Nijmegen, 2017

PROGRESS REPORT 2017

Donders Hearing & Implants

Donders Institute for Brain,
Cognition and Behaviour

Radboud University,
Department of Biophysics

Radboudumc,
Department of Otorhinolaryngology

Donders Institute

Radboud University Nijmegen

Radboudumc

Addresses:

Department of Otorhinolaryngology
PO Box 9101, 6500 HB Nijmegen,
the Netherlands

Department of Biophysics
Huygens Building, HG00.800
Heyendaalseweg 135, 6525 AJ Nijmegen
the Netherlands

Dear reader,

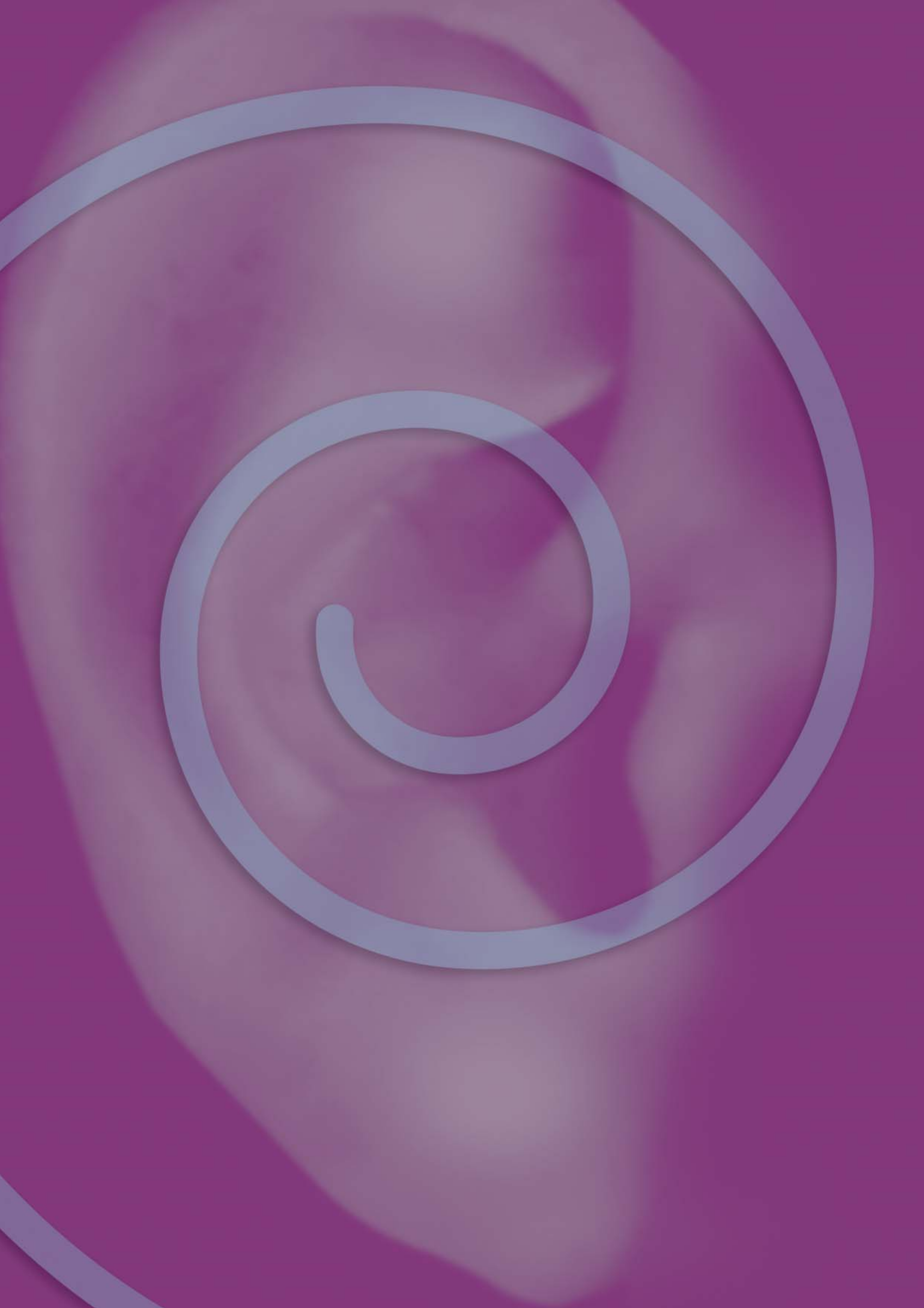
It is with pleasure that we are writing the introduction of the second Progress Report of Donders Hearing & Implants. This interdisciplinary research platform is firmly rooted within the Donders Institute for Brain, Cognition and Behaviour at Radboud University. Our interdisciplinary group consist of audiologists, clinicians, biophysicists, psychologists and neuroscientists from the department of Otorhinolaryngology (RadboudUMC), and the department of Biophysics (Radboud University). During the last four years, we further bridged the gap between academic fundamental research of the human auditory system, and clinical applications in the field of hearing rehabilitation. The interdivisional collaboration improved the quality of care for hearing-impaired subjects, and led to a better understanding of the mechanisms underlying hearing disorders. On the other hand, we experience a changing scientific and clinical environment. Increasing regulation, rapidly changing protocols, and insufficient funding for the variety of treatment options, seems to put the best possible clinical care under pressure.

With this Progress Report, we present an overview of the current activities at DHI. This report does not aim to give a complete overview of all ongoing research projects. We do hope, however, that this Report will further stimulate (international) collaborations, and that your expertise will help to further improve the objective evaluation of hearing rehabilitation.

We hope to share our enthusiasm for the potential of our work, and we hope that you will enjoy reading this Progress Report.

Prof. Emmanuel Mylanus
Prof. John Van Opstal
Prof. Ad Snik
Dr. Martijn Agterberg
Dr. Lucas Mens
Dr. Marc Van Wanrooij

DONDERS INSTITUTE Radboud University Nijmegen Radboudumc

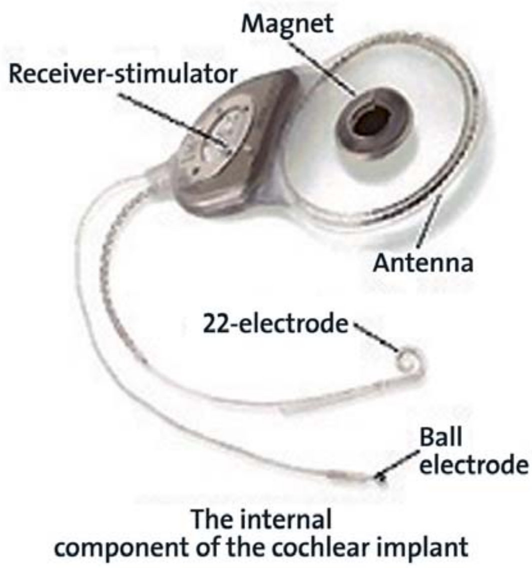


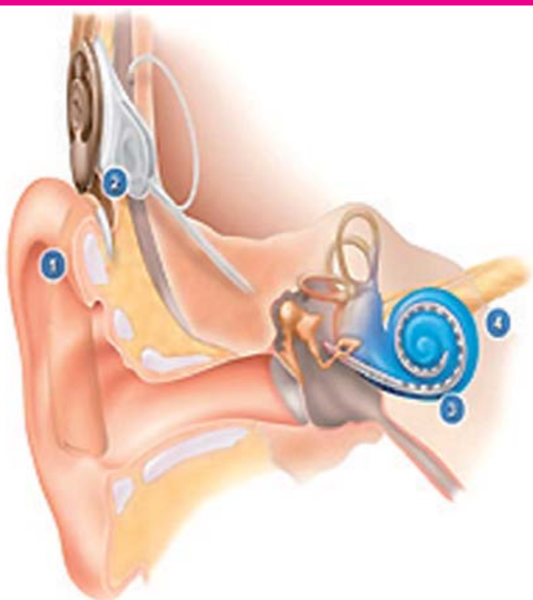
CONTENTS

Historical Background

In 1987, the first deaf adult patient received a cochlear implant in Nijmegen. The first child was implanted in 1992. In April 2017, more than two thousand deaf adults and children had been implanted. Cochlear implants have been developed for patients with profound hearing loss or total deafness. The actuator is an electrode array, typically 22 electrodes in a row, which is

The Cochlear Implant (device, and in situ).





surgically placed in the deaf cochlea (in the scala tympany). An externally worn audio processor is coupled trans-cutaneously to an implanted receiver unit that drives the electrode array. The electric current in the cochlea stimulates the remaining nerve endings, in such a way that the tonotopical organisation of the cochlea is used optimally.

Fitting of implantable bone-conduction devices (BCDs) was started in Nijmegen in 1988. The first child was implanted in the next year. At the end of 2016, close to two thousand patients had received an implantable bone-conduction device, about 20% being children. It comprises an externally worn audio processor with vibrator (as actuator), coupled percutaneously to the skull. Amplified acoustic signals are transferred into vibrations that are transmitted by the skull bone and stimulate the cochlea. This device was developed for patients with blocked or absent external ear canal, and/or malfunctioning middle ear, and to replace the rather ineffective conventional bone-conduction devices.

Implantable hearing aids or active middle ear implants are on the market since the mid-nineties. In the Nijmegen clinic, the first middle ear implantation was carried out in 1997. At the end of 2016, approximately 150 adults have been implanted but, so far, no children. Primarily, this auditory implant was developed for cosmetic reasons. However, most widely applied is the semi-implantable version. In principle, this auditory implant is a conventional acoustic device with the telephone exchanged for a small vibrating actuator. That actuator is implanted in the middle ear, driving directly one of the middle ear osscicles, or cochlear windows. In Nijmegen, middle ear implants were mainly applied in hearing impaired patients with co-morbid severe chronic external otitis, and in patients with severe mixed hearing loss, who didn't profit sufficiently from using an implantable bone-conduction device.

The the Middle-Ear Implant and BAHA

Introduction

Because hearing impairment directly affects the ability to communicate with other humans, it has a significant impact on the patient's social activities, and on the perceived quality of life. For children, hearing impairment also affects their mental development, not only with respect to maturation and organization of their auditory system and language acquisition skills, but also on the development of their cognitive and socio-emotional abilities.

Hearing rehabilitation technology has improved spectacularly over the last decades, not only because of the introduction of fast digital sound processing systems, but also because of growing knowledge in the field of biomaterials. These improvements have led to better conventional hearing solutions with enhanced sensitivity and selectivity, and increased signal bandwidth. The technological advancements have also enabled the clinical application of (partly) implantable

hearing devices, which have created new sound-amplification options for patients who suffer from previously untreatable hearing problems.

The ENT department at the RadboudUMC has become a leading clinic in the application of auditory implant technologies for over almost

30 years. We apply cochlear implants (CI), middle ear implants (MEI) and bone-conduction devices (BCDs) to patients with a wide variety of hearing disorders. In a continuous search for the best amplification options, new technological developments were recognized as innovative treatments for specific hearing problems (e.g. CI for total deafness, MEI for chronic external otitis, and semi-implantable BCDs for chronic draining ears, atresia and single-sided deafness). The main research focus on the technology of temporal bone-implants (TBIs) has been on safety and stability issues, and on their effectiveness in objective terms (audibility, speech recognition, spatial hearing), subjective terms (remaining disability, handicap) and in health technology studies.

The close collaboration between the department of Biophysics from the Faculty of Science, and the ENT department, has resulted in an increased number of academic research projects. We extended the research activities on hearing impairment and hearing rehabilitation with some valuable international partnerships. By its increased research mass and its novel expertise, we succeeded in receiving substantial external funding, and in initiating new projects using innovative technologies.

In what follows, we briefly describe the highlights of our current research projects. We summarize our current funding sources, and preview our near-future plans and long-term goals within Donders Hearing & Implants. In Chapter I (Academic research) special attention is paid to binaural hearing and the auditory brain. Chapter II describes current research projects investigating bilateral cochlear implantation, and clinical research projects related to acoustic implants. In Chapter III (Behavioral research projects) we focus on the development of deaf children with cochlear implants, and of children with severe hearing impairment who are listening with hearing aids.

Our aim is to continue our leading and pioneering position in the field of auditory implant technology, by extending our research efforts to the objective evaluation of auditory impairment and implant effectiveness, and by studying the potential neural mechanisms that underlie auditory rehabilitation and neural plasticity.

Academic research projects

Binaural Hearing

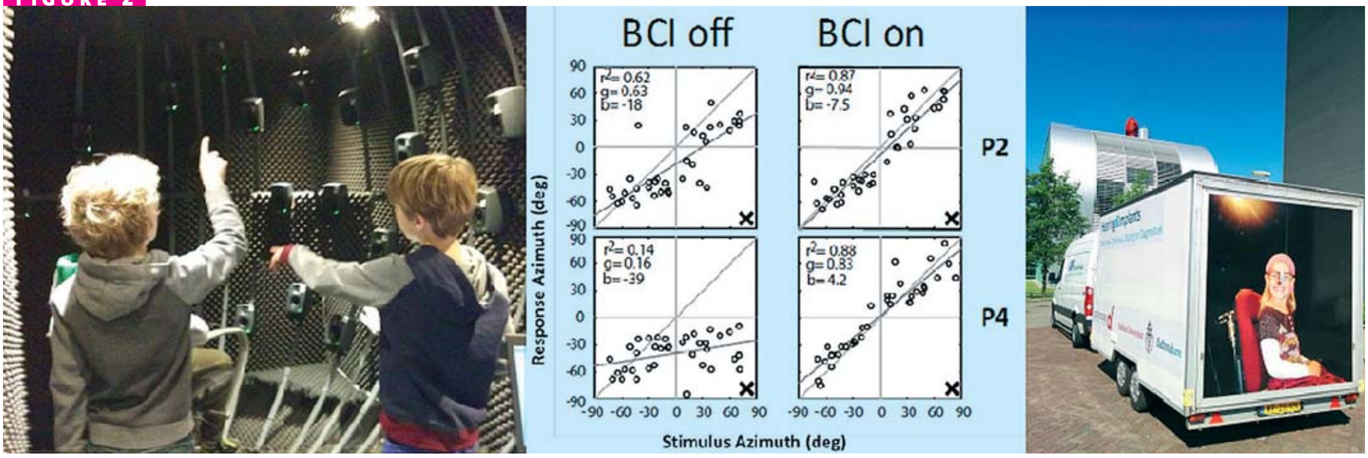
Binaural hearing refers to the proper neural integration of interaural time differences (ITDs for frequencies below about 1.5 kHz) and interaural level differences (ILDs for frequencies above 3 kHz). It enables normal hearing listeners to localize sounds and to understand speech in noisy listening situations. In Nijmegen, in the last five years, sound localization behaviour has been studied in different populations of patients with increasing interest. The laboratories of Hearing & Implants, reflecting the collaboration between the departments psychophysics and otorhinolaryngology, contain several experimental setups in which we can present sounds from all possible directions. We can investigate sound localization during whole body rotation (see later in this progress report), in a completely dark sound attenuated room *(Fig. 1)*, and in our mobile laboratory *(Fig. 2)*. Sound localization ability is measured with the magnetic eye-coil technique or with one of our different head-tracking techniques. We can study binaural processing of moving and static sound stimuli.

One of the major challenges is to relate the limitations in sound localization with hearing implants to possible imperfect processing

Figure 1

One of the sound localization setups (Hoop)

Figure 2



Children in the mobile lab (left). Sound localization responses for two listeners with UCHL (middle). Responses are plotted in the bone-conduction implant off (BCI off) and BCI on condition. Both listeners localize better with the BCI on. However, localization is not perfect. Mobile sound localization setup (right)

strategies or imperfect designs of the hearing implants. Our studies demonstrated considerable plasticity of the auditory system. In several high-impact research papers, we demonstrated that (impaired) human hearing listeners can relearn to re-acquire accurate sound localization abilities. Hearing-impaired listeners can learn to adapt their localization strategies under a wide variety of challenging hearing conditions. In several publications we have now demonstrated the increased localization abilities of patients with unilateral conductive hearing loss when fitted with a bone-conduction device. We expanded our studies to patient populations who are not present in the Netherlands. For example, cochlear implantation is a treatment option for adult with single-sided deafness in Germany, and cochlear implantation of unilateral deaf infants is already offered in some clinics outside the Netherlands, while, to our opinion, scientific evidence of the overall benefit of this treatment is limited. Furthermore, we evaluated the effect of advanced signal processing in hearing impaired patients and patients with hereditary deaf-blindness.

Children with unilateral conductive hearing loss who are implanted with a middle ear implant, are tested in Germany and the results are compared to the results obtained in children who are implanted with a bone-conduction device in the Netherlands. Because of our mobile auditory lab, the same method is used to test sound localization in an increasing number of different clinics. Therefore, we can investigate one of the important factors affecting performance with a bone-conduction device, namely the additional stimulation, through bone conduction, of the cochlea contralateral of the implanted side. This so called cross-hearing is possible because of the limited transcranial attenuation of sound vibrations in the skull. We demonstrated that although cross-hearing might affect directional hearing, patients implanted with a middle ear implant did not outperform patients with a bone-conduction device on a sound localization test in our setup.

Ultimately we restore binaural hearing and succeed in providing useful binaural cues. The ability to use binaural cues for the localization

FIGURE 3

One of the sound localization setup (Sphere)

of sounds is difficult to measure at a young age. Our results are the first that demonstrate accurate sound-localization performance under open-loop conditions in a completely dark environment by children from 7 to 11 years of age. We demonstrated that children performed as good as young adults (age 20-35). Our experience with performing tests in children is now helpful to investigate the best hearing solution for different populations of patient with a young age. One of the challenges is to provide fundamental evidence for the optimal moment of implantation of children with unilateral hearing loss. Another challenge is to avoid nonuse of hearing implants and provide evidence-based clinical guidelines for treatment of single sided deafness.

CONTACT

Martijn Agterberg
m.agterberg@donders.ru.nl
martijn.agterberg@radboudumc.nl
31 (0) 24 36 14238

SELECTED PUBLICATIONS IN THE LAST 3 YEARS:

- *Agterberg MJ, Van Opstal AJ, Hol MK, Van Wanrooij MM, Snik AF.* **Single-sided deafness and directional hearing: contribution of spectral cues and high-frequency hearing loss in the hearing ear.** *Front. Neurosc. 8:188, 2014.*
- *Ent van der L, Agterberg M, Wolter A.* **Met de audiowagen naar de basisschool.** *Audiology INFOS, 2016.*
- *Hartel BP, Agterberg MJ, Snik AF, Kunst HP, Van Opstal AJ, Bosman AJ, Pennings RJ.* **Hearing aid fitting for visual and hearing impaired patients with Usher Syndrome type IIa.** *Clinical Otolaryngology. 2016.*
- *Snik, A., Agterberg, M., Bosman, A.* **How to quantify binaural hearing in patients with unilateral hearing using hearing implants.** *Audiol Neurootol. 20 Suppl 1:44-7, 2015.*

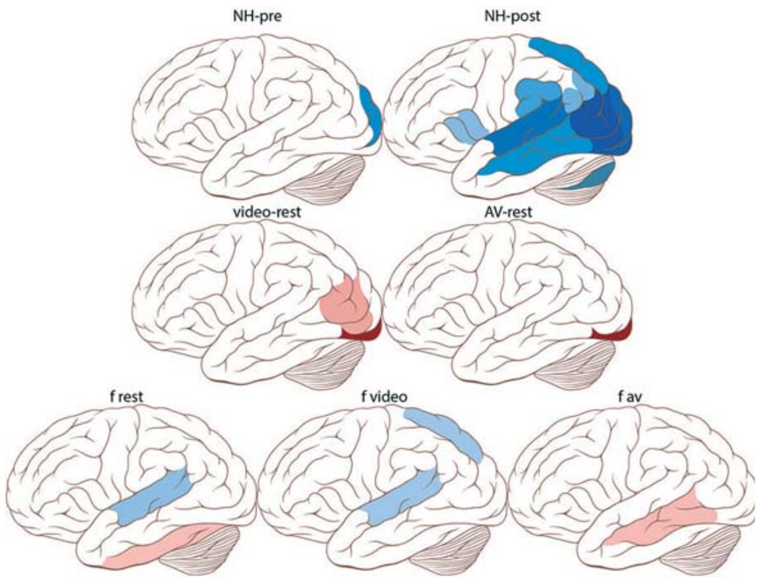
through positron emission tomography (PET). This technique has the benefit of having a high spatial resolution, which allows us to accurately localize the activity in auditory, visual and multisensory areas of the brain before and after implantation. Comparing individual differences in localized activity with idiosyncratic hearing performance after implantation (as determined by psychophysical measures, see elsewhere), we aim to predict the effectiveness of implantation *(Fig. 1)*.

Auditory brain

Despite tremendous advances in implantable hearing solutions, the prediction of substantial communication benefits after cochlear implantation in patients with pre-lingual deafness is still a clinical dilemma. This wide range in performance might be related to widely-varying brain activity patterns in these patients. At *Donders Hearing & Implants*, we use several techniques to provide an objective measure for the efficacy of cochlear implantation. Functional neuroimaging techniques allow for investigation of human central auditory processing and assessing human auditory cortical activity.

Unfortunately, several of the neuroimaging methods (magnetic-resonance imaging and magneto-encephalography) are severely limited in their usefulness in CI patients, as they are affected by and/or affect the metal, magnetic components of the CI. Therefore, we have studied neural reorganization of auditory cortical areas in prelingually deafened CI users by measuring metabolic changes in the brain

Figure 1



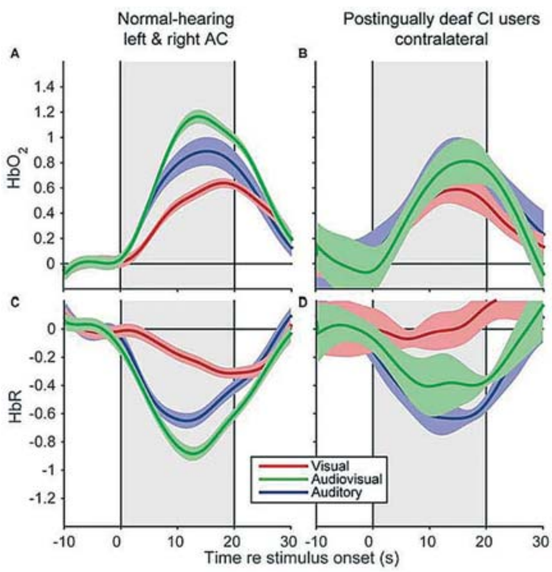
Glucose use. Regional differences in neuronal activity as measured through [18F]-FDG uptake between normal-hearing (NH) and pre-lingually (pre) or post-lingually (post) deaf CI-users are shown on top. Middle: differences in neural activity between rest and visual (video) or audiovisual (AV) stimulation. Bottom: Correlation between neural activity at rest, visual or audiovisual stimulation and phoneme score (blue = negative, red = positive).

PET has the disadvantage that it is invasive (an injection with a radioactive isotope is required). Therefore, we also combine two promising non-invasive neuroimaging techniques: electroencephalography (EEG) and functional near-infrared spectroscopy (fNIRS). Both techniques allow for measurements in a comfortable and ☛

natural environment. They can be utilized in infant and children studies, are portable, easy to handle, and have a relatively low cost. This allows for studying the rapid changes in auditory information processing, that are crucial for speech understanding; for investigating functional networks and interhemispheric specializations of the auditory system of CI patients; and furthermore, for learning the processes underlying impaired binaural hearing and sound localization, which are deemed essential for normal-hearing sound perception in noisy environments.

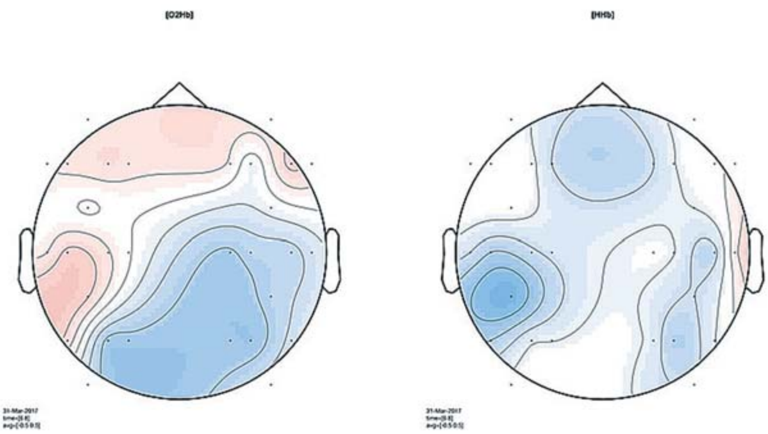
With fNIRS, we can measure how activity in the auditory cortex is influenced by auditory and visual speech. Comparisons between normal-hearing subjects and postlingually deafened CI users indicate how the auditory-impaired process sounds differently *(Fig. 2)*.

FIGURE 2



Functional hemodynamic response in temporal cortex to auditory, visual and audiovisual speech stimulation. Average changes in oxy- (top) and deoxyhaemoglobin (bottom) concentrations of normal-hearing subjects (left) and CI users (right) during stimulus activation (grey patch).

FIGURE 3



Functional hemodynamic response over the cortex to an auditory oddball. Peak changes in oxy- (left) and deoxyhaemoglobin (right) concentrations of one normal-hearing subject after presentation of a 1500 Hz oddball.

Recently, we expanded our fNIRS setup in order to measure all over the cortex, in order to determine lateralization of neural activity and hemispheric specialization of temporal cortices, and to infer listening effort from activity in frontal cortex *(Fig. 3)*. Classical acoustic experiments (such as the auditory oddball) give us a precise estimate of hemodynamic responses in unilateral, bilateral and bimodal CI users.

CONTACT

Marc van Wanrooij
m.vanwanrooij@donders.ru.nl
31 (0) 24 36 52428

SELECTED PUBLICATIONS IN THE LAST 3 YEARS:

- *van de Rijt, L.P.H., van Opstal, A.J., Mylanus, E.A.M., Straatman, L. V., Hu, H.Y., Snik, A.F.M., & van Wanrooij, M.M. (2016)*
  Temporal Cortex Activation to Audiovisual Speech in Normal-Hearing and Cochlear Implant Users Measured with Functional Near-Infrared Spectroscopy. Front. Hum.
  Neurosci., 10.
- *L.V. Straatman, M.M. van Wanrooij, L.F. de Geus-Oei, E.P. Visser, J.J.S. Mulder, A.F.M. Snik*
  Multisensory brain metabolic activity in prelingually deaf adults varies with speech recognition after cochlear implantation.
  In: Straatman, L.V. (2015) Cochlear Implantation in the prelingually deaf. Thesis, Ch. 4, pg. 55

Figure 1

Two-axis rotational vestibular chair in the Biophysics Laboratory at the Huygens building.

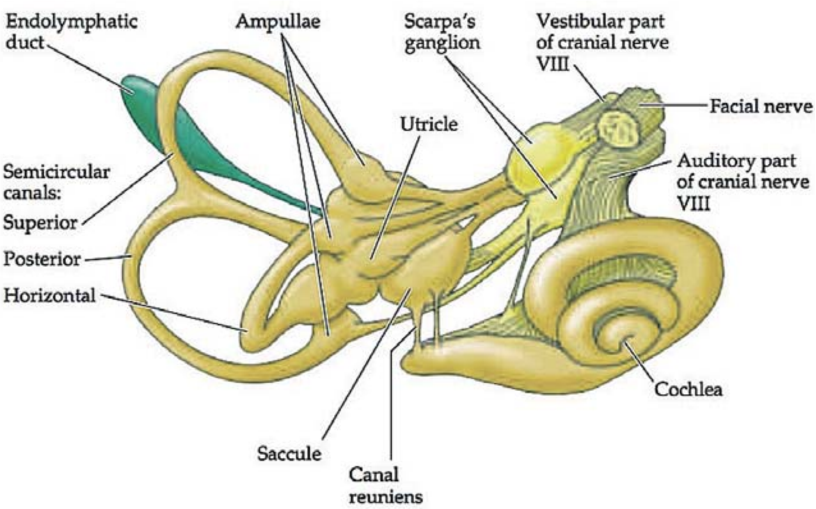
Vestibular Function

From March, 2017 onwards, the department of Biophysics will start a new research line on multisensory integration, in which the combined information processing of the visual, auditory, and vestibular senses will be studied within a new vestibular facility. This custom-built, unique machine will provide novel opportunities to quantify vestibular canal function in health and disease across all three rotational axes, and spatial perception under a wide variety of sensory conditions. Figure 1 shows the two-axis vestibular chair. It consists of two independent rotation frames (black and blue in the photograph), each equipped with 7.5 kW motors that enable whole-body rotation of the subject around an earth-fixed vertical axis (horizontal canal stimulation, black outer frame), and a nested horizontal axis (stimulation of the anterior and posterior canals around different directions, blue inner frame). In a first project, we will characterize the rotational mechanics (transfer characteristics) of the entire chair in all directions, and then measure eye-movement responses of healthy subjects to very brief target flashes

- during vestibular rotation in complete darkness (visuo-vestibular integration; e.g. Van Barneveld et al., 2011a).

The vestibular system *(Figure 2)* contains three pairs of mutually orthogonal canals (horizontal canal, superior, and posterior canals) that measure rotations of the head in three-dimensional space, and two additional otolith organs (the saccule and utricle), which measure linear translation of the head through space, and the head's orientation relative to gravity. Through this sensory system our brain is capable to determine the head movements and orientation in space, which is of crucial importance for maintaining our balance, as well as for keeping our eyes centred on objects of interest while the body (and head) is moving, either actively (walking, running, driving), or passively (while sitting in a train, or car).

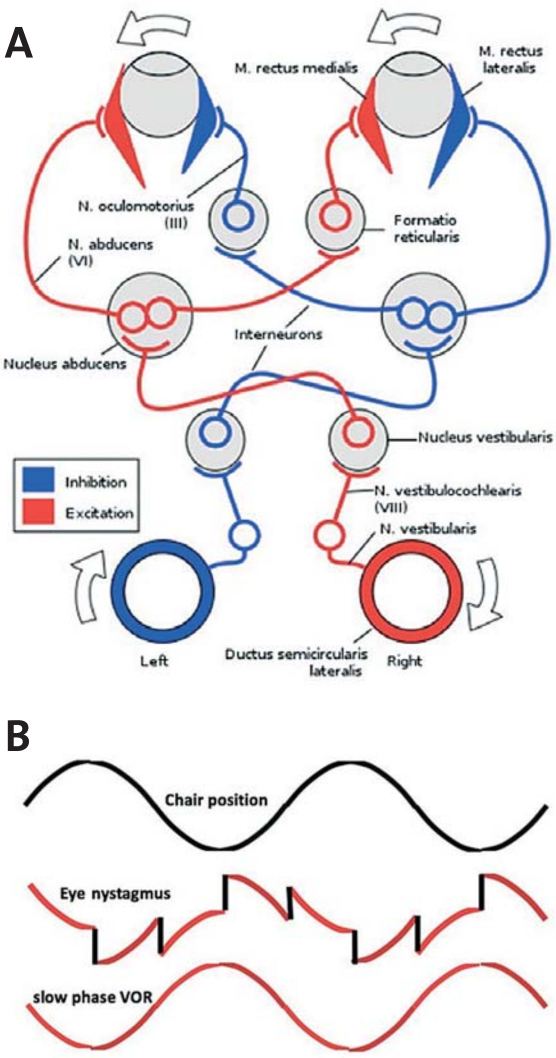
FIGURE 2



The vestibular system, showing the three vestibular canals and the otoliths (saccule and utricle), together with the cochlea. The vestibular system and cochlea share the same fluid-filled bony structures, which are fed through the endolymphatic duct. Disturbances of this latter system may cause e.g. Menieres disease.

The eyes are kept stable in space through a rapid reflex system, the so-called vestibular-ocular reflex (VOR). The VOR compensates any movement of the head in space by a precise and fast (15 ms reaction time) opposite movement of the eyes in the head. In this way, the visual image on the retina is stabilized, allowing the visual system to analyse fine detail of the object of interest. Any movement of an object across the retina causes visual blur, and therefore

FIGURE 3



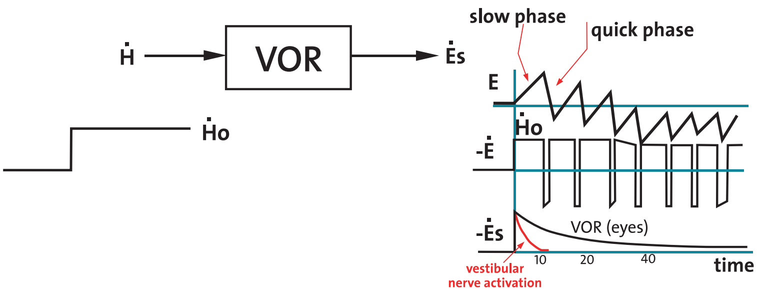
Shows the neural circuitry in the brainstem for the horizontal VOR, together with an example of the vestibular eye movements (nystagmus pattern of the VOR slow phase (red) and quick phase (black)) that are evoked during horizontal sinusoidal rotation of a normal subject. Because of the continuous acceleration of the head, the healthy vestibular reflex is always active.

disables clear vision. Thus, when the VOR is not functioning properly, stable vision is either impossible, or it becomes very fatiguing, as visual stabilization will have to be achieved through relatively slow (60-100 ms), and highly attentive, visually-driven feedback. Moreover, VOR malfunctioning is cause for strong nausea. Patients suffering from acute vestibular malfunction are very sick and cannot perform their normal functions of daily life, nor can they properly navigate through the environment. This is an extremely debilitating condition, which causes tremendous decrease of the patient's quality of life.

However, when a subject is suddenly rotated at a constant velocity (i.e., only an initial rapid acceleration, followed by no acceleration at all), the slow-phase VOR will gradually decay to zero, in about 40-50 seconds. At that point in time, the subject no longer senses the whole-body rotation, and thinks she is stationary in space *(Figure 4)*. When the chair is suddenly stopped, the subject senses a 40 seconds rotation in the opposite direction (but now she is standing absolutely still)!

Interestingly, the ocular nystagmus patterns in these cases by far exceed the activation of the canals and vestibular nerve, which already stop reacting after about 10 seconds, because of the canal hydrodynamics. Hence, the sensation of head rotation is kept in vestibular memory for about 30 seconds longer, by a neural mechanism that is called 'velocity storage'. In the Biophysics chair we can test subjects and patients for the integrity of these mechanisms across all directions of rotation.

Figure 4



Constant rotation of the head causes a slow-phase ocular VOR that decays over time, because the canals only react to changes in head velocity (i.e., head acceleration). To a step-change in head velocity (left), the canals react as a high-pass linear filter with a time constant of about 7 sec. Interestingly, the VOR will last for ~40 sec, due to the velocity storage mechanism in the brainstem.

On March 21, 2017 TV Gelderland broadcasted their news program "Trots op Gelderland", in which the vestibular chair is demonstrated with a human participant.

See: https://www.youtube.com/watch?v=LTL-owN52jc&t=367s

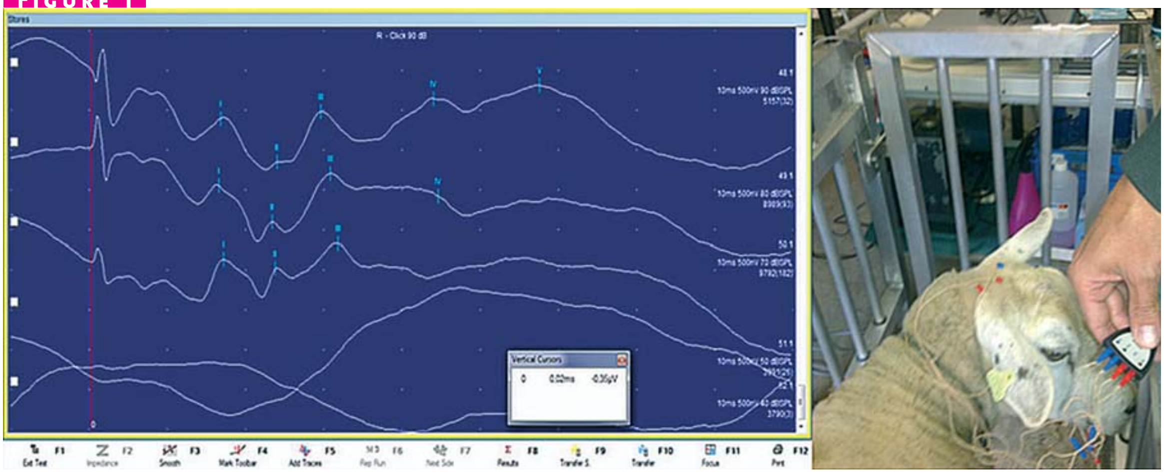
CONTACT

John Van Opstal
j.vanopstal@donders.ru.nl
+31 (0) 24 36 14 251

SELECTED PUBLICATIONS IN THE LAST 3 YEARS:

- *Oonk AM, Beynon AJ, Peters TA, Kunst HP, Admiraal RJ, Kremer H, Verbist B, Pennings RJ.* **Vestibular function and temporal bone imaging in DFNB1.** *Hear Res. 327:227-34, 2015.*
- *A.J. van Opstal* **"The Auditory System and Human Sound Localization Behavior."** *Elsevier Publishers, Academic Press, Amsterdam, the Netherlands, 431 pages, ISBN 978-0-12-801529-2 (2016).*

FIGURE 1



Auditory brainstem responses could be measured in awake animals. Placement of the electrodes was well tolerated by the sheep. By measuring ABRs in awake animals we avoid transportation and use of anesthetics.

Animal model for auditory implants

As the development of acoustic implant technology continues and evolves, the necessity for a large animal model, for preclinical device testing, is increasing. Due to the relatively large size of human hearing implants (~3–5 cm) cats, chinchillas, guinea pigs, rats and mice generally are unsuitable for these preclinical tests. Because of the unique animal research facilities in Nijmegen and the interdisciplinary collaboration between the departments Biomaterials, Psychophysics and Otorhinolaryngology, we were able to investigated whether a sheep model was suitable for testing (new) human hearing implants.

After implantation of bone-conduction hearing implants, middle ear implants or cochlear implant, animals were housed at the farm of the animal facilities. To reduce discomfort by transportation of the animals for functional measures, we develop a protocol to measure auditory brainstem responses (ABRs) in awake sheep. ABRs could be recorded in awake animals. Correct device placement was verified by cone beam CT and histology. Histological sections of the osseointegrated large titanium devices were, produced with a modified sawing microtome technique.

The developed sheep model is suitable as in vivo model for (preclinical) testing of human hearing implants. For successful implantation of middle ear implants and cochlear implants sheep should at least be two-years old. The sections evidenced that sheep middle ear and cochlea were, although smaller, morphologically highly similar to the human middle ear and cochlea.

CONTACT
Martijn Agterberg
m.agterberg@donders.ru.nl
martijn.agterberg@radboudumc.nl
31 (0) 24 36 14238

SELECTED PUBLICATIONS IN THE LAST 3 YEARS:

- *Klymov A, Neves CR, Riet J, Agterberg MJ, Mylanus EA, Snik AF, Jansen JA,* **Walboomers XF. Nanogrooved Surface-Patterns induce cellular organization and axonal outgrowth in neuron-like PC12-Cells.** *Hear Res. 320:11-17, 2015.*


Hearing&Implants
Onderzoek, Onderwijs, Nazorg en Diagnostiek
Radboud Universiteit
Radboudumc

Clinical research projects

Cochlear implantation in adults

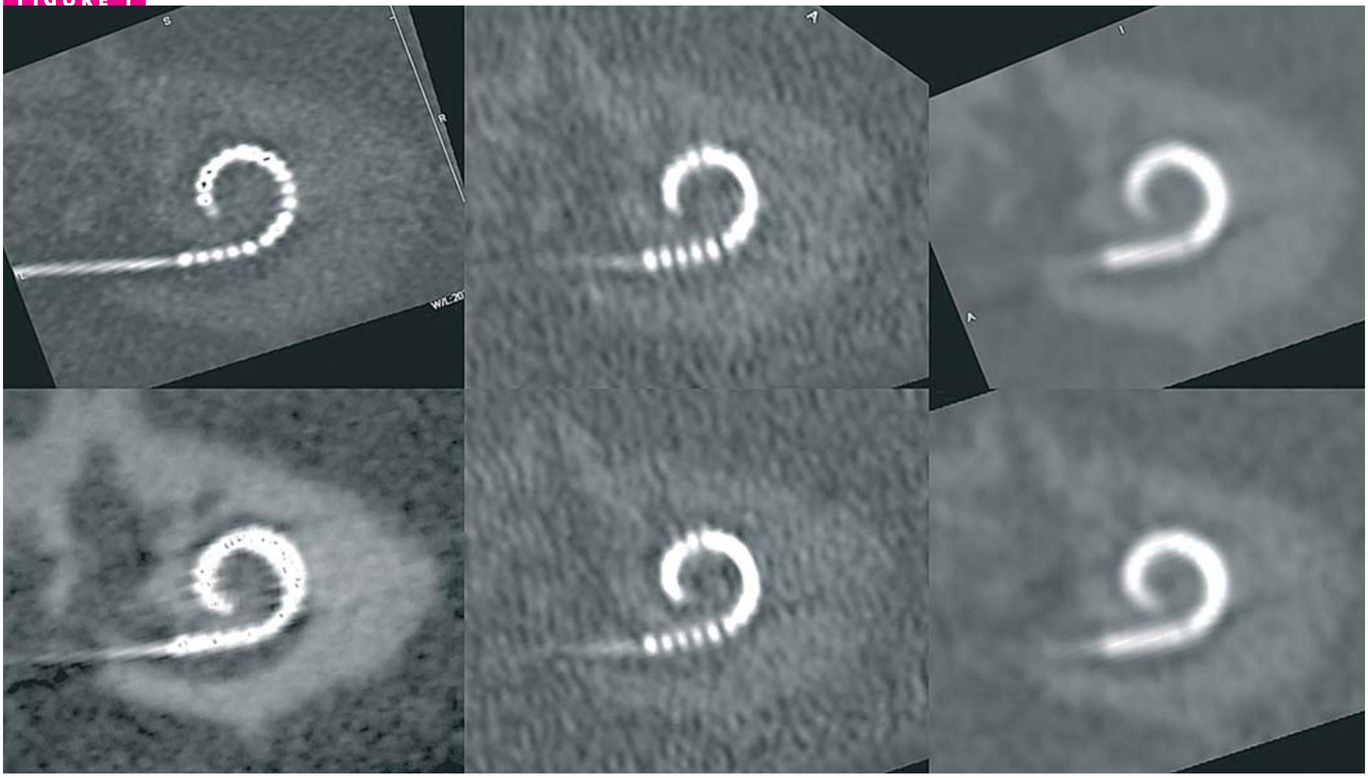
post-implantation imaging of the electrode array's position and its' relation to performance outcome

Using per- and post-implantation imaging of the patient is useful for the evaluation of the actual position of the electrode array within the cochlea. Since the recent designs of the electrodes of the various CI systems available tend to be thinner and more flexible designed for minimal traumatic insertions and preservation of residual hearing, the chance for a tip-fold over, or misplaced array may be higher.

Although some advocate the use of backward telemetry only to prove a tip fold-over, imaging provides direct information and allows the surgeon to act accordingly. In addition, a precise assessment of the array in relation to the modiolus wall, the basilar membrane and the depth of insertion is of use in the endeavour to improve the design of new electrode arrays. The quality of the imaging should be optimal in terms of the visibility of the cochlear structures, ideally of both bony and soft tissue structures, the visibility of the individual electrode contacts, with minimal dose of radiation and artefacts. There are three imaging techniques that are commonly used for postoperative evaluation of cochlear implants: plain X-ray imaging, single- or multi-slice (fan-beam) CT and more recently, flat-panel volume or cone-beam CT (CBCT).

With the advent of multi slice computer tomography (MSCT) volume scanning with low metallic artefacts and the possibility of reconstructing images in different planes became feasible. When applied to cochlear implant imaging, it renders information on insertion depth, insertion trauma and precise electrode position which is of interest for frequency mapping studies. Given the detailed view on the cochlear anatomy provided by MSCT also

Figure 1



Images of matched-dose protocols of the same specimen. Upper row (from left to right): ILUMA (0.10 mSv), Sensation 64 (0.08 mSv) and Aquilion 64 (0.08 mSv), bottom row: iCAT (0.04 mSv), Sensation 64 (0.07 mSv) and Aquilion 64 (0.03 mSv).

differences in operation technique may be evaluated. There is however a great variety in resolution among different scanners and not all 64-slice scanners are able to identify individual electrode contacts of a 22-electrode array. Another matter of concern is the radiation dose and in particular assumed risk to the eye lens. In regard to this the use of CBCT has lately been advocated as a low dose alternative to MSCT with superior image quality. These systems operate a conical shaped X-ray beam and provide high resolution imaging volumes of high contrast structures in restricted anatomic areas.

In order to compare imaging quality of MSCT and CBCT of in situ electrode arrays a temporal bone study was conducted. Five formalin-fixed human temporal bones were implanted with a Nucleus 24 Contour Advance practice electrode consisting of 22 half-banded platinum electrodes with non-uniform electrode spacing (0.8 mm at the basal end to 0.4 mm apically). Acquisitions were performed on two MSCT systems and two CBCT systems: Aquilion 64 (Toshiba Medical Systems, Otawara, Japan), Somaton Sensation 64 (Siemens Healthcare, Erlangen, Germany), iCAT 3D Imaging System (Imaging Sciences International Inc, Hatfield, USA) and ILUMA Ultra Cone Beam CT scanner (3M IMTEC Imaging, Ardmore, USA), respectively. The phantoms including the implanted cochleae were positioned perpendicular to the axis of the CT scanners to simulate clinical conditions. Methods of the study involved measuring the radiation dose and spatial resolution, as well as the subjective image quality assessment per scanning system by four independent observers.

☛ The study demonstrated that CBCT is indeed adequate for post-operative CI imaging with a fraction of the radiation dose that is used in clinical MSCT protocols. However, we also established that low-dose MSCT is a suitable alternative for CBCT, because in a dose-matched comparison, MSCT systems were rated equally to CBCT systems on overall image quality and most other variables. And while CBCTs are advantageous in the imaging of high density structures, they lack the flexibility of MSCT systems on acquisition and reconstruction parameters. For both CBCT and MSCT performance differences between systems of different manufacturers do exist and should be taken into account when choosing an imaging modality.

Current and future research on post-implantation imaging focusses on the observed position of the electrode array within the cochlea and the relation with performance outcome. In previous studies, the position of the electrode within scala tympani or scala vestibule has been shown to be significantly correlated.

Alternative parameters concerning the position of the electrode have been proposed, like the insertion depth and the electrode position relative to the modiolus. Our aim is to assess the predictive value of the electrode position, together with patient related factors like duration of deafness and audiologic factors, in a single cochlear implant center with a large number of participants with the same type of cochlear implant system. In an additional prospective study, we will evaluate the added value of the use of fused pre-implantation MRI and per- or post-implantation CT images in the assessment of the electrodes' position relative to bony and to soft tissue structures like the basilar membrane. Possibly, these data will provide more insight in the extent of insertion trauma and the exact position of the array. The benefit of having a greater insight in which factors influence outcome of cochlear implantation, both in terms of residual hearing preservation and performance outcome are obvious. First, it will aid in predicting outcome and therefore is of value in counseling. Second, it may lead to improved electrode designs and surgical techniques.

CONTACT

Emmanuel Mylanus
emmanuel.mylanus@radboudumc.nl
+31 (0) 24 36 14934

SELECTED PUBLICATIONS IN THE LAST 3 YEARS:

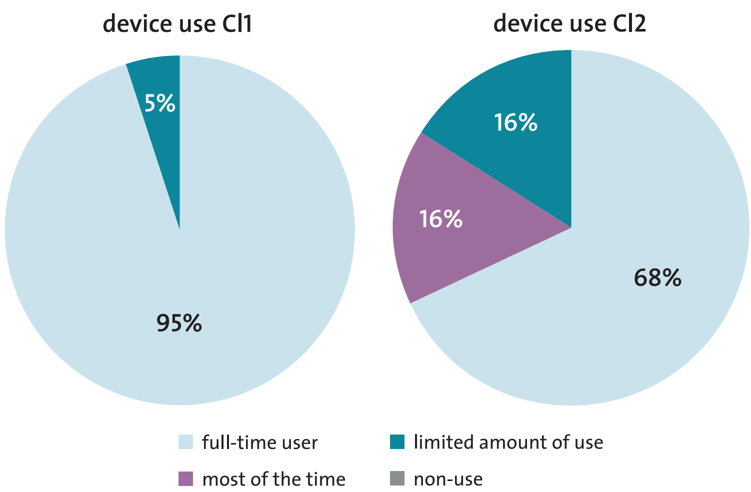
- *Theunisse HJ, Joemai RMS, Maal TJJ, Geleijns J, Mylanus EAM, Verbist BM.* **Cone-Beam CT Versus Multi-slice CT Systems for Postoperative Imaging of Cochlear Implantation-A Phantom Study on Image Quality and Radiation Exposure Using Human Temporal Bones.** *Otol Neurotol 2014:36;592-599.*

Paediatric cochlear implantation

Paediatric cochlear implantation has always been a cornerstone of clinical care within the department of otorhinolaryngology ever since the very first implantation of a deaf child in 1987. Research from our department and the Donders Institute for Brain, Cognition and behavior has been of societal importance. Two hallmarks in the area of reimbursement underpin this statement; in 1999 reimbursement for unilateral cochlear implantation was approved based on clinical evaluative reports on cochlear implant research projects in adults and children from our center. In 2012, the national board for health care provisionists and advising body for the Minister of Health CVZ issued a positive advice regarding the reimbursement of bilateral cochlear implants for children, in part based upon our publications on primary auditory and subjective benefits of bilateral cochlear implantation in children. In the meanwhile, longterm results have been published.

Interesting results were obtained using objective measures. On a brainstem and cortical level, maturation of the auditory processing of the first and of the second cochlear implant was observed, with a reduction in latencies of the cortical wave responses in time. In fact, we observed that the latency of the second implant caught up with the first to almost the same level. The morphology of the cortical wave generated by the second cochlear implant did however deteriorate with longer intervals between the first and second implantation and the age at which the second implantation took place. ☛

Figure 1

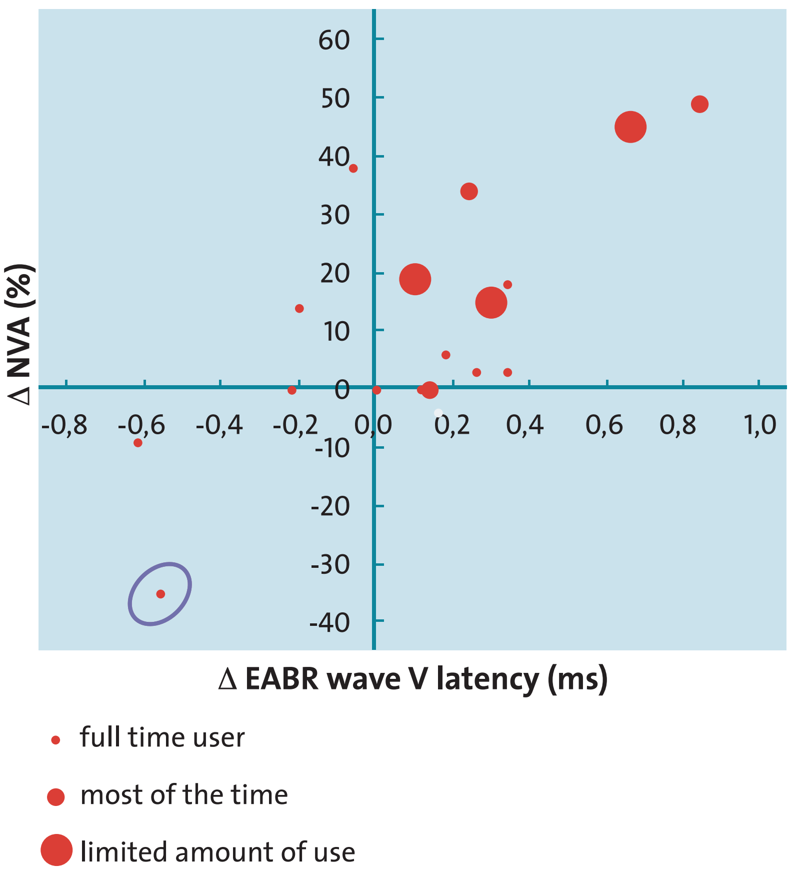


Device use of the first and second CI.

In a recent study involving assessment of brainstem latencies the aim of the study was to assess the long-term effect of sequential bilateral cochlear implantation on auditory brainstem maturation in children with early-onset deafness, when device use was taken into account. We hypothesized that auditory brainstem maturation is mostly functionally driven by auditory stimulation and therefore influenced by device use and not mainly by the inter-implant delay. Besides auditory brainstem maturation, the effect of device use and inter-implant delay was assessed on the long-term difference in speech recognition scores between the CI1 and CI2. The difference in device use of the first and second CI in the study group is depicted in Figure 1.

The results of our study showed that after sequential bilateral cochlear implantation in children with early onset deafness, in the long term, device use has a significant influence on both auditory brainstem maturation and speech recognition. According to our hypothesis, when the CI2 was worn less, EABR latencies evoked by the CI2 became longer in comparison with those evoked by the CI1 and differences in speech recognition became larger detrimental to that of the CI2 *(Figure 2)*. The difference in speech recognition between both CIs for an reduction of 1 category of device use of the CI2 was on average 13.8%. Speech recognition differences between both CIs increased with 3.5% for every increase of 0.10 ms of interaural EABR wave V latency difference. Multiple regression analyses revealed that interaural EABR wave V latency differences acted as a significant mediator between CI2 device use and interaural differences in speech recognition. This indicates that the less the second device is used, the larger the difference in interaural EABR wave V latencies, which consequently leads to larger differences in speech recognition between both implants. In our group, no significant effect of inter-implant delay was found.

FIGURE 2



Raw data on ƒEABR wave V latency against ƒNVA. The different categories of device use are shown in the legend. The encircled outlier, shows data for a child who only uses her CI1 for a limited amount of time.

The outlier in our data suggests that this framework also applies to device use in general. After sequential bilateral cochlear implantation, this particular child was no longer a full-time user of the CI1 as opposed to her CI2. Over time, device use of the CI1 decreased and consequently EABR wave V latencies of the CI1 became longer than those evoked by the CI2. As a consequence, speech recognition of the CI1 decreased, compared to that of the CI2 *(Figure 2, encircled datapoint)*.

In conclusion, in children with early onset deafness after various periods of unilateral deprivation, a sequentially placed CI2 can lead to similar auditory brainstem responses as the experienced CI1. The current study suggests that device use is of major importance for auditory brainstem maturation and speech recognition. Intensifying device use consequently leads to smaller or no interaural EABR latency differences, which consequently leads to smaller or no interaural differences in speech recognition in quiet scores. Results, however, must be interpreted as preliminary findings, because at the time of the study, device use could not be retrieved by a robust measure like data logging. For future studies and for guidance of children with a sequentially placed CI2 and their parents, device use indicated by data logging should be considered as a relevant factor contributing to the outcomes to be obtained.

Ongoing and future research…

Future research goals pertain to optimization of bilateral and bimodal fitting of children with severe to profound hearing loss. For optimal binaural hearing, balancing both devices is of great importance. To improve ILD cues it is important that interaural loudness is balanced. Another important aspect of the processing in bilateral implanted children will be the synchronization of bilateral input in order to provide access to useful and reliable binaural temporal cues. In a current research project the effect of loudness balancing will be tested on speech perception in noise and localization. In the localization task stimuli of different bandwidth will be presented in order to fully understand the processing of bilaterally presented sounds. This fitting method will be investigated in children with simultaneously and sequentially implanted CIs. If possible, this method will also be tested in children with bimodal stimulation.

CONTACT
Marloes Sparreboom
marloes.sparreboom@radboudumc.nl
+31 (0) 24 36 14817

Selected publications in the last 3 years:

- *Sparreboom M, Langereis MC, Snik AFM, Mylanus EAM.* **Long-term outcomes on spatial hearing, speech recognition and receptive vocabulary after sequential bilateral cochlear implantation in children.** *Res Dev Disabil 2014:36;328-337.*
- *Sparreboom M, Beynon AJ, Snik AFM, Mylanus EAM.* **The effect of device use after sequential bilateral cochlear implantation in children: an electrophysiological approach.** *Int J Pediatr Otorhinolaryngol 2016:86;161-166.*
- *Theunisse HJ, Joemai RMS, Maal TJJ, Geleijns J, Mylanus EAM, Verbist BM.* **Cone-Beam CT Versus Multi-slice CT Systems for Postoperative Imaging of Cochlear Implantation-A Phantom Study on Image Quality and Radiation Exposure Using Human Temporal Bones.** *Otol Neurotol 2014:36;592-599.*

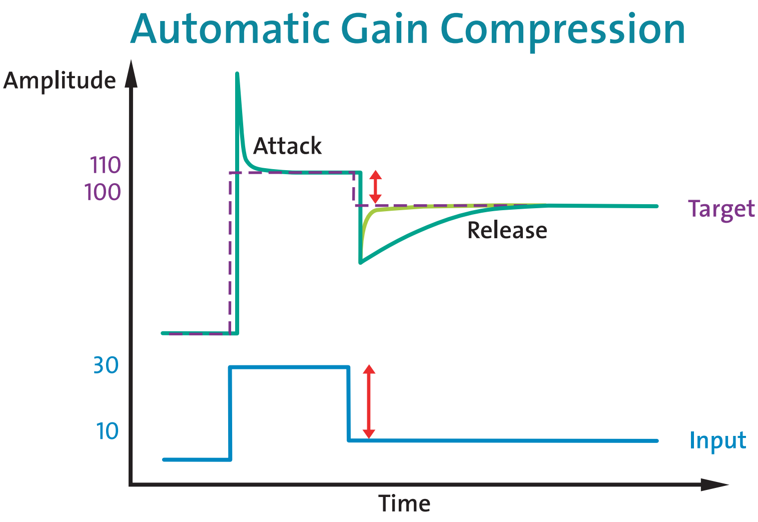
Bimodal Hearing

Traditionally, the use of cochlear implantation has been restricted to people who are deaf in both ears. Cochlear implants have shown increased reliability with respect of saving residual hearing in the implanted cochlea, and increased speech understanding. As a result, now candidates are offered surgery even if they have considerable residual hearing. More than half of recently implanted CI users now wear a hearing aid in the non-implanted ear. The combined use of electrical and acoustical stimulation is called "bimodal" hearing, see Figure 1.

Figure 1

Many cochlear implant users benefit from amplification of the acoustical signal in the non-implanted ear in addition to electrical stimulation by the CI: Bimodal Hearing. The benefit of bimodal hearing depends on patient characteristics, but also to avoidable incongruities in signal processing between devices affecting interaural level differences (ILDs). Or hypothesis is that eliminating unnecessary distortions of ILD cues will improve bimodal hearing.

FIGURE 2



Automatic Gain Compression. Sudden changes in the input (bottom) lead to smaller changes in the output in order to encompass the decreased dynamic range in the affected cochlea. Compression typically reacts with a short attack time avoiding uncomfortable loud sensations and a release time that is much longer to avoid a "pumping" response that is distracting. In our experiment, AGC time constants in the hearing aid were matched to that in the CI processor (dual attack, slow release time of 1.5 ms instead of 50 ms in the original hearing aid setting), possibly improving ILDs.

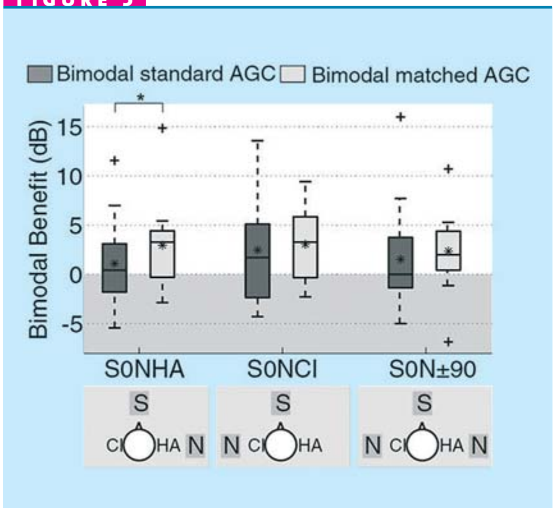
Ideally, the acoustical and electrical inputs complement each other leading to a benefit that compares to the benefit that is possible with a second cochlear implant. Such a bimodal benefit has been shown for speech perception in noise and for voice pitch perception. Horizontal plane localization is improved in some subjects, but this is less consistent across subjects. In a series of experiments, we are investigating fundamental aspects of bimodal hearing as well as technical solutions to improve bimodal benefit.

Automatic Gain Control is used in hearing aids to limit the dynamic range of input signals to fit within the limited dynamic range of the affected cochlea. Hearing aids differ in the time over which increases in intensity are integrated before compression kicks in (attack time), and even more in the time after which a softer input leads to less compression (release time, see Figure 2).

In a cross-over study, 15 users of the same CI device were provided with a hearing aid engineered to match AGC time constants to that of the CI processor. Fifteen bimodal users were tested after at least 3 weeks acclimatization to the new signal processing. All subjects were able to use the experimental device. Everyday sentences were presented from the front, and non-sense speech maskers from several different locations. If the masker was presented at the hearing aid side, AGC-matching resulted in a significant improvement of the critical signal-to-masker level of 1.9 dB (an increase of up to 20% correct).

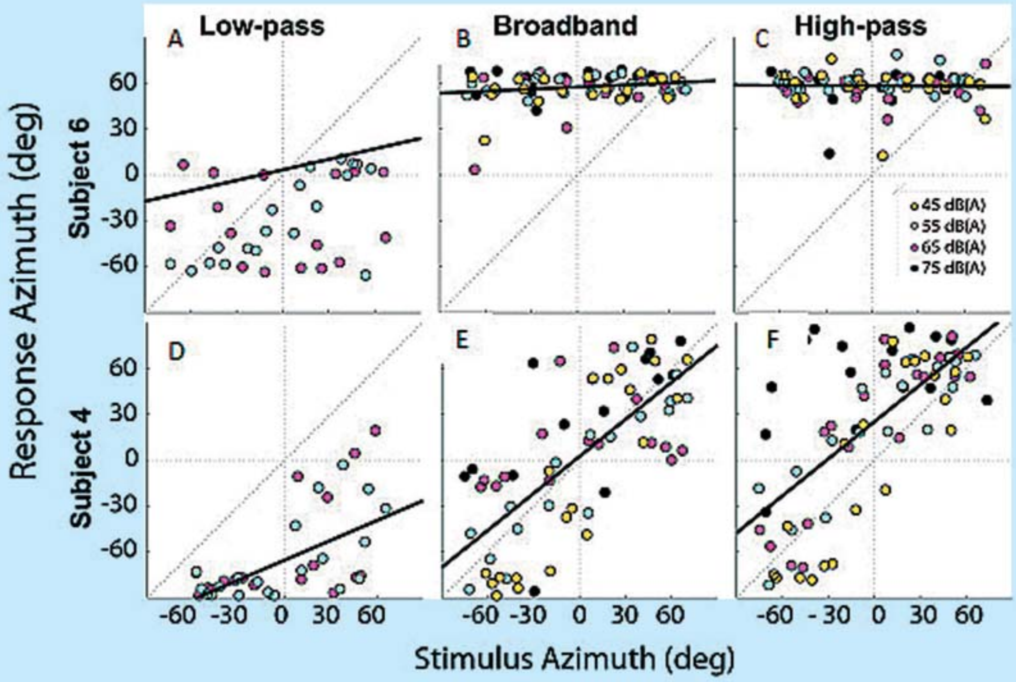
Localization has been tested in the same subjects, after matching the AGC time constants. Our hypothesis was that matching leads to an improved protection of ILD cues and thus in adequate horizontal sound localization. Figure 3 shows results from two subjects. For subject 6, all sounds were localized at the CI side (+60°) whenever the signal contained frequencies

FIGURE 3



Bimodal benefit of adding a hearing aid. A significant additional bimodal benefit of 1.9 dB was found when noise was presented at the hearing aid side.

FIGURE 4



Subjects were presented short noise bursts from unpredictable angles in a dark room. Perfect localization in the horizontal plane would result in responses on the diagonal. Subject 4 shows some ability to localize if the signal contains frequencies above 1500 Hz.

higher than 1500 Hz (only audible through the CI). Signals containing mainly low frequencies were localized at the hearing aid side. Thus, subject 6 responses were based on which side was loudest and no evidence of true binaural processing was seen. Subject 4, with considerable residual hearing up to 2 kHz, performed best among all subjects but many responses were still inaccurate and sounds missing high frequencies were again mainly heard at the hearing aid side.

The localization experiments suggest that the bimodal subjects that participated in our experiments had little or no access to timing cues and heavily depended in intensity cues. Intensity cues in the low frequencies are small and can easily be corrupted by uncoordinated signal processing in the left and right device. We have shown that the matching of AGC time constants supports speech understanding in some situations. Based on this result and similar findings of other researchers, Advanced Bionics has marketed a dedicated hearing aid specifically for bimodal use. Future research is planned to explore possibilities to further improve ILD cues using this new technological platform.

CONTACT
Lucas Mens
Lucas.mens@radboudumc.nl
+31 (0) 24 36 19749

SELECTED PUBLICATIONS IN THE LAST 3 YEARS:

- *Veugen LC, Chalupper J, Snik AF, Opstal AJ, Mens LH. Matching* **Automatic Gain Control Across Devices in Bimodal Cochlear Implant Users.** *Ear Hear. 37:260-70, 2016*
- *Veugen LC, Hendrikse MM, van Wanrooij MM, Agterberg MJ, Chalupper J, Mens LH, Snik AF, John van Opstal A.* **Horizontal sound localization in cochlear implant users with a contralateral hearing aid.** *Hear Res. 336:72-82, 2016.*
- *L.C.E. Veugen, J. Chalupper, A.F.M. Snik, A.J. Van Opstal, and L.H.M. Mens* **Frequency-Dependent Loudness Balancing in Bimodal Cochlear Implant Users.** *Acta Otolaryngology. 136: 775-781, 2016.*
- *L.C.E. Veugen, J. Chalupper, L.H.M. Mens, A.F.M. Snik, and A.J. Van Opstal.* **Effect of Extreme Adaptive Frequency Compression in Bimodal Listeners on Sound Localization and Speech Perception.** *Cochlear Implants International, Accepted for publication.*

Temporal Bone-Implants

A great deal of our research efforts in the years 2013 – 2016 focused on clinical implant trials, investigating novel titanium implants in terms of stability, survival and tolerability. These recent years, development of temporal bone implants and bone conduction devices (BCDs) gained momentum. Partially, this has been stimulated by the introduction of a second manufacturer entering the market, as competition is known to stimulate progress and further improve quality. Furthermore, new developments such as transcutaneous coupling and active implants have been introduced recently. Next, during the last years we have been able to acquire long term results of these novel implants.

Figure 1

Resonance frequency analysis (RFA). First, the SmartPeg is screwed on the abutment. Second, the handheld electronic analyses device excites the SmartPeg through electromagnetic pulses and analyses the implant stability quotient (ISQ). Figures courtesy of Osstell AB and Cochlear Bone Anchored Solutions AB.)

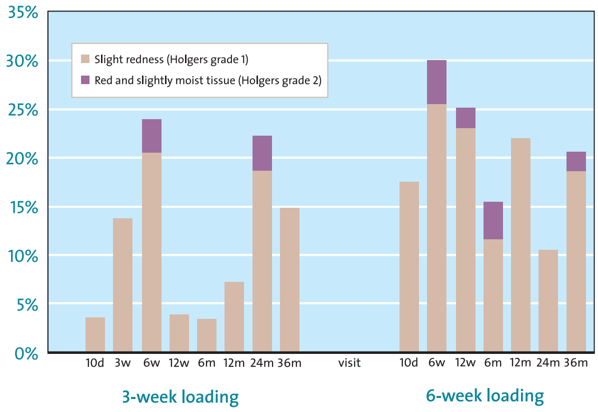
Since the commercial introduction of the BAHA® in 1984 until 2009, there was only a single implant system available, the titanium machined flange fixture, which was obviously subject to some evolutions over time. This system has been marketed by several companies and is currently known as the Cochlear Baha system (Cochlear Bone Anchored Solutions AB, Mölnycke, Sweden). The outcomes of these implants are well known. A new implant design was commercially introduced in 2010, the Baha BI300, with a wider diameter, small-sized threads at the implant neck, and a moderately rough surface on the intra-osseous portion of the implant. Also the abutment had evolved: the initial 5.5-mm conically shaped abutment was changed to a 6-mm rounded, apically converging design. This implant and abutment were found superior to the previous generation flange fixture in a multicenter randomized controlled clinical trial in terms of implant stability quotient (ISQ) and soft tissue tolerability after 5 years of follow-up. In 2009, Oticon's Ponto system (Oticon Medical AB, Askim, Sweden) was introduced as an alternative bone-anchored hearing implant with accompanying BCDs. A retrospective analysis of these first 31 implants from our center with a mean follow-up of 16.9 months showed positive results. In 2012, the Ponto wide implant was introduced. The major change in the implant's design was the wider diameter (3.75 mm to 4.5 mm) and, additionally, a different cutting geometry and threading compared with the previous generation implant. The first clinical case series of 20 patients presented promising one-year results with 100% implant survival, generally increasing ISQ trends, and good soft-tissue tolerability. The 3 year data of a randomized controlled clinical trial comparing the Ponto wide implant with the previous generation implant of in total 60 patients are currently being analyzed.

As a result of these higher initial ISQ values of the wide implants and the increasing trends in ISQ, earlier loading the BAHI with the BCD was studied. This concept was mostly stimulated by dental research where earlier (and even immediate) loading protocols are common practice. Promising, yet, relatively short-term, outcomes have been reported on early loading at three weeks with a three-year follow-up have been published in the past years and 5 year data are being collected. Next to this a clinical approach on how to use and interpret the ISQ values.

1) Implant and abutment type and length influence ISQ and should always be specified when presenting ISQ values. The correct SmartPeg (as recommended by the manufacturer) should be used, and the specific type used should be stated when reporting outcome. The SmartPeg-to-abutment/implant connection needs to be identical to ensure comparable data between different implants/abutments.
2) Changes in ISQ from baseline and over time define the tendency of implant-bone stability.
3) At present, absolute stand-alone ISQ values should not be interpreted individually. ISQ values are at this moment most meaningful as a trend in the individual patient or in a population over time. Therefore, in clinical use, no conclusions should be based on individual ISQ values at a certain moment in time. We suggest performing a baseline measurement at the time of implant insertion and measure again when applicable.
4) Standardized time points for RFA in research should be determined prospectively. RFA at surgery should be established as a baseline. Depending on the research question, follow-up moments may vary.
5) After abutment replacement, individual ISQ trends from baseline cannot be interpreted anymore if abutments differ in length. A new baseline ISQ value should be established after replacement.
6) It is encouraged to present case series of clinically unstable implants with baseline and event related ISQ values. With a large pool of such data, an individual absolute ISQ value for a specific implant might be of clinical use to predict its clinical behavior.

The abutment design is arguably the most important implant related factor for soft tissue tolerability, as this is the actual percutaneous part of the system. Besides the recent change in abutment design from conical to concave and shoulder shaped, which has been mentioned earlier, different abutment lengths have been introduced. The first longer (8.5-mm) abutment was introduced in 2003. This longer abutment provided a solution for patients with frequent soft tissue related problems such as Holgers grade 2 (or higher) skin reactions and soft tissue overgrowth, as well as patients with a thick scalp and preserved them from further surgical interventions. Not only was scalp thickness found to correlate with body mass index (94),

Figure 2



Soft tissue reaction as a percentage of visits according to Holgers' classification for the study population (3-week loading) and the comparison population (6-week loading).

obese patients (BMI > 30) are more prone to have soft tissue complications resulting in partial or total overgrowth of skin over the abutment. Ethnic disparity in soft tissue complications had been reported: patients with dark skin experience significantly more keloid or hypertrophic scar formation compared to patients with lighter skin. Longer abutments have proven to be specifically beneficial in surgery of patients with thick scalp or tendency to hypertrophic scarring. Currently, the Baha BA300 abutment is available in 6, 9, and 12 mm and the Ponto abutment in 6, 9, 12, and 14 mm. Increasing abutment lengths was considered safe because of the higher implant stability and survival of wide implants.

The availability of these longer abutments allowed surgeons to further evolve the linear incision technique to a technique without subcutaneous tissue thinning. Besides this technique being quicker and the outcomes are reported to be more cosmetically pleasing, fewer and less severe subcutaneous tissue infections are expected to be encountered, healing time is faster, and numbness and pain around the implant are minimized compared to the previously used techniques. Placing the implant either inside or outside the line of incision turned out to be non-relevant to the soft tissue reactions.

Next to changes in implant and abutment design and surgical techniques, the bone conduction devices itself have evolved over time. They became smaller, more powerful, wireless and compatible with several mobile devices i.e. adjusted to the current era of digital innovations. Another important aspect of our research over the past years is long-term evaluations of patients satisfaction and usage, especially in the extended indications like single-sided deafness and unilateral conductive hearing loss. Especially in these patient groups the directional hearing abilities are of main interest. The contribution of spectral cues and high frequency hearing loss in the hearing ear has been studied in SSD patients. In patients with bilateral conductive hearing loss the hearing ability improved with bilateral bone conduction devices.

CONTACT

Myrthe Hol
myrthe.hol@radboudumc.nl
+31 (0) 24 36 14934

SELECTED PUBLICATIONS IN THE LAST 3 YEARS:

- *Den Besten CA, Stalfors J, Wigren S, Blechert JI, Flynn M, Eeg-Olofsson M, Aggarwal R, Green K, Nelissen RC, Mylanus EA, Hol MKS.* **Stability, Survival, and Tolerability of an Auditory Osseointegrated Implant for Bone Conduction Hearing: Long-Term Follow-Up of a Randomized Controlled Trial.** *Otol Neurotol. 37:1077-83. 2016.*
- *Bosman AJ, Mylanus EA, Hol MKS, Snik AF.* **Wireless and acoustic hearing with bone-anchored hearing devices.** *Int J Audiol. 2015 Jul;55(7):419-24. 2015.*
- *den Besten CA, Nelissen RC, Peer PG, Faber HT, Dun CA, de Wolf MJ, Kunst HP, CremersCW, Mylanus EA, Hol MKS.* **A Retrospective Cohort Study on the Influence of Comorbidity on Soft Tissue Reactions, Revision Surgery, and Implant Loss in Bone-anchored Hearing Implants.** *Otol Neurotol. 36:812-8. 2015*
- *Agterberg MJ, Hol MKS, Van Wanrooij MM, Van Opstal AJ, Snik AF.* **Single-sided deafness and directional hearing: contribution of spectral cues and high-frequency hearing loss in the hearing ear.** *Front Neurosci. 4;8:188. 2014.*
- *Dun CA, Agterberg MJ, Cremers CW, Hol MK, Snik AF.* **Bilateral bone conduction devices: improved hearing ability in children with bilateral conductive hearing loss.** *Ear Hear. 34:806-8. 2013.*

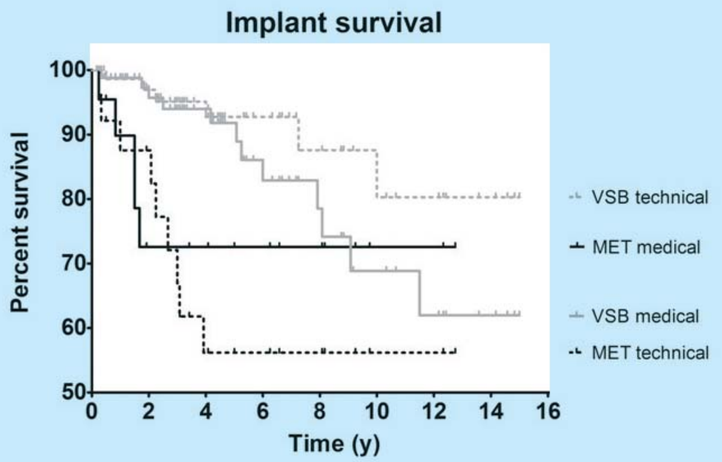
Middle ear implants, clinical studies

The development of active middle ear implants or implantable hearing aids started in the nineteen-seventies. To deal with the stigma of hearing aids, invisible implantable hearing devices were envisioned. Unfortunately, progress has been slow, although from a technological point of view, achievements are impressive. Clinical studies showing good patient performance, comparable to conventional hearing aids, are lacking. As cost is high and the implant surgery complex, today's fully implantable devices are rarely applied.

Semi-implantable devices are more often applied. Such devices are commercially available since the late nineties. In sensorineural hearing loss, the implanted actuator directly stimulates the ossicular chain, driven by an externally worn sound processor. Research through the years showed that results obtained with these semi-implantable devices were comparable to those obtained with today's advanced behind-the-ear device (BTE), not better. Therefore, nowadays, the manufacturers advocate these devices for patients with sensorineural hearing loss who, for whatever reasons, cannot use a BTE. In Nijmegen, we applied semi-implantable devices in patients with sensorineural hearing loss and comorbid chronic external otitis. A recent retrospective study showed that long-term device use was acceptable (87%; mean follow up of 7 years) and the long-term satisfaction scores were comparable to those obtained one year after the intervention.

Another application concerns the coupling of the implanted actuator directly to the cochlea, which makes these devices suitable for the treatment of conductive and mixed hearing loss. This application of middle ear implants is rather successful. Complications and long-term stability of the Nijmegen cohort were studied and published *(Fig. 1)*.

Figure 1



Explantations during the 'growing pains' follow up period. Per half year implant explantation because of technical and medical reasons is indicated

Classification system of amplification options for conductive and mixed hearing loss

An ongoing research topic comprise the development of a classification system of all amplification options for patients with conductive or mixed hearing loss, including middle ear implants with the actuator directly coupled to the cochlea (Vibrant Soundbridge device, Med-El; Codacs device, Cochlear) as well as percutaneously coupled bone conduction implants (Baha device, Cochlear BAS; Ponto device, Oticon Medical), transcutaneous coupled passive bone conduction devices (Sophono device, Medtronic; Baha Attract device, Cochlear) and transcutaneous active bone-conduction implants (Bonebridge device, Med-El).

First outcomes of this classification study have been published (Zwartenkot et al., 2014). The studied devices were classified according to their capacity in terms of output, or, in other words how effectively they work as hearing aids. More recently, the outcomes have been interpreted in more detail (http://www.snikimplants.nl). We defined application areas in terms of the maximum allowable sensorineural hearing loss component for mentioned devices and addressed issue like longevity and MRI compatibility and stability. As the reviewed literature showed a large spread in gain (amplification) outcomes, an attempt was made to formulate a fitting rule, using an existing, well-validated rule for sensorineural hearing loss, adapted on pragmatic grounds. A straightforward analysis indicated that percutaneous bone conductors outperform the transcutaneous ones. Furthermore, it was concluded that the VSB device is another option that may outperform bone-conductors in patients with a moderate-severe sensorineural hearing loss component.

Concerning the Codacs device, long-term stability and effectiveness was studied in patients with advanced otosclerosis. Stable results over a period of 3 to 5 years were found. According to the classification system, the Codacs device was the most powerful device. In contrast to the other devices, the Codacs device is not limited in its output. Early 2017, owing to commercial reason, the manufacturer of this device has decided to no longer promote this device.

When searching for a solution for a given patient, the capacity of a device is of utmost importance, however factors like cost, complexity and invasiveness of the surgery and ease of use also play a role.

Binaural hearing with implantable devices

Implantable bone conductors stimulate the skull bone. The skull vibrations stimulate the cochleae what results in sound perception. However, both cochleae are stimulated with a somewhat higher efficacy of the ipsilateral cochlea. Better acoustic isolation can be achieved when using middle ear implants directly stimulating the cochlea instead of bone conductors. This subject, as well as the application of implantable bone-conductors and middle ear implants in unilateral conductive hearing loss is on-going. Special attention is given to the 'auditory preference syndrome', referring to the dominant ear (first aided ear in bilateral hearing loss or the normal hearing ear in unilateral hearing loss) and the other, deprived ear. Device use, the volume setting of the device, speech perception and binaural hearing capacity affect each other mutually. This complicates the effectiveness of this intervention; the development of binaural hearing is not obvious and non-use is an issue.

CONTACT

Jef Mulder
Jef.mulder@radboudumc.nl
+31 (0) 24 36 14934

SELECTED PUBLICATIONS IN THE LAST 3 YEARS:

- **Snik AFM. Auditory implants. 2017, http:\\www.snikimplants.nl**
- *Zwartenkot JW.* **Auditory implants in otology.** *Thesis, Radboud University Nijmegen, 2017.*
- *Zwartenkot JW, Snik AF, Mylanus EA, Mulder JJ.* **Amplification options for patients with mixed hearing loss.** *Otol Neurotol. 2014;35:221-226.*
- *Breukels-van Barneveld D, Kok H, Bosman A, Snik A.* **Determining fitting ranges of various bone conduction hearing aids.** *Clin. Otolaryngol; 2017, in press.*

Behavioural research projects

Development of deaf children with cochlear implants

These days, a cochlear implant is indicated for deaf and very severe hearing-impaired children (> 85dBHL). These children with CI have the abilities to develop a good speech recognition and understanding in a quiet environment. For children with no additional problems this results in an age-appropriate vocabulary development. For the first time we see a large group of children participate successful in mainstream education, with proper guidance. Children who are bilaterally implanted even have the possibility to recognize speech in a noisy environment, which leads to even more complex language development. These children can develop with relatively little guidance. In the clinic we see that these children function similarly to children with moderate hearing loss who use hearing aids (50-70 dBHL).

Often we get feedback from family counseling services and teachers of the deaf. They say that the children with severe hearing impairment with hearing aids (70-85 dBHL) achieve, despite the intensive support, less language and academic skills. These children experience more psychological and behavioral problems. In general, little is known about the relationship between hearing ability and long-term psycholinguistic and socio-emotional development in audiological centers. Often the speech recognition and understanding in the test situation is reasonably, which is seen as a sufficient condition. But in real life these children perform less well in complex listening situations such as school and home environment. Opportunities to develop higher social and cognitive functions are restricted because of the communication problems they experience.

The moderate to severe hearing loss group does not get the same opportunities for optimal development, that are provided to deaf and severe to profound hearing-impaired children with CI. We think it is socially unacceptable to allow this situation. Therefore we want to investigate the relationship between speech perception in noise, and soft speech (like the child hears in the back of the classroom) with the cognitive and personality/behavioral development in the longer term. We expect that a substantial group of children with severe or even moderate hearing loss will benefit more from a CI, above hearing aids.

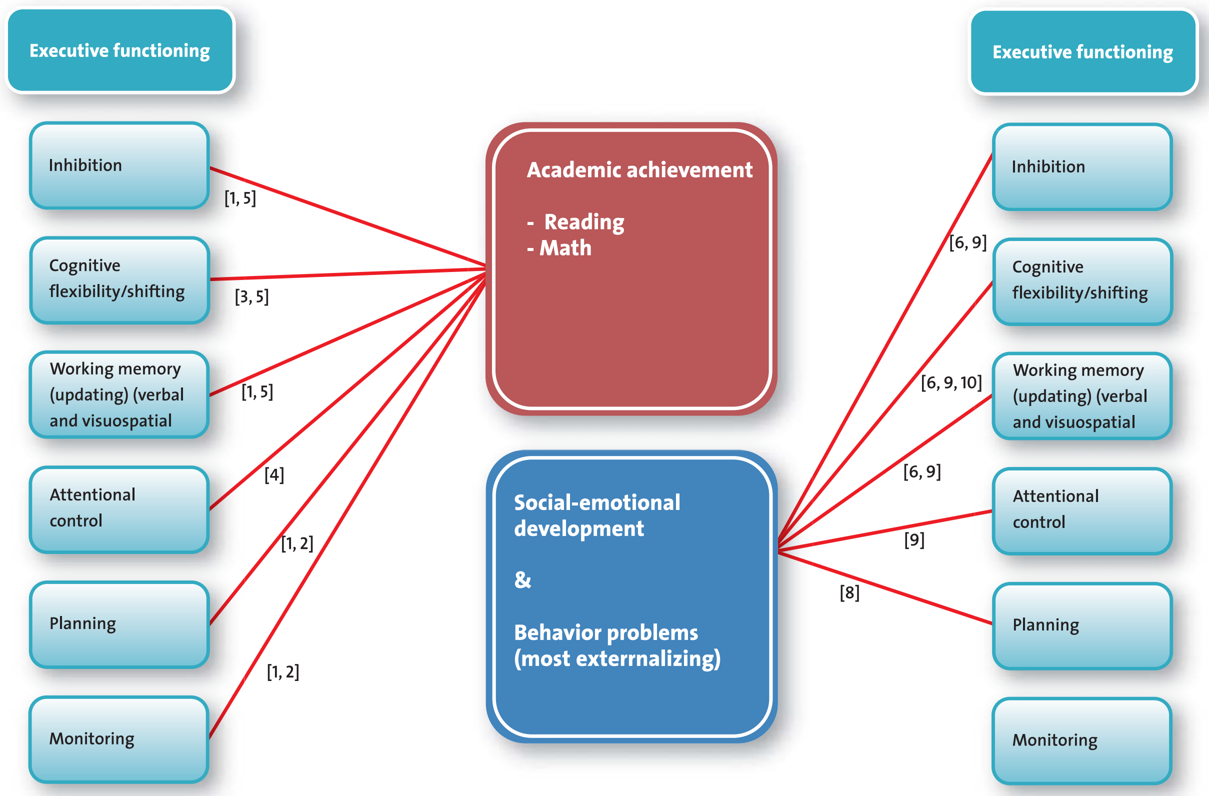
In the past there have been several studies that showed correlations between IQ and behavioral problems such as aggression, conduct disorder and criminality. Correlations were also found between IQ and academic achievement.

In addition, comorbidity was reported between school problems (reading disorders, academic underachievement and school dropout and failure) and disruptive behavior disorders.

The consideration of executive functioning in relation to children's skills has become a relatively common occurrence in recent years. Executive functioning refers to a set of higher order cognitive processes, which are involved in the self-regulation of thought, action and emotion. It is an umbrella term that includes mental processes such as planning, working memory, inhibition of inappropriate responses, flexibility in adaptation to changes and decision making. They are necessary for adaptive and goal-oriented behavior.

Various studies have been carried out among different populations, including children with

FIGURE 1



1. Best, J.R., P.H. Miller, and J.A. Naglieri, *Relations between Executive Function and Academic Achievement from Ages 5 to 17 in a Large, Representative National Sample.* Learn Individ Differ, 2011. **21**(4): p. 327-336.
2. Bull, R., K.A. Espy, and S.A. Wiebe, *Short-term memory, working memory, and executive functioning in preschoolers: longitudinal predictors of mathematical achievement at age 7 years.* Dev Neuropsychol, 2008. **33**(3): p. 205-28.
3. Neuenschwander, R., et al., *How do different aspects of self-regulation predict successful adaptation to school?* J Exp Child Psychol, 2012. **113**(3): p. 353-71.
4. Lan, X., et al., *Investigating the links between the subcomponents of executive function and academic achievement: a cross-cultural analysis of Chinese and American preschoolers.* J Exp Child Psychol, 2011. **108**(3): p. 677-92.
5. Bull, R. and G. Scerif, *Executive function as a predictor of childrens's maghematics ability: Inhibition, switching, and working memory.* Developmental Neuropsychology, 2001. **19**: p. 273-293.
6. Schoemaker, K., et al., *Executive functions in preschool children with externalizing behavior problems: a meta-analysis.* J Abnorm Child Psychol, 2013. **41**(3): p. 457-71.
7. Raaijmakers, M.A., et al., *Executive functions in preschool children with aggressive behavior: impairments in inhibitory control.* J Abnorm Child Psychol, 2008. **36**(7): p. 1097-107.
8. Hughes, C., et al., *Antisocial, angry, and unsympathetic: "Hard-to-manage" preschoolers' peer problems and possible cognitive influences.* Journal of Child Psychology and Psychiatry and Allied Disciplines, 2000. **41**(2): p. 169-179.
9. Cole, P.M., B.A. Usher, and A.P. Cargo, *Cognitive Risk and Its Association with Risk for Disruptive Behavior Disorder in Preschoolers.* Journal of Clinical Child Psychology, 1993. **22**(2): p. 154-164.
10. Kusche, C.A., E.T. Cook, and M.T. Greenberg, *Neuropsychological and Cognitive-Functioning in Children with Anxiety, Externalizing, and Comorbid Psychopathology.* Journal of Clinical Child Psychology, 1993. **22**(2): p. 172-195.

learning disabilities, language and comprehension problems. As well among children with behavioral problems. These studies have found that executive functioning is a good predictor of performance in everyday life.

Results indicate that hearing loss, and especially greater hearing loss, is significantly associated with lower scores on measures of executive functioning (working memory, inhibition, cognitive flexibility) in adults.

Lin and colleagues devote the significant association to poor verbal communication, less access to social situations and cognitive load.

Also research on executive function in children with hearing loss and CI has been conducted. Is has been found that de children with CI scored lower than the NH sample and test norms on several measures of short-term/working memory, fluency-speed, inhibition, behavioral regulation and sustained attention. In addition, deficits in executive function related to working memory and fluency-speed were associated with poor performance on traditional speech and language measures that require a great deal of cognitive control such as hearing in noise and general language.

Relations between executive functioning and academic achievement

A number of studies have focused on the relation between executive functioning and academic achievement. In particular, correlations were found between executive functioning and academic achievement in reading, writing and math. Most investigated and strongest correlations were found on inhibition, cognitive flexibility (shifting) and working memory (updating). Analyses revealed that executive functions were also predictive of learning-related behavior such as listening to instructions, following directions, and accomplishment of tasks in a limited period of time. Research shows that children's classroom behavior did not account for the relation between executive functioning and math achievement, suggesting executive functioning and math performance are directly associated.

Relations between executive functioning and behavioral problems

Executive functions also tend to have a vital role in children's social- emotional development. Research indicates a medium mean effect size for the relationship between overall executive functioning and externalizing behavior problems. In particular inhibition, cognitive flexibility (shifting) and working memory (updating) correlate with aggressive and disruptive behavior problems. Figure 1 depicts the relation between executive functioning and academic achievement & social-emotional development.

CONTACT
Anneke Vermeulen
anneke.vermeulen@radboudumc.nl
+31 (0) 24 36 14817

SELECTED PUBLICATIONS IN THE LAST 3 YEARS:

- *Evi Jacobs, Margreet Langereis, Johan Frijns, Rolien Free, Andre Goedegebure, Cas Smits, Robert Stokroos , Saskia Ariëns, Emmanuel Mylanus, Anneke Vermeulen.*
  Benefits of simultaneous bilateral cochlear implantation on verbal reasoning skills in prelingually deaf children Res. *Dev. Disabil,2016, 58:104-113*
- *Brigitte de Hoog; Margreet Langereis; Marjolijn van Weerdenburg; Jos Keuning; Harry Knoors; Ludo Verhoeven.*
  Auditory and verbal memory predictors of spoken language skills in children with cochlear implants. *Research in Developmental Disabilities: 57:112-124, 2016.*
- *Margreet Langereis & Anneke Vermeulen.*
  School performance and wellbeing of children with CI in different communicative-educational environments. *International Journal of Pediatric Otorhinolaryngology 79(6). DOI:10.1016*
- *B. de Hoog, M. Langereis, M van Weerdenburg, H.Knoors, L. Verhoeven.*
  Linguistic profiles of children with CI as compared with children with Hearing or Specific Language Impairment. *Int. Journal of Language and Communication disorders, 2016.*
- *Leo De Raeve, Anneke Vermeulen, Ad Snik.*
  Verbal cognition in deaf children using cochlear implants: effects of unilateral and bilateral stimulation. *Audiology and Neurotology 20(4):261-266.*

Funding sources since 2014

iCARE
improving Children's
Auditory REhabilitation

- Source: William Demands og Hustra Ida Emilies Fond.
  Title project: Improving the benefit of a second hearing implant

- Source: NWO STW-Perspectief, NeuroCIMT
  Title project: *OtoControl:* Improved spectral-temporal sensitivity and binaural integration in the hearing impaired through automated sensorineural feedback.

- Advanced Bionics
- Cochlear BAS
- Cochlear Benelux
- Med-El
- Oticon

EU FP7 / Horizon 2020 projects:

- PEOPLE-2013 – ITN: iCARE, "Improved Children Auditory Rehabilitation"
- PEOPLE-2013 – ITN: HealthPAC, "Perception and Action in Health and Disease"
- Horizon-2020-ERC Advanced grant: "ORIENT" (AJvOpstal)

Group Members of DH&I

Staff:

- Prof. dr. E. Mylanus (ENT)
- Prof. dr. J. van Opstal (Biophysics)
- Prof. dr. ir. A. Snik (ENT)
- Dr. M. Agterberg (Biophysics / ENT)
- Dr. L. Mens (ENT)
- Dr. M. van Wanrooij (Biophysics)

Researchers:

- Dr. A. Beynon (ENT)
- Dr. A. Bosman (ENT)
- Dr. M. Hol (ENT)
- Dr. W. Huinck (ENT)
- Dr. M. Langereis (ENT)
- Dr. R. Miserus (ENT)
- Dr. J. Mulder (ENT)
- Dr. R. Pennings (ENT)
- Dr. M. Sparreboom (ENT)
- Dr. A. Vermeulen (ENT)

Technicians

- Ing. C. Beerendonk
- Drs. R. Lof
- S. Martens
- Ing. G. Windau

PhD students and postdocs on grants:

- Drs. S. Ausili (HealthPAC)
- Drs. M. Boerrigter (ENT)
- Drs. C. den Besten (ENT)
- Drs. B. Hartel (ENT)
- Drs. I. Kruyt (ENT)
- Dr. R. Nelissen (ENT)
- Drs. E. Noordanus (STW OtoControl)
- Drs. L. van de Rijt (ENT)
- Dr. A. Roye (Biophysics)
- Drs. S. Sharma (HealthPAC)
- Drs. E. Theunisse (ENT)
- Drs. L. Veugen (Biophysics)
- Drs. K. Vogt (iCARE)
- Dr. J. Zwartenkot (ENT)