

# Department of Otorhinolaryngology – Head and Neck Surgery

## Chair of Otorhinolaryngology

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### Director

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### Research focus

- Ultrasound, endoscopy, and salivary glands
- Division of Phoniatrics and Pediatric Audiology
- Experimental Oncology/nanomedicine (SEON)
- Speech perception with hearing aids and Cochlear implants
- Allergology/clinical immunology and rhinology
- Experimental otology/audiology
- Laboratory for sleep disorders/somnology

### Structure of the Department

Professorships: 5

Personnel: 355

- Doctors (of Medicine): 43
- Scientists: 34 (thereof funded externally: 18)
- Graduate students: 32

### Clinical focus areas

- Minimal invasive surgery of salivary glands
- Lancer surgery
- Cochlear implantat surgery
- Nose/paranasal surgery
- Clinical and surgical treatment of voice disorders
- Pediatric hearing disorders
- Diagnosis and treatment of sleep disorders

### Research

The Department of Otorhinolaryngology – Head and Neck Surgery is one of the largest hospitals in Germany and has a comprehensive research repertoire. In the clinical area, the focus is on ultrasound, the diagnosis/treatment of salivary gland diseases, tumor and voice disorders, vestibular and hearing impairments as well as somnology and allergology. These foci are reflected in the basic research area. Nanomedicine, which carries out translational projects as well as extensive basic research, is another highly interdisciplinary focus. Ultrasound, endoscopy, and salivary glands in modern ultrasound systems and endoscopy units, studies on sonographic imaging of head and neck malignancies and salivary gland tumors remain a cornerstone of scientific work. The role of ultrasonography for the diagnosis of

sialolithiasis was systematically examined using a large group of patients. Our results show an accuracy of approximately 95% for the diagnosis of sialolithiasis. Gland-conserving surgery for benign salivary gland diseases is one of our priorities. The main topics are currently the long-term results after limited, extracapsular resection especially of cystadenolymphomas and pleomorphic adenomas of the glandula parotis. Minimally invasive interventions of the salivary glands and their excretory ducts are not only applications in daily practice, but have been systematically reviewed and evaluated scientifically. Combined endoscopic and open surgical procedures provide a new way of treating obstructive salivary gland disorders. The application of Pneumatic Intracorporeal Lithotripsy, introduced in 2015, has been expanded in our Department, particularly in the context of the multimodal treatment of the difficult cases of sialolithiasis, which until recently required resection of the affected salivary gland under general anesthesia.

### Division of Phoniatrics and Pediatric Audiology

Our clinical research focuses on the development of new methods allowing for quantitative voice diagnostics. The major part is the objective analysis of endoscopic high speed recordings during voice production. Within our basic research we concentrate on physical interactions during voice production. We develop and analyze numerical models (lumped-mass models, finite-volume-models) and experimental models (synthetic silicon vocal folds and ex-vivo animal cadaver larynx models). We expect to gain more insight into the interaction between airflow, vocal fold dynamics and resulting acoustics for physiologic and pathologic voice production. We apply state-of-the-art methods from the scientific area of artificial intelligence. Since 2016, we have been analyzing the vocal fold tissue from the molecular-biological point of view. All these topics have the goal to enhance diagnostics and the treatment of our patients.

### Experimental Oncology/nanomedicine (SEON)

PI: Prof. Dr. C. Alexiou

The Section for Experimental Oncology and Nanomedicine (SEON) has successfully expanded the main topics of oncology, cardiovascular diseases, regenerative medicine, imaging and nanotoxicology and has added the area of infection research as a new pillar. The research work here relates to the nanoparticle-based magnetic isolation of specific bacteria and toxins for the therapy and diagnosis of bacterial infectious diseases. Here, we were able to acquire extensive funding from the Doctor Robert Pflieger Foundation. The basic research

gained from this grant helped us to scientifically address the challenges in the context of the emerging corona pandemic. For example, with the support of the Manfred Roth Foundation, we were able to acquire the project "Functionalized Superparamagnetic Iron Oxide Nanoparticles (SPIONs) as a Platform Technology for the Diagnosis and Therapy of Enveloped Viruses" (including SARS COV-2) and we are working on developing an antigen test. In the field of regenerative medicine, SEON is successfully funded as a project partner together with the Universities of Würzburg, Bayreuth and partners from FAU in the DFG-SFB/Transregio 225 "From the basics of biofabrication to functional tissue models". A special highlight was the 10th anniversary of SEON on September 18, 2019, which we celebrated with a scientific symposium and numerous visitors. The world's first installation of a robot-controlled magnet for nanoparticle therapy was also presented to the public at this event. This was also extensively reported in the media. In summer 2019, we received the prestigious Medical Valley Award for the project "Safe contrast agents for magnetic resonance imaging (MRI)". As part of the AI competition organized by the Bavarian State Government, we were successful with the complementary joint application Medical-Nano-Micro-Robotics together with the TU-Munich, the University of Applied Sciences Munich and the University of Applied Sciences Ansbach. With this extensive funding, it is now possible to fill a W2 professorship and pending equipment positions. In this reporting period, our work was again honored with numerous scientific awards at various national and international congresses and, among others, Dr. med. dent. Magdalena Alev received the doctoral award of the STAEDTLER Foundation on October 22, 2020 for her doctoral thesis, which was evaluated summa cum laude.



Installation of a TX 200 high-performance 6-arm robot from Stäubli in SEON's animal operating room for precise control and positioning of the magnetic field.

### Speech perception with hearing aids and Cochlear implants

Restoring hearing performance with technical devices such as hearing aids or cochlear implant systems is one of the most important challenges in audiological research. The focus of this project

is the prediction of speech comprehension based on audiological characteristics. Based on an existing hearing loss, the attenuation and distortion of the speech signal are estimated and the speech intelligibility is predicted. On the basis of clinical data and special hearing tests, models were developed that can predict hearing and speech understanding with a CI system based on speech understanding with hearing aids, the etiology and anamnestic data. The data are used to evaluate hearing aid fittings and to substantiate the indication for CI fittings.

#### **Allergology/clinical immunology and rhinology**

Endonasal endoscopic sinus surgery and following oral desensitization with ASS come into question as a treatment for NSAID-intolerant patients. The aim of the study is to elaborate and perform a treatment scheme for a treatment with an intravenous desensitization with ASS. The collected data of the intravenous desensitization as an efficient therapy for patients with NSAID-intolerance is going to be evaluated and compared to oral desensitization with ASS.

#### **Experimental otolaryngology**

In our group, we investigate among others the development of tinnitus. We developed a new model based on information-theoretical approaches in which tinnitus is a by-product of a mechanism that is able to improve hearing thresholds. Based on the model we developed a new therapy that gave promising results in first pilot studies. In addition, data from animal research support this model. With a new statistical method developed by us, we investigate space-time patterns of cortical activity and are able to describe tinnitus-specific activity in the brain that may be diagnostically used. Additionally, we were able to categorize human sleep stages from EEG data with this method and generate new insight for the sleep medicine. Furthermore, we develop new methods for the determination of sensory thresholds in humans and animals with which it is now possible to determine thresholds, e.g. of auditory brainstem responses, in a completely automatic and objective manner. For all these and other questions, we additionally develop artificial neuronal network models and applications for artificial intelligence

#### **Sleep laboratory / experimental sleep medicine**

On the part of the clinic, the sleep medicine department offers a comprehensive spectrum of current diagnostics and therapy of all sleep disorders according to ICSD-3 with a focus on "sleep-related breathing disorders". Within the framework of experimental sleep medicine, a DFG-funded research focus is on the analysis of sleep architecture with respect to the macro- as well as microstructure of sleep. A major goal is the establishment of a novel, fully objectified and thus automatable method of sleep stage analysis by means of a global pattern analysis of the cortical activity distribution. Further goals are the investigation of spatiotemporal developments of cortical activity during sleep stage changes and the investigation of local sleep

phenomena in patients with obstructive sleep apnea. With the goal of a deeper understanding in the field of sleep electrophysiology, methods such as non-supervised dimensional reduction (deep autoencoders), time series analysis (Bayesian superstatistics), and statistical cluster analysis (combination of Gaussian mixture models with evidence-based Bayesian model selection) are applied.

Another translational research focus lies on the optimization of diagnostics and the individualization of therapeutic concepts for patients with obstructive sleep apnea. A key objective in this respect is the validation of different circulating biomarkers on a serological basis. The use of biomarkers as a screening tool in primary diagnostics as well as for individual cardiovascular risk stratification and for monitoring of the treatment response will be investigated. The aim of this project is the use of circulating biomarkers in clinical routine in order to enable individualized therapy strategies in the context of personalized medicine in the future.

#### **Teaching**

The Department of Otorhinolaryngology - Head and Neck Surgery is involved in the curricular teaching of Medicine, Dentistry and Logopedics with compulsory and elective subjects. Particularly the interdisciplinary teaching concerning medical technology, nanotechnology, toxicology and integrated life sciences has to be pronounced.

Bachelor's and Master's theses as well as MD and PhD theses are supervised.

#### **Selected publications**

Hoppe U, Hocke T, Hast A, Iro H. Cochlear Implantation in Candidates With Moderate-to-Severe Hearing Loss and Poor Speech Perception. *Laryngoscope*, 2020.

Karawacka W, Janko C, Unterweger H, Mühlberger M, Lyer S, Taccardi N, Mokhir A, Jira W, Peukert W, Boccaccini AR, Kolot M, Strauss R, Bogdan C, Alexiou C, Tietze R. SPIONs functionalized with small peptides for binding of lipopolysaccharide, a pathophysiologically relevant microbial product. *Colloids Surf B Biointerfaces*, 2019, 174: 95-102

Friedrich RP, Schreiber E, Tietze R, Yang H, Pilarsky C, Alexiou C. Intracellular Quantification and Localization of Label-Free Iron Oxide Nanoparticles by Holotomographic Microscopy. *Nanotechnol Sci Appl*, 2020, 13:119-130

P. Gomez, A. M. Kist, P. Schlegel, D. A. Berry, D. K. Chhetri, S. Dürr, M. Echternach, A. M. Johnson, S. Kniesburges, M. Kunduk, Y. Maryn, A. Schützenberger, M. Verguts, M. Döllinger. BAGLS, a multihospital benchmark for automatic glottis segmentation. *Scientific Data*, 7(1):186; 2020.

P. Schlegel, M. Kunduk, M. Stingl, M. Semmler, M. Döllinger, C. Bohr, A. Schützenberger. Influence of spatial camera resolution in highspeed videoendoscopy on laryngeal parameters. *PLoS ONE*, 14(4):e0215168; 2019.

#### **International cooperations**

D.A. Berry, PhD, University of California Los Angeles, Los Angeles: USA

M. Kunduk, PhD, Louisiana State University, Baton Rouge: USA

C. Madell, PhD, The University of Sydney, Sydney: Australia

N. Li-Jessen, PhD, McGill University, Montreal, Canada

Prof. Dr. M. Kaltenbacher, TU-Graz, Graz: Austria