ear implant to assist patients with moderate to severe sensorineural hearing loss, because of its larger dynamic range.

References

1. Dietz TG, Ball GR, Katz BH. Partial implantable vibrating ossicular prosthesis *IEEE Electron Device Society.* Chicago, 1997:433-6.
2. Labassi S, Beliaeff M. Retrospective of 1000 patients implanted with a vibrant Soundbridge middle-ear implant. *Cochlear.Implants.Int.* 2005;6 Suppl 1:74-7.
3. Verhaegen VJ, Mylanus EA, Cremers CW, Snik AF. Audiological application criteria for implantable hearing aid devices: a clinical experience at the Nijmegen ORL clinic. *Laryngoscope* 2008;118:1645-9.
4. Jenkins HA, Niparko JK, Slattery WH, Neely JG, Fredrickson JM. Otologics Middle Ear Transducer Ossicular Stimulator: performance results with varying degrees of sensorineural hearing loss. *Acta Otolaryngol.* 2004; 124:391-4.
5. Kasic JF, Fredrickson JM. The Otologics MET ossicular stimulator. *Otolaryngol.Clin.North Am.* 2001;34:501-13.
6. Venail F, Lavieille JP, Meller R, Deveze A, Tardivet L, Magnan J. New perspectives for middle ear implants: first results in otosclerosis with mixed hearing loss. *Laryngoscope* 2007;117:552-5.
7. Beltrame AM, Martini A, Prosser S, Giarbini N, Streitberger C. Coupling the Vibrant Soundbridge to cochlea round window: auditory results in patients with mixed hearing loss. *Otol Neurotol* 2009;30:194-201.
8. Dumon T, Gratacap B, Firmin F, et al. Vibrant Soundbridge middle ear implant in mixed hearing loss. Indications, techniques, results. *Rev Laryngol Otol Rhinol (Bord)* 2009;130:75-81.
9. Kontorinis G, Lenarz T, Mojallal H, Hinze AL, Schwab B. Power stapes: an alternative method for treating hearing loss in osteogenesis imperfecta? *Otol Neurotol* 2011;32:589-95.
10. Bernhard H, Stieger C, Perriard Y. New implantable hearing device based on a micro-actuator that is directly coupled to the inner ear fluid. *Conf.Proc.IEEE Eng Med.Biol.Soc.* 2006;1:3162-5.
11. Hausler R, Stieger C, Bernhard H, Kompis M. A novel implantable hearing system with direct acoustic cochlear stimulation. *Audiol.Neurootol.* 2008;13:247-56.
12. Snik AF, Cremers CW. Vibrant semi-implantable hearing device with digital sound processing: effective gain and speech perception. *Arch.Otolaryngol.Head Neck Surg.* 2001;127:1433-7.
13. Snik AF, Noten J, Cremers C. Gain and maximum output of two electromagnetic middle ear implants: are real ear measurements helpful? *J.Am.Acad.Audiol.* 2004;15:249-57.
14. Dillon H. *Hearing Aids.* New York: Thieme Verlag, 2001.
15. Byrne D, Dillon H, Ching T, Katsch R, Keidser G. NAL-NL1 procedure for fitting nonlinear hearing aids: characteristics and comparisons with other procedures. *J.Am.Acad.Audiol.* 2001;12:37-51.
16. Morgan DE, Dirks DD, Bower DR. Suggested threshold sound pressure levels for frequency-modulated (warble) tones in the sound field. *J.Speech Hear.Disord.* 1979;44:37-54.
17. Gatehouse S, Browning GG. The output characteristics of an implanted bone conduction prosthesis. *Clinical otolaryngology and allied sciences* 1990;15:503-13.
18. Ohno T, Kajiya T. Performance of the middle ear implants. *Adv Audiol.* 1998;4:85-96.
19. Dillon H, Storey L. The National Acoustic Laboratories' procedure for selecting the saturation sound pressure level of hearing aids: theoretical derivation. *Ear Hear* 1998;19:255-66.

4.2.

Amplification options for patients with mixed hearing loss

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Amplification options for patients with mixed hearing loss.
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Abstract

Objective: To compare all amplification options for patients with mixed hearing loss by determining the maximum output of the available devices.

Patients and methods: Patients with mixed hearing loss who were implanted with either the Vibrant Soundbridge (VSB) or Cochlear's Direct Acoustic Cochlear Stimulator (Codacs) were compared to standard non-patient related measurements of one acoustic hearing aid, two percutaneous bone conduction devices (BCD) and one transcutaneous BCD. The dynamic range was determined by ear canal microphone measurements of the maximum output per frequency, which is the highest sound level that can be produced by a device without distortion, in combination with loudness scaling tests.

Results: The dynamic range is largest in the Codacs device, since 4 of 5 patients had unlimited output up to uncomfortable loudness. The VSB maximum output varies between 65 and 85 dBHL. BCD maximum output levels vary around 70dBHL and 80dBHL for the Baha Cordelle. The transcutaneous Sophono reached 56dBHL.

Conclusion: The best dynamic range is achieved by surgical closure of the air-bone gap and application of a regular hearing aid. By implantation of a Codacs device the utility of the complete dynamic range can also be achieved. Coupling of the VSB to the round or oval window results in a smaller dynamic range, but the surgery is less invasive. Stability of coupling of this device may vary and application in atretic or obliterated ears is possible. For moderate to severe mixed hearing loss a BCD is a straightforward solution which is independent of the middle ear status, although the transcutaneous device is only suitable for (sub-)normal sensorineural hearing.

Introduction

Mixed hearing loss is a common otological condition. Mostly, it is caused by some abnormality of the middle ear or outer ear or by otosclerosis or middle ear disease in combination with sensorineural hearing loss of any cause. The first option to treat a patient with mixed hearing loss is reconstructive surgery. If reconstructive surgery is impossible because of medical reasons (e.g. aural atresia), technical reasons (remaining sensorineural hearing loss needs amplification) or personal reasons, then fitting the patient with a hearing device should be considered. Conventional acoustic devices, however, are not always an option because of medical reasons (chronic otorrhoea or aural atresia) or technical reasons (lack of power in case of a severe air-bone gap). In this case, the next option is to consider a transcutaneous or percutaneous bone-conduction device (BCD) or a middle ear implant directly coupled to the cochlea (1). This latter application is relatively new; in 2006, Colletti and co-workers published their results on the use of the Vibrant Soundbridge middle ear implant (VSB) with its actuator coupled directly to the round window instead of to the incus (the 'classic' application for patients with sensorineural hearing loss)(2). As shown later by Linder et al. (2009), this new VSB application is also effective after subtotal petrosectomy and obliteration of the middle ear cavity by filling it with abdominal fat, in patients with chronically infected ears (3). Furthermore, several papers have addressed the application of the VSB in atretic ears (4,5). Coupling the actuator to the oval window has also been described (6,7).

Recently, Häusler et al. (2008) introduced a new implant, the DACS device (Direct Acoustic Cochlear Stimulation), developed for patients with advanced otosclerosis (8). The actuator of the DACS device is anchored in the mastoid cavity and its vibrating piston, called the artificial incus, is connected to a stapes prosthesis. This device was recently further developed and renamed the Codacs device and has been tested in a phase 1 clinical study (9).

Percutaneous BCDs have been available since 1987; viz. the Baha system (Bone Anchored Hearing Aid) (10). Research showed superior audiological results compared to conventional bone conductors (11). Despite its audiological superiority, there is still a search for transcutaneous solutions, as the skin-penetrating abutment of Baha requires lifelong daily care and infections around the abutment, although rare, can occur (11). Transcutaneous BCDs typically use a subcutaneously placed magnet, solidly connected to the skull bone. The externally worn driver, the audioprocessor, is coupled transcutaneously using a second coupling magnet, part of the audioprocessor. Recently, Siegert introduced such a transcutaneous BCD, called the Otomag device (12).

The aim of this paper is to compare all amplification options for patients with mixed hearing loss (conventional acoustic devices, transcutaneous and percutaneous BCDs, middle ear implants) by determining the maximum output of the available devices. The maximum output is the output level at which the device no longer behaves linearly and

saturates (13). In other words, the maximum output is the highest sound level that can be produced by a device without distortion. It was decided to express the maximum output level of all the devices in dB HL.

Patients and methods

Study design

For the acoustic device, the maximum output level was measured on an ear simulator, part of TBS25 Test Chamber connected to the Affinity 2.0 Hearing Aid Analyzer (Interacoustics, Assems, Denmark) and the output was expressed in dB HL(14). We measured the maximum output of a standard, powerful acoustic device (Oticon Tego Pro Power; Oticon, Copenhagen, Demark) for matters of comparison.

For the percutaneous BCD, the skull simulator was used, which measures the output of this BCD in 'dB output force level'(15). The skull simulator was integrated in a second TBS 25 Test Camber, connected to the Affinity Hearing Aid analyzer (Interacoustics). As described by Carlsson et al. (1997), the dB output force level can be transformed to dB HL by using the RETEL*dbc* (Reference Equivalent Threshold Force Level for *d*irect *b*one *c*onduction) (16). The Baha Divino (standard Baha; Cochlear BAS, Göteborg, Sweden) and the most powerful Baha Cordelle (Cochlear BAS, Göteborg, Sweden) were measured on the skull simulator and the maximum output was determined and expressed in dB HL. Nowadays, as percutaneous BCD, not only Baha devices are available but also Ponto devices (Oticon Medical, Copenhagen, Denmark). The maximum output of the Ponto device was also determined on the skull simulator as the coupling of the Ponto and Baha soundprocessors are compatible.

Håkansson et al. (1990) showed that the skull simulator can also be used to measure the output of transcutaneous bone-conduction implants (17). They connected the to-be-implanted magnet solidly to the skull simulator, used a layer of fresh skin over that magnet and then coupled the external sound processor. In this way, they studied the Audiant Xomed device, which is no longer on the market. The new transcutaneous bone-conduction implant, the Otomag Alpha 1 device (Sophono, Boulder, CO, USA) was studied in the same way (18).

As simulators for middle ear implants are lacking, in vivo experiments have been carried out to determine the maximum output (following Snik et al., 2004) (19). When stimulated, the implanted actuator radiates sound that can be picked up in the occluded ear canal by a probe microphone. This enabled the measurement of the actuator's output as a function of the input level (19, 20). Next, they calculated the maximum output, being the input level at which the output levelled off, and the gain (or amplification) of the device. It should be realized that in mixed hearing loss the actuator directly stimulates the cochlea and surpasses the middle ear. Therefore, by definition, the gain at a given frequency is the

(post-implant) bone-conduction threshold minus the aided threshold.
Such microphone measurements in the ear canal might be compromised in ears with aural atresia or with obliteration of the middle ear cavity. In such cases, the input-output behaviour was studied with loudness scaling measurements. following the procedures proposed by Moser (1987) (21). A 7-point categorical scale was used, with categories from inaudible to uncomfortably loud. The loudness categorization test was carried out with 0.5, 1, 2 and 4 kHz narrow band noise.

Patients

The maximum output of the VSB and Codacs implantable devices was measured in 11 patients with mixed hearing loss, who were recruited for this study. Six patients used a VSB device (Med-El, Innsbruck, Austria) with the actuator coupled either to the isolated stapes (n=5) or the round window membrane (n=1) and all used the VSB Amadé speech processor (Med-El, Innsbruck, Austria). The average (post-intervention) bone conduction threshold of this group at 0.5, 1 and 2 kHz (PTAbc) ranged from 45 to 68 dB HL. The history of the patients has been described in detail previously (7). The other patient group contained five patients with mixed hearing loss due to advanced otosclerosis who were fitted with a Codacs device (Cochlear, Mechelen, Belgium) as part of the European phase 1 clinical trial (9). The post-implant PTAbc ranged from 25 to 75 dB HL. Details of these patients are described elsewhere (9). Note that except for the unknown effectiveness of the coupling of the implant actuator to the cochlea, individual patient characteristics do not play any role in the present maximum output measurements.
During all measurements the hearing devices were set in an unlimited linear amplification mode with noise reduction and speech enhancement functions switched off. The microphone mode was set to omnidirectional.

Results

Figure 1 presents the format for presenting the data. The x-axis presents the sensorineural hearing loss component of patients (mean value at 0.5, 1 and 2 kHz) and the vertical axis presents the maximum output of the tested hearing devices (averaged over the same frequencies). If the maximum output value is lower than the lower thick black diagonal line, the amplified sound is inaudible. The bold line at the top of the figure represents the highest output level that is tolerated by patients as reported by Dillon and Storey (1998) and expressed in dB HL (again mean value at 0.5, 1 and 2 kHz)(13). The desired dynamic hearing range is the area between the diagonal line and Dillon and Storey's loudness discomfort line.

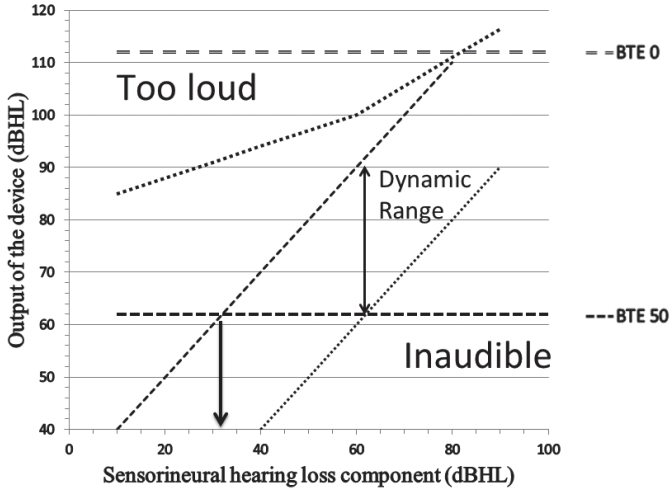


Figure 1 Maximum output as a function of hearing impairment.

The y-axis presents the maximum output averaged at 0.5, 1 and 2 kHz and expressed in dB HL. The x-axis presents the sensorineural hearing loss component averaged over the same frequencies. If a data point lies below the thick black diagonal line, it is inaudible. The middle dashed line presents the desired maximum output level of 30 dB (taken from Dillon and Storey, 1998). The area between this line and the diagonal line presents the dynamic hearing range. The upper thick dashed line represents the loudness discomfort line. The horizontal lines display the maximum output of the behind-the-ear (acoustic) device assuming no air-bone gap (label BTE-0) and assuming a 50 dB air-bone gap (label BTE-50).

It is obvious that the maximum output should be loud enough for the whole dynamic hearing range of the patient to be utilized. Since this is not always achieved, we formulated a minimum criterion: a device is considered sufficiently effective if its maximum output reaches 30 dB louder than the inaudible diagonal line. This score is indicated by the dotted diagonal line in the figure running parallel to the inaudible value line). Thus, the hearing range should be at least 30 dB, which is the dynamic range of normal speech(22).

The horizontal lines in **figure 1** present the average maximum output level of the conventional acoustic device, assuming absence of an air-bone gap (line labelled BTE-0) and assuming an air-bone gap of 50 dB (line labelled BTE-50).

The three horizontal lines in **figure 2** present the maximum output of the standard Baha (Baha Divino), the Baha Cordelle (most powerful Baha) and the Sophono device. Following the criterion of at least a 30 dB dynamic range, the maximum output levels indicate that the standard Baha Divino, the Baha Cordelle and the Sophono can be used up to 40 dB HL, up to 50 dB HL and up to 25 dB HL sensorineural hearing loss component, respectively.

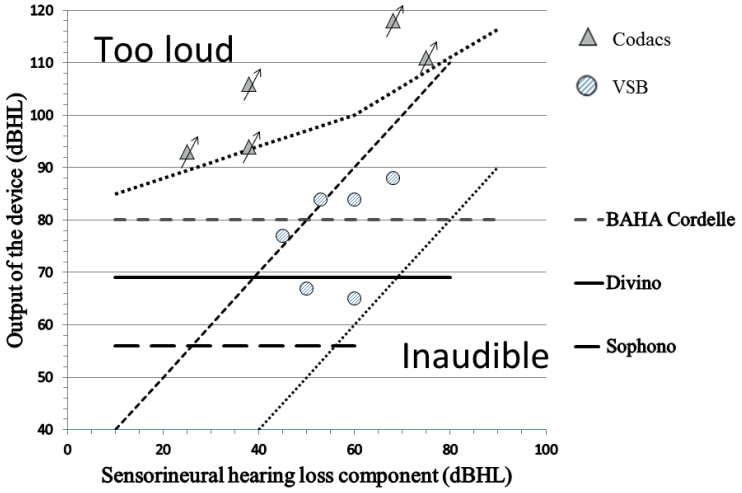


Figure 2 The maximum output of the different hearing devices (for BCDs presented as horizontal lines) and for the VSB and Codacs directly coupled to the cochlea (presented as individual points).

The maximum output of the standard Ponto device was found to be 66 dB HL which is comparable to that of the Baha Divino. The Baha Cordelle is a unique device with respect to the maximum output which is unmatched by any other BCD.

Irrespective of the applied measurement (microphone measurement in the ear canal or loudness scaling), the maximum output could not be determined for four of the five patients using a Codacs device. Non-linear behaviour did not occur up to the patients' loudness discomfort levels. For the remaining patient, saturation was found at input levels of 80-85 dB HL. However, the gain could not be determined properly as bone conduction thresholds at 500 Hz and 2 kHz were beyond the limits of the audiometer (> 75 dB HL). From these data we concluded that the maximum output was louder than 102 dB HL. The arrows in **figure 2** indicate that the maximum output of the other four patients was above their uncomfortable loudness level.

The VSB data points are also presented in **figure 2**. Measurements obtained with a microphone in the ear canal were only feasible for one patient. For the other patients, loudness scaling measurements were carried out. **Figure 2** shows an obvious variation in the results. We expect variability owing to coupling effectiveness of the actuator to the cochlea and whether or not the middle ear cavity was air-filled or obliterated with fat (7). For two of the six patients, the maximum output was considered rather low (around 65 dB HL) whereas for the other four patients, a rather stable result was found around 85 dB HL.

Figure 3 presents the mean maximum output data, however, this time separated per individual frequency: 0.5, 1, 2 and 4 kHz. The highest maximum output for all the devices is found at 2 kHz. The data of the VSB users were averaged, with the two lower outliers were excluded for the averaged calculations. This figure suggests a best bandwidth for the percutaneous BCD devices. No Codacs data could be included as the maximum output values remained unknown.

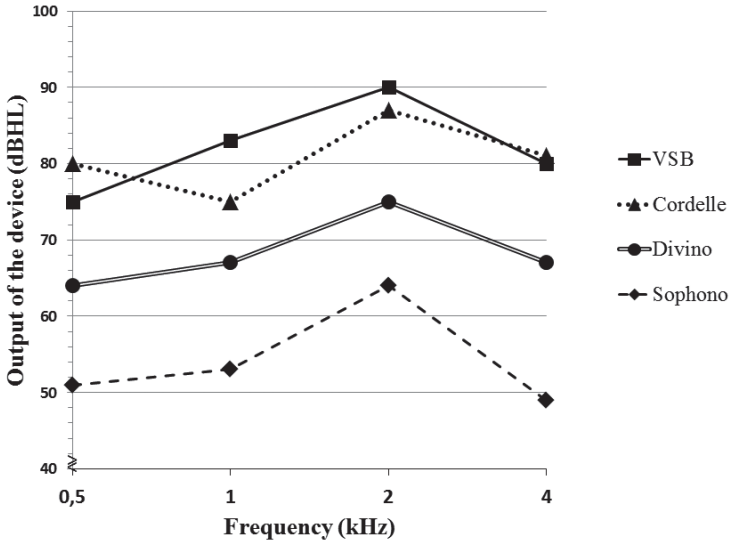


Figure 3 The mean maximum output level per device for the individual frequencies of 0.5, 1, 2 and 4 kHz. Note that to calculate the mean for the VSB, the two lower outliers were excluded.

Discussion

Figure 1 shows the maximum output of the acoustic hearing aid. The output depends proportionally on the size of the patient's air-bone gap; e.g. for patients without any air-bone gap, the entire dynamic hearing range is available. However, in case of a patient with an air-bone gap of 50 dB and accepting the minimum criterion of 30 dB dynamic range, this acoustic device should only be used in patients with (sub)normal cochlear functioning with up to 30 dB sensorineural hearing loss component.
The maximum output of the Baha Divino, as presented in **figure 2**, is in accordance with published data on the device's predecessors (16). **Figure 2** shows that this device can be effectively applied for patients with a sensorineural hearing loss component of up to 40

dB HL. This value is in agreement with the consensus in literature (11). For the Baha Cordelle, the upper application level of 50 dB HL is lower than the 60 dB HL that has been previously suggested by Bosman et al. (23). However, they used a less strict criterion, namely 50% word recognition.

The Sophono Alpha 1 device has a maximum output approximately 15 dB less than the Baha Divino. This limits the application range of the Sophono Alpha. In principle, the Sophono device is a standard transcutaneous BCD with magnetic coupling instead of the classical coupling with a headband (12). Håkansson et al. showed that transcutaneous coupling is indeed 10 to 15 dB less effective than percutaneous BCD coupling, which explains the observed difference between the maximum output of the Baha Divino and the Sophono Alpha 1 devices (10). Recently Sylvester et al. published their first data on the application of the Sophono device in patients with conductive and mixed hearing loss. In agreement with our results they concluded that the Sophono device should only be used in patients with (sub-) normal cochlear function (24).

The maximum output of the Codacs device is very loud, which means that, unlike the other devices, the patient's full hearing range can be utilized. Also, in contrast with the other devices, this means that special attention has to be paid to output limitation when fitting this device.

The results of the VSB with its actuator coupled to one of the cochlear windows shows a variable result; coupling effectiveness may play a role. Previous studies have addressed such questions as whether the VSB actuator could be coupled effectively to the (remains of the) stapes; how to assure proper contact between the actuator and the round window membrane; and what options would be best in atretic ears (2, 4-7). Recently, publications by Maier et al. (25) and Schwab et al.(26) indicate that the coupling of the transducers to the cochlea may vary as much as 20 dB, depending on various circumstances. The Med-El company suggests that the VSB coupled to the round or oval window can be used in patients with a sensorineural hearing loss component of up to 55 dB HL (27). Our presented results support this claim.

In a previous study, the maximum output of the VSB in its classic application was studied in 8 patients with pure sensorineural hearing loss and chronic external otitis (19). A mean maximum output level of 102 dB SPL was found, what equals 98 dB HL, in the 1 to 2 kHz region. The calculated mean at the same frequencies of the present data is 83 dB HL. Comparison of the two means suggest that the present VSB application on the round window and stapes suprastructure is 15 dB less effective than the classic VSB application.

Conclusion

In summary, four amplification options to treat patients with mixed hearing loss have been considered. The first option, if possible, is surgical closure of the air-bone gap and fitting of a conventional acoustic device. This option enables full use of the patient's dynamic hearing range. The second option is the application of a Codacs implant (pending certification). This option will also enable full use of the patient's dynamic hearing range. So far, the Codacs device has only been applied in patients with advanced otosclerosis, and long term stability data are still lacking. A stapedotomy is an essential part of the surgical procedure and carries its own risks.

The third option involves application of the VSB device connected to the round or oval window. Although application of the VSB device is less invasive than that of the Codacs device, the coupling effectiveness is not yet well defined. In contrast to the Codacs device, it has been shown that the VSB device can be used in chronically diseased middle ears (after subtotal petrosectomy with obliteration of the middle ear cavity) and in atretic ears. Structural long-term data on the stability of the coupling between actuator and the cochlear windows have not yet been published.

The fourth option is a percutaneous BCD, which offer effective amplification for patients with a moderate to severe sensorineural hearing loss. BCD surgery is relatively straight forward and the main advantage of a percutaneous BCD is that neither surgery nor performance is affected by the status of the middle ear.

The search for transcutaneous BCDs remains, as the skin-penetrating abutment of percutaneous BCDs requires lifelong daily care and infections around the abutment may occur. However, the 10-15 dB improvement in effectiveness that was achieved by changing from transcutaneous to percutaneous transmission of sound vibrations would be lost (10). Nevertheless, the maximum output of the transcutaneous Sophono device is relatively low and makes this device only suitable for patients with normal or subnormal cochlear function.

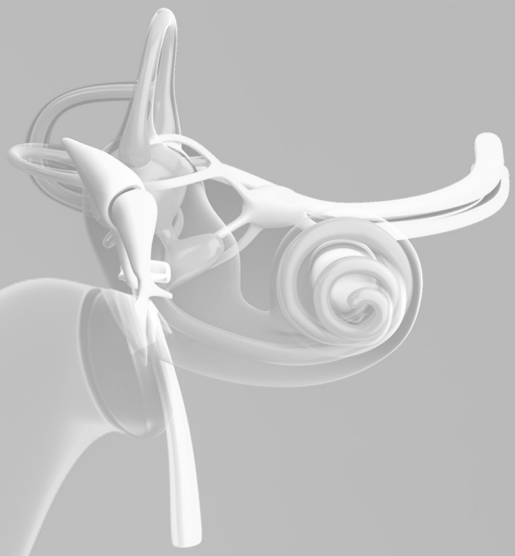
References

1. Snik A. (2011) Implantable hearing devices for conductive and sensorineural hearing impairment. In *Auditory Prostheses; new horizons*, Zeng F. (ed), pp. 85-108. Springer Handbook of Audiology Research, New York (NY; USA)
2. Colletti V., Soli S.D., Carner M. & Colletti L. (2006) Treatment of mixed hearing losses via implantation of a vibratory transducer on the round window. *Int J Audiol.* **45,** 600-608
3. Linder T., Schlegel C., DeMin N. & van der Westhuizen S. (2009) Active middle ear implants in patients undergoing subtotal petrosectomy: new application for the Vibrant Soundbridge device and its implication for lateral cranium base surgery. *Otol Neurotol.* **30,** 41-47
4. Frenzel H., Hanke F., Beltrame M., Steffen A., Schonweiler R. & Wollenberg B. (2009) Application of the Vibrant Soundbridge to unilateral osseous atresia cases. *Laryngoscope.* **119,** 67-74
5. Mandala M., Colletti L. & Colletti V. (2011) Treatment of the atretic ear with round window vibrant soundbridge implantation in infants and children: electrocochleography and audiologic outcomes. *Otol Neurotol.* **32,** 1250-1255
6. Beleites T., Neudert M., Beutner D., Huttenbrink K.B. & Zahnert T. (2011) Experience with vibroplasty couplers at the stapes head and footplate. *Otol Neurotol.* **32,** 1468-1472
7. Verhaegen V.J., Mulder J.J., Cremers C.W. & Snik A.F. (2012) Application of active middle ear implants in patients with severe mixed hearing loss. *Otol Neurotol.* **33,** 297-301
8. Häusler R., Stieger C., Bernhard H. & Kompis M. (2008) A novel implantable hearing system with direct acoustic cochlear stimulation. *Audiol Neurootol.* **13,** 247-256
9. Lenarz T., Zwartenkot J., Stieger C. *et al.* (2013) Multicenter study with a Direct Acoustic Cochlear Implant. *Otol Neurotol.* **accepted for publication**
10. Håkansson B., Tjellstrom A. & Rosenhall U. (1984) Hearing thresholds with direct bone conduction versus conventional bone conduction. *Scand Audiol.* **13,** 3-13
11. Snik A.F., Mylanus E.A., Proops D.W. *et al.* (2005) Consensus statements on the BAHA system: where do we stand at present? *Ann Otol Rhinol Laryngol Suppl.* **195,** 2-12
12. Siegert R. (2011) Partially implantable bone conduction hearing aids without a percutaneous abutment (Otomag): technique and preliminary clinical results. *Adv Otorhinolaryngol.* **71,** 41-46
13. Dillon H. & Storey L. (1998) The National Acoustic Laboratories' procedure for selecting the saturation sound pressure level of hearing aids: theoretical derivation. *Ear Hear.* **19,** 255-266
14. Bentler R.A. & Pavlovic C.V. (1992) Addendum to "transfer functions and correction factors used in hearing aid evaluation and research". *Ear Hear.* **13,** 284-286
15. Håkansson B. & Carlsson P. (1989) Skull simulator for direct bone conduction hearing devices. *Scand Audiol.* **18,** 91-98
16. Carlsson P.U. & Håkansson B.E. (1997) The bone-anchored hearing aid: reference quantities and functional gain. *Ear Hear.* **18,** 34-41
17. Håkansson B., Tjellstrom A. & Carlsson P. (1990) Percutaneous vs. transcutaneous transducers for hearing by direct bone conduction. *Otolaryngol Head Neck Surg.* **102,** 339-344
18. Hol M., Nelissen R., Agterberg M., Cremers C. & Snik A. (2013) Comparison between a new implantable transcutaneous bone conductor and percutaneous bone-conduction hearing implant. *Otol neurotol* ***Epub ahead of print***
19. Snik A., Noten J. & Cremers C. (2004) Gain and maximum output of two electromagnetic middle ear implants: are real ear measurements helpful? *J Am Acad Audiol.* **15,** 249-257
20. Zwartenkot J.S., AFM, Kompis M. & Stieger C. (2012) Gain and maximum output of implantable hearing devices in patients with moderate to severe sensorineural hearing loss. *Journal of Hearing Science.* **2,** 35-40
21. Moser L.M. (1987) [The Wurzburg auditory field, a test for prosthetic audiometry]. *HNO.* **35,** 318-321
22. Dillon H. (2001) *Hearing Aids.* Thieme Verlag, New York
23. Bosman A.J., Snik A.F., Mylanus E.A. & Cremers C.W. (2006) Fitting range of the BAHA Cordelle. *Int J Audiol.* **45,** 429-437
24. Sylvester D.C., Gardner R., Reilly P.G., Rankin K. & Raine C.H. (2013) Audiologic and Surgical Outcomes of a Novel, Nonpercutaneous, Bone Conducting Hearing Implant. *Otol Neurotol* ***Epub ahead of print***

25. Maier H., Salcher R., Schwab B. & Lenarz T. (2012) The effect of static force on round window stimulation with the direct acoustic cochlea stimulator. *Hear Res*
26. Schwab B., Salcher R.B., Maier H. & Kontorinis G. (2012) Oval window membrane vibroplasty for direct acoustic cochlear stimulation: treating severe mixed hearing loss in challenging middle ears. *Otol Neurotol.* **33,** 804-809
27. Wagner F., Todt I., Wagner J. & Ernst A. (2010) Indications and candidacy for active middle ear implants. *Adv Otorhinolaryngol.* **69,** 20-26

5.

Closure



5.1.

General discussion

General discussion

Limitations of the studies

This thesis focuses on the clinical outcome of the implantation of active middle ear implants (AMEI) and direct acoustic cochlear implants (DACI). Although most of the data has been prospectively acquired (baseline and long term data in chapter 2.2 and the studies presented in part III), the long term clinical outcome of the AMEI cohort has been retrospectively studied (surgical results in chapter 2.1 and 2.3). The retrospective method of these latter studies may have invoked an under-reporting in the occurrence of minor complications. Potentially, the clinical observations might be influenced due to a heterogenic description, as data were not acquired in a pre-study well defined, structured and periodic order like in a prospective study. Nevertheless, the descriptive studies present a new and unprecedented follow up duration and detail of clinical results in implantable hearing implants in terms of safety and stability. The publication of these studies appeals to our strong belief that reporting these long term data is of great importance for the post market release experience of new implantable technologies for the rehabilitation of hearing loss.

No randomized studies have been conducted in this thesis. The lack of randomization introduces the possibility of bias, e.g. selection and/or confounding bias. None of the patients chose for an implantable hearing implant as a result of dissatisfaction with the hearing performance or quality with the conventional device. In all cases described, conventional hearing aids were contra-indicated as a result of the medical problems they caused. Implantable hearing aids were simply the last resort. Therefore, no comparison to another treatment was available for a controlled study and a pre and post intervention analysis was considered adequate. Previous studies have reported that recipients of active middle ear implants were critical about the quality of sound of the devices. This was caused by the restricted bandwidth and output capacity of their devices. Nevertheless, the quality of life of the patients improved significantly as a result of the fact that the patients were able to use their device all day. This certainly reflects the value of the availability of these devices for those who could otherwise not be rehabilitated.

In the structured prospective multicenter study on the Codacs device, independently monitored by an external monitor, no randomized comparison to conventional hearing aids was conducted. The purpose of this study was to determine the safety and efficacy of the experimental device. Therefore, a specific narrow selection was applied. Since the indication criteria was set for otosclerosis, which is a chronic stable disease, the patients were suitable for a pre- and post comparison of their own measurements. It is however of importance to note that beneficial changes in terms of speech recognition-in-quiet, and in-noise may be explained by the improvement in pure tone thresholds with the Codacs. These results were consistent with the subjective results obtained in the recipients. The results of this study provide evidence that the device is safe to apply and that it provides a sufficient audiological benefit for the specific selection of patients.

The comparative articles on maximum output of the various devices (part IV) present original data which are patient independent and therefore individual patient characteristics or selection criteria have not influenced these results.

Benefit of the devices

The studies in this thesis present evidence that both the AMEI as DACI provide adequate benefit for the implanted patients. In chapter 2.2, the long term benefit in quality of life of AMEI has been reported for a mean follow up duration of 7.5 years. This study focused on a selection of the total patient cohort, because the first implanted patients were not prospectively evaluated with questionnaires. Although the level of benefit gradually decreased over time, a significant improvement is still found in the long term evaluation for 3 different quality of life questionnaires. No long term reports on quality of life outcome in AMEI surgery are present in the literature. These results are in accordance with the results on short term studies in the literature (1-4).

In chapter 2.3 the long term evaluation of the technical outcome of AMEIs is studied. Many of the first implantations were experimental or part of phase I trials. Therefore, growing pains occurred like, for example, the application of ionomeric glass cement to improve the coupling of the actuator to the middle ear ossicular chain. This application proved disappointing. Another example is the technically poor results of the Otologics Middle Ear Transducer (MET), which caused many revision surgeries (5). Fortunately, the quality of the implants and the implant surgery improved gradually over the years leading to less revisions and less explantations. Eventually, an overall explantation rate of 7% was found for the Vibrant Soundbridge (VSB) which is comparable to the rates of cochlear implants (6, 7). The overall explantation rate of the MET (28%) was high, but the rate has decreased in time, with no explantations with the newer Cochlear MET model (applied since 2010; chapter 2.3 and unpublished data).

For the DACI, two prospective studies have been conducted to evaluate the safety and efficacy of the investigational Codacs device. In chapter 3.1 the results of a multicenter study are presented. This study reported a significant decrease in difficulties with hearing compared to the pre-operative hearing aid or unaided situation, tested by the APHAB questionnaire (8). The audiometric benefit was evident. Most important was the finding of better hearing in the high frequencies compared to conventional hearing aids and, consequently, the improved results of speech-in-noise tests. Chapter 3.2 presented the long term stability of the Dutch cohort of Codacs implanted patients. The results were stable compared to a previous short term evaluation, both on the APHAB outcome as the audiometric evaluation. Most surprising was the ease of the fitting of the device. Apart from the evaluation visits initiated by the hospital, no further visits were necessary to adapt the fittings of these implants (unpublished data).

Complications in surgery

As in any surgical procedure, implantation of AMEI and DACI comes with surgical risks and complications. These risks are comparable to other otologic operations that include a mastoidectomy, atticotomy and posterior tympanotomy. It mostly concerns the risk of damage to the inner ear and vestibule, facial and chorda tympani nerves and postoperative problems of infection in the middle ear or surrounding the implant under the skin. In chapters 2.1, 2.3 and 3.2 we have described the complications that occurred in our series. Especially the so-called transcanal approach through the ear canal for the implantation of the VSB proved to be unsafe in our hands. When applying it in patients with external otitis, the wire of the device repeatedly extruded through the skin of the ear canal. For the regular approach, 20 complications have been described in chapter 2.3, classified as minor or more serious. For some of the complications revision surgery was required. Although device failure might not be classified as a medical complication but rather a technical failure, in most cases it still required a revision operation to explant or replace the device.
In part III we have described the study cohort for the DACI. In our own study group of 5 patients, one patient suffered a decrease in sensorineural hearing. We could not identify any specific cause for this hearing loss, and treatment with corticosteroids did not improve his hearing thresholds. In the final evaluation, the thresholds were stable on the level of the postoperative deteriorated measurement. The patient had no postoperative improvement in speech understanding, which was explained by the advanced level of hearing loss and long period of hearing deprivation in the operated ear.

Selection of the best acoustic implant

Since several options are available in the treatment of sensorineural, mixed or conductive hearing loss, selecting the most adequate solution is challenging. Therefore, all patient characteristics should be taken into account: age, general health, fitness for surgery and anesthesia, hearing levels, life expectancy and the personal wishes and choices of the patient. When the level of hearing loss is evaluated, care should be taken to pay attention to the progressiveness of the hearing loss. If this is neglected, the implant might only be temporarily beneficial for the patient. This so called longevity issue is often neglected (9). The sensorineural hearing will deteriorate due to presbyacusis and in certain hereditary forms of hearing impairment even at a fast rate. For otosclerosis, both the sensorineural thresholds as the air-bone gap may deteriorate over time. Since the maximum output of the implantable devices vary strongly, as presented in part IV, some implants are not indicated when the sensorineural hearing (component) thresholds exceeds a certain level. Not only should the maximum output level of the device be powerful enough to reach the levels of the patient's hearing, it should provide at least 35 dB dynamic range of hearing to provide acceptable speech audibility (see chapter 4.1). As a consequence, dealing with patients with mixed hearing loss, a maximum application range was set of 35 dB HL mean sensorineural hearing loss component for standard percutaneous bone

implants, 50 dB HL for the Baha Cordelle, 45-50 dB HL for the VSB and 65 dB HL for Codacs, although the latter might even be larger due to the loudness discomfort at maximum output. These maximum ranges need to be considered, when the actuator of the implant would be directly coupled to the remaining ossicles or round window.

Magnetic resonance imaging (MRI) compatibility

Considering the increasing availability of high-field MRI scanners, some technical and medical challenges may arise in patients with acoustic implants. In a large US report in 2012 an increase in MRI usage between 1996 and 2010 is presented (10). The authors report an increase from 1.7% to 6.5% of the enrolled patients and 10 percent increase per year. Azardamaki et al and Fritsch and Mosier have published about the interactions that need to be considered related to the magnetic field in the MRI-scanner and the metallic and magnetic parts of implantable hearing aids (11, 12). Most implants consist of an internal processor carrying a magnet which will couple to the externally worn sound processor. One risk might be displacement of the implant in the patient because of translational and rotational forces. Another risk is the production of heat due to the effect of radiofrequency absorption. Another problem might be demagnetization of the implanted magnets. Finally, the diagnostic use of the MRI itself is obscured due to the artifacts that will be created due to the metallic and magnetic implant parts. Especially in the VSB the torque effects need to be considered since the FMT is an active magnet which is coupled directly to the middle ear ossicles.

Another problem is demagnetization of the magnet, part of the FMT, which might influence the output of the device. In an extensive publication in 2011, Wagner et al have described a review on the results of all published in vivo en ex vivo experiments with the VSB and MRI scanning (13). Although no severe torque on the FMT was measurable, some displacement of the position of the FMT onto the incus had occurred. Demagnetization of the implant and receiver magnet was only limited. The voltage induction in experimental setting showed no limits that would damage the implant. Nevertheless, it might lead to hearable activation of the FMT, which did occur in some patients. No significant heating of the device was measurable in an experimental setting. In the in vivo reports dislocation of the FMT and VORP as well as bending and rotation of the attachment to the incus have been reported. This has also been confirmed in temporal bone studies (14). Wagner et al state that, for the VSB, an MRI up to 1.5 Tesla can be performed at calculated risk, although the possible side effects of loud hearing sensations and possible dislocation of the FMT should be weighed against the necessity of the imaging. Since 2014, the Med-El company has introduced the newest version of the VSB implant and states a MRI-compatibility up to 1.5 Tesla (company information). In contrast, the percutaneous bone-conduction implants with its titanium coupling is not affected by MRI and its effect on the MRI image is less then 1 cm.

Future developments

Miniaturization and battery improvement

A problem in acoustic devices might be cosmetics, or the size of the device. The actuator is one of the bigger elements which has decreased in size over the years. Most of the size of the AMEI audioprocessor is the actuator and the magnet to couple the audio processor to the implanted receiver, part of the internal part of the implant. Because of the ongoing development, each generation of implants has led to some decrease in size. This so called miniaturization will hopefully lead to even smaller sizes for the external processors and for AMEIs to smaller internal components, to facilitate easier and less traumatic implantation procedures.

Improvement of implantable microphones and fully implantable devices

For the totally implantable device used in our studies, the FIMOS, a drawback has been the feedback of sounds in and to the skull itself. As the microphone is implanted just underneath the retroauricular skin of the cranium, many of the sounds to the skull (e.g. combing of the hair, scratching) are picked up and amplified. Another problem is the distortion of the own voice because of amplification and suppression issues. These problems cannot be easily solved. Reducing the volume is not appropriate but effective. Better acoustic isolation of the microphone is the better option. In addition, improvement of the implanted rechargeable battery might lead to longer battery lifetime, requiring fewer revision surgery.

Reimbursement issues

In the local situation in the Netherlands, direct reimbursement of AMEIs is not provided by the health insurance companies. However, about ten years ago, the implantation of the VSB and MET were approved as regular health care by the national healthcare authority council (CvZ). Therefore, they can be applied under the formulated indication criteria, namely for hearing impaired patients who could not benefit from conventional behind-the-ear devices, caused by chronic external otitis or patients with a severe hearing loss. Reimbursement has to be supplied by the hospitals. In other European countries like the United Kingdom, Switzerland and Germany these devices are directly reimbursement by the health insurance. More recently, in Belgium, the VSB has also been accepted for reimbursement, with the limitation that the application of a bone conduction implant is contra-indicated (personal communications).

Nowadays, the indications for AMEIs have broadened to mild and severe mixed hearing loss. As the knowledge of the expanding indications for AMEIs has not yet spread adequately amongst otolaryngologists in the Netherlands, the number of eligible patients for middle ear implantation will probably increase in the future. Until this moment, the reimbursement of the devices is indirectly funded through hospital budgets, since the number of implantations is too few to develop a specific funding category. Not only the

costs of the implant should be considered, but also the replacement costs of the external audioprocessor (after e.g. 5 years as is the case for percutaneous bone conduction implants). The cost effectiveness of middle ear implants was determined in two previous studies (15, 16). Therefore, a dedicated diagnosis related group (DRG) also called 'diagnose behandel code' (DBC) should be introduced, specifically for AMEI and DACI. It should cover the costs for a newly created procedure code that includes the implantation of the device, the actual costs of the device itself and the audioprocessor and the fitting appointments in an audiological center. These DRG's have been available for the implantation of bone implants and cochlear implants for many years.

General conclusion

The studies that have been conducted for this thesis provide evidence that the application of AMEIs nowadays in patients with SNHL and comorbid external otitis, as well as severe mixed hearing loss, is associated with a low incidence of complications, which decreased over time. The initial medical-technical challenges with the implants seem to have been solved by the manufacturing companies and recent explantations are few. The so-called transcanal approach in the implantation of the VSB should be avoided in patients suffering from external otitis, due to complications with wire extrusions in the ear canal. So far, the complication rate for DACI seems to be low. Long term evaluation with quality of life questionnaires (after a mean of 7.5 years) resulted in a report of significant decrease in disability due to implantation. Overall more than 80% of the patients that still use the device is content with the device and 90% of them use it daily.

A new alternative in the surgical treatment of advanced otosclerosis was studied and described in two chapters. A direct acoustic cochlear implant (Codacs) was tested in a trial study. The study showed that the device was both safe and effective. Compared to the pre-operative situation with a conventional hearing aid, better audiological results were obtained. In a long term study the audiological results proved to be stable in all 5 patients, evaluated at 20 and 40 months, post device fitting. Only one complication occurred, for which no explicit relation with the device was found.

Two chapters present evidence that the maximum output of acoustic implants vary greatly. The comparison between the VSB, MET and Codacs devices showed that the VSB has a smaller aided dynamic range of hearing than the MET for patients with sensorineural hearing loss. The dynamic range of hearing with the Codacs was even larger than for the MET. A criterion was set to provide a dynamic range of hearing of at least 35dB. With that criterion applied to patients with conductive or mixed hearing loss, maximum allowable levels for the sensorineural hearing loss component were defined. Non-audiological factors that play a role have been discussed; an international consensus on the application of acoustic implants has not yet been determined.

In conclusion, this thesis provides additional scientific evidence to the literature that acoustic implants have a key position in surgical restoration of selected hearing impaired

patients for whom conventional solutions are contra-indicated or provide insufficient benefit. Active middle ear implants can be considered as alternative to conventional treatments like reconstructive surgery and bone-conduction implants in specific patient groups

References

1. Mosnier I, Sterkers O, Bouccara D, Labassi S, Bebear JP, Bordure P, et al. Benefit of the Vibrant Soundbridge device in patients implanted for 5 to 8 years. Ear and hearing. 2008;29(2):281-4.
2. Rameh C, Meller R, Lavieille JP, Deveze A, Magnan J. Long-Term Patient Satisfaction With Different Middle Ear Hearing Implants in Sensorineural Hearing Loss. Otol Neurotol. 2010;31(6):883-92.
3. Schmuziger N, Schimmann F, aWengen D, Patscheke J, Probst R. Long-term assessment after implantation of the Vibrant Soundbridge device. Otol Neurotol. 2006;27(2):183-8.
4. Sterkers O, Boucarra D, Labassi S, Bebear JP, Dubreuil C, Frachet B, et al. A middle ear implant, the Symphonix Vibrant Soundbridge: retrospective study of the first 125 patients implanted in France. Otol Neurotol. 2003;24(3):427-36.
5. Verhaegen VJ, Mulder JJ, Cremers CW, Snik AF. Application of active middle ear implants in patients with severe mixed hearing loss. Otol Neurotol. 2012;33(3):297-301.
6. Theunisse HJ, Mulder JJ, Pennings RJE, Kunst HPM, Mylanus EaM. A database system for the registration of complications and failures in cochlear implant surgery applied to over 1000 implantations performed in Nijmegen, The Netherlands. J Laryngol Otol. 2014;128:952-7.
7. Wang JT, Wang AY, Psarros C, Da Cruz M. Rates of revision and device failure in cochlear implant surgery: a 30-year experience. Laryngoscope. 2014;124:2393-9.
8. Cox RM, Alexander GC. The abbreviated profile of hearing aid benefit. Ear and hearing. 1995;16(2):176-86.
9. Snik A. Snik Implants. Available from: www.snikimplants.nl.
10. Smith-Bindman R, Miglioretti DL, Johnson E, Lee C, Feigelson HS, Flynn M, et al. Use of diagnostic imaging studies and associated radiation exposure for patients enrolled in large integrated health care systems, 1996-2010. Jama. 2012;307(22):2400-9.
11. Azadarmaki R, Tubbs R, Chen DA, Shellock FG. MRI information for commonly used otologic implants: review and update. Otolaryngology--head and neck surgery : official journal of American Academy of Otolaryngology-Head and Neck Surgery. 2014;150(4):512-9.
12. Fritsch MH, Mosier KM. MRI compatibility issues in otology. Current opinion in otolaryngology & head and neck surgery. 2007;15(5):335-40.
13. Wagner JH, Ernst A, Todt I. Magnet resonance imaging safety of the Vibrant Soundbridge system: a review. Otol Neurotol. 2011;32(7):1040-6.
14. Todt I, Rademacher G, Wagner F, Schedlbauer E, Wagner J, Basta D, et al. Magnetic resonance imaging safety of the floating mass transducer. Otol Neurotol. 2010;31(9):1435-40.
15. Snik, A, Duijnhoven van N, Mylanus E, Cremers C. Estimated Cost-effectiveness of Active Middle-Ear Implantation in Hearing-Impaired Patients With Severe External Otitis. Arch Otolaryngol Head Neck Surg. 2006;132(11):1210-1215
16. Snik A, Verhaegen V, Mulder J, Cremers C. Cost-Effectiveness of Implantable Middle Ear Hearing Devices. Adv Otorhinolaryngol. Basel, Karger, 2010, vol 69, pp 14–19

5.2.

Summary

Summary

Active middle ear implants or AMEI have been applied for over two decades in the surgical rehabilitation of hearing loss. It comprises the implantation of an actuator that is coupled to the middle ear ossicles and a receiver. The (external) soundprocessor communicates with the receiver by radiofrequency or electromagnetical signals. These signals are decoded and transformed into a vibration of the actuator, thereby vibrating the ossicles and subsequently stimulating the cochlea. More recently, direct acoustic cochlear implants or DACI have been developed which provide a method to directly drive the fluids in the inner ear. The DACI is a type of middle ear implant that provides a powerful vibration to a stapes prosthesis (coupled to its actuator) that is inserted through an opening in the stapes footplate.
This thesis has focused on the long term results of AMEI on several outcome factors, such as quality of life, complications and implant failures. The results of the first clinical application of a DACI have been evaluated in a short term multicenter trial and a long term follow-up study. Furthermore, two studies have been conducted to evaluate the device characteristics for maximum output and saturation of the amplified sounds. The first chapter offers an introduction to the theory of hearing and hearing loss and to the various acoustic implants.

Active middle ear implants

In chapter 2.1, a selected study group of 13 subsequent patients suffering from sensorineural hearing loss and therapy resistant external otitis was evaluated after an experimental procedure to implant the Vibrant Soundbridge or VSB. Shortening of the time of surgery and decrease in perioperative complications was hypothesised, using an approach through the outer ear canal, rather than using the regular approach through the mastoid cavity. In this study, the connecting wire of the implant between the receiver and the actuator was guided through the ear canal and buried in an artificial groove in the bony part of the canal. During a mean follow-up period of 51 months, apart from 2 perioperative sacrificed chorda tympani nerves, 7 postoperative complications were observed in 6 of the 13 patients (46%). The complications were a collapse of the ear canal (n = 1), repeated extrusions of the conducting wire (n = 5) in the ear canal and a perforation of the tympanic membrane (n = 1). No further postoperative complications occurred during the follow-up period and no postoperative complications were observed for the other 7 patients. After careful consideration, it was concluded that this so called transcanal approach for VSB implantation is unfavourable in patients with therapy-resistant external otitis.

In the chapter 2.2, the effects on quality of life and the level of handicap for the patients implanted with a VSB implant or a semi- implantable Middle Ear Transducer (MET) were studied using validated questionnaires. The Abbreviated Profile of Hearing Aid Benefit

(APHAB and the Glasgow Benefit Inventory (GBI) were administered pre-operatively and at short and at long term intervals, postoperatively. Data of 33 patients (80%) were available, with a mean post-operative duration of 7.5 years. No difference in subjective results was found between the VSB and MET patient groups. The total percentage of non-use was 13%. The long-term APHAB results showed a significant decrease in overall disability for 43% of the patients compared to 54% at 1-year postoperative. The GBI results show a significant long-term increase in quality of life with positive scores for 82% of the 33 assessed patients. These results are lower compared to the 12-month results in which 23 patients (92%) had a positive GBI score. The results of all questionnaires showed a negative trend over time, but the evaluated AMEI provide a significant long-term benefit in disability and quality of life with a benefit that was slightly better than the results reported in the literature.

In chapter 2.3, the result of a long term evaluation of the complete cohort of AMEI patients is presented. This study evaluated the number of explanted devices due to a medical or technical reason, the number of revision procedures and the total complication rate. The VSB and MET devices were implanted as well as a fully implantable middle ear ossicular stimulator (FIMOS).
In total 94 patients were implanted, of whom 12 patients eventually with a round window or stapes coupling rather than the regular application to the incus. A number of 28 patients (30%) were lost to follow up: 7 patients had deceased, 12 patients were definitively explanted, and 6 patients were lost to follow-up appointments. The average follow-up duration was 4.4 years (range 1 month to 15 years). Altogether, 128 devices were evaluated: (92 VSB, 32 MET, 4 FIMOS). 36 devices (28%) were explanted or replaced (18 VSB, 14 MET, 4 FIMOS). The device failure rate was 7% for VSB, 28% for MET and 100% for FIMOS.
In 16 patients (17%) revision surgery (n=20) was performed, which mostly concerned revision of the skin and the implanted magnet and middle ear inspections to evaluate the coupling of the device to the incus. Finally, 20 patients (21%) suffered a medical complication of which the erosion of the long process of the incus and extrusions of the wire in the ear canal were the most notable. The complication rate decreased steadily over time and no complications were found in the last 3 years of the evaluation, whereas the number of implantations increased over time. This trend is best explained by the learning curve and experimental procedures in the explorative first years of middle ear implantation. Because of incompatibility with an MRI scanner, 12 of the 92 VSB implants were explanted. This issue has more recently been addressed by the industry. The VSB is now compatible for low-strength magnetic fields. For the other implants, this issue is still ongoing.
Although the number of complications, device failures and revision procedures in the past can be considered high, the decreasing trend over time shows that experimental phase in the development and implantation procedure of AMEIs has passed. Therefore, AMEI may be considered as a valuable and safe contribution in the surgical rehabilitation of hearing

loss, since the benefits in audiological and quality of life outcome have been previously established.

Direct acoustic cochlear implants

Chapter 3.1 presents a phase 1 prospective multicenter trial conducted in Germany, Switzerland and the Netherlands. Fifteen patients who suffered from severe mixed hearing loss as a result of advanced otosclerosis were included to be implanted with an experimental direct acoustic cochlear implant (DACI). Rather than performing a regular stapes replacing surgery, this procedure comprised the implantation of a device that was made up of a vibrating rod, the actual actuator, and a sound processor. The vibrating rod was coupled to the stapes replacing prosthesis, which connects directly to the perilymph fluid in the inner ear. A previous study provided evidence of an additional benefit in the higher frequencies compared to a regular stapedotomy combined with conventional hearing aids. The study goal of this trial was to confirm the audiological efficacy and safety of the device.

The pre- and post-operative air and bone conduction thresholds did not change significantly by the implantation with the DACI. The mean sound field thresholds (0.25 to 8 kHz) improved significantly by 48 dB compared to the pre-operative unaided situation and by 15dB compared to aided with a hearing aid (n=11). The improvement of the DACI aided sound-field thresholds postoperatively compared with the HA aided sound-field thresholds preoperatively was significant in all frequencies except at 2 and 8 kHz (n=5). The word recognition scores at 50, 65 and 80 dB SPL improved significantly by 30, 75 and 78% respectively compared to the pre-operative unaided condition and 29%, 36%, and 26% respectively to the preoperative aided condition (n=11). The speech in noise test improved significantly by 4.2 dB and 2.4 dB signal to noise ratio (SNR), measured with two different tests (n=7). In eight patients, no pre-operative speech in noise was measureable. Three of these patients did not improve in speech in noise results, whereas the five other patients improved from not measureable to 0.5 dB SNR on average. Difficulty in hearing, measured by the APHAB questionnaire, decreased by 27% after implantation with the investigational DACI. Three patients suffered deterioration in bone conduction thresholds, which could not be related to the procedure or the experimental device. Two patients fully recovered. One revision procedure was necessary to change the position of a transducer that contacted the bony wall of the external ear canal.

The study concluded that the DACI investigational device is safe to implant and beneficial for severe to profound hearing loss in patient with otosclerosis, compared to the preoperative situation with hearing aids. An important criterion for success is the need for patients to still have measurable bone conduction speech recognition in the ear to be implanted.

In chapter 3.2, a long term follow up study of the Dutch cohort of five patients implanted with the experimental DACI is presented. The stability of the audiometric, functional en quality of life results was evaluated after approximately 1.5 and 3.5 years.
One patient suffered from decrease in sensorineural hearing of 10 dB. This hearing loss has remained stable during the follow up. He did not improve in speech understanding after implantation, despite adequate aided thresholds with the DACI. For the other patients, the overall aided and unaided thresholds showed stable values compared with the short term results. The mean unaided pure tone average was 83 dB HL and the long term aided results 35 dB HL for 3 months, 39 dB HL for 19 months and 41 dB HL for 40 months. The pure tone averaged results did not differ significantly from the pre-operative hearing aid results. The aided speech reception and speech in noise recognition values showed a significant improvement compared to the baseline. Four patients used hearing aids and were tested in pre-operative aided conditions with an average speech reception threshold of 42 dB HL, which is a benefit of 35.5 dB HL. With the DACI, these results were 36.4 dB HL at 3 months and an improved benefit compared to the preoperative hearing aids of 12.6 dB HL and 7.8 dB HL at 19 an 40 months. The mean speech-to-noise ratio (S/N) improved from 4.5 dB pre-operatively with hearing aids to 0.6 dB (3 months) and 0.4 dB (19 months) postoperatively. The APHAB questionnaire scores were equally improved from the pre-operative situation. In total, a significant improvement was found for all follow up moments, almost halving the percentage of difficulty in hearing from 58% to 30%. All five patients used their implant on a daily basis and were content with the device. No device failure or complications occurred.
This study concluded that the DACI experimental device provided stable results up to at least 40 months after implantation. A significant improvement of speech understanding, speech in noise and disability was found compared to pre-operative hearing aid results.

Comparison of auditory implants

Chapter 4.1 evaluates a study on 22 selected patients suffering from severe sensorineural hearing loss with a VSB or MET middle ear implant or with a first-generation DACI. The implants were tested to determine a gain per frequency related to the cochlear hearing level, best estimated by bone conduction thresholds (thus a gain-threshold ratio). This value is independent of the patient's degree of hearing loss and it can be compared to the commonly used NAL-NL hearing aid prescription rule. The second parameter was a measure of the input level at which the tested device saturated, which means that the amplification was no longer advancing at a linear mode and the sounds were no longer properly processed by the device. At that certain input level the maximum output of the device could be determined by simply adding the gain. Next, this maximum output was related to the level of sensorineural hearing loss of the patient to determine the dynamic range of hearing that the device offers for the amplification of sounds. Data were gathered in 9 patients (three MET, four VSB and two DACI users).

The gain-threshold ratio varied from approximately 0.2 at 0.5 kHz to 0.45 at 2 kHz and no significant difference was found between the three devices. The desired gain ratio, according to the NAL rule, should be at least 0.46 (at 1, 2, and 4 kHz). This ratio was found at 1 kHz and 2 kHz for the DACI users and at 2 kHz for the VSB users; for MET users, the values at 1 kHz and 2 kHz approached this target value. The input level at saturation was higher for the DACI than for the MET or VSB. As a consequence, the dynamic range of hearing was the largest for the DACI. This means that the DACI is better able to prevent the distortion of loud sounds due to device saturation.
The results of this study suggested that the DACI has an amplification capacity that exceeds the VSB and has a comparable or better capacity than the MET because of this larger dynamic range of hearing. It could therefore be outperforming the other implants in the rehabilitation of patients with severe sensorineural hearing loss that would need an acoustic implant. However, in contrast to the other two systems, implantation of a DACI is cochlear invasive.

In chapter 4.2, the methods of the study in chapter 4.1 were applied to evaluate the amplification options for patients suffering from mixed hearing loss with varying levels of sensorineural hearing loss. In this study the VSB (coupled to the stapes or round window) and DACI were measured in patients and compared to three bone conducting devices (BCD), viz. the Sophono transcutaneous BCD, the regular BAHA Divino (percutaneous BCD) and the more powerful BAHA Cordelle percutaneous BCD. The BCDs were tested on a skull simulator for the maximum output level. This maximum output was determined per frequency. These mean values were considered in relation to patients' level of the sensorineural hearing loss component.
The mean maximum output (at 0.5, 1 and 2 kHz) was 55dB HL for the Sophono, 70dB HL for the Divino and 85dB HL for the Cordelle. For the VSB, varying results were found. For two patients a poor result was found, which was explained by a poor coupling of the transducer to the oval or round window of the cochlea. Without these outliers excluded, the VSB provided a mean maximum output of 85 dB HL. For the DACI, all five patients could be stimulated louder than their loudness discomfort levels. This means that the DACI saturates at levels above a level around 110 dB HL. Assuming a minimal dynamic range of hearing of 35 dB HL, this study suggested that the maximum level of the sensorineural hearing loss component in mixed hearing loss should not be more than 20, 35, 50, and 50 dB HL for the Sophono, the BAHA Divino, the BAHA Cordelle, and the VSB device respectively. No maximum level of sensorineural hearing loss is set for the DACI, since it provides the ability to amplify the sounds to the loudness discomfort levels and therefore offers the full dynamic range of hearing amplification to the patient.

In the chapter 5.1, the previous chapters are discussed and the pros and cons for the various types of AMEI are discussed. The selection criteria for the most adequate acoustic

implant and the considerations on MRI compatibility are outlined. Furthermore, the future developments and reimbursement issues are discussed.

In conclusion, this thesis provides new scientific evidence that AMEI and DACI have a key position in the surgical restoration of selected hearing impaired patients. AMEIs should be considered in conductive and mixed hearing loss and DACIs can be beneficial for patients with severe to profound mixed hearing loss owing to advanced otosclerosis. When the treatment of chronic external otitis fails in patients suffering from sensorineural hearing loss, an AMEI provides a safe and well accepted solution, with adequate and stable benefits in quality of life. The transcanal approach is contra-indicated in this category of patients. AMEI and DACI can also be applied after surgery for chronic otitis media or cholesteatoma after subtotal petrosectomy.

When an acoustic implant is considered for a patient, the sensorineural levels of hearing loss need to be thoroughly evaluated. Progressiveness of hearing loss should be considered as well as MRI compatibility.

5.3.

Samenvatting (summary in Dutch)

Samenvatting

Actieve middenoorimplantaten (AMOI) worden al sinds 2 decennia toegepast in de chirurgische revalidatie van gehoorverlies. Het implantaat is opgebouwd uit een actuator die gekoppeld is aan de gehoorbeentjes en een implanteerbare signaalprocessor. Deze processor verwerkt en versterkt de geluiden die door een in- of uitwendige microfoon worden aangeboden. In het geval van een semi-implanteerbaar middenoorimplantaat communiceert een uitwendige geluidsprocessor met het implantaat via radio- of magnetische golven. Deze signalen worden gedecodeerd en omgezet in een vibratie van de actuator, waardoor de gehoorbeenketen in trilling wordt gebracht om in het binnenoor te worden waargenomen.
Recentelijk zijn directe akoestische cochleaire implantaten (DACI) ontwikkeld waarmee een toepassing beschikbaar komt om de vloeistof in het binnenoor direct in trilling te brengen. Een DACI is een middenoorimplantaat dat een sterke vibratie kan overbrengen op een gekoppelde stijgbeugel prothese die door een opening in de voetplaat van de stijgbeugel contact maakt met de binnenoorvloeistoffen in het geval van ernstig gehoorverlies bij geavanceerde otosclerose.

Dit proefschrift is toegespitst op de lange termijn resultaten van AMOI op verscheidene uitkomsten, waaronder de kwaliteit van leven, complicaties en implantaat falen. De resultaten van de eerste klinische toepassing van DACI zijn geëvalueerd in een korte termijn multicenter onderzoek en een lange termijn vervolgstudie. Daarnaast zijn er twee studies verricht naar de implantaat karakteristieken qua maximale versterking en saturatie van deze versterkte geluiden. Ter introductie worden de theorie van gehoor, gehoorverlies en de verscheidene implantaten beschreven.

Actieve middenoorimplantaten

Hoofdstuk 2.1 beschrijft een studie onder een geselecteerde studiegroep van 13 opeenvolgende patiënten met perceptief gehoorverlies en therapieresistente otitis externa. Deze patiënten ontvingen een zogenaamde Vibrant Soundbridge (VSB) implantaat dat middels een nieuwe experimentele procedure geplaatst werd. De hypothese was een verkorting van de procedure en een afname van perioperatieve complicaties door een benadering van het middenoor via de gehoorgang in plaats van de reguliere procedure door de mastoidholte. De verbindende draad tussen het implantaat en de actuator werd door de gehoorgang geleid en in een groeve in het bot van de gehoorgang begraven. Gedurende een follow up periode van 51 maanden werden 7 postoperatieve complicaties waargenomen bij 6 patiënten (46%). Deze complicaties bestonden uit een samenvallende gehoorgang (1), terugkerende extrusie van de verbindende draad (5) en een perforatie van het trommelvlies (1). Perioperatief werd bij 2 patiënten de chorda tympani zenuw opgeofferd. Er werd geconcludeerd dat

deze zogenaamde 'transcanal' methode om de VSB te implanteren ongunstig is voor patiënten met therapieresistente otitis externa.

In hoofdstuk 2.2 wordt een studie beschreven waarin de kwaliteit van leven en de mate van beperkingen werden bestudeerd middels gevalideerde vragenlijsten bij patiënten met een VSB of een semi-implanteerbare 'Middle ear transducer' (MET). De toegepaste vragenlijsten waren de Abbreviated Profile of Hearing Aid Benefit (APHAB) en de Glasgow Benefit Inventory (GBI), welke preoperatief en op korte en lange termijn postoperatief werden afgenomen. De gegevens van 33 patiënten (80%) waren beschikbaar, waarbij de gemiddelde postoperatieve duur 7,5 jaar was. Er werd geen verschil gevonden tussen de beide implantaat types. Het totale percentage van niet-gebruikers was 13%. De lange termijn APHAB-resultaten lieten een significante afname van klachten zien voor 43% van de patiënten vergeleken met 54% 1 jaar postoperatief. De GBI-resultaten laten een significante verbetering in de kwaliteit van leven zien voor de lange termijn met een positieve score voor 82% van de patiënten, vergeleken met 92% na 1 jaar (23 patiënten). De uitkomsten van de vragenlijsten lieten een negatieve trend zien, maar de uitkomsten bleven significant ten opzichte van preoperatief. De verbetering was enigszins hoger dan de resultaten in de literatuur.

In hoofdstuk 2.3 zijn de resultaten uiteengezet van een lange termijn evaluatie van het complete cohort van AMOI-patiënten. In de studie zijn de aantallen geëxplanteerde apparaten geëvalueerd, evenals het aantal revisie ingrepen en de complicatie frequentie. De explantaties werden onderverdeeld in een medische of een technische reden. De VSB, de MET en de zogenaamde experimentele 'fully implantable middle ear ossicular stimulator' (FIMOS) implantaten werden toegepast.
In totaal werden 94 patiënten geimplanteerd, van wie 12 patiënten middels een ronde venster of stapes koppeling in plaats van de reguliere koppeling van het implantaat aan de incus. Een totaal van 28 patiënten (30%) werden verloren in de follow-up: 7 patiënten stierven, 12 patiënten werden definitief geëxplanteerd en 6 patiënten verschenen niet meer voor de vervolgconsulten. De gemiddelde vervolg-duur was 4,4 jaar met een spreiding van 1 maand tot 15 jaar. In totaal werden 128 implantaten geëvalueerd: 92 VSB, 32 MET en 4 FIMOS. Hiervan werden 36 implantaten (28%) geëxplanteerd of vervangen (18 VSB, 14 MET, 4 FIMOS). Dit bracht de totale technische faal frequentie per implantaat type op 7% voor de VSB, 28% voor de MET en 100% voor de FIMOS.
Bij 16 patiënten (17%) werd een revisie operatie verricht (in totaal 20 operaties). De meeste operaties betrof een revisie van de huid of de geïmplanteerde magneet. Verder werd de koppeling van het implantaat aan de incus geverifieerd door middel van een middenoor-inspectie in 8 patiënten. Twintig patiënten (21%) leden aan een medische complicatie. De meest opvallende waren erosie van het lange been van de incus (4 patiënten) en extrusie van de draad in de gehoorgang (5 patiënten). De complicatie frequentie naam af met de

tijd en in de laatste drie jaar van de evaluatie kwamen er geen complicaties meer voor, terwijl de implantatie frequentie juist toenam. Deze trend is het best te verklaren door de leercurve en de verschillende experimentele toepassingen in de eerste jaren van de toepassingen van AMOI.
Vanwege de incompatibiliteit van de vroege generatie VSB-implantaten met MRI-scanners, werden 12 van 92 implantaten geëxplanteerd omdat er voor de patiënt een noodzaak voor een scan was. Dit probleem is recentelijk door de fabrikant opgelost. De VSB is nu compatibel met MRI-scans tot 1,5 Tesla. Voor de overige implantaten is dit probleem nog steeds aan de orde.
Hoewel het aantal complicaties, falende apparaten en revisie procedures als hoog kan worden bestempeld, laat de afnemende trend in de tijd zien dat de experimentele fase van de toepassing van AMOI voorbij is gegaan. De implantaten mogen beschouwd worden als een waardevolle en veilige bijdrage in de chirurgische revalidatie van gehoorverlies. De voordelen op zowel audiologisch gebied als de kwaliteit van leven zijn al in eerdere studies vastgesteld.

Directe akoestische cochleaire implantaten

Hoofdstuk 3.1 presenteert de resultaten van een eerste fase prospectieve multicenter studie die in Duitsland, Zwitserland en Nederland is uitgevoerd. Vijftien personen met ernstig gemengd gehoorverlies door gevorderde otosclerose werden geïncludeerd voor een implantatie met een experimenteel direct akoestisch cochleair implantaat (DACI). Dit implantaat bestaat uit een geluidsprocessor en een zogenaamde actuator, wat een titanium behuizing met een trillend uiteinde omvat. In plaats van een reguliere stijgbeugel vervanging, waarbij een prothese gekoppeld worden aan het aambeeld, wordt de stijgbeugel vervangende prothese tijdens de operatie aan de actuator gekoppeld, zodat deze direct met de perilymfe vloeistof in het binnenoor contact maakt. In een eerdere studie was reeds aangetoond dat het implantaat een toegevoegde versterking biedt in de hoge frequenties, vergeleken met een reguliere stijgbeugelvervanging in combinatie met een hoortoestel. Het doel van deze studie was de audiologische werkzaamheid en de veiligheid van het implantaat aan te tonen.
De pre- en postoperatieve beengeleidingsdrempels werden niet beïnvloed door de implantatie met het DACI. De gemiddelde vrije veld geluidsdrempel (0,25 tot 8 kHz) verbeterde significant met 48 dB vergeleken met de ongeholpen preoperatieve situatie en met 15 dB vergeleken met de preoperatieve geholpen situatie met een hoortoestel (11 patiënten). Voor alle frequenties behalve de 2 en 8 kHz drempels werd een significant verschil gevonden vergeleken met het hoortoestel preoperatief (5 patiënten). De scores van het woordverstaan bij 50, 65 en 80 dB verbeterde significant met 30, 75 en 78% respectievelijk vergeleken met de ongeholpen preoperatieve situatie en met 29, 36 en 26% respectievelijk vergeleken met de preoperatieve hoortoestel situatie (11 patiënten). De spraakverstaan-in-ruis scores verbeterden significant met 4,2 decibel voor de ongeholpen

en met 2,4 decibel voor de geholpen situatie (7 patiënten). In de overige 8 patiënten was preoperatief geen score meetbaar. Postoperatief was er voor 3 patiënten nog geen spraak in ruis test meetbaar, voor de overige 5 patiënten was er een verbetering tot een score van 0,5 decibel signaal/ruis verhouding. De beperkingen van het gehoorverlies op het dagelijks leven werden met een gevalideerde APHAB-vragenlijst geëvalueerd, waarbij sprake was een een afname met 27% na de operatie. Drie patiënten leden toch aan een milde vermindering van hun spraak verstaan, waarbij geen relatie met het implantaat kon worden gerelateerd en bij twee patiënten was het probleem reversibel. Voor 1 patiënt was een revisieoperatie nodig omdat het implantaat contact maakte met het het bot in de gehoorgang, wat succesvol werd verholpen.
De conclusie van de studie was dat het DACI veilig was om te implanteren voor patiënten met ernstig tot zeer ernstig gehoorverlies bij otosclerose en een goede verbetering van het gehoor werd bereikt vergeleken met de preoperatieve situatie met hoortoestellen. Een belangrijk criterium voor het succes met het implantaat is de meetbaarheid van de begeleidingsdrempels en beengeleide spraak in het te implanteren oor.

In hoofdstuk 3.2 wordt een lange termijn vervolgstudie gepresenteerd voor het Nederlands cohort van geïmplanteerde patiënten met een DACI. De stabiliteit van de audiometrische, functionele en kwaliteit van leven resultaten werd gerevalueerd na ongeveer 1,5 en 3 jaar.
Bij één patiënt werd een perceptief gehoorverlies van 10 decibel vastgesteld. Dit gehoorverlies bleef stabiel aanwezig gedurende de evaluatieperiode. Zijn spraak verstaan verbeterde niet na de implantatie, ondanks adequate geholpen drempels met het implantaat. Voor de overige patiënten waren de lange termijn evaluaties van de geholpen en ongeholpen drempels stabiel. De gemiddelde ongeholpen preoperatieve score was 83 decibel en de postoperatieve geholpen drempel 35, 39 en 41 decibel voor respectievelijk 3, 19 en 40 maanden postoperatief. Voor de vier patiënten die preoperatief een hoortoestel droegen, kon een vergelijking worden gemaakt met het implantaat. Het hoortoestel leverde gemiddeld een verbetering van de gehoordrempel van 35,5 decibel. Met het DACI kon een additionele verbetering boven dit niveau worden bereikt van 12,6 en 7,8 decibel bij 19 en 40 maanden respectievelijk. De gemiddelde spraak-ruis verhouding verbeterde van 4,5 decibel preoperatief met een hoortoestel naar 0,4 decibel bij 19 maanden. De APHAB-vragenlijsten werden opnieuw afgenomen, waarbij een stabiele verbetering van 58% naar 30% beperking in het dagelijks leven werd gevonden. Alle patiënten droegen het implantaat dagelijks en waren tevreden met het resultaat. Er traden geen complicaties op en er waren geen technische mankementen.
Concluderend toont deze studie aan de resultaten met het DACI een stabiel resultaat tonen tot 40 maanden na implantatie. Er werd een stabiele en significante verbetering gevonden voor het spraakverstaan in rust en in rumoer en voor de beperkingen in het dagelijks leven vergeleken met de preoperatieve situatie met een hoortoestel.

Vergelijking van akoestische implantaten

In hoofdstuk 4.1 wordt een evaluatie beschreven van 22 geselecteerde patiënten met een ernstig gehoorverlies, waarvoor zij geimplanteerd waren met een VSB, MET of DACI. De toestellen werden getest om een versterking per frequentie te bepalen, in relatie tot de perceptieve hoordrempel, de zogenaamde gain-threshold ratio (GTR). Deze ratio is onafhankelijk van de ernst van het gehoorverlies van de patiënt en kan worden vergeleken met de gebruikelijke NAL-NL-regel voor het afstellen van reguliere hoortoestellen. De tweede parameter was het bepalen van de saturatie van het implantaat, oftewel de maximale versterking die het implantaat nog zuiver kon versterken zonder bijgeluiden of volumeverlies bij een bepaald volume van het binnenkomende geluid. Het verschil tussen de maximale versterking van het implantaat en het perceptieve drempelniveau van de patiënt werd als het dynamisch bereik vastgesteld. De gegevens van 9 patiënten konden hiervoor worden geanalyseerd (3 MET, 4 VSB en 2 DACI gebruikers).
De GTR varieerde van ongeveer 0,2 bij 0,5 kHz tot 0,45 bij 2 kHz en er werd geen significant verschil gevonden tussen de implantaten. De gewenste GTR volgens de NAL-NL-regel zou tenminste 0,46 moeten zijn (gemiddeld van 1, 2 en 4 kHz). Deze ratio kon alleen worden gevonden voor 1 en 2 kHz bij de DACI-gebruikers en voor 2 kHz bij de VSB-gebruikers. Voor de MET-gebruikers benaderde de GTR deze waarde. Het grootste dynamische bereik werd gevonden voor het DACI en het kleinste bereik voor de VSB.
De resultaten van deze studie suggereren dat het DACI een grotere versterking kan bieden dan de VSB en een vergelijkbare of betere capaciteit heeft dan het MET implantaat. Daarom kan het DACI mogelijk beter presteren bij patiënten met een ernstig tot zeer ernstig gehoorverlies. Het is echter wel meer invasief dan de overige implantaten omdat er een open verbinding met de cochlea nodig is.

In hoofdstuk 4.2 werd een vergelijkbare studie verricht als in het voorgaande hoofdstuk, maar dan bij patiënten met een gemengd gehoorverlies, met een gevarieerd niveau van de perceptieve drempel. De implantaten VSB, gekoppeld middels de irreguliere toepassing aan de stapes of het ronde venster, het DACI en 3 typen beengeleidingsapparaten werden vergeleken. De typen beengeleider waren de Sophono trancutane toepassing, de reguliere Baha Divino percutane toepassing en de Baha Cordelle, welke een sterkere percutane toepassing benut. Deze drie apparaten werden op een zogenaamde schedel simulator getest voor hun maximale versterking per frequentie. De gemiddelde waarden werden gerelateerd aan het perceptief gehoorverlies van de patiënt om opnieuw het dynamische bereik te bepalen.
De gemiddelde maximale versterking (bij 0,5 , 1 en 2 kHz) was 55 decibel voor Sophono, 70 decibel voor Divino en 85 decibel voor de Cordelle. Voor de VSB werden variërende resultaten gevonden. Bij twee patiënten was sprake van een slechte koppeling, wat een slecht resultaat gaf. Met de exclusie van deze afwijkende resultaten, was de gemiddelde uitkomst voor de VSB 85 decibel. Voor het DACI werd bij alle 5 patiënten een versterking

gevonden die luider was dan hun oncomfortabele luidheidsgrens. Dit betekent dat een DACI pas saturatie vertoont boven een luidheid van 110 decibel. Uitgaande van een minimaal dynamisch bereik van 35 decibel, levert deze studie de suggestie dat er een maximale grens aan het perceptieve gehoorverlies kan worden toegepast voor de implantaten. Dit is namelijk 20 decibel voor Sophono, 35 decibel voor Divino en 50 decibel voor Cordelle en VSB. Voor DACI geldt geen maximale grens aangezien dit implantaat het geluid kan versterken tot de luidheidsgrens en dus een volledig dynamisch bereik kan benutten.

In hoofdstuk 5.1 wordt een discussie over de voorgaande hoofdstukken gevoerd en worden de voor en nadelen van de diverse middenoorimplantaten afgewogen. De selectiecriteria voor het meest adequate akoestische implantaat worden uiteengezet en de overwegingen ten aanzien van MRI-compatibiliteit worden benadrukt. Tot slot worden de toekomstige ontwikkelingen en de problemen met de vergoedingen bediscussieerd.

Concluderend levert dit proefschrift nieuwe wetenschappelijke inzichten dit aantonen dat actieve middenoorimplantaten en directe akoestische cochleaire implantaten een essentiële positie hebben ingenomen in de chirurgische mogelijkheden van gehoorverbetering voor slechthorende patiënten. AMOI moeten overwogen worden in conductief en gemengd gehoorverlies en DACI zijn van toegevoegde waarde in de behandeling van ernstig tot zeer ernstig gehoorverlies bij patiënten met gevorderde otosclerose. Indien de behandeling van chronische otitis externa faalt bij patiënten met een hoortoestel, kan een AMOI een veilige en goed getolereerde oplossing bieden met stabiele resultaten op de kwaliteit van leven. Wel is de zogenaamde transkanaal methode gecontra-indiceerd voor deze categorie van patiënten. AMOI en DACI kunnen eveneens worden toegepast na eerdere chirurgie voor chronische otitis media, cholesteatoom of in combinatie met een subtotale petrosectomie.
Wanneer een akoestisch implantaat wordt overwogen voor een patiënt is het relevant dat zowel het niveau van het perceptieve gehoor als de eventuele progressiviteit goed worden geëvalueerd. Daarnaast dient de MRI-compatibiliteit altijd een onderdeel van de afweging te zijn.

5.4.

Addendum

List of abbreviations

AC	Air conduction (threshold)
APHAB	Abbreviated Profile of Hearing Aid Benefit
AMEI	Active middle ear implant(s)
BAHA or BAHI	Bone anchored hearing aid(s) or implant(s)
BC	Bone conduction (threshold)
BCI	Bone conduction implant(s)
BCD	Bone conduction device(s)
BI	Bone implant
BTE	Behind the ear device
CHA	Conventional hearing aid(s)
CHL	Conductive hearing loss
CI	Cochlear implant
cMET	Cochlear Middle ear transducer
Codacs ID	Cochlear's direct acoustic cochlear stimulator investigational device
DACS	Direct acoustic cochlear stimulator
DACI	Direct acoustic cochlear implant(s)
dB	Decibel(s)
dBHL	Decibel(s) of hearing loss
dBSPL	Decibel(s) sound pressure level
EAC	External auditory canal
FF	Free field audiometry
FG	Functional gain
FIMOS	Fully implantable middle (ear) ossicle stimulator
FMT	Floating mass transducer
FU	Follow up
GBI	Glasgow Benefit Inventory
GR	Gain ratio
HA	Hearing aid(s)
Hz / kHz	(kilo-)Hertz
HL	Hearing loss
IL(O)S	input level at output saturation
MEI	Middle ear implant(s)
MET	Otologics Middle ear transducer(s)
MRI	Magnetic resonance imaging
NCIQ	Nijmegen Cochlear Implant Questionnaire
NIHL	Noise induced hearing loss
oMET	Otologics middle ear transducer(s)
PTA	Pure tone average of 0.5, 1 and 2 kHz thresholds
PTA4	Pure tone average of 0.5, 1, 2 and 4 kHz thresholds
RF	Radiofrequency
SIN	Speech in noise test
SMA	Suprameatal approach
SNHL	Sensorineural hearing loss
SNR	Signal to noise ratio
SRT	Speech reception threshold
TM	Tympanic membrane
TMA	Transmeatal approach
UCL	Uncomfortable loudness level
VORP	Vibrating ossicular replacement prosthesis
VSB	Vibrant Soundbridge
WRS	Word recognition scores

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Curriculum vitae

Joost Willem Zwartenkot werd op 12 oktober 1982 geboren in Franeker en groeide op in Leeuwarden. Als zoon van een psychiater en een psychotherapeute was zijn interesse in de mens en het menselijk lichaam al vroeg gewekt. In 2000 behaalde hij zijn vwo-diploma aan het Stedelijk Gymnasium Leeuwarden. Na uitloting voor geneeskunde in datzelfde jaar volgde een studiejaar in Groningen, waar hij zijn propedeuse Biologie behaalde aan de Rijksuniversiteit Groningen in 2011. Vervolgens startte hij met de studie geneeskunde aan de Erasmus Universiteit Rotterdam. Deze studie werd een jaar onderbroken voor een bestuursfunctie bij de Rotterdamse studentenroeivereniging 'Skadi'.
Na de coschappen verrichtte hij een afstudeeronderzoek binnen de KNO-heelkunde onder leiding van dr. Hans Hoeve en dr. Hans Borgstein in het Sophia kinderziekenhuis te Rotterdam, waarna hij onder de hoede van dr. René Poublon een half jaar oudste coschap volgde op de afdeling KNO-heelkunde in het Erasmus MC te Rotterdam. In het NKI-AVL te Amsterdam was hij nog enkele maanden te gast op de afdeling hoofd-hals oncologie bij prof.dr. A.J.M. Balm.
In 2009 werd de basis voor dit proefschrift gelegd op de afdeling KNO-heelkunde van het Radboudumc onder leiding van prof.dr.ir. Ad Snik, dr. Emmanuel Mylanus en dr. Jef Mulder. In april 2011 startte hij op dezelfde afdeling met de opleiding tot KNO-arts onder supervisie van prof.dr. Henri Marres en dr. Frank van den Hoogen. Zijn perifere stages volgde hij in het Rijnstate ziekenhuis te Arnhem onder supervisie van dr. Henk Bouman en in Viecuri MC te Venlo onder supervisie van dr. Eric Theunissen. Tijdens zijn opleiding tot KNO-arts heeft Joost zich met name in de otologie ontwikkeld. Daarnaast heeft hij 2 jaar lang deel mogen uitmaken van de visitatiecommissie-opleidingen van de landelijke beroepsvereniging voor KNO-artsen en volgde hij in zijn laatste jaar een management leergang voor specialisten in opleiding in het Radboudumc. Zijn KNO-opleiding heeft hij voltooid per 1 juni 2016, waarna hij in het St. Antonius ziekenhuis te Nieuwegein/Utrecht is gaan werken als chef de clinique. Vanaf 1 juli 2017 zal hij een fellowship neurotologie volgen in het St Vincents hospital in Sydney, Australië.
In 2013 is hij getrouwd met Ingeborg Ligteringen, met wie hij al een relatie heeft sinds 2004. Zij zijn de trotse ouders van hun dochters Féline en Julie.

List of publications

1. Zwartenkot JW, Hoeve LJ, Borgstein JA.
   Inter observer reliability for localization of recorded stridor sounds in children.
   Int J Ped Otorhinolaryngol. 2010;74(10):1184-1188.

2. Zwartenkot JW, Mulder JJ, Snik AFM, Cremers CWRJ.
   Vibrant Soundbridge surgery in hearing impaired patients with severe otitis externa: evaluation of a transcanal approach.
   Otology & Neurotology 2011;32(3):398-402.

3. Zwartenkot JW, Snik AFM, Kompis M, Stieger C.
   Gain and maximum output of implantable hearing devices in patients with moderate to severe sensorineural hearing loss.
   Journal of Hearing Science 2012;2(3):35-40.

4. Zwartenkot JW, Hashemi J, Cremers CWRJ, Mulder JJ, Snik AFM.
   Active middle ear implantation for patients with sensorineural hearing loss and external otitis: long-term outcome in patient satisfaction.
   Otology & Neurotology 2013;34(5):855-61.

5. Lenarz TH, Zwartenkot JW, Mylanus EAM, Snik AFM et al.
   Multi-center study with a Direct Acoustic Cochlear Implant.
   Otology & Neurotology 2013;34(7):1215-25.

6. Zwartenkot JW, Snik AFM, Mylanus EAM, Mulder JJ.
   Amplification options for patients with mixed hearing loss.
   Otology & Neurotology 2014;35(2):221-26.

7. Zwartenkot JW, Cremers CWRJ, Mylanus EAM, Snik AFM, Mulder JJS
   Long term evaluation of medical and technical complications and implant stability in active middle ear implantation.
   Otology & Neurotology 2016;37(5):513-519.