

Institute of Anatomy

Chair of Functional and Clinical Anatomy

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Research focus

- Pathomechanisms of the Meibom Gland Dysfunction
- Biopolymer hydrogels for tissue replacement
- HistoDigital® (HiD) and Cinematic Anatomy
- Mechanisms of tear outflow
- Surfactant proteins
- Test anxiety among medical and dental students
- Diagnostics of neuropathic pain via the eye
- Ocular tissue interactions of a refractive UV femtosecond laser

Structure of the Chair

Professorships: 2

Personnel: 30

- Doctors (of Medicine): 2
- Scientists: 17 (thereof funded externally: 7)
- Graduate students: 35

Special structural features

- Lecture room for lessons in histology with 160 microscopes
- Electron microscopy unit
- Digital Anatomy unit
- Management of the body donation unit

Both chairs collegially lead the Institute of Anatomy.

Research

The Chair of Functional and Clinical Anatomy deals with questions concerning the eye, in particular the ocular surface and the draining tear ducts (ocular surface group) as well as the role of various proteins and peptides (including surface-active proteins) on the ocular surface, in joints (osteoarthritis and rheumatoid arthritis) and in other body localizations. In addition, clinical-anatomical questions are addressed and new methods for anatomy education are intensively developed and teaching research is conducted.

Pathomechanisms of the Meibom Gland Dysfunction

PI: Prof. Dr. F. Paulsen, PD Dr. F. Garreis
Meibomian gland dysfunction (MGD), a term used to describe a diffuse abnormality of the meibomian glands, which are specialized sebaceous glands in

the eyelids, is considered the most common cause of dry eye syndrome (DES), a disease with an estimated prevalence of 12 million people alone in Germany. It is currently thought that MGD is caused primarily by terminal duct obstruction due to hyperkeratinization of the ductal epithelium and an increased viscosity of meibum. However, the molecular mechanisms that underlie this process are unclear. We investigate the influence of different hormones on the keratinization process, the importance of the formation of adhesion contacts (Desmosomes) for the maturation process of the meibocytes and the influence of various proteins which contribute to a hyperkeratinization of the ducts and the increasing viscosity of the meibum. Our goal is to gain deeper insights into the pathophysiology of MGD. To this end, experiments will be carried out in an established mouse model of the DED as well as in two and three-dimensional cultivation models with human meibomian epithelial cells. This serves to determine factors that could possibly be used as therapeutic treatment options in MGD.

Novel Biopolymer Hydrogels for Understanding Complex Soft Tissue Biomechanics

PI: Prof. Dr. F. Paulsen (together with Prof. Dr.-Ing. P. Steinmann [Tech], Prof. Dr.-Ing. A. Boccaccini [Tech], Prof. Dr. B. Fabry [Nat])

In a joint project, biopolymer hydrogels are produced and mechanically characterized. These serve as proxy materials to understand and model the highly complex behavior of soft biological tissues. This will result in a proxy material catalog that combines various characteristic features of the mechanical response with a validated modeling approach. It will serve as an important basis for selecting suitable materials for tissue engineering, reducing experiments on human and animal tissues, and increasing the potential of numerical approaches that can be applied in clinical and industrial settings.

HistoDigital® and Cinematic Anatomy

PI: Prof. Dr. M. Scholz, Prof. Dr. F. Paulsen

In close cooperation with Chimaera GmbH (Erlangen), HiD, a digital application is being developed that enables the user to create a digital volumetric reconstruction of the anatomical tissue structures from the data sets of histological section series. The goal is the future use of this application in research and teaching.

The cinematic rendering (CR) technology was originally developed by Siemens Healthineers (Dr. Klaus Engel) as a medical image visualization technology. It enables the generation of 3D photorealistic images of the human body. Existing imaging methods (CT, MRT, etc.) provide the raw data for the volumetric visualizations. In direct cooperation with Siemens, this technology is to be made applicable for teaching and learning the human anatomy.

New insights into the lacrimal pump

PI: Prof. Dr. F. Paulsen, Prof. Dr. M. Scholz

To date, there are many theories on the transport of tears through the canaliculi of the efferent lacrimal system into the lacrimal sac, but few with

hard data. We have shown that contraction of the Horner-Duverney muscle leads to closure of the canaliculi in their first two thirds due to the special arrangement of muscle fibers and connective tissue fibers. As a result, the tear fluid in the canaliculi is pushed/transported toward the lacrimal sac. The medial third of the vertical portions of the canaliculi, the canaliculus communis, and the intrasaccal portion of the canaliculus are compressed by the shortening and thickening of the Horner-Duverney muscle from the dorsal side, resulting in compression of the canaliculi lumen in this part of the system, thereby pushing the tear fluid further toward the lacrimal sac. The mixture of rapidly contracting and fatigue-resistant muscle fibers is ideally suited for the blink mechanism, which is complexly regulated by the nervous system. In further studies, we are currently analyzing the lymphatic drainage of the human lacrimal system.

Surfactant proteins

PI: Prof. Dr. L. Bräuer, PD Dr. M. Schicht, Prof. Dr. F. Paulsen

The successive characterization of surfactant proteins, in particular the proteins SP-G and SP-H described by us, demonstrate the immense spectrum of action of these proteins in the human organism. Within the research group it could be shown that SP-H has stimulatory effects on the activity of alveolar macrophages and furthermore leads to an increased phagocytosis activity. Meanwhile, further own studies suggest that both surfactant proteins might play an important role in inflammation and wound healing processes also outside the lung (e.g. at the ocular surface or inside the kidney). The properties described so far could make SP-G and SP-H potential candidates for diagnosis, prophylaxis and possibly therapy of different diseases.

Test anxiety among medical and dental students

PI: PD Dr. C.M. Hammer, Prof. Dr. M. Scholz, Prof. Dr. F. Paulsen

Test anxiety is a common phenomenon among students, often affecting academic performance. To date, there is a scarcity of valid data concerning prevalence, severity, and types of test anxiety among German medical and dental students. Hence, there are only few reports on effective therapeutic or preventive strategies tackling the problem of test anxiety. Repetitive application of a validated psychological test anxiety questionnaire yielded more than 50% of the evaluated students showing pronounced signs of test anxiety. Moreover, it revealed medical hypnosis as a potent intervention to significantly alleviate test anxiety. Medical hypnosis was proved especially effective in the amelioration of the test anxiety subtype "lack of confidence".

Biomarkers and novel therapeutic approaches for neuropathic pain of different etiologies

PI: Prof. Dr. E. Lütjen-Drecoll, Prof. Dr. F. Paulsen

Within the project, different models of neuropathic pain will be investigated separately, as the mechanisms of neuropathic pain differ considerably depending on the etiology of the pain.

For this reason, therapeutic approaches also differ in the respective neuropathic pain syndromes. For example, effective therapy requires differentiation between tumor- and chemotherapy-induced neuropathic pain. Therefore, to cover the widest possible range of different neuropathic pain types, we are investigating different models of neuropathic pain such as chemotherapy-induced or diabetes-induced neuropathic pain. Results generated therein will be applied to the eye as a window to the peripheral nervous system e.g. by measuring axonal corneal degeneration in neuropathic models, by multi-epitope-ligand mapping as well as tear film lipidomics and -proteomics.

Ocular tissue interactions of a refractive UV femtosecond laser

PI: Dr. C.M. Hammer, Prof. Dr. F. Paulsen

The already established cooperation with the Department of Ophthalmology and WaveLight GmbH was further intensified with regard to this project. Intraoperative gas production and interface quality after extraction of refractive lenticles from porcine eyes was examined and compared between the novel UV-laser and an infrared laser system already established for this procedure (VisuMax). Histological investigations demonstrated the superiority of the UV laser as far as gas production is concerned. Since the UV laser produces significantly less gas than the VisuMax system, it may also have the potential to achieve a much higher degree of surgical precision. Comparative scanning electron microscopical examinations showed similar interface properties with respect to surface smoothness and regularity. This is supportive of the assumption that the UV laser may be as well suited for refractive lenticle extractions as the clinical VisuMax system.

Teaching

The Chair of Functional and Clinical Anatomy is involved in the teaching of macroscopic anatomy at the Institute of Anatomy. Each semester a variety of elective subjects can be offered for medical and dental students in the preclinical semesters. Virtual courses of histology, macroscopy, and embryology are offered in cooperation with the virtual university of Bavaria (vhb). Moreover, Bachelor's and Master's theses as well as MD and PhD are supervised.

Selected publications

Ali MJ, Zetzsche M, Scholz M, Hahn D, Gaffling S, Heichel J, Hammer CM, Bräuer L, Paulsen F. New insights into the lacrimal pump. *Ocul Surf* 2020, 18:689-698

Culemann S, Grüneboom A, Nicolás-Ávila JA, Weidner D, Lämmle KF, Quintana JA, Kirchner P, Krljanac B, Eberhardt M, Ferrazzi F, Kretschmar E, Schicht M, Fischer K, Gelse K, Faas M, Pfeifle R, Rothe T, Ackermann JA, Pachovsky M, Renner N, Haseloff RF, Ekici A, Bäuerle T, Blasig IE, Vera V, Voehringer D, Paulsen F, Schett G, Hidalgo A, Krönke G. Spatiotemporal molecular profiling of synovial macrophages reveals a locally renewing barrier of membrane-forming macrophages shielding the joint. *Nature* 2019, 572:670-675

Hammer CM, Bischofsberger L, Burger P, Paulsen F, Scholz M. Feasibility of clinical and experimental hypnosis. *Int J Clin Exp Hypnosis* 2020, 68:511-520

Popp J, Schicht M, Garreis F, Klinger P, Gelse K, Sesselmann S, Tsokos M, Etzold S, Stiller D, Claassen H, Paulsen F. Human synovia contains

trefoil factor family (TFF) peptides 1-3 although synovial membrane only produces TFF3: implications in osteoarthritis and rheumatoid arthritis. *Int J Mol Sci* 2019, 20:E6105

Weizel A, Distler T, Scheiderei D, Friedrich O, Bräuer L, Paulsen F, Detsch R, Boccaccini AR, Budday S, Seitz H. Complex mechanical behavior of human articular cartilage and hydrogels for cartilage repair. *Acta Biomater* 2020, 118:113-128

International cooperations

Prof Dr. M.J. Ali, FAU Humboldt Fellow, LV Prasad Eye Institute, Hyderabad: India

PD Dr. Dr. P. Burger, Psychiatrische Universitätsklinik Zurich: Switzerland

Prof. C.S. de Paiva, Baylor College of Medicine, Houston, Texas: USA

Prof. Dr. S. Dydekin, Sechenov University, Moscow: Russia

Prof. Dr. M. Ito, National Defense Medical College, Saitama: Japan

Prof. Dr. L. Olewnik, Medical University of Lodz: Poland

Dr. S. Singh, Lala Jagannath Eye Institute, Ambala: India

Dr. S. Wosniak, Wroclaw Medical University, Wroclaw: Poland

Prof. D. Zoukhri, Tufts University School of Dental Medicine, Boston: USA