Department of Neurosurgery

Chair of Neurosurgery

Address
Schwabachanlage 6
91054 Erlangen
Phone: +49 9131 8534566
Fax: +49 9131 8534476
www.neurochirurgie.uk-erlangen.de

Director
Prof. Dr. med. Michael Buchfelder

Contact
Prof. Dr. med. Ilker Y. Eyüpoglu
Phone: +49 9131 8544756
Fax: +49 9131 8534569
ilker.eyupoglu@uk-erlangen.de

Research focus
- Functional neuronavigation and intraoperative imaging
- Neuroendocrinology
- Neurooncology

Structure of the Department

Professorships: 2
Personnel: 182
- Doctors (of Medicine): 21
- Scientists: 10 (thereof funded externally: 3)
- Graduate students: 34

Clinical focus areas
- Endocrine neurosurgery
- Neurooncology
- Scull base surgery
- Epilepsy surgery
- Vascular neurosurgery
- Spine surgery
- Neurotramatology
- Pediatric neurosurgery

Research

The scope of research of the Department of Neurosurgery is primarily clinical, with special focus on the field of intraoperative imaging, neuroendocrinology, and neuro-oncology.

Functional neuronavigation and intraoperative imaging

The research group "functional neuronavigation and intraoperative imaging" is divided in three subgroups that work in part independently, but use the intraoperative 1.5 T MRI-scanner as a common interface.

• Intraoperative imaging

A major effort of this group is the acquisition of all parameters that are connected to intraoperative imaging of pituitary and suprasellar tumors, intra- and extraaxial brain tumors, and epilepsy-associated procedures. The analysis of these data is currently in progress. In addition, the group worked on the visualization of important eloquent brain areas with the implementation of diffusion-tensor-imaging, functional MRI, and magnetoencephalography. Moreover, studies of implementation of tractography data in the surgical treatment of brain stem lesions were completed. Two important studies analyzed the connectivity of eloquent brain areas with different DTI algorithms using probabilistic fiber tracking and investigated the amount of susceptibility artifacts in linear registration of fiber tracts. We further established the novel DiVA-protocol which combines the fluorescence-guided resection with intraoperative MRI resulting in an increased glioblastoma patient survival.

• Functional imaging

This group focused on correlative studies for cortical plasticity after resection of gliomas. Also the connectivity of receptive and expressive language areas was investigated with fMRI and DTI following reports of other groups with electrical stimulation.

• Metabolic imaging

Major focus of this group was on studies of metabolic imaging for the characterization of the infiltration of gliomas with proton MR spectroscopy and FET-PET. Furthermore, studies of the tumor invasion into fiber tracts and its influence on their reconstruction and neurologic symptoms and studies of metabolic changes in temporal lobe lesions with 1H MR spectroscopy were investigated. Furthermore, we investigate the cortical plasticity after gliome resection adjacent to eloquent brain areas and intraoperative MR spectroscopy in gliomas.

Neuroendocrinology

The Department of Neurosurgery is a nationally and internationally specialized center for the whole spectrum of sellar pathologies. Clinically we investigate the influence of interventional/operative, radiotherapeutic, and pharmacological approaches on normal and hypersecretory pituitary gland function in the course of the "Acrostudy" (treatment and MRI follow-up of the medicinal therapy with Somavert®). Also, investigations on somatostatin analoga and their clinical relevance in the treatment of growth hormone secreting pituitary adenoma represent a central part. Our clinical and laboratory chemical analyses and screening studies are supported by the companies Pfizer and Novartis. The efficacy of novel intra-operative technologies in pituitary adenoma surgery and craniopharyngiomas is evaluated. Novel procedures include endoscopic surgery, such as endoscopic assisted microsurgery and intraoperative MRI. These techniques allow controlling resections in cases of intrasellar and suprasellar tumors. Goal of these clinical long-term studies is to define the relapse frequencies of sellar tumors, including different prognostic factors.

The field of neuroendocrinology within the Department of Neurosurgery was established in 2007 in the framework of an endowed professorship for clinical and experimental neuroendocrinology (Prof. Dr. C. Schöfl, now Department of Medicine 1). In cooperation with the Institute of Radiology, body composition, liver and muscle fat content are determined by MRI in patients with various hypothalamic-pituitary diseases (e.g. pituitary deficiency, acromegaly, and M. Cushing). The results are correlated with various metabolic characteristics and with novel parameters involved in the metabolic control. The aims of these studies are to obtain novel insights in the neuroendocrine control of metabolic and energetic processes.

Another translational scientific project involves the functional characterization of mutations of the metabotropic calciumsensing receptor (CaSR) that occur in patients with specific disorders of calcium homeostasis. The CaSR is also expressed in pituitary cells and in hypothalamic nuclei involved in the control of endocrine systems. In this project, the patients are screened for clinical evidence of neuroendocrine dysfunction, and clinical and *in-vitro* data are correlated to define a potential genotypephenotype relation. Furthermore, agonists and antagonists of the CaSR are tested *in vitro* whether they can rescue the molecular defect of the mutated CaSR. This potentially offers a therapeutic approach specifically tailored to patients' molecular CaSR defect (individualized medicine).

Further projects investigate various aspects of growth-hormone secreting human adenoma cells *in vitro*, like the expression of certain membrane receptors (e.g. somatostatin receptors) and the characteristics of signaling cascades (cAMP- and Ca2+-PI-signaling pathway). The *in vitro* data are related to various clinical data in order to extract potential prognostic factors concerning therapeutic outcome and to define potential new therapeutic targets.

Neurooncology

Gliomas are the most common primary tumors of the brain and about 70% of these tumors are malignant gliomas. Currently, there is no promising therapy for the treatment of malignant tu-

mors which targets the high proliferation and diffuse brain invasion. Therefore, investigation and characterization of the molecular mechanisms of glioma growth and invasion are essential steps in developing novel therapeutic strategies.
The neurooncology research group deals with the biology and therapy of brain tumors and could demonstrate that malignant gliomas secrete high amounts of the neurotransmitter glutamate which results in neuronal cell death in the peritumoral brain parenchyma and induces perifocal edema. These data correlate with a reduced quality of life of patients suffering from malignant gliomas.
Another focus of the group is to decipher the interaction of different brain cells and glioma proliferation. One candidate molecule for tumor-associated cell interaction is the protein MIF (macrophage migration inhibitory factor). This cytokine is secreted by glioma cells and interacts with the adjacent parenchyma. The aim of this project is the analysis of MIF effects on immune competent cells in the brain, such as microglial cells, and its role in glioma proliferation and invasion. Moreover, the preliminary data indicate that microglial cells participate at edema formation surrounding malignant gliomas.

Teaching

The Department of Neurosurgery is involved in the curricular teaching of Medicine and Dentistry with compulsory and elective subjects. In addition, the students are exposed to the practical aspects of neurosurgery within the framework of the block practical course system through guided tours in operating rooms during live surgery. A special aspect is the interdisciplinary nature of teaching within the framework of the neurosurgery/neurology block.
The Department of Neurosurgery supervises Bachelor's and Master's theses as well as MD and PhD theses.

Selected publications

Ackermann A, Karagöz AÇ, Ghoochani A, Buchfelder M, Eyüpoglu I, Tsogoeva SB, Savaskan N. Cytotoxic profiling of artesunic and betulinic acids and their synthetic hybrid compound on neurons and gliomas. Oncotarget. 2017 Jun 7;8(37):61457-61474

Chen D, Fan Z, Rauh M, Buchfelder M, Eyupoglu IY, Savaskan N. ATF4 promotes angiogenesis and neuronal cell death and confers ferroptosis in a xCT-dependent manner. Oncogene. 2017 Oct 5;36(40):5593-5608

Buchfelder M, van der Lely AJ, Biller BMK, Webb SM, Brue T, Strasburger CJ, Ghigo E, Camacho-Hubner C, Pan K, Lavenberg J, Jönsson P, Hey-Hadavi JH. Long-term treatment with pegvisomant: observations from 2090 acromegaly patients in ACROSTUDY. Eur J Endocrinol. 2018 Dec 1;179(6): 419-427

Stadlbauer A, Zimmermann M, Doerfler A, Oberndorfer S, Buchfelder M, Coras R, Kitzwögerer M, Roessler K. Intratumoral heterogeneity of oxygen metabolism and neovascularization uncovers 2 survival-relevant subgroups of IDH1 wild-type glioblastoma. Neuro Oncol. 2018 Oct 9;20(11): 1536-1546

Stadlbauer A, Mouridsen K, Doerfler A, Bo Hansen M, Oberndorfer S, Zimmermann M, Buchfelder M, Heinz G, Roessler K. Recurrence of glioblastoma is associated with elevated microvascular transit time heterogeneity and increased hypoxia. J Cereb Blood Flow Metab. 2018 Mar;38(3):422-432

Stadlbauer A, Roessler K, Zimmermann M, Buchfelder M, Kleindienst A, Doerfler A, Heinz G, Oberndorfer S. Predicting Glioblastoma Response to Bevacizumab Through MRI Biomarkers of the Tumor Microenvironment. Mol Imaging Biol. 2018 Oct 25

International cooperations

Prof. DS Olsson, MSc, MD, PhD, University of Gothenburg, Göteborg: Sweden

Prof. Dr. JP Martinez-Barbera, UCL GOS Institute of Child Health, London: UK