

# Department of Anesthesiology

## Chair of Anesthesiology

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### Director

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### Research focus

- Clinical and experimental pharmacology of anesthesia
- Experimental pain research
- Medical technology of diagnostic and therapeutic procedures
- Clinical research in perioperative medicine
- Research projects furthering the medical education

### Structure of the Chair

Professorships: 2

Personnel: 479

- Doctors (of Medicine): 151
- Scientists: 8 (thereof funded externally: 3)
- Graduate students 2019: 9
- Graduate students 2020: 13

### Clinical focus areas

- Clinical anesthesiology
- Operative intensive care medicine
- Pain management center
- Emergency medicine
- Palliative medicine

### Special structural features

- 50 anesthesia workplaces
- Anesthesia outpatient department
- Pain outpatient department, pain ward (four hospital beds)
- Two intensive care units (35 critical care beds), during the covid pandemic two more intensive care units with 22 critical care beds.
- Pain management unit (in cooperation with the Department of Neurology)
- Medical management of the emergency service (Erlangen, administrative district Erlangen-Höchstadt, Herzogenaurach)
- Medical care in air rescue services and in transport within UK Erlangen

### Research

Research at the Department of Anesthesiology is focused on the clinical and experimental pharmacology of anesthesia and on the experimental and clinical pain research. In

addition, innovative techniques for drug administration and patient monitoring are investigated, and projects dealing with the quality improvement of teaching and training are part of the Department's research program.

### Clinical and experimental pharmacology of anesthesia

In a clinical phase I study in young healthy volunteers, the pharmacokinetics and clinical pharmacodynamics (including sedation, hemodynamics, respiration and electrocardiogram) of the new short acting benzodiazepine remimazolam were investigated. An integrated pharmacokinetic model for remimazolam and its metabolite and a pharmacodynamic model for the sedative effect of remimazolam were developed within this study.

During the reporting period and within the framework of a research cooperation with the Department of Anesthesiology, Wenzhou Medical University, China, the pharmacokinetics of dexmedetomidine, a selective  $\alpha_2$  adrenergic receptor agonist for sedation, was investigated after intranasal administration during general anaesthesia in Chinese children aged 4 to 10 years.

### Experimental pain research

The Heisenberg professorship of Experimental Pain Research was tenured in 2019. Research topics of this program included the pathomechanism of cold pain as well as the investigation of the role of TRP channels in the somatosensory system and in thermoregulation. To investigate afferent nerves innervating striated muscle tissue, a new muscle-nerve preparation was established which allows to stimulate receptive fields in the muscle specifically and locally. This allowed to investigate the effect of lactate and rising temperature, such as in the working muscle, on metaboreceptors and other muscle afferents, such as muscle spindles. Further projects addressed the differences in mouse behavioral activity patterns, food intake, and energy consumption in a large number of inbred strains which are commonly used in mouse pain behavioral models and our currently ongoing haplotype mapping studies. In these studies, differences between mouse strains were quantified and serve as a basis for the interpretation of future haplotype-based studies.

Another research area deals with the analysis of rare hereditary pain syndromes using human induced pluripotent stem cells (hiPSCs). In cooperation with the Department of Stem Cell Biology, we differentiate hiPSC-derived pain sensing neurons (nociceptors) from skin biopsies of healthy donors and affected pain patients. These sensory neurons are hardly available for analysis in humans and have therefore mainly been investigated using animal models. Species-specific differences are likely to be one explanation for the poor translation of preclinical findings into effective pain therapeutics. This project aims to contribute to bridge this gap. In our *in vitro* disease model we found that hiPSC-derived nociceptors of our patients show pathological spontaneous activity in electrophysiological recordings which is also found in patients suffering from neuropathic

pain.

### Medical technology of diagnostic and therapeutic procedures

The main research focus in this area was the processing and analysis of the EEG signal recorded during sedation with the new benzodiazepine Remimazolam in a phase I study in volunteers. Using an artificial neuronal network trained on specific artifact patterns of EEG signals and new processing techniques in the time-frequency domain, it was able to identify concentration-induced remimazolam-characteristic changes in the EEG activity of Beta, Alpha and Delta frequency bands. Concentration dependent changes of a processed parameter in the Beta frequency band (BetaRatio) highly correlated with the remimazolam-induced sedation. Thus, BetaRatio can be used as a surrogate parameter for monitoring remimazolam sedation.

During the reporting period, we further investigated the analgesic efficiency of the new therapeutic algorithm Patient-Controlled-Analgesia with Target-Controlled-Infusion. For the opioid hydromorphone, the algorithm showed analgesic equivalence but higher patient comfort compared to standard Patient-Controlled-Analgesia.

### Clinical research in perioperative medicine

The research in perioperative medicine was focused on the evaluation of airway devices and complex procedures to secure the airway and following intraoperative ventilation in the field of thoracic surgery. Videolaryngoscopy as a relevant tool for anesthesia and emergency medicine was studied comparing different designs. Results revealed favorable designs for safe care. In the field of anesthesia during thoracic surgery a complex combination of neuromonitoring to prevent harm from intraoperative nerve lesions and providing single-lung-ventilation simultaneously was described and studied in terms of feasibility and safety. This topic was addressing patient safety in both anesthesiology and surgery. A systematic development of a cognitive aid representing the anesthesiological issue of emergency medicine. The cognitive aid was supported by the professional society of anesthesiology and is now implemented nationwide. Another focus in emergency medicine was set on physical and psychological loads of EMS personnel. Results delimited occupational reality of EMS professionals as well as required support more precise.

### Research projects furthering the medical education

A major focus of research on patient safety was the further development of a cognitive aid for crisis management in Anaesthesia which had been implemented in the department several years ago. Since there are currently no officially endorsed cognitive aids for intraoperative emergencies available in Germany, the Professional Association of German Anesthesiologists (BDA) and the German Society of Anesthesiology and Intensive

Care (DGAI) set up a project to develop such a comprehensive set of digital cognitive aids for intraoperative emergencies under the leadership of staff from the Erlangen department of Anesthesiology. Within the scope of this project, clinicians from different university hospitals („German Cognitive Aid Working Group“) worked together with human factors engineers and software developers. The development of the cognitive aid „eGENA“ (elektronische Gedächtnis- und Entscheidungshilfe für Notfälle in der Anästhesie) was based on the user-centered design (UCD) process of ISO 9241-210, that has been performed for the development of other applications in the medical context. A thorough analysis of the physical and organizational environment, the application context, and the technical and task-specific requirements of the end-users was performed. The project resulted in a progressive web application that runs with multiple software platforms as well as stationary and mobile devices.

As the main function of cognitive aids consists in supporting expert teams to remember and excel, rather than helping novices perform procedures beyond their expertise, a qualitative study explored how novice and expert anaesthetists understand expertise in anaesthesia.

As a result of the COVID-19 pandemic and the related restrictions on face-to-face teaching for students, new concepts to qualify medical students to support intensive care staff during a pandemic (TIP) were developed and evaluated.

## Teaching

The Department of Anaesthesiology is involved in the curricular and extracurricular student teaching of the Medical Faculty of the Friedrich Alexander University in many ways. In 2019, two digitisation projects within the framework of the QuIS II funding phase (Quality in Study and Teaching) were the focus of the further development of teaching. Triggered by evaluation and student surveys, two project groups created blended learning concepts in the form of flipped classrooms for the cross-sectional area 14 "Pain Medicine" and Q8 "Emergency Medicine 6th Semester". Interactive learning modules preparing for the attendance phase were created in the StudOn learning platform. With the Covid-19 pandemic in 2020, the teaching and learning conditions changed rapidly. The two projects were now able to unfold their full effectiveness. Due to the complex requirement profile of emergency medicine of theoretical knowledge, technical skills in combination with non-technical skills and high interactivity in the team, classroom training is indispensable. Flipped classroom concepts set knowledge impulses in advance and activate latent knowledge. In the classroom phase, these knowledge impulses are applied in practical case scenarios. The focus of the concept is on a concentrated presence phase at the simulation manikin. This concept and the experiences from QuIS II were also transferred to the block practical course "Anaesthesia, Intensive Care Medicine and Emergency Management" (10th semester). In a similar way, teaching was implemented for the block practical course in pain medicine. Here, students work out contents in advance in case-based learning modules in order to reflect on them in a video seminar (Zoom) with a lecturer and to deepen them in practice on a simulation patient (SP). Evaluations were linked to these curricular seminars and practical courses, which were always evaluated very positively and contributed to further optimisation of the courses. Building on these experiences, lectures, seminars

and practical courses could be offered in digital or hybrid form. The concept of blended learning as a flipped classroom offers the opportunity for concentrated, in-depth attendance phases and will continue to play an important role in curricular development in order to prepare students for their medical work.

## Selected publications

Schüttler J, Eisenried A, Lerch M, Fechner J, Jeleazcov C, Ihmsen H. Pharmacokinetics and pharmacodynamics of remimazolam (CNS 7056) after continuous infusion in healthy male volunteers: Part I. Pharmacokinetics and clinical pharmacodynamics. *Anesthesiology*. 2020; 132(4): 636-651. doi: 10.1097/ALN.0000000000003103

König C., Plank A., Kapp A., Timotius I., von Hörsten S., Zimmermann K. (2020) Thirty mouse strain survey of voluntary physical activity and energy expenditure: Influence of strain, sex and day-night variation. *Frontiers in Neuroscience* 14:531. doi: 10.3389/fnins.2020.00531.

Lampert A., Bennett D.L., McDermott L.A., Neureiter A., Eberhardt E., Winner B., Zenke M. Human sensory neurons derived from pluripotent stem cells for disease modelling and personalized medicine. *Neurobiology of Pain* 8:100055 (2020)

Eisenried A, Schüttler J, Lerch M, Ihmsen H, Jeleazcov C. Pharmacokinetics and Pharmacodynamics of Remimazolam (CNS 7056) after Continuous Infusion in Healthy Male Volunteers: Part II. Pharmacodynamics of Electroencephalogram Effects. *Anesthesiology*. 2020;132(4):652-666. doi:10.1097/ALN.0000000000003102

Wehrfritz A, Ihmsen H, Fuchte T, Kim M, Kremer S, Weiß A, Schüttler J, Jeleazcov C. Postoperative pain therapy with hydromorphone; comparison of patient-controlled analgesia with target-controlled infusion and standard patient-controlled analgesia: A randomised controlled trial. *Eur J Anaesthesiol* 2020 Dec;37(12):1168-1175. doi: 10.1097/EJA.0000000000001360.

St Pierre, M. and J. M. Nyce (2020). "How novice and expert anaesthetists understand expertise in anaesthesia: a qualitative study." *BMC Med Educ* 20(1): 262.

## International cooperations

Prof. E. Jørum, Department of Neurology, Oslo University Hospital-Rikshospitalet, Oslo: Norwegen

Prof. G. Peltz, Department of Anesthesia, Pain and Perioperative Medicine, Stanford University, Stanford: USA

Prof. Teijo Saari, Department of Anesthesiology and Intensive Care at Turun yliopisto - University of Turku, Finland

Dr. Hua-Cheng Liu, MD, Department of Anesthesiology, the Second Affiliated Hospital & Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, China

Prof. Johan Bergstrom, PhD, Division of Risk Management and Societal Safety, Director MSc. Programme in Human Factors & Systems Safety, Lund University, Sweden