Hearing4all Vision Workshop

The Future of Hearing Implants

13th April – 14th April 2023

Abstract Book

www.hearing4all.de

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Contact

Hearing4all
Hannover Medical School
Phone +49 (0) 511 532 - 9151
events-hno@mh-hannover.de

Content

 

Dear colleagues, friends, and guests,

It is a great honor for us to work for you all here in Hannover to our Vision Workshop on Future of Hearing Implants. We are very glad that you all could make it in order to discuss with us the future perspectives of research and development. This topic of hearing implants has been our focus both in clinical work and research as over the last 40 years.

Starting in 1984 so far, more than 11.000 patients have been served with cochlear implants and acoustic implants. The huge clinical work was always based on solid research and we are proud to say that we were able to establish the full circle of research and development from bench to bedside and back. The research activities are mainly supported by huge federal government grants as well as the industry in this field. We are glad that we can demonstrate you also facilities we were able to build up over the years mainly with the NIFE as our research institute for basic research and the German Hearing Center for clinical research. We hope you will enjoy this workshop very much and we would be glad if you could also stimulate our future work in the most productive way.

Thank you for being our guests. We are looking forward to an exciting, scientific event together with you!

Thomas Lenarz
Chairman ORL-Department
Hannover Medical School

Andrej Kral
Chairman Institute for AudioNeuroTechnology (VIANNA)
Hannover Medical School

Time	**Room 1**
from 07:30	Registration
08:00 - 08:30	Welcome and Introduction Prof. Michael P. Manns, Prof. Thomas Lenarz, Prof. Andrej Kral, Prof. Birger Kollmeier
08:30 - 11:05	**Cochlear Implant Future Developments** Chair: Prof. Thomas Lenarz
08:30 - 08:45	Overview by Prof. Thomas Lenarz Hannover Medical School
08:45 - 09:15	Prof. Stephen O'Leary, University of Melbourne, Australia Cochlear implant after-care: the emerging role of implant-derived objective measures
09:15 - 09:45	Prof. Bruce Gantz, University of Iowa, USA Importance of Preserving Low Frequency Acoustic Hearing: Central Auditory Processing
09:45 -10:15	Prof. Philippe Lefèbvre, CHU Liège, Belgium Totally implantable cochlear implant
10:15 -10:45	Prof. Manuel Manrique Rodrígez, Clinica Universidad de Navarra, Spain Cochleo-Vestibular Implants (Electrical stimulation of the Otolith Organs)
10:45 -11:05	Discussion
11:05 - 11:30	Coffee Break

Thursday, 13th April 2023 | 07:30 - 19:00

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Time	Room 1
11:30 - 13:35	**Advanced Diagnostics** Chair: Prof. Anke Lesinski-Schiedat, Hannover Medical School
11:30 - 11:45	Overview by Prof. Athanasia Warnecke Hannover Medical School
11:45 - 12:15	Prof. Nicolas Verhaert, UZ Leuven, Belgium Optical Coherence Tomography for Image-guided Cochlear Implantation and diagnostics: a near future?
12:15 - 12:30	Prof. Georg Berding, Hannover Medical School Functional and molecular diagnostics of the auditory system with PET including new perspectives from translational research
12:30 - 12:45	Prof. Birger Kollmeier, University of Oldenburg, Germany Audiological Diagnostics supported by Machine Learning and auditory models
12:45 - 13:15	Prof. Hung Thai-Van, Hôpital Edouard Herriot Lyon, France Auditory neuropathy
13:15 -13:35	Discussion
13:35 - 14:30	Lunch Break
14:30 - 19:00	**Advanced Implants: drug delivery, regeneration, gene therapy** Chairs: Prof. Athanasia Warnecke, Hannover Medical School Prof. Marcelo Rivolta, University of Sheffield, UK
14:30 - 14:45	Overview by Prof. Theodor Doll Hannover Medical School
14:45 - 15:15	Prof. Brigitte Malgrange , University of Liège, Belgium Regeneration and biology in the inner ear: input of human induced pluripotent stem cells

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Time	Room 2
11:30 - 13:35	**Individualized, Adaptive Implants And Additive Manufacturing Technologies** Chair: PD Verena Scheper Ph.D.
11:30 - 11:45	Overview by Prof. Theodor Doll Hannover Medical School
11:45 - 12:15	Prof. Thorsten Buzug, Fraunhofer IMTE, Germany Navigation of magnetic micro-robots
12:15 - 12:45	Prof. Dr.-Ing. Hoc Khiem Trieu, Technische Universität Hamburg, Germany 3D patterning for individualized implantable MEMS
12:45 - 13:15	PD Verena Scheper, Hannover Medical School Hearing4all Patient-individualized drug delivering Implants in Otorhinolaryngology
13:15 - 13:35	Discussion
13:35 - 14:30	Lunch Break
14:30 - 18:00	**Robotics and computer assisted technologies for precision surgery** Chair: Samuel John, Hannover Medical School
14:30 - 14:45	Overview by Rolf Salcher Hannover Medical School
14:45 - 15:15	Prof. Greg Eigner Jablonski / Ralf Greisiger University of Oslo, Norway / Oslo University Hospital, Norway Fluoroscopy and intra-OP imaging as quality control for Minimal Invasive CI Surgery

Thursday, 13th April 2023 | 07:30 - 19:00

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Time	**Room 1**
15:15 - 15:45	Prof. Lawrence Lustig, Columbia University, USA
15:45 - 16:15	Michael Hoa, Porter Neuroscience Research Center, USA Deep Phenotyping of Hearing Instability Disorders: Searching for Biomarkers and Re-purposable Therapeutics
16:15 – 16:40	Coffe Break
16:40 – 17:10	Prof. Jian Zuo, Creighton School of Medicine, USA Repurposing drugs against hearing loss
17:10 – 17:40	Prof. Gerry O'Donoghue, Queen's Medical Centre, UK Stem Cells for Hearing Regeneration: towards a first-in-human clinical trial
17:40 – 18:10	Prof. Gwenaelle Geleoc, Boston Children's Hospital & Harvard Medical School, USA Development of Therapeutic Approaches for Usher Syndrome
18:10 – 18:40	Prof. Vincent can Rompaey, University of Antwerp, Belgium Progressive non-syndromic sensorineural hearing loss: towards a disease-modifying gene therapy
18:40 – 19:00	Discussion
From 19:15	Shuttle to Evening Event
19:30 - 22.30	Evening Event: Gartensaal, Townhall

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Time	**Room 2**
15:15 – 15:45	Prof. Marco Caversaccio, Inselspital – Universitätsspital Bern, Switzerland Robotics and computer assisted surgery on ear
15:45 – 16:15	Prof. Yann Nguyen, Sorbonne Université, France Robot-based assistance for middle ear and cochlear implant surgery
16:15 – 16:40	Coffee Break
16:40 – 17:10	Thomas Rau Ph.D., Hannover Medical School Precision control of critical parameters: Surgical tools to increase the reliability of cochlear implants
17:00 – 17:30	Prof. Bruce Gantz, University of Iowa, USA Preservation of Functional Residual Hearing Comparing Manual and Robotic Insertion of Cochlear Implants
18:20 – 18:30	Discussion
19:15	Shuttle to Evening Event
19:30 – 22:30	Evening Event: Gartensaal

Friday, 14th April 2023

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Time	Room 1
08:00 – 08:05	Welcome Prof. Andrej Kral, Hannover Medical School
08:05 – 11:35	**Artificial intelligence for hearing devices** Chair: Prof. Waldo Nogueira, Hannover Medical School
08:05 – 08:15	Overview by Prof. Waldo Nogueira Hannover Medical School
08:15 – 08:45	Prof. Fan-Gang Zeng, University of California, USA How can artificial intelligence advance hearing devices and research, or vice versa?
08:45 – 09:05	Prof. Bernd Meyer, University of Oldenburg, Germany Low-complexity models for speaker separation in hearing aids
09:05 – 09:35	Prof. De Liang Wang, The Ohio State University, USA Location-based training for multi-channel speaker separation
09:35 – 10:00	Coffee Break
10:00 – 10:20	Prof. Holger Blume, Leibniz Universität Hannover, Germany
10:20 – 10:50	Prof. Sarah Verhulst, Ghent University, Belgium Personalised neural-network-based closed-loop systems for augmented hearing
10:50 – 11:20	Prof. Nima Mesgarani, Columbia University, USA Brain-controlled assistive hearing technologies
11:20 – 11:35	Discussion
11:35 – 13:15	Tour NIFE / DHZ including Lunch

Friday, 14th April 2023 | 08:00 - 18:45

Time	Room 1
13:15 – 16:40	**Central Auditory Implants** Chair: Prof. Kerstin Schwabe
13:15 – 13:30	Overview by Prof. Andrej Kral Hannover Medical School
13:30 – 14:00	Prof. Hubert Lim, University of Minnesota, USA Future opportunities for central auditory prosthetics
14:00 – 14:30	David Moses Ph.D., UCSF Weill Institute for Neurosciences, USA Developing a speech neuroprosthesis
14:30 – 15:00	Prof. Amir Samii, International Neuroscience Institute – Hannover, Germany Auditory Midbrain Implant – hearing beyond the brainstem
15:00 – 15:25	Coffee Break
15:25 – 15:55	Prof. Kirill Nourski, University of Iowa, USA Intracranial electrophysiology of auditory processing in the human cortex
15:55 – 16:25	Marcus Janssen M.D. PhD., Maastricht UMC+, The Netherlands Deep Brain Stimulation for Tinnitus: from bench to bed
16:25 – 16:40	Discussion
16:40 – 17:40	**Future Care Concepts** Panel Discussion / Round Table Presented by Prof. Jill B. Firszt, Washington University School of Medicine, USA and Prof. Andreas Büchner, Hannover Medical School Participants: Stefan Launer, Sonova AG, Switzerland Prof. Hubert Lim, University of Minnesota, USA Prof. Fan-Gang Zeng, University of California, USA Prof. Stephen O'Leary, University of Melbourne, Australia PD Dr. Angelika Illg, Hannover Medical School, Germany
18:30 – 18:45	Closing Remarks
19:30 – 22:30	Dinner

Time	Room 2
13:15 – 16:40	**Hearing and cognition, education, societal impact** Chair: PD Angelika Illg Ph.D., Hannover Medical School Prof. Christiane Thiel Ph.D., University of Oldenburg
13:15 – 13:30	Overview by PD Angelika Illg Hannover Medical School
13:30 – 14:00	Prof. Ulrike Lüdtke, Leibniz Universität Hannover, Germany Improving the assessment of hearing impairment in children globally
14:00 – 14:30	Prof. Mickael L.D. Deroche, Concordia University, Canada Use of EEG and fNIRS to predict language outcomes in children with cochlear implants
14:30 – 15:00	Dr. Margreet Langereis, Pento Speech and Hearing Centers, The Netherlands Defining working memory profiles in children with auditory/communicative disorders
15:00 – 15:25	Coffee Break
15:25 – 15:55	Prof. Rachel R. Romeo, University of Maryland, USA How early language experience influences brain and cognitive development
15:55 – 16:25	Ellen Andries Ph.D., Antwerp University Hospital, Belgium Implementation of the ICF model in adult Cochlear Implant users
16:25 – 16:40	Discussion

Abstracts

Thursday, 13th April 2023

Thomas Lenarz
Hannover Medical School, Germany

Cochlear Implant Future Developments

The field of cochlear implant has developed tremendously over the last decades. Today it is the role model for successful neuroprosthesis mainly in the field of sensory neural restoration. Currently the main topics are in the field of the electrode nerve interface, the more natural speech coding, the closed loop systems to use the central processing as an important source for information, the precision surgery including robotics, the advanced implants who are using additional biological components for the improvement of electrode nerve interface, hearing preservation and regeneration and the focus on hearing preservation cochlear implantation. Individual treatment concepts have become most important due to the fact that more and more patients with residual hearing and different conditions of hearing loss are being treated. Despite all this progress there is still a huge gap between the number of potential candidates and those who are implanted.

The following session will highlight many of these aspects and give the future directions.

Prof Stephen O'Leary
William Gibson Chair of Otolaryngology
University of Melbourne
Royal Victorian Eye and Ear Hospital, Melbourne

Cochlear implant after-care: the emerging role of implant-derived objective measures

Surgery on the inner ear is likely to remain a foundational methodology for the treatment of hearing loss, whether this be for cochlear implantation or the delivery of genes/ drugs into the cochlea. We have focussed upon ensuring that inner ear can be done safely, that is, conducted without loss of residual acoustic hearing. We have developed a suite of intra-operative and post-operative monitoring tools to warn of impending hearing loss, and to better understand its cause.

Electrocochleography, recorded directly from cochlear implant electrodes during surgery, has been shown to predict loss of residual hearing, and immediate surgical intervention in response to a drop in signal amplitude can prevent permanent loss of hearing.

Four-point electrode impedance provides new insights into the biological status of the cochlea after implantation. Impedance reflects a reduction in the conductance of current in the local cochlear environment surrounding the electrode, reflecting either a change in electrode geometry or the biological response to implantation. If raised during implant surgery, or three months later, residual hearing is poorer. Similarly, high four-point impedance 3 months after implantation is associated with loss of residual hearing.

The best prediction of residual hearing loss is seen when electrocochleography and four-point impedance are combined. For example, from these data we find evidence that delayed hearing loss is likely caused by progressive fibrosis and fixation of the basilar membrane.

Our experience suggests that monitoring directly from cochlear prostheses can provide detailed information on the likelihood of hearing loss, and its cause. The interpretation of monitoring measure depends upon a good understanding of the characteristics of the intracochlear device, and must be timely.

Prof. Stephen O`Leary
The University of Melbourne, Department of Otolaryngology
32 Gisborne Street
East Melbourne VIC 3002, Australia
sjoleary@unimelb.edu.au
catherine@olearyent.com.au

Gantz, Bruce; Choi, Inyong; Griffiths, Tim; McMurray, Bob; Dunn, Camile; and Hansen, Marlan
The University of Iowa Cochlear Implant Clinical Research Center, The University of Iowa Carver College of Medicine
Iowa City, Iowa, USA

Importance of Preserving Low Frequency Acoustic Hearing: Central Auditory Processing

Background: Understanding speech in background noise is challenging especially for hearing-impaired listeners. The variance in the speech-in-noise (SiN) understanding ability is significant in cochlear implant (CI) users. Acoustic + Electric (A+E) processing has been shown to enhance word understanding in noise. Variation in the neural encoding of acoustic information, measured as early auditory-cortical evoked responses, is known to contribute to the behavioral variance, while its interaction with cognitive processing mediated by frontal cortex is unclear.
Materials and Methods: We explored relationships between the evoked responses from auditory cortex (AC), frontal cortex, and behavioral performance in SiN understanding by examining CI listening based on EEG and O-15 water PET scanning. We tested evoked responses to words in multi-talker babble background in 114 CI users. Rate of lexical word processing was recorded in a subset of those undergoing EEG using an eye tracking paradigm.
Results: Multivariate analysis of SiN EEG recordings demonstrated that N1-P2 complex amplitude predicts single word in noise perception. We found that poor CI SiN performers exhibit stronger late response (later than around 600ms after the word onset) in the frontal area as well as weaker and delayed N1 response at the auditory cortex region. O-15 water PET experiments with SiN established this as a reliable single-subject brain measure in CIs. Comparison between CI users and normal listeners demonstrated a different auditory cortical mechanism for SiN in CI users in high-level cortex. We also showed significant correlation between left auditory cortex activity and performance and negative correlation between frontal cortex activity and performance. Eye tracking **demonstrated those with larger N1-P2 EEG amplitudes recognized words more rapidly.**
Conclusion: Our results suggest that EEG and O-15 PET demonstrate different central processing features in those with acoustic and electric CI processing and electric only CI processing. Those with large early N1-P2 amplitudes separate speech from noise while those with late frontal cortex responses (electric only processing) negatively correlate with SiN. These findings suggest that low frequency acoustic hearing provides more rapid lexical recognition and assists in separation of speech in noise. Preservation of low frequency functional acoustic hearing is important to improve SiN performance for those with residual acoustic hearing undergoing CI.

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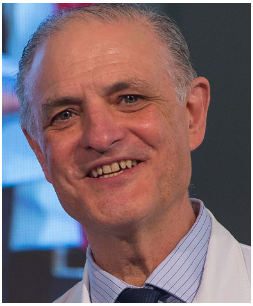
Prof. Dr. Bruce Gantz
University of Iowa, Dept of Otolaryngology--Head and Neck Surgery/ Neurosurgery
University of Iowa Hospitals and Clinics
200 Hawkins Drive (21201 PFP)
Iowa City, Iowa 52242-1078, USA
bruce-gantz@uiowa.edu

Philippe Pierre Lefebvre[1], Joachim Müller[2], John-Martin Hempel[2],
Gerhard Mark[3], Ingeborg Hochmair[3]
[1]Service ORL, Liège University, Liège, Belgium
[2]Klinik und Poliklinik für Hals-Nasen-Ohren-Heilkunde, München, Germany
[3]MED-EL Elektromedizinische Geräte GmbH, Innsbruck, Austria

A Totally Implantable Cochlear Implant shows potential benefits for adults with hearing loss

People with hearing impairment have several specific expectations: advanced technology providing superior outcomes, aesthetics, and reliability. The newly developed totally implantable cochlear implant (TICI) was designed to provide these. Advanced technology considers now and the future. Users experience benefits in speech understanding in quiet, speech understanding in noise (1), using the telephone (2), and listening to music(3). Aesthetics means having no visible audio processor, while still allowing a person to hear when they are in the shower, swimming, or when sleeping. Therefore, an increasing number of individuals with hearing loss might decide for cochlear implantation and enjoy the benefits thereof.A TICI comprises the housing and electrode of a conventional cochlear implant, while incorporating the microphone, the signal processing and the batteries previously contained in the external audio processor (Figure 1a). A first-in-human clinical investigation using the MED-EL TICI system in six post-lingually deafened adults (21.3-73.2y) collected data over 52 weeks. The surgical procedure for the TICI is similar to the one used to implant currently marketed cochlear implants, except for the microphone positioning under the skin.Safety of the investigational device was closely monitored throughout this clinical investigation, no unexpected adverse events were reported, indicating a favourable benefit versus risk ratio for the Mi2000 TICI. Self-reported overall satisfaction was measured daily on a VAS scale. Figure 1b shows individual and average data over time. There was clear improvement from first fitting to 20 weeks. Monosyllable scores (Freiburger(4) and Listes de mots monosyllabiques de Fournier(5)) (Figure 1c) with the TICI improved from 6.3% pre-operatively to an average of 63.8% at 3-months post-operatively, further increasing to 70.3% at one year. The OLSA sentence test in noise (Figure 1d) determines the signal-noise ratio where 50% of sentences can be understood. No subject could complete the test pre-operatively. At 3-months post-operative, mean SRT with the TICI was -1.2 dB SNR and remained stable up to the one-year assessment. These scores were similar when comparing the TICI with the SONNET audio processor. (1).The evaluation of the TICI in a first-in-human study, showed that expectations of users can be met. Surgeries were completed without incident. Speech-scores matched scores using an external audio processor. User satisfaction showed increasing satisfaction with the TICI over time. No unexpected safety events were recorded. The TICI shows the new way forward for cochlear implants.

Prof. Philippe Lefèbvre
CHU de Liège, Oto-rhino-laryngologie et chirurgie cervicofaciale
Avenue de l'Hôpital 1
4000 Liège, Belgium
PP.Lefebvre@uliege.be



Manuel Manrique[1], Raquel Manrique-Huarte[1], Marta Alvarez de Lnera[1], Nicolas Pérez[1], Andrzej Zarowski[2], Morgana Sluydts[2], Erwin Offeciers[2], Angel Ramos De Miguel[3], Maurizio Barbara[4], Angel Ramos Macias[3]

[1]Otorhinolaryngology Department, Clinica Universidad de Navarra, Pamplona, Spain
[2]European Institute for Otorhinolaryngology, Antwerp, Belgium
[3]Hearing Loss Unit, Otorhinolaryngology, Head and Neck Department, Complejo Hospitalario Universitario Insular Materno Infantil, Las Palmas of Gran Canaria, Spain
[4]NESMOS Department, ENT Clinic, Sapienza University, Rome, Italy

Cochleo-Vestibular Implants (Electrical stimulation of the Otolith Organs)

Introduction: Bilateral vestibular areflexia is a severe disability leading to chronic instability and oscillopsia, a multiple increase in the risk of falls and a significantly reduced quality of life. The possible etiologies are ototoxicity, autoimmune damage to the inner ears, bilateral Menière's disease, genetic disorders (e.g. DFNA9), neurodegenerative diseases, meningitis, etc. In patients with bilateral vestibulopathy, the classic treatment options, such as medication and/or vestibular rehabilitation, are often insufficient. Therefore, electrical vestibular stimulation (EVS) is a possible alternative for restoring peripheral vestibular functions. Three approaches to EVS are currently being investigated: galvanic vestibular stimulation (GVS), vestibular co-stimulation with a cochlear implant (CI) and the direct vestibular stimulation with a vestibular implant (VI). The classic VI approach involves stimulating the ampullas of the semicircular channels. This presentation describes a new approach based on stimulation of the otolith organs and pay special attention to the surgical technique for its placement.

Material and methods: So far, 12 patients have been implanted with a follow-up period of 9 -24 months as part of the European Horizon 2020 project. In all patients, double ipsilateral vestibular and cochlear implantation was performed with a new Nucleus CI-VI 19+3 system. The cochlear stimulation is performed by a Contour AOS electrode. For vestibular stimulation, a full-band straight electrode array is used with three band electrode contacts with a width of 0.3 mm and a diameter of 0.4 mm at the electrode tip. Following the same principles as in standard cochlear implant surgery, cortical mastoidectomy extended to the attic. Posterior tympanotomy was performed at this time with a clear exposure of the long process of incus, stapes and oval window. After regular insertion via round window of the cochlear implant component, opening of the vestibule was performed by performing a 0.6 mm stapedotomy just medial and inferior to the anterior crura of the stapes to reach the closest area to inferior vestibular nerve afferent near the saccule macula. Vestibular stimulation is performed with a constant pulse train delivered interleaved to all 3 vestibular contacts.

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Results: No relevant surgical complications were observed and the surgical technique was successfully reproducible in the four centers participating in the study. Most patients show good improvement in vestibular functions, especially in the dark and on unstable surfaces. This was confirmed by significant improvements in the Dizziness Handicap Inventory (DHI), the Dynamic Visual Acuity (DVA), the Timed Up and Go Test (TUG), the Dynamic Gait Index (DGI) and the Subjective Visual Vertical (SVV) scores and the results of the posturography. All patients use their systems throughout the day and do not show significant dizziness when the system is switched off.

Conclusion: EVS with VI is feasible and gives a chance of rehabilitation in patients with bilateral vestibular dysfunction. Stimulation of the otolith organ is an interesting alternative to stimulation of the ampullary nerves and opens up new possibilities for generating observations of gravito-inertial accelerations by electrical stimulation.

Prof. Manuel Manrique
Clinica Universidad de Navarra, Otorhinolaryngology Department
Av. de Pío XII, 36, 31008 Pamplona, Navarra, Spain
mmanrique@unav.es / agancino@unav.es

Nicolas Verhaert [1,2,3], Lore Kerkhofs[1,2], Anastasiya Starovoyt[1,2],
Tristan Putzeys[1,2,4], Jan Wouters[1,2]
[1]Research Group Experimental Oto-Rhino-Laryngology, Department of Neurosciences,
KU Leuven, University of Leuven, Leuven, Belgium
[2]Leuven Brain Institute, Department of Neurosciences, KU Leuven, 3000 Leuven, Belgium
[3]Department of Otorhinolaryngology, Head and Neck Surgery, UZ Leuven,
University Hospitals of Leuven, Leuven, Belgium
[4]Laboratory for Soft Matter and Biophysics, Department of Physics and Ast+ronomy,
KU Leuven, University of Leuven, Leuven, Belgium

Optical Coherence Tomography for Image-guided Cochlear Implantation and diagnostics: a near future?

Advancements in intracochlear diagnostics, as well as prosthetic and regenerative inner ear therapies, rely on a good understanding of cochlear microanatomy. The human cochlea is very small and deeply embedded within the densest skull bone, making nondestructive visualization of its internal microstructures extremely challenging. Current imaging techniques used in clinical practice, such as MRI and CT, fall short in their resolution to visualize important intracochlear landmarks, and histological analysis of the cochlea cannot be performed on living patients without compromising their hearing. Recently, optical coherence tomography (OCT) has been shown to be a promising tool for nondestructive micrometer resolution imaging of the mammalian inner ear. First, we present an atlas of intracochlear OCT images, which were acquired in a series of 7 fresh and 10 fresh-frozen human cadaveric cochleae through the round window membrane and describe the qualitative characteristics of visualized intracochlear structures. Likewise, in this work in progress, we will try to describe several intracochlear abnormalities, which could be detected with OCT and are relevant for clinical practice.

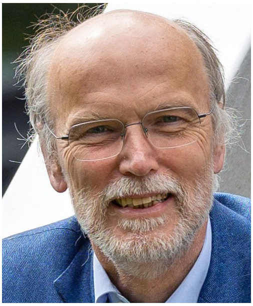
Prof. Nicolas Verhaert
University Hospitals Leuven, Department of Otorhinolaryngology, Head and Neck Surgery
KU Leuven
Research Group Experimental Oto-rhino-laryngology, Dept of Neurosciences
ON2 Herestraat 49 - box 721
3000 Leuven, Belgium
nicolas.verhaert@kuleuven.be

Prof. Georg Berding
Hannover Medical School
Germany

Functional and molecular diagnostics of the auditory system with PET including new perspectives from translational research

In the 1980s and 1990s, PET (positron emission tomography) was frequently used for functional studies of the auditory system in healthy subjects and patients. Since then, such studies have been performed by fMRI for most indications, except for those in which fMRI is contraindicated due to the risks associated with the magnetic field, such as in users of auditory implants. In addition, PET provides the unique possibility of investigating molecular targets related to hearing, e.g., neuro-receptors. For PET examinations, fundamental advances have been made in the last decades in terms of device technology (20-fold increase in sensitivity, improved resolution of 3.5 mm for clinical and 0.7 mm for preclinical systems) and in terms of the variety of molecular targets, e.g. also intracellular, which can be measured using radiopharmaceuticals manufactured in compliance with GMP. Current device technology allows to detect with minimal radiation exposure (below the natural annual exposure) smallest structures like the auditory nuclei in the brainstem. From a translational perspective, the ß+-emitting radiotracers offer the possibility to image functional or molecular processes from the insect (using storage phosphor screens and 30 µm resolution) to the patient. Thus, PET provides biomarkers / endpoints for control / new development of therapies for the auditory system. In preclinical studies, for example, the relevance of CNS related factors for age-related hearing loss could be elaborated. For example, a study of inhibitory neurotransmission (GABAA receptors using 18F-flumazenil) showed significant reductions in regions of the auditory system in the CNS in middle-aged gerbils before there was a reduction of auditory brainstem potentials indicative of peripheral disorders. In another study in guinea pigs, 68Ga-FAPI PET revealed increased fibroblast activity in the cochlea after cochlear implantation as a possible pathophysiological correlate of increased impedance/variable treatment response. Both preclinical studies suggest benefit from translation to patients. In patients with CI, functional PET studies have already revealed essential factors for therapy response - such as the absence of maladaptive changes before implantation or favorable cross-modal neuronal plasticity afterwards. The method thus has considerable potential to detect correlates of variable response after implantation and to support goal-directed auditory rehabilitation. For example, the processing of music in CI users can be objectively investigated as a possible therapeutic factor and also as an essential factor for quality of life. In these contexts, the synchronous combination of PET with EEG, especially the registration of event-related potentials, is particularly interesting in order to conceive correlates of the cognitive processing of auditory information in a spatially and temporally differentiated manner.

Prof. Georg Berding
Hannover Medical School, Department of Nuclear Medicine
Carl-Neuberg-Str. 1, 30625 Hannover
berding.georg@mh-hannover.de



Birger Kollmeier, Anna Warzybok,
Medizinische Physik & Cluster of Excellence Hearing4All,
Universität Oldenburg

Audiological Diagnostics supported by Machine Learning and auditory models

Precision diagnostics in rehabilitative audiology is concerned with understanding and quantifiying the underlying factors (or causes) of a given hearing impairment with a minimum amount of measurement time and effort for the individual patient. Both statistical learning methods (e.g., the CAFPA approach to quantify the underlying factors in an abstract, data-representation-independent and interpretable way, Buhl et al., 2019) and auditory models are important tools to optimize the inference from given diagnostic data.

Recently, a remarkable precision in predicting the individual benefit from a hearing device (aided performance prediction) has been achieved with a machine-learning based model for speech recognition, denoted as FADE (Framework for auditory discrimination experiments) (Schädler et al., 2020). This will have a great impact on how we will construct and individually fit hearing aids in the future: We build on the Plomp (1978) A&D approach separating a compensable part of the hearing loss (attenuation component A) from a suprathreshold distortion or D component which can not be compensated for by amplification and which should be determined to set realistic fitting targets. Moreover, the binaural contribution to speech recognition can well be modelled by a contralateral inhibition approach (FADE-CAIN, Hülsmeier et al., 2021, motivated by Lopez Poveda et al., 2018) which in certain situation supersedes automatic better ear listening (FADE-ABEL) and calls for a preservation of temporal varying interaural level differences (ILDs) in hearing devices.

To experimentally test and verify these approaches independent from manufacturer-specific commercial solution, a portable Hearing Lab (Kayser et al., 2022) has been developed together with open-source software (open Master Hearing Aid) within the Cluster of Excellence Hearing4All. This talk will therefore provide some hints on how you as an audiologist can set realistic fitting expectations for a given patient and be part of the international hearing instrument research community.

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Prof. Birger Kollmeier
University of Oldenburg, Department of Medical Physics and Acoustics
26111 Oldenburg, Germany
birger.kollmeier@uni-oldenburg.de

Thorsten. M. Buzug
Fraunhofer Research Institution for Individualized and Cell-Based Medical Engineering (IMTE), Lübeck, Germany

Navigation of magnetic micro-robots

We propose a spiral magnetic microrobot that can be controlled by magnetic fields in an untethered mode. This is demonstrated by navigating the microrobot through an additively manufactured phantom. The microrobot is fabricated by a stereolithographic printing process. After printing, the microrobot was coated with a sealing varnish containing magnetic nanoparticles. Magnetic fields are applied using a magnetic particle imaging (MPI) scanner, which allows navigation and tomographic visualization with the same device. With MPI, the actuation process can be visualized with a localization accuracy of 0.68 mm. Preliminary in vitro phantom experiments are presented to give an idea of robotic treatment.

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Prof. Dr. rer nat. Thorsten Buzug
Universität zu Lübeck, Institut für Medizintechnik
Ratzeburger Allee 160
23562 Lübeck, Germany
buzug@imt.uni-luebeck.de; harms@imt.uni-luebeck.de

Hoc Kiem Trieu
Institute of Microsystems Technology,
Hamburg University of Technology

3D patterning for individualized implantable MEMS

Microsystems, also known as MEMS (Micro-Electro-Mechanical Systems) [1], are well established and indispensable in daily life, with great potential in life sciences. Many implantable MEMS devices, among others pressure sensors and micro stimulators, have been developed [2,3] or are under development, including implantable sensors for hearing devices [4]. MEMS have their origin in semiconductor technology, a typical subtractive planar technology for the manufacturing of microelectronic devices and integrated circuits with high pattern resolution and large scale integration. Enhanced by specific process modules such as surface and bulk micromachining, 3D freely moving structures have been realized. However, due to the techniques used, such as photolithography, thin film deposition and reactive ion etching, the achievable devices are limited to components with planar 2D geometry and low thickness or to extruded 2.5D structures with high aspect ratio. MEMS with more complex structures such as microvalves and micropumps have been implemented by bulk micromachining combined with wafer bonding techniques [5]. Furthermore, manufacturing of MEMS in a batch process is a time consuming procedure. 3D patterning with additive manufacturing such as photopolymerization, extrusion, powder bed fusion or direct writing [6] and subtractive 3D approaches such as selective laser-induced etching (SLE) [7] are highly versatile manufacturing techniques differing in technology, materials and precision.

Other advantages besides high degree of design freedom include efficiency, customization and manufacturing speed. However, although 3D printed devices can be very complex in shape, their functionality remains limited in complexity due to creating the entire structure in one fabrication step using usually only one material. Recent trends in multi-material additive manufacturing show more complex 3D printed parts [8] with applications for printed electronics [9]. Nevertheless, the complexity of functionality and integration density of MEMS remain unmatched. Manufacturing of 3D MEMS with high degrees of design freedom, as known from additive manufacturing, in combination with complex functionalities of traditional microsystems is still in its infancy and subject of current research. The successful combination of 3D printing and micromachining of MEMS is demonstrated in this presentation with some basic technology investigations that pave the way to an extended toolbox for MEMS with high degrees of design freedom in 3D as known from 3D printing. Extending the typical one-step manufacturing approach of 3D printing to multiple processing cycles, as is common in manufacturing of microsystems and semiconductor devices, will enable 3D patterning with more complex structures and unprecedented integration density. Particularly, the high degree of design freedom and customizability of 3D patterning combined with its manufacturing speed enable the realization of individualized implantable 3D MEMS.

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Prof. Dr. Ing. Hoc Khiem Trieu
Technische Universität Hamburg, Institut für Mikrosystemtechnik
Eißendorfer Straße 42, 21073 Hamburg
trieu@tuhh.de

Verena Scheper
Department of Oto-Rhino-Laryngology, Hannover Medical School, Hannover, Germany
Lower Saxony Centre for Biomedical Engineering, Implant Research and Development, Hannover, Germany

Patient-individualized drug releasing implants in Otorhinolaryngology

Specific ear and rhinologic disorders such as recurrent outer ear canal infections, middle ear infections, tinnitus, and hearing loss or chronic rhinosinusitis as well as implant based pathologies such as peri-implant fibrosis or implantation related hearing loss can and should be treated by pharmacotherapy. Local pharmacotherapy to the inner ear and frontal sinus is very challenging due to physiological barriers like the blood-labyrinth barrier (BLB) or the close proximity of the frontal sinus to easily vulnerable structures like the orbital cavity and the skull base. Up to now the results of otologic and rhinologic drug therapy are heterogeneous since the drug delivery devices are not exactly tailored to the patients needs. Individualized implants, exactly fitting to the patient's anatomy, will help to overcome this lack of therapeutics. To allow an atraumatic implantation of individualized implants into the anatomical niches and sinuses, the implant needs to be mechanically flexible. We developed a process chain from clinical images (cone beam computed tomography), semi-automated segmentation of the region of interest using a custom-made software, 3D-printing of drug containing material to clinical application. Implants for the outer ear canal, round window niche and frontal sinus are manufactured containing different drugs. Implants are 3D printed by a 3D-Bioplotter using medical-grade silicone. The printed specimens are tested for drug release, biocompatibility and –efficacy in vitro and in vivo. The additive manufacturing method allows the development of implants in a large volume range. The precision is acceptable for the intended applications; drug is released out of the samples and causes biological effects in vitro. Biocompatibility is given and first named patient use with this novel generation of implants are performed and suggest safety and compliance.

PD Dr. Verena Scheper
Hannover Medical School, Department of Otolaryngology
Carl-Neuberg-Str. 1
30625 Hannover, Germany
Scheper.Verena@mh-hannover.de

Prof. Brigitte Malgrange
University of Liège, Belgium

Regeneration and biology in the inner ear: input of human induced pluripotent stem cells

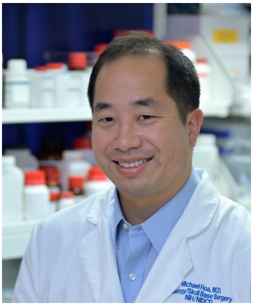
The inner ear development involves several complex and tightly coordinated processes that include the proliferation and fate commitment of otic progenitor cells into sensory epithelial hair cells and supporting cells which primarily relies on spatio-temporal regulation of gene expression. Given the developmental complexity, genetic mutations in transcription factors, ion channels and diverse ranges of proteins including ciliary proteins can impair inner ear development and can cause hearing loss. In this context, numerous gene mutations have been reported in patients affected with profound sensorineural hearing loss.

Here, we showed that human induced pluripotent stem (hIPS) cells generated from fibroblasts of healthy and patients are very useful to decipher the pathophysiological role of mutated genes in deafness. We established hiPS cells from patient fibroblasts using non-integrative Sendai viral vectors. These cell lines were validated in vitro and in vivo. Using a 3D protocol, we generate inner ear organoids and demonstrate that healthy and pathological hiPSCs can generate a population of otic progenitor cells that are then able to differentiate into hair cells (HCs), supporting cells and neurons. Using this model, we characterized proliferative capabilities, differentiation aptitudes and cell death in normal and pathological organoids. This new human derived organoid model provides insights regarding molecular mechanisms that drive pathological inner ear development.

Prof. Brigitte Malgrange
Université de Liège, Bât. B36 Pharmacologie
Quartier Hôpital
Avenue Hippocrate 15
4000 Liège 1, Belgium
bmalgrange@uliege.be

Prof. Lawrence R. Lustig, MD
Columbia University
New York, USA

Prof. Lawrence R. Lustig, MD
Columbia University Vagelos College of Physicians and Surgeons
NewYork-Presbyterian/Columbia University Irving Medical Center
Department of Otolaryngology-Head & Neck Surgery
Harkness Pavilion Suite 850
180 Fort Washington Ave
New York, NY 10032, USA
lrl2125@cumc.columbia.edu; lh2022@cumc.columbia.edu



Michael Hoa[1], Jennifer Chisholm[2], Talah Wafa[2], Carmen Brewer[2], Samuel Adadey[1], Alison Benner[1], Dillon Strepay[1], Shoujun Gu[1,] Li-Yueh Hsu[3], John Butman[3], Rafal Olszewski[1]

[1]Auditory Development and Restoration Program, National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Bethesda, MD;
[2]Audiology Unit, National Institute on Deafness and Other Communication Disorders, National Institutes of Health, Bethesda, MD;
[3]Department of Radiology and Imaging Sciences, NIH Clinical Center, National Institutes of Health, Bethesda, MD

Longitudinal Deep Phenotyping of Hearing Instability Disorders: Searching for Biomarkers and Repurposable Therapeutics

Introduction: Clinical assessment of human diseases often starts with the identification of a phenotype, defined as an observable set of traits. Some hearing loss disorders, including Meniere's disease (MD), sudden sensorineural hearing loss (SSNHL), autoimmune/autoinflammatory inner ear disease (AIED/AID), are characterized by either fluctuating and/or sudden changes in hearing, which can be termed hearing instability (HI) as a prominent phenotype. In some cases, HI disorders are characterized by endolymphatic hydrops (EH), which is expansion of the endolymph-containing compartments (Figure 1), in the cochlea and vestibule EH can now be visualized in vivo in patients utilizing contrast-enhanced delayed fluid-attenuated inversion recovery (CED-FLAIR) MR imaging. While treatments, both medical and surgical, exist for the vestibular symptoms that accompany some of these disorders, effective treatments for hearing loss in these diseases remain limited. Deep phenotyping of human diseases has been utilized to gain a better understanding of poorly understood diseases and to identify potential biomarkers and therapeutic targets in these settings. We recently initiated a deep phenotyping study of HI disorders utilizing a combination of physiologic, immunologic, and magnetic resonance imaging-based investigations. In this presentation, we introduce this NIDCD-sponsored longitudinal deep phenotyping protocol for HI disorders at the NIH Clinical Center (NIH CC) and describe the phenotyping measures utilized to assess an initial cohort of HI patients. We characterize the baseline characteristics of an initial cohort of recruited patients.

Methods: Patients with presentations consistent with HI disorders were recruited for longitudinal deep phenotyping at the NIH CC. Recruited patients are assessed longitudinally during periods of both hearing instability and stability, respectively, over the course of 15 months. Deep phenotyping measures include audiometric and vestibular physiologic tests, CED-FLAIR MRI, and immunophenotyping of immune cells and peri-

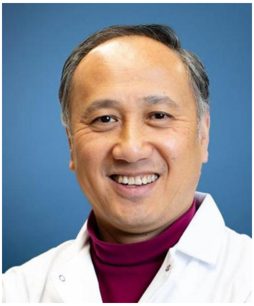
see next page

pheral plasma. Immunophenotyping consists of full spectrum flow cytometry (FSFC), single-cell RNA-sequencing (scRNA-Seq), and cytokine and proteome profiling of peripheral plasma.

Results: Results of longitudinal assessments will be presented for the initial cohort of HI patients. An overview of phenotyping with audiometric and vestibular measures, as well as the use of CED-FLAIR MRI to both identify and quantify endolymphatic hydrops (EH) will be detailed. Preliminary findings related to an immunoprofiling efforts will be discussed.

Conclusions: We present a structural overview of a deep phenotyping clinical protocol for HI disorders that is actively recruiting subjects. Deep phenotyping efforts may improve our understanding of the underlying pathophysiology of these poorly understood disorders and may lead to the identification of potentially druggable targets.

Dr. Michael Hoa
Porter Neuroscience Research Center, Division of Intramural Research, NIDCD/NIH
35 Convent Dr., Room 1F-226
Bethesda, Maryland 20892-3745, USA
michael.hoa@nih.gov



Prof. Jian Zuo
Creighton University
Omaha, USA

Repurposing drugs against hearing loss

Hearing loss induced by noise, cisplatin, and antibiotics is an unmet medical need that lacks effective therapeutic treatment. We performed in vitro and in silico screens for a large number of existing drugs that can be repurposed against hearing loss and identified multiple biological pathways and drug candidates. We further validated top drug candidates in zebrafish and mouse models with noise-, cisplatin- and antibiotics-indued hearing loss. We also determined inner ear perilymph pharmacokinetics of several top drug candidates. Our studies provided preclinical basis for future clinical trials to prevent and treat hearing loss.

Prof. Jian Zuo
Creighton University, Department of Biomedical Sciences
2500 California Plaza
Omaha, NE 68178, USA
JianZuo@creighton.edu / JohnBolas@creighton.edu

Gerard M. O'Donoghue
National Institute Health Research, Nottingham Biomedical Research Centre and Nottingham University Hospitals NHS Trust, Nottingham

Stem Cells for Hearing Regeneration: towards a first-in-human clinical trial

The neurosensory structures of the human inner ear are post-mitotic with little capacity for regeneration if lost or damaged. While auditory prostheses (cochlear implants and hearing aids), provide useful access to sound, they do not treat the underlying pathology causing the deafness, are often perceived as stigmatising, and do not restore normal auditory inputs. Induced pluripotent stem cells have the capacity to self-renew, express the same human pluripotent markers, and can differentiate into all three germ layers creating patient-specific cells of any lineage. They are thus ideal for cell substitution therapy such as may be needed to renew the inner ear's neurosensory apparatus for hearing restoration. While stem cell colonies for research use in the laboratory are relatively easy to produce substantial challenges are incurred when developing cells for clinical use. The regulatory requirements are rigorous and are established in the US by the Food and Drug Administration (FDA), in the European Union by the European Medicine's Agency (EMA) and in the UK by the Medicines and Healthcare Regulatory Agency (MHRA). The manufacturing process of stem cells must meet current Good Manufacturing Practice (cGMP) which regulates every step in the process from tissue collection, cell reprogramming, cell expansion, media, reagents, cryopreservation, cell banking and post-thaw recovery. Standard operating procedures are needed at each step for compliance with cGMP with rigorous documentation and traceability of all components along the manufacturing and delivery pathways. Meticulous testing is required to ensure the culture medium is optimised to ensure good quality cell proliferation which is quality-controlled through a range of tests (karyotype analysis, flow cytometry, whole genome analysis, cancer predisposition testing etc). Maintaining the sterility of the culture medium (for endotoxins, mycoplasma, bacteria) without compromising the viability of the stem cells is a particularly challenging requirement. Once regulatory approval of the induced stem cells is awarded, precise delivery to their target structures is a critical requirement. Our primary interest is the use of stem cells to renew the spiral ganglion cells (SGC) of the auditory nerve as well as its terminal filaments in the sensory end-organ. In order to identify the exact location of these structures we used synchrotron phase-contrast imaging using volume-rendering software to construct highly accurate 3-dimensional representations of the inner ear (1). The cell bodies of the SGCs are arranged in a bony helical canal that spirals from the base of the cochlea to its apex; the canal volume is 1.6 µL but with a diffusion potential of 15 µL. Modelling data from 10 temporal bones enabled definition of safe trajectories for therapeutic access while preserving the cochlea's internal architecture and vasculature. We validated two such surgical approaches (one to Rosenthal's canal and the other directly to the auditory nerve) through surgical simulation, anatomical dissection, and micro-radiographic analysis. The necessity for clinical trials. their opportunities and perils along with their prohibitive costs will be elaborated.

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Prof. Gerry O'Donoghue
Queen's Medical Centre
Nottingham Hearing BRU, ENT Department, UK
g.odonoghue@nottingham.ac.uk

Gwenaelle S.G. Géléoc[1,2] and Jennifer J. Lentz[3,4]
[1] Department of Otolaryngology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA;
[2] Kirby Neurobiology center, Boston Children's Hospital, Boston, MA, USA;
[3] Department of Otorhinolaryngology, LSUHSC, New Orleans, LA, USA;
[4] Neuroscience Center of Excellence, LSUHSC, New Orleans, LA, USA

Antisense oligonucleotides or gene replacement therapy? Lessons learned from USH1C preclinical studies

Usher syndrome (Usher) is the most common genetic cause of concurrent hearing and vision impairment. Over the past decade, we have explored different strategies to target the USH1C c.216G>A (216A) mutation responsible for nearly all USH1 cases in the Acadian population in Louisiana, USA and Canada. The 216A mutation creates a cryptic splice site that results in a truncated mRNA and the protein product, harmonin. In the inner ear, USH1C is expressed in sensory hair cells of the auditory and balance organs. One strategy that we have explored consists of replacing the faulty gene with a correct copy that is provided to the sensory cells via viral vectors injected into the inner ear (Pan et al. 2017). This gene therapy approach applied to neonatal Ush1c. c.216G>A knock-in mice promoted recovery of sensory cell function and restoration of hearing and balance to near wild type levels. Another strategy, originally developed by Lentz et al. (2013) uses short splice-switching antisense oligonucleotides (ASOs) to block the aberrant de novo splicing and restore RNA processing and expression of a functional protein. We have now demonstrated that localized ASOs delivery to the middle and inner ear of neonatal Ush1c. c.216G>A knock-in mice also leads to significant improvements of auditory and balance function (Lentz et al. 2020).

For this presentation, I will discuss the advantages and disadvantages of these two approaches. Preclinical studies have shown that both gene and antisense therapies lead to robust hearing and balance outcomes (Lentz et al 2013 and 2020; Pan et al 2017, Géléoc and Amraoui, 2020). ASOs are desirable in that they target pre-mRNA and preserve endogenous regulation of gene expression. However, for long-term improvement, this strategy requires repeated dosing. Gene replacement therapy using viral vectors only requires a single dose, however, regulating the expression of the target gene has not yet been established. Before either approach can be advanced to the clinic for USH1C, several aspects must be considered, including the use of specific promoters that can lead to physiological expression of the target gene, the choice of viral capsid with the appropriate cell tropism, as well as the duration of therapeutic effect of either treatment.

Clinically, both ASOs and viral vectors used to treat other diseases have been shown to elicit limited immune responses, highlighting the importance of safety studies for any investigational new drug. Lastly, it will be essential, for either strategy, to define the critical time window for intervention, whether we are targeting the hearing or balance organs.

Prof. Dr. Gwenaelle Geleoc
Boston Children's Hospital & Harvard Medical School
Center for Life Sciences, CLS 03001
3 Blackfan Circle
Boston, MA 02115, USA
Gwenaelle.Geleoc@childrens.harvard.edu

Vincent Van Rompaey
University of Antwerp – Antwerp University Hospital

Disease-modifying therapy for autosomal dominant hereditary hearing loss in DFNA9

DFNA9 is the most frequent hereditary disorder in Belgium and the Netherlands causing hearing loss at 20-30 years and evolving towards deafness by 60-70 years. Additionally, patients suffer from bilateral vestibulopathy by the age of 40 years. Over 30 different pathogenic variants in the COCH gene have been reported worldwide. Currently, there is no cure available although we can restore speech understanding to some level with hearing aids and cochlear implants. Ideally, a disease-modifying therapy would have the ability to delay or stop the progression of hearing loss in DFNA9. In DFNA9, only one of the two copies of the COCH gene (one inherited from either parent), is mutated and encodes for a toxic protein that affects the aging inner ear in general, and the spiral ligament and spiral limbus more specifically. It therefore presents us with a target anatomically as well as genomically. The DFNA9 population is particularly relevant to develop and evaluate a disease-modifying gene therapy for sensorineural hearing loss because: potential carriers are aware of their hearing-impaired relatives, potential carriers can get routine genetic testing and know their carrier status, once aware of their carrier status, a significant pre-symptomatic stage of several years starts, carriers are aware they will inevitably develop severe-to-profound SNHL and are open to future clinical trials with gene therapy, as identified during a patient advocacy meeting.

Prof. Vincent van Rompaey
University of Antwerp, Departement - Translationele Wetenschappen
Campus Drie Eiken - T.498
Universiteitsplein 1
2610 Wilrijk, Belgium
vincent.vanrompaey@uantwerpen.be

Prof. Greg Eigner Jablonski MD PhD[1 2],
Ralf Greisiger PhD[1]
[1]Department of Otorhinolaryngology and Head & Neck Surgery, Oslo University Hospital, Norway
[2]University of Oslo, Institute of Clinical Medicine, Norway

Fluoroscopy and intra-OP imaging as quality control for Minimal Invasive CI Surgery

A feasibility study about the minimal invasive Cochlear Implant surgery system from OtoJig was carried out at Oslo University Hospitals Intervention Centre. For this study two cadaver heads were used and bilaterally implanted. For the planning procedure the Flat-Detector CT-scans were done with the Siemens Artis Pheno system. The planning of the drill channel was done with the OtoJig software. The surgical procedure was done with per-operative fluoroscopy using the Siemens Artis Pheno FD-CT-scanner. Microscope video and fluoroscopy video were post-op analyzed to investigate the surgical and insertion procedure. Especially the step of opening the round window is a critical one and has been performed with a sharp cannula through the drill tunnel. The electrode array insertion is equally important for the overall success. Both steps can be observed intraoperatively with the help of fluoroscopy.

Removal of the insertion tube and placement of the electrode array have caused unwanted movements and our investigation has led to an improved redesign of the insertion procedure. Intra op fluoroscopy combined with microscope video has been shown to be a feasible procedure to detect unwanted electrode placements in this new surgical procedure an will lead to an improved surgical protocol.

Prof. Greg Eigner Jablonski
University of Oslo, Institute of Clinical Medicine
Postboks 4950 Nydalen
OUS, Rikshospitalet
0424 Oslo, Norway
g.e.jablonski@medisin.uio.no

Ralf Greisiger
Department of Otorhinolaryngology and Head & Neck Surgery
Oslo University Hospital, Norway
ralf@greisiger.org

Caversaccio M[1,2], Weber S[2], Aebischer P[1,2], Weder S[1], Mantokoudis G[1], Wimmer W[1,2]
[1]Department of ENT, Head and Neck Surgery, Inselspital, Bern University Hospital, University of Bern, Bern, Switzerland
[2] ARTORG Center for Biomedical Engineering Research, University of Bern, Bern, Switzerland

Robotics and computer assisted surgery on ear

Robotics has recently gained popularity in otology as an effective tool to overcome the surgeon's limitations such as tremor, drift and accurate force control feedback. Several products are on the market but the use of endoscope included in the robot or guided is still limited. Computer assisted surgery is the "predecessor" of robotic surgery.

Robotic cochlear assisted implantation as tunnel procedure is a minimally invasive approach for CI surgery. The prototype of our developed robot and the procedure was created and evaluated in a first clinical trial as a translational project at the University ARTORG Center and the Hospital in Bern, Switzerland.

The clinical study was approved by the local IRB and regulatory body. Access to the middle ear was drilled using a previously developed task specific image-guided robotic system. Sufficient clearance of the drill trajectory from the facial nerve was confirmed using intraoperative cone beam CT imaging. The electrode array was manually inserted in the round window using a specifically manufactured insertion tube. Correct placement and nominal function of the implant was verified by telemetry and postoperative CT imaging. We have demonstrated that a CI electrode can be successfully inserted into the cochlea through a 1.8 mm keyhole created by a surgical robot. The crucial key point remains the size of the facial-chorda angle.

During the last years the development of our prototype to a commercial robot system has been reinforced by the industry. The inner ear approach with the robot seems possible for the future. 2020 the prototype received the CE-mark.

Since 2021 we include robotic cochlear implantation with the commercialized system (Hearo™) and the planning system (Otoplan™) to evaluate the performance. It's an ongoing study (ClinicalTrials.gov) J Vis Exp 2022, 16(184).

Additionally in a multicenter study the robot will be tested by the University hospitals of Antwerp, Brussels, Vienna, Düsseldorf and Montpellier. Before the robot can become the standard approach for CI, several points still need to be addressed, primarily imaging, accuracy, cost and duration of the procedure

Prof. Dr. med. Marco Caversaccio
Inselspital - Universitätsspital Bern, HNO-Klinik
Freiburgstrasse 18
CH-3010 Bern, Switzerland
Marco.Caversaccio@insel.ch / Irene.Zintel@insel.ch

Yann Nguyen, Hannah Daoudi, Renato Torres, Ghizlene Lahlou, Evelyne Ferrary, Isabelle Mosnier, Olivier Sterkers
AP-HP, GHU « Sorbonne Université »; site Pitié Salpêtrière; DMU «ChIR» Chirurgie Innovation et recherche, Service ORL, Paris, France.
Sorbonne Université/ Inserm / Institut Pasteur : UMR-S 1120, «Technologies et thérapie génique pour la surdité», Paris, France

Robotic assistance for otological procedures

Accurate positioning, sub-millimetric displacements, tremor filtration, and preservation of the microscope vision field are the primary requirements for a robotic assistance in ear surgery. Applications are mainly represented by middle ear surgery and cochlear implantation,

RobOtol (Collin, Bagneux, France) is a robotic arm device, designed to assist middle ear surgery and cochlear implantation and tele-operated by the surgeon through a SpaceMouse® (3Dconnexion). In this presentation, we will describe our experience with this robotic device concerning more than 200 procedures.This system can be used in all indications of otologic surgery. The first application concerns the atraumatic insertion of the cochlear implant electrode. Different array devices from five manufactures (Advanced Bionics, Cochlear, Medel, Nurotron, Oticon) can be adapted to the robotic arm. RobOtol® allows a slow and constant insertion speed (0.1-0.3 mm/s) of the electrode array into the cochlea. It also offers the possibility to modify the insertion axis following the optimal axis of insertion within the basal turn of the scala tympani. According to the robotic-assistance procedure, the rate of translocations from scala tympani towards the scala vestibuli was reduced depending on the electrode array type. We describe how the CI procedure is performed and how a slow and continuous insertion can be obtained with the robot.The second application is otosclerosis surgery. The robot was used to guide a laser fiber (Iridex KTP, USA) to perform the section of the stapes muscle tendon and the posterior branch of the stapes (1.5W, 200ms), the platinotomy (1W, 200ms) before calibration with the Oto-tool skeeter motor (Medtronic, USA) and tightening the Nitibond prosthesis (Kurz, Germany, 0.5W, 200ms).The third application is endoscopic ear surgery using the robot as an endoscope holder which allows bi-manual surgery for tympanic grafts, ossicular repairs and control of cholesteatoma removal during chronic otitis. A case series of patients operated with an endoscopic exposure with a robot based assistance will be reported. We will describe how a robot-based holder may combine the benefits from endoscopic exposure and a two-handed technique.

Prof. Yann Nguyen
Sorbonne Université, Greater Paris University Hospitals, Institut de l'Audition
63, rue de Charenton
75012 Paris, France
yann.nguyen@aphp.fr

Thomas Rau Ph.D.
Hannover Medical School

Precision control of critical parameters: Surgical tools to increase the reliabil-ity of cochlear implants

Dr. Thomas Rau
Hannover Medical School, Department of Otolaryngology
Carl-Neuberg-Str. 1
30625 Hannover, Germany
Rau.Thomas@mh-hannover.de

Bruce Gantz, Marlan Hansen, Alex Clausen, Camile Dunn
Iowa Cochlear Implant Clinical Research Center
Carver College of Medicine at the University of Iowa
Iowa City, Iowa USA

Preservation of Functional Residual Hearing Comparing Manual and Robotic Insertion of Cochlear Implants

Objective: To compare manual and robotic-assisted cochlear implant insertion system in subjects with residual low frequency hearing that are candidates for EAS.

Setting: All procedures were performed, and all data were collected, at a single tertiary referral center.

Patients: 43 postlingually deafened adult subjects with a PTA of <60dB for 125-500 Hz that met FDA indication criteria for Hybrid cochlear implantation were implanted with MedEl Flex 20, 24 cochlear implants.

Intervention: All patients underwent standard-of-care surgery for unilateral cochlear implantation with the addition of a single-use robotic-assisted insertion device during cochlear electrode insertion or standard manual insertion using soft surgical principles.

Main outcome measures: Post operative ability to maintain functional acoustic hearing at 125, 250, and 500 Hz of 85dB or less.

Results: Successful robotic-assisted insertion of lateral wall cochlear implant electrode arrays was achieved in 15 of 15 subjects. Manual insertion was performed in 28 subjects. Postoperative functional acoustic hearing was measured at initial activation, 2, 3, 6, and 12 months post operative.

Conclusions: Initial results with robotic insertion of hearing preservation lateral wall cochlear implant electrodes resulted in better functional acoustic hearing preservation compared to manual insertion of similar devices. Longer term follow-up is ongoing to determine if these results are maintained.

Prof. Dr. Bruce Gantz
University of Iowa, Dept of Otolaryngology--Head and Neck Surgery/ Neurosurgery
University of Iowa Hospitals and Clinics
200 Hawkins Drive (21201 PFP)
Iowa City, Iowa 52242-1078, USA
bruce-gantz@uiowa.edu

Abstracts

Friday, 14th April 2023

Fan-Gang Zeng
UC Irvine

How can artificial intelligence advance hearing devices and research, or vice versa?

Like telephones, computers and internet, artificial intelligence (AI) will fundamentally change our life. Compared with its impact on speech, language and vision, AI application to hearing devices is less developed, or even primitive. One reason for this lack of advances is the stringent requirement of hearing devices, such as short latency, low power, and local processing, making AI implementation difficult if not impossible. The other reason is that hearing and vision are different, specializing in time and space processing, respectively. I will review the status of AI application to hearing devices and discuss potential solutions to overcoming the latency, power, and locality limitations. I will then focus on the "cocktail party problem" to illustrate technical approaches, including generative AI models, that may provide solutions to the problem. I will argue for research and development of a hearing-driven, biologically-plausible and interpretable AI system that not only restores impaired hearing and enhances normal hearing, but also serves as a general man-machine interface.

Prof. Fan-Gang Zeng
University of California, Hearing and Speech (HESP)Laboratory
110 Medical Science E
Irvine, CA 92697-5320, USA
fzeng@uci.edu

Prof. Bernd Meyer
University of Oldenburg

Low-complexity models for speaker separation in hearing aids

The enhancement of degraded speech signals has seen major breakthroughs in recent years through deep learning. Separating signals from speakers in many-talker (cocktail party) situations is a feature that should be very important in future hearing aids, since it could enable isolating voices for selective listening with drastically decreased noise levels. A requirement for the underlying algorithms are are causal and low-latency systems, which have not been in the main focus of the community in the last few years. In this talk, I will introduce models for speech enhancement (and particularly separation) which are relatively lightweight, exhibit low latencies (of a few milliseconds) and take into account information from multiple channels which are typically available in current hearing aids. Since model size and computational complexity are crucial parameters in the context of assistive listening, I will present results for the tradeoff between objective listening metrics and model complexity.

Prof. Bernd Meyer
University of Oldenburg
Communication Acoustics
26111 Oldenburg, Germany
bernd.meyer@uni-oldenburg.de

DeLiang Wang
Perception and Neurodynamics Laboratory
Ohio State University

Location-based training for multi-channel speaker separation

Permutation ambiguity is a crucial issue for deep learning based talker-independent speaker separation. Deep clustering and permutation invariant training (PIT) are widely used for addressing the permutation ambiguity problem in monaural scenarios. Although both approaches have been extended to multi-microphone scenarios, the permutation ambiguity problem may be naturally resolved by leveraging the spatial relations of multiple speakers. We present location-based training (LBT), a new approach to achieve talker independency in multi-channel speaker separation. Unlike PIT that examines all possible permutations, LBT assigns speakers according to their positions in physical space. With a linear training complexity to the number of concurrent speakers, LBT is computationally much more efficient than PIT when many overlapped speakers need to be separated. Specifically, we propose two training criteria: azimuth-based and distance-based training, using speaker azimuths and distances relative to a microphone array. Evaluation results show that LBT significantly outperforms PIT on two-speaker and three-speaker mixtures with different array geometries and in various acoustic conditions. In addition, a joint training strategy is proposed to integrate azimuth-based and distance-based training, further improving separation performance.

Prof. DeLiang Wang
The Ohio State University, Department of Computer Science and Engineering
2015 Neil Avenue
Columbus, OH 43210-1277, USA
dwang@cse.ohio-state.edu

Prof. Holger Blume
Leibniz Universität Hannover

Prof. Holger Blume
Leibniz Universität Hannover, Institut für Mikroelektronische Systeme
Appelstr. 4
30167 Hannover, Germany
blume@ims.uni-hannover.de

Prof. Sarah Verhulst
Ghent University, Belgium

Personalised neural-network-based closed-loop systems for augmented hearing

Prof. Dr. Sarah Verhulst
Ghent University, Hearing Technology - Waves
Technologiepark 126
9052 Zwijnaarde, Belgium
sarah.verhulst@ugent.be

Prof. Nima Mesgarani
Columbia University (New York)
Electrical Engineering Department

Brain-controlled assistive hearing technologies

Listening in noisy and crowded environments is a challenging task. Assistive hearing devices can suppress certain types of background noise, but they cannot help a user focus on a single conversation amongst many without knowing which speaker is the target. Our recent scientific discoveries of speech processing in the human auditory cortex have motivated several new paths to enhance the efficacy of hearable technologies. These possibilities include, I) speech neuroprosthesis which aims to establish a direct communication channel with the brain, II) auditory attention decoding where the similarity of a listener's brainwave to the sources in the acoustic scene is used to identify the target source, and III) increased speech perception using electrical brain stimulation. In parallel, the field of auditory scene analysis has recently seen great progress due to the emergence of deep learning models, where even solving the multi-talker speech recognition is no longer out of reach. I will discuss our recent efforts in bringing together the latest progress in speech neurophysiology, brain-computer interfaces, and speech processing technologies to design and actualize the next generation of assistive hearing devices, with the potential to augment speech communication in realistic and challenging acoustic conditions.

Speaker BIO: Nima Mesgarani is an associate professor at Zuckerman Mind, Brain, Behavior Institute of Columbia University in the City of New York. He received his Ph.D. from the University of Maryland and was a postdoctoral scholar at the Center for Language and Speech Processing at Johns Hopkins University and the Neurosurgery Department of the University of California San Francisco. He received the National Science Foundation Early Career Award in 2015, Pew Scholar for Innovative Biomedical Research Award in 2016, and Auditory Neuroscience Young Investigator Awards in 2019. His research was selected among the top-10 innovations of 2018 by UNICEF-Netexplo, top-10 breakthroughs of 2019 by Institute of Physics, and top-10 health innovations of 2019 by Healthcare Innovation. His interdisciplinary research combines experimental and computational methods to study speech communication in the human brain which critically impacts research in artificial models of speech processing and speech brain-computer interface technologies.

Prof. Nima Mesgarani
Columbia University (New York), Electrical Engineering Department
nm2764@columbia.edu

Prof. Hubert Lim Ph.D
University of Minnesota, USA

Future opportunities for central auditory prosthetics

Prof. Hubert Lim
University of Minnesota, Departments of Otolaryngology and Biomedical Engineering
312 Church Street SE
Minneapolis, MN 55455, USA
hlim@umn.edu

David Moses Ph.D.
UCSF Weill Institute for Neurosciences, USA

Developing a speech neuroprosthesis

Speech is a fundamental mode of human communication. However, patients suffering from severe paralysis may not be able to speak or even type, drastically limiting autonomy and self-expression. To address this, we started a clinical trial to assess the feasibility of using a brain-computer interface and advanced decoding algorithms to restore speech to persons with paralysis. In our approach, participants are surgically implanted with an electrocorticography (ECoG) array, enabling recording from neural populations in the sensorimotor cortex. Through the application of deep-learning and natural-language models, we demonstrate a proof-of-concept speech neuroprosthesis that decodes brain activity into intended messages as a clinical-trial participant with severe paralysis attempted to speak. In subsequent work, we expand the vocabulary of the neuroprosthesis by implementing a spelling interface. Ultimately, we hope to bring this technology closer to a clinical solution that can restore fully expressive communication to those who have lost the ability to speak.

Dr. David Moses
UCSF Weill Institute for Neurosciences, USA
505 Parnassus Ave, San Francisco, CA 94143
David.Moses@ucsf.edu

Amir Samii[1], Karl-Heinz Dyballa[2], Waldo Nogueira[2],
Rolf Salcher[2], Hubert Lim[3], Thomas Lenarz[2]
[1]International Neuroscience Institute, Hannover, Germany
[2]Hannover Medical School, Hannover, Germany
[3]University of Minnesota, Minneapolis, USA

Auditory Midbrain Implant – hearing beyond the brainstem

During 2017-2019 five deaf patients with neurofibromatosis type II (NF2) were implanted at Hannover Medical School with a novel central auditory prosthesis known as the two-shank Auditory Midbrain Implant (AMI). The AMI consists of two penetrating shanks each 5 mm long with 11 electrode contacts inserted in the central nucleus of the inferior colliculus of the midbrain. The AMI was developed as an alternative to the Auditory Brainstem Implant (ABI) for patients with NF2 in whom hearing rehabilitation is not possible, for example, due to damage to the cochlear nucleus. The two-shank AMI is a further development of a single-shank array, which was already implanted in five patients between 2006 and 2008, but led to limited hearing performance, probably due to insufficient temporal coding and suppression effects in the neurons [1].

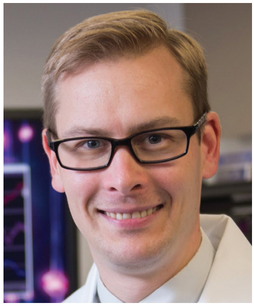
Method: The AMI is implanted via a retrosigmoid (suboccipital) approach. Reaching and exposing the inferior colliculus will be discussed as well as the optimal positioning of the shanks in a restricted surgical corridor.

Results: Nearly all requirements in terms of positioning and insertion angle of the shanks in the inferior colliculus across patients was achieved. All patients can hear at least environmental sounds and partly understand numbers and monosyllables. Some of them were previously provided with an ABI and could increase their performance with the AMI. One patient for example could raise his score in numbers by a factor of four (40 % instead of 10 %).

Conclusion: In a surgical challenging condition, a successful positioning of the shanks in the inferior colliculus has been demonstrated. Overall, the AMI enhanced lip-reading capabilities and provided some hearing with the AMI alone, at least for numbers. Word understanding with the AMI is still challenging, which is also not readily possible with the ABI. Further research is needed to get even better results.

References: [1] Lim HH, Lenarz T. Auditory midbrain implant: research and development towards a second clinical trial. Hearing research. 2015 Apr 1;322:212-23.

Prof. Amir Samii
International Neuroscience Institute - Hannover
Rudolf-Pichlmayr-Str. 4
30625 Hannover, Germany
a.samii-office@ini-hannover.de



Prof. Kirill Nourski
University of Iowa, USA

Intracranial electrophysiology of auditory processing in the human cortex

Electrical stimulation of the auditory nerve with a cochlear implant (CI) is the method of choice for treatment of severe-to-profound hearing loss. Understanding how the human cortex responds to acoustic stimuli may be useful in facilitating development of CI stimulation paradigms and rehabilitation strategies. Further, studies of cortical processing of spectrally degraded speech in normal-hearing individuals may serve as a model of how sound information is processed by CI users.

Intracranial electroencephalography (iEEG) in neurosurgical epilepsy patients offers an opportunity to study auditory processing at multiple levels of the cortical hierarchy with high spatiotemporal resolution (Nourski, Laryngoscope Investig Otolaryngol. 2017, 2:147-156). Systematic iEEG investigations demonstrate that core auditory cortex within the posteromedial portion of Heschl's gyrus represents spectrotemporal features of sounds with high precision and short onset latencies. At this level, iEEG activity in the high gamma band (70-150 Hz), thought to reflect neuronal spiking, is minimally modulated by task demands. Non-core auditory areas within superior temporal cortex facilitate transformation of acoustic attributes of speech into phonemic representations. Prefrontal cortex exhibits complex response patterns related to stimulus intelligibility, task relevance, and behavioral performance.

Feasibility of iEEG during CI stimulation was established in a case study in a neurosurgical epilepsy patient with a 20-year history of deafness and CI use (Nourski et al., J Assoc Res Otolaryngol. 2013, 14:435-50). Responses were recorded from non-core auditory cortex overlying lateral superior temporal gyrus. Activity was stable across recording sessions, underwent changes in latency and magnitude with stimulus level, exhibited phase locking to temporal stimulus modulations, and was abolished under general anesthesia. These response patterns were comparable to those obtained from normal hearing participants, suggesting that prolonged deafness with CI use did not result in gross maladaptive changes in auditory cortical processing.

In hearing individuals, spectrally degraded speech can be used to approximate the CI output to the central auditory system (Nourski et al., Hear Res. 2019, 371:53-65). Cortical responses to utterances /aba/ and /ada/, degraded using a noise vocoder, were studied in a cohort of 13 participants. The stimuli yielded chance identification performance when degraded to 1-2 spectral bands, variable performance in the 3-4 band conditions, and near-ceiling in the clear condition. Analysis of iEEG responses revealed tiered differences in cortical activation with respect to spectral complexity and intelligibility. A progressive preference for clear speech emerged in areas along both the ventral and the dorsal auditory processing pathways. Better task performance in the 3-4 band conditions was associated with high gamma activation in the posterior portion of the superior temporal gyrus and alpha (8-14 Hz) suppression in the supramarginal gyrus in response to all vocoded stimuli.

Direct recordings from the human brain reveal a hierarchical organization of speech processing within and beyond canonical auditory cortex. Data obtained with noise-vocoded speech can provide insights into the neural bases of variability in speech perception in CI users. Future non-invasive studies may assist in developing novel objective measures to assess CI performance and improve rehabilitation strategies.

Prof. Dr. Kirill Nourski
The University of Iowa, Human Brain Research Laboratory
Department of Neurosurgery
Iowa City, IA 52242 USA
kirill-nourski@uiowa.edu

Dr. Marcus Janssen
Maastricht University Medical Center

Deep Brain Stimulation for Tinnitus: from bench to bed

Electrical stimulation of multiple targets within and outside the auditory pathway have shown to suppress tinnitus in experimental settings. In patients who underwent deep brain stimulation (DBS) to treat movement disorders, a concurrent reduction of their co-existing tinnitus has been reported. A handful of case reports and case studies in human have shown that electrical stimulation of varying non-auditory structures can attenuate tinnitus. We hypothesize that neuromodulation within the tinnitus network may alleviate tinnitus. Efficacy of DBS in central auditory structures on tinnitus suppression in preclinical setting, as well as central mechanisms underlying tinnitus pathophysiology will be shared. In succession of the animal studies in which DBS was tested and proven effective, MGB-DBS is currently investigated in a clinical intervention study in humans using a crossover-design. Six subjects will receive bilateral DBS electrodes in the MGB. First results of this clinical feasibility study will be presented.

Prof. Mark Janssen
Maastricht UMC+, Afdeling Klinische Neurofysiologie
P. Debyelaan 25 6229 HX Maastricht
mlf.janssen@mumc.nl

Prof. Dr. habil. Ulrike Lüdtke
Leibniz Universität Hannover,
Institut für Sonderpädagogik, Abteilung für
SprachPädagogik- und Therapie

Improving the assessment of hearing impairment in children globally

Data will be presented from two projects focusing on elements of assessment relevant to children with hearing impairment globally. Firstly, the implementation of Universal Newborn Hearing Screening (UNHS) in Subsahara-Africa with results from a pilot study in Tanzania (n = 922 newborns). Secondly, the development of machine learning applications to automate the process of language sample analysis (transcription, annotation and analysis) in children with preliminary results from Germany (n = 94).

Prof. Ulrike Lüdtke
Leibniz Universität Hannover, Institut für Sonderpädagogik
Schloßwender Str. 1
30159 Hannover, Germany
ulrike.luedtke@ifs.uni-hannover.de

Prof. Mickael L.D. Deroche
Concordia University, Canada

Use of EEG and fNIRS to predict language outcomes in children with cochlear implants

Despite their remarkable success, cochlear implants fail to provide the expected benefits for some (arguably a minority of) users. This is true even for children implanted very early in life. The challenge of developing age-appropriate skills in speech, language, and reading is dependent on many factors, from the deleterious impact of sensory deprivation to the timing and quality of surgical intervention, the degree and kind of post-implant intervention / rehabilitation, device parameters, and an emphasis on oral-aural communication at home; they all have some impact on developmental outcomes. We postulate that we can understand some of the heterogeneity in these outcomes with brain imaging. To this aim, we used electroencephalography (EEG) and functional near-infrared spectroscopy (fNIRS) to scan the brain of 75 children (7 -18 year old), 50 of whom wore implants but had disparate language skills. Children participated in a number of tasks: visual processing (checkerboard), auditory processing (oddball with spectrally-modulated noises), motor/somatosensory processing (squeezing a joystick's triggers), audio-visual integration (McGurk), phonological processing (words and sudo-words), emotional processing (child-friendly video) and resting-state recording. This presentation will review our findings to date, highlighting evidence that the brain of some children with cochlear implants has undergone cross-modal and intra-modal changes (compared to the brain of normally-hearing children) that are undesirable for processing linguistic stimuli which are intrinsically audio-visual.

Prof. Mickael L.D. Deroche
Concordia University, Laboratory for Hearing and Cognition
7141 Sherbrooke Street West
Montreal, QC H4B 1R6, Canada
mickael.deroche@concordia.ca

dr. Margreet Langereis

dr. Anneke Vermeulen

Dr. Margreet Langereis & dr. Anneke Vermeulen,
Pento Speech and Hearing Centers,
research department, Apeldoorn,

Defining working memory profiles in children with auditory/communicative disorders

Objective

The application of advanced technical-medical devices in Hard-of-Hearing and Deaf (DHH) children and adults has increased their auditory abilities to a large extent, which improved access to perception of spoken language. The large variability however, remains unaccounted for. Verbal Working Memory is an important factor in language proficiency. Our presentation focusses on Verbal Working Memory in DHH children and adults.

Background

We present four studies we conducted on working memory components which are underlying mechanisms of language learning.

In a first study we found that 25% of the DHH children with CI and HA showed a similar linguistic profile as children with a Developmental Language Disorder (DLD).

A following study on children with cochlear implants showed that the phonological storage component of working memory was significantly disrupted as compared to the phonological processing component. Both working memory components were associated to receptive vocabulary.

A third study in adults with cochlear implants revealed different patterns for pre and post lingually deaf persons. In prelingually deaf adults speech perception at 45 dB was predictive for receptive vocabulary, whereas in post lingually deaf adults non-word repetition (phonological encoding) was a predictive factor.

Present Study

Next, preliminarily results of our present large scale study will be presented. This study assesses working memory components in order to define profiles that capture the strengths and weaknesses of underlying working memory mechanisms in language learning of children with hearing impairments (DHH) or developmental language disorders (DLD). We hypothesize that performance on working memory tasks will reveal disharmonic outcomes, from which several distinct profiles can be inferred.

We applied assessments of verbal working memory, visual sequential memory, executive functioning, auditory speech perception and language ability. The key range of ver-

see next page

bal working memory components that underpin language learning include encoding, recoding, storage, processing, and retrieval assessed with standardized tests. The study group comprises DHH children with cochlear implants or hearing aids and children diagnosed with DLD, aged 8 - 10 years, with typical cognitive abilities. Factor analysis is carried out to identify distinct working memory components. Subsequently, a cluster analysis is performed to define different working memory profiles. Linear regression is performed to analyze the relation between factor scores and sentence comprehension.

Results

Preliminary data of 42 children will be presented, twenty-two DHH children and 20 diagnosed with DLD. Average performances of the total group on all subtests ranged between below average to low average. Varimax rotation factor loadings suggested three components representing a 'recoding-attention' factor, a 'verbal-phonological' factor and a 'processing' factor. The standardized factor scores derived from the factor analyses yielded two clusters. The profile of the first cluster (32%) indicated relatively low scores on recoding-inhibition/switching and relatively high scores on verbal-phonology and processing. The profile of the second cluster (68%), conversely, indicated relatively high scores on recoding-inhibition/switching and relatively low scores on verbal-phonology and processing. The first cluster consisted largely of children with DLD, whereas the second cluster contained children with both DLD and DHH. Linear regression showed significant relations between sentence comprehension and 'verbal-phonology' and 'processing'.

Conclusion

In different DHH subgroups, various working memory components show deficits, however, phonological storage is relatively poor in all subgroups. Analyses of working memory components in language learning in children with DHH or DLD reveal two clusters (i.e., groups of children) that were formed on the basis of the data and not solely on the basis of their diagnoses DHH or DLD. In language learning about 25% of DHH children demonstrate 'characteristics of DLD working memory mechanisms' with relatively poor recoding and attention abilities.

Dr. Margreet Langereis
University of Nijmegen, Pento Utrecht
Burgemeester Verderlaan 15
3544 AD Utrecht, Netherlands
m.langereis@pento.nl

Prof. Rachel R. Romeo
University of Maryland, USA

How early language experience influences brain and cognitive development

Within the first years of life, children develop a remarkable set of language and communication skills, which set the foundation for later academic learning. Yet, individual children vary widely in their developmental trajectories, due to differences in both physical (e.g., hearing impairment) and environmental (e.g., language exposure) factors. My research aims to understand how children's early experiences—both favorable and adverse—interact with mechanisms of developmental neuroplasticity to shape cognitive and academic development, and how this can inform clinical and educational practice. In this talk, I will present a series of studies investigating how children's early language exposure experiences influence their linguistic, cognitive, and brain development; how developmental differences and social inequality drive disparities in language experience; and how a brief, family-based intervention induces cortical neuroplasticity that improve children's language development. I will discuss implications of this work for designing clinical interventions and social policies that enhance children's early language experiences and reduce disparities in language and cognitive development.

Prof. Dr. Rachel R. Romeo
University of Maryland, Department of Human Development and Quantitative Methodology
3942 Campus Drive
College Park, MD 20742, USA
rromeo@mit.edu

Ellen Andries1,2, Artur Lorens3, Piotr Henryk Skarżyński3, Henryk Skarżyński3, Miryam Calvino4,5, Javier Gavilán4, Luis Lassaletta4,5, Dayse Tavora-Vieira6, Aanand Acharya6, Anja Kurz7, Rudolf Hagen7, Ilona Anderson8, Edda Amann8, Paul Van de Heyning1,2, Vincent Van Rompaey1,2, Griet Mertens1,2

1Department of Otorhinolaryngology, Head and Neck Surgery, Antwerp University Hospital (UZA), Antwerp, Belgium

2Experimental Laboratory of Translational Neurosciences and Dento-Otolaryngology, Faculty of Medicine and Health Sciences, University of Antwerp (UA), Antwerp, Belgium

3World Hearing Center, Institute of Physiology and Pathology of Hearing, Warsaw/Kajetany, Poland

4Department of Otolaryngology, La Paz University Hospital, Madrid, Spain. IdiPAZ Institute for Health Research.

5Biomedical Research Networking Centre on Rare Diseases (CIBERER-U761), Institute of Health Carlos III, Madrid, Spain

6Department of Otolaryngology, Head & Neck Surgery, Fiona Stanley Fremantle Hospital Group, Perth, Australia

7Department of Otolaryngology, University Clinic of Würzburg, Würzburg, Germany

8Clinical Research Department, MED-EL GmbH, Innsbruck, Austria

Implementation of the International Classification of Functioning, Disability and Health model in Cochlear Implant recipients: a multi-center prospective follow-up cohort study

Purpose: to define a Cochlear Implant (CI) outcome assessment protocol based on the International Classification of Functioning, Disability and Health (ICF) model and apply it in clinical routine.

Methods: An international multidisciplinary core group of CI experts selected the most relevant ICF categories and codes for CI users out of the existing ICF core set for hearing loss. A well-known commonly used and internationally validated instrument or method was identified and assigned to each ICF category along with quantified ICF qualifiers. The ICF-based CI outcome assessment protocol was applied in clinical routine in a prospective longitudinal multicenter study assessing 72 adult CI candidates before and six months after implantation.

Results: The ICF-based CI outcome assessment protocol was successfully implemented and positively received in all participating centers. Overall, the CI users in our study either improved or showed stable ICF qualifiers after cochlear implantation across all ICF domains (e.g., Body Functions and Structures, Activities and Participation and Environmental factors). Auditory perception-related and communication-related categories generally improved the most after cochlear implantation, with 46% to 73% of CI users perceiving an improvement postoperatively.

Conclusion: The ICF-based CI outcome assessment protocol provides a common language and comprehensive assessment protocol for the description and measurement

of CI outcomes worldwide. It can and should be adopted in the rehabilitation process of CI users to enable a patient-centered approach, addressing a unique combination of not only body functions and structure impairments but also relevant activity limitations, participation restrictions and environmental barriers, which would ultimately benefit CI outcomes.

Dr. Ellen Andries PhD
Antwerp University Hospital
Drie Eikenstraat 655
2650 Edegem, Belgium
Ellen.Andries@uza.be

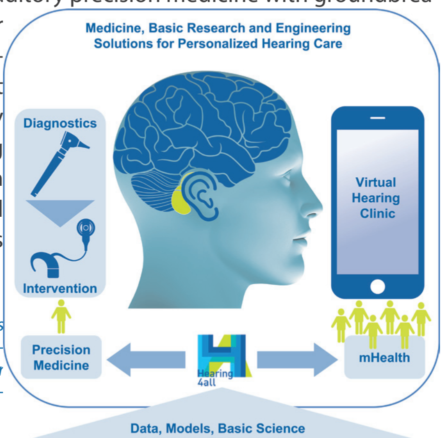
Hearing4all

Overview

Hearing4all 2.0 –
Medicine, Basic Research and Engineering Solutions for Personalized Hearing Care

The long-term aim of Hearing4all is to solve the major problem of hearing impairment in our communication-oriented, ageing society by providing research-driven solutions to improve hearing for all listeners, i.e., for all kinds of hearing impairments, in all acoustical situations, and for all domains of everyday life. Hearing impairment is the most frequent chronic neurosensory disease (progressively affecting 17% of our population); it has one of the highest impacts on the quality of life and often leads to social isolation. Hearing aids, auditory implants and other treatments therefore need to become more effective than the currently unsatisfactory state-of-the-art. Hearing4all encompasses all the research expertise needed to fulfil patients´ needs through groundbreaking, individually tailored hearing solutions for all kinds of hearing impairment, ranging from near-normal listeners to deaf patients. By combining science-based functional auditory diagnostic methods with models of auditory processing in the normal and hearing-impaired auditory system, the most effective hearing solutions and medical treatment for the future will be sought, based on highly innovative algorithms, biomaterials and architectures for future generations of individually tailored hearing devices. The wide spectrum of combined expertise from basic science, engineering, and machine learning oriented towards clinical medicine allows a personalized approach to identify the causes of hearing impairment and of its amelioration. The research consortium from universities, non-university research institutions, and industry in the "Auditory Valley" network is in an internationally leading position to achieve solutions for the long-term goal of the Cluster of Excellence and to attain a paradigm shift in rehabilitative audiology from a descriptive empirical discipline towards a quantitative, model- and data-driven science.

Hearing4all 2.0 builds on the achievements and unique innovations from the current first funding period of the cluster. These include multilingual speech recognition tests, auditory mid-brain implants or precise, aided patient performance prediction with machine learning, which aim at better diagnosis, better hearing devices and better assistive technology in hearing support. To further advance Hearing4all into mobile Health solutions with a "virtual hearing clinic" for everyone - that includes a "software hearing device" and builds up auditory precision medicine with groundbreaking hearing device technology - we will pursue four ambitious and comprehensive research threads. These span two orthogonal dimensions: "Development chain: from basic research to solutions" and "Severity of hearing loss". The Excellence Centre for Hearing Research (Oldenburg/Hannover), the Joint Research Academy, and the Translational Research Centre will be developed as sustainable joint structures across the participating universities, coordinating basic, clinical and translational research.



Basic research on auditory brain function and on hearing devices is connected with medical research on precise diagnostics and treatment. This paves the way for hearing devices of the future and for mobile health (mHealth) apps in a data-driven and model-based approach.

Auditory processing deficits throughout the lifespan

Coordinators
Christiane Thiel (UOL), Andrej Kral (MHH), Georg Klump (UOL)

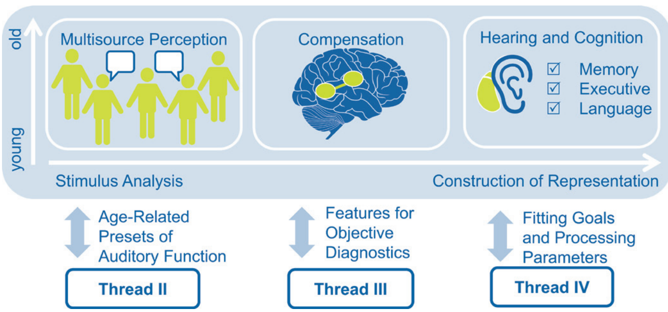
Objectives: Auditory deficits will be traced to structural and functional changes in the developing and ageing brain in a comparative approach focussing on three areas of research: multisource perception, hearing loss and compensation, and the relationship between hearing and cognition. An unprecedented array of neuro-scientific methods will be applied to understand the complex interplay throughout the lifespan between audition, the brain and cognition as the basis for developing auditory diagnostics and therapy.

We will concentrate on the three most important aspects of characterising individual hearing ability across the lifespan that are especially important for diagnostics and treatment with hearing devices: Hearing in complex, multisource environments (including better understanding of source segregation and of temporal processing deficits), plasticity as a compensatory function in hearing impairment (including cross-modal plasticity) and interaction between hearing and cognition (including the relationship between hearing impairment and cognitive decline). These fields highlight different representation levels in the auditory system from stimulus analysis to the internal reconstruction of the outer world (representation construction) and provide the relevant knowledge on central physiological mechanisms to the other research threads (see Fig.), for example:

- Physiological signatures of source segregation, temporal processing and central auditory representation and compensation will provide objective measures to Research Thread II to diagnose impairments typical of multisource environments. Moreover, easily accessible and validated diagnostic methods will be shared with Research Thread II. Research Thread I will provide normative data from these measures to be inserted into the "virtual hearing clinic" for a better interpretation of the outcomes.

- Cognitive fingerprints and research methods will be shared with Research Thread III, to support rehabilitation strategies in the young and old.

- The most important changes observed with ageing in interaction with hearing devices and their consequences for the fitting and functioning of hearing devices will be provided to Research Thread IV, which will deliver prototype hearing devices for testing the interaction between aided performance, age and the performance domains considered in Research Thread I.



Research Thread I analyses auditory and cognitive performance across development and ageing, comparing stimulus-driven vs. cognition-driven processes linked to the construction of (internal) representation. It delivers results and data for the other research threads and receives input from them.

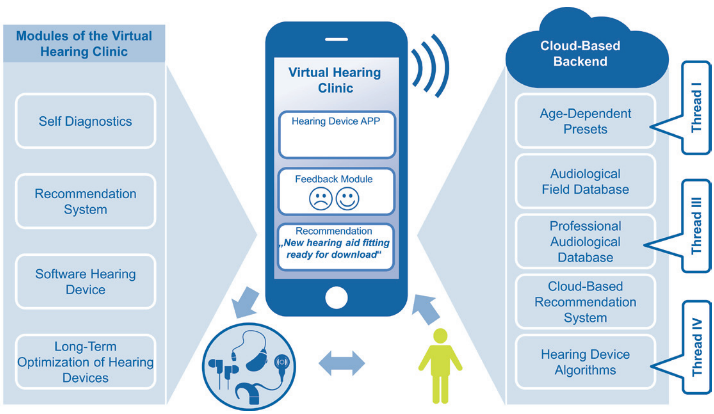
IT-based diagnostics and rehabilitation

Coordinators
Andreas Büchner (MHH), Birger Kollmeier (UOL), Simon Doclo (UOL)

Objectives: Groundbreaking data- and model-driven approaches towards self-controlled hearing tests and fitting of hearing devices will be advanced for listeners with a beginning, a mild or a moderate hearing impairment. Using machine learning techniques and professional databases, the aim is a multilingual "virtual hearing clinic" providing a low-threshold, affordable access and basic hearing support for every smartphone user (see Fig.).

To achieve this, we strive to develop a comprehensive system of multilingual diagnostic methods, functional auditory models, and hearing-aid fitting tools for smartphone-based devices in combination with data-driven, machine-learning-supported inference techniques. We aim at generating and exploiting a suitable "big" audiological data pool to quantify any possible relationships between audiological screening, diagnostic and hearing-aid benefit parameters and hence to verify or falsify the auditory model predictions developed in Hearing4all. The aim is to be able – by machine learning techniques employing probabilistic (Bayesian) approaches – to automatically deduce from an incomplete, error-prone individual diagnostic data set not only a potential diagnosis, but also the optimum treatment option and a related prediction of the benefit with the lowest possible uncertainty. Research Thread II will interact with the other research threads in various ways:

- Research Thread I will provide age-related expectations to be used for the various auditory functional parameters as well as ways to interpret the relationships between auditory functions across age.
- Research Thread III will manage and analyse the professional, clinical database and will provide access to it in order to classify patients as far as possible using their self-assessed data obtained within the virtual hearing clinics. Moreover, a common set of diagnostic methods and a classification and recommendation system for best treatment will be jointly developed with Research Thread III.
- The interface between auditory diagnostics and (virtual) hearing devices with respect to hearing device fitting and functioning will connect Threads II and IV.



Functionality of the virtual hearing clinic approach from Research Thread II. A cloud-based backend with knowledge-based decision making provides treatment recommendations and settings for the subject's hearing device based on the individual user data obtained through the app.

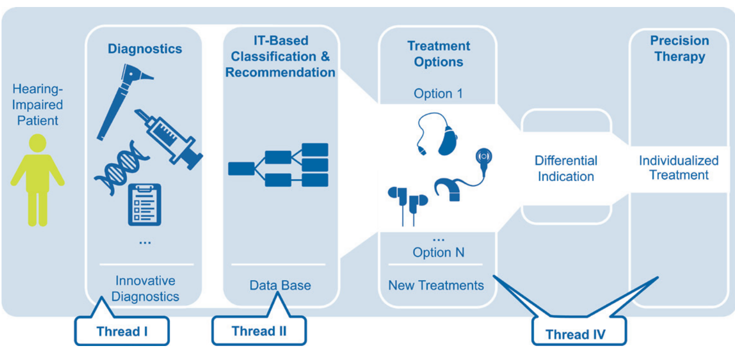
Auditory precision medicine: research-based novel intervention methods

Coordinators
Thomas Lenarz (MHH), Birger Kollmeier (UOL), Peter Behrens (LUH)

Ojectives: The precision of the auditory diagnostic procedure for patients with hearing loss will be substantially advanced. This will allow for an innovative, precisely individualized rehabilitative treatment, also involving newly developed therapeutic measures.

Prevention, diagnosis and treatment of hearing loss with respect to the wide variety of the different causes will require the development of novel approaches for extensive and in-depth diagnosis and targeted novel therapy options for precision treatment that supplement the technological and clinical interventions achieved in H4A 1.0. The goal is to determine the patient-specific, functional hearing deficit and to provide innovative therapies for individualized treatment as well as prevention strategies in a highly optimised way. The diagnostic methods (organized in a rational diagnostic decision tree, see Fig.) will be developed to yield the most relevant information and provide unprecedented precision in selecting the best treatment options, the most accurate prognosis and predicting a valid outcome for each individual patient. The aspired therapy options will supersede current treatment concepts by providing novel auditory implants including superselective electrodes, multimodal stimulators of the inner ear with additional biological components including local drug delivery to enhance the electrode-nerve interface, gene therapy to stop progression of hearing loss, and cell therapies to improve the neurobiological substrate for stimulation of the auditory system. The interaction with the other research threads is characterized as follows:

- Diagnostical methods, their results and interpretation throughout the lifespan is shared with Research Thread I that provides suggestions and data for objective diagnostics derived from auditory brain functions and cognition across developmental stages and ageing.
- The patient-centred database with statistical and knowledge-based methods to connect different patient's parameters for model-based diagnostics and interpretation will be shared with Research Thread II, thus creating a close link between the subclinical population, persons with a mild to moderate hearing loss (primarily covered by Research Thread II) and the moderate-to-severe hearing-impaired patients to be considered in Research Thread III.
- The technology of the "hearing device of the future" and the options to simulate and predict aided performance, as pursued by Research Thread IV, underlies to the development of actuators and biological components for precision therapy performed in Research Thread III.



Research Thread III provides auditory precision diagnostics and therapy and interacts with results and data from the other research threads.

The H4A hearing devices of the future

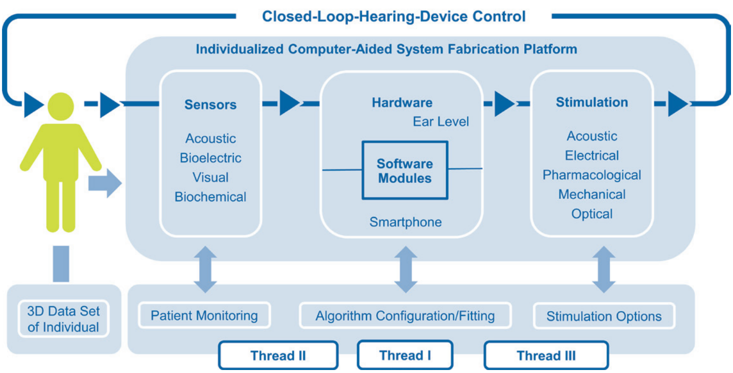
Coordinators
Volker Hohmann (UOL), Holger Blume (LUH), Andreas Büchner (MHH)

Objectives: Based on the solutions from H4A 1.0, unprecedented, highly integrated system concepts, hardware and software solutions for research and applications will result from interdisciplinary research on comprehensive system technology. This translational research focus will enable the cluster to serve all degrees of hearing impairment and to achieve its ultimate goal of Hearing for All in the future.

The fourth research thread integrates research and development towards functional concepts, novel stimulation principles, hardware, software and algorithms for a groundbreaking hearing device system technology. This will enable the cluster to achieve its ambitious goals, i.e., to implement the "IT-based diagnostics and rehabilitation" and "auditory precision medicine" research threads utilizing the most advanced hearing device technology available worldwide. Devices of the future will be "human-centred", i.e., the subject will be the centre of all technology. In particular, closed-loop concepts utilizing biosignals for device adaptation and the empowerment of the patient, giving them control over their own device through the use of intelligent software interfaces, will define a new era of hearing devices (see Fig.). To this end, device concepts based on the research results from H4A 1.0 and from the results of Research Thread I will be employed to design innovative functional principles and algorithms of next-generation devices while covering the whole range of acoustic, electric and alternative modes of stimulation including any combinations thereof. The connection to the other research threads are as follows:

The technology of the "hearing device of the future" and the options to simulate and predict aided performance, as pursued by Research Thread IV, underlies to the development of actuators and biological components for precision therapy performed in Research Thread III.

- The characterisation of the patient throughout their life time and its consequences for hearing device system design is shared with Research Thread I.
- The connection between the virtual hearing device developed and maintained in Research Thread IV and its integration into the virtual hearing clinic (Research Thread II) is shared by both Threads.
- The clinical parameters, experience and application data to specify and modify hearing devices will be received from Research Thread III, which will receive technical solutions (prototypes) to be used within clinical rehabilitative audiology.



Research Thread IV develops hearing devices of the future and interacts with the other research threads by exchanging concepts, results and data.

Staff

The groups contributing to the cluster provide a unique set of competencies in basic science, applied and translational research, and clinical medicine in a transdisciplinary structure from physics, chemistry, engineering, biology, physiology, psychology as well as the clinical specialties otology, audiology, and neurology. Likewise, the whole range of research expertise required for the developmental chain from patient needs via diagnostics, models, devices and clinical applications towards comprehensive hearing solutions is covered.

Spokespersons

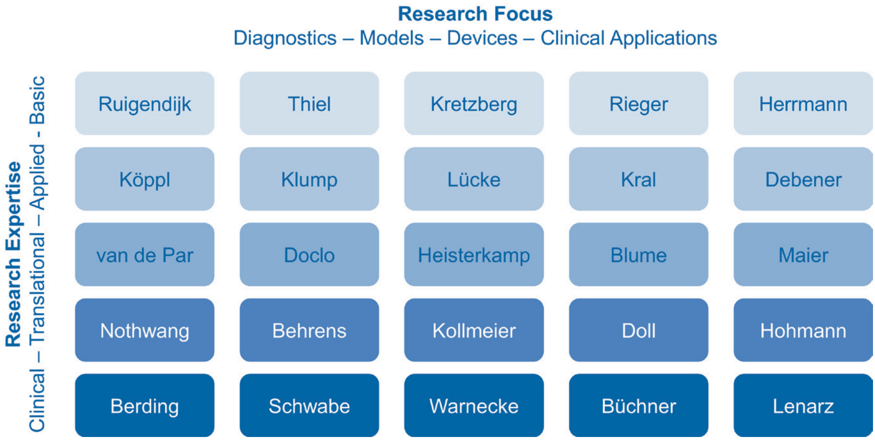
Birger Kollmeier (Authorised Spokesperson)
Carl von Ossietzky University of Oldenburg

Thomas Lenarz (Clinical Spokesperson)
Hannover Medical School

Principal investigators

Peter Behrens (LUH)
Georg Berding (MHH)
Holger Blume (LUH)
Andreas Büchner (MHH)
Stefan Debener (UOL)
Simon Doclo (UOL)
Theodor Doll (MHH)
Alexander Heisterkamp (LUH)
Christoph Herrmann (UOL)
Volker Hohmann (UOL)
Georg Klump (UOL)
Birger Kollmeier (UOL)
Christine Köppl (UOL)

Andrej Kral (MHH)
Jutta Kretzberg (UOL)
Thomas Lenarz (MHH)
Jörg Lücke (UOL)
Hannes Maier (MHH)
Hans Gerd Nothwang (UOL)
Jochem Rieger (UOL)
Esther Ruigendijk (UOL)
Kerstin Schwabe (MHH)
Christiane Thiel (UOL)
Steven van de Par (UOL)
Athanasia Warnecke (MHH)



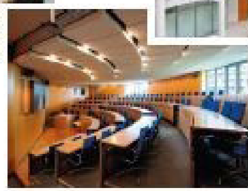
In addition to the PIs, a number of internationally visible, non-PI researchers participate as members of H4A 2.0 with financial support. They qualify for a prominent role within the cluster either by a professorship or a group leader position in one of the institutions supporting the cluster or have shown a high potential for a future leadership position or professorship. Their involvement in the projects of H4A 2.0 also secures the close interaction with non-university research institutions that provide strategic advantages in some of the fields to be addressed by H4A 2.0, e.g.:

- Access to the hearing-aid manufacturers worldwide through their strong collaboration with Hörzentrum Oldenburg GmbH and HörTech gGmbH
- Access to the cochlear implant manufacturers worldwide through Deutsches HörZentrum Hannover (DHZ) at the Hannover Medical School, Hörsys GmbH, Fraunhofer ITEM and Hörzentrum Oldenburg GmbH
- Access to the consumer electronic industry and to IT-market global players via the Fraunhofer IDMT/HSA
- Access to international research networks and organizations in neuroscience and the social sciences relevant for technology follow-up research through the Hanse-Wissenschaftskolleg, Delmenhorst

Venue:

Forum Niedersachsen
Feodor-Lynen-Str. 27
30625 Hannover

Map: HNO der MHH



Photos: Forum Niedersachen (3)