# **Department of Orthodontics and Orofacial Orthopedics**

Chair of Dental, Oral, and Maxillofacial Medicine - especially Orofacial Orthopedics

#### Address

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#### **Research focus**

- MRI in orthodontic diagnosis
- Material scientific examinations of orthodontic materials
- Quality of life of mothers of children with cleft lip and/or palate
- Identification of genetic risk variants by molecular genetics
- Mechanisms of dental brace-induced immune tolerance against nickelions

## **Structure of the Department**

Professorship: 1

- Personnel: 26 • Doctors (of Medicine): 10
- Scientist: 1
- Graduate students: 3

#### **Clinical focus areas**

- Treatment of newborn babies with cleft lip and/or palate
- Orthodontic treatment of cleft lip and/or palate
- Orthodontic treatment of dysgnathia / malformations of the upper and/or lower jaw
- Orthodontic treatment of craniofacial anomalies and syndromes
- Orthodontic treatment of tooth displacement
- Orthodontic treatment of tooth agenesis (hypo- or oligodontia)
- Evidence-based orthodontics

## Research

Research of the Department of Orthodontics and Orofacial Orthopedics includes the implementation of three-dimensional diagnosis in orthodontics. Other research areas are material scientific examinations of orthodontic materials and the quality of life of mothers of children with cleft lip and/or palate (CL/P). Besides this, we are currently building up a molecular genetics laboratory to identify genetic causes for many of our patients' conditions: CL/P, craniofacial dysgnathia, tooth agenesis (hypo- or oligodontia) as well as molar incisor hypomineralization and periodontitis.

## **MRI** in orthodontic diagnosis

Our department has focused on the application of three-dimensional diagnosis in orthodontics for several years. The conventional technique, computer tomography (CT), has become a well-established gold standard. In spite of excellent accuracy and image quality, each new CT scan exposes patients to radiation. In contrast, magnetic resonance imaging (MRI) allows a three-dimensional, radiation-free medical imaging. Therefore, we are collaborating with the Fraunhofer Institute for Integrated Circuits IIS in Würzburg and the Institute of Radiology of UK Erlangen to develop new MRI sequences with ultra-short echo times in order to enable imaging of hard tissue like teeth and bones. Aim of this study is the development of a platform to examine the practicability of three-dimensional (3D) MRI imaging in orthodontic issues due to the statement of the German society of Orthodontics (DGKFO) on the indication of 3Dimaging and the evaluation of MRI as an alternative imaging technique to CBCT (cone beam computed tomograph), MSCT (multi slice computed tomograph), and industrial MSCT. Moreover, we develop methods of analysis to enable the use of established two-dimensional cephalometric analysis in three-dimensional MRI data sets. The long-term aim of this project is to replace the routine orthodontic X-ray imaging with radiation-free MRI.



Representation of the newly developed cephalometric analysis in three-dimensional MRI data set

# Material scientific examinations of orthodontic material

Further research fields are material scientific examinations of orthodontic materials, their biocompatibility, and the development of antibacterial material for orthodontic applications in collaboration with the Technical University of Munich. In the long term, by using these materials as bonding material for brackets we want to reduce number and size of demineralized areas after removal of fixed multibracket appliances, thus minimizing risk of caries for patients.

# Quality of life of mothers of children with cleft lip and/or palate

We want to assess the quality of life of mothers having a baby with CL/P. The aim of this study with 12 participating university hospitals is the prospective evaluation of mothers' quality of life, their sense of coherence, and social support after birth of a baby with CL/P. In order to measure changes in quality of life we collect data at three specific time points during the first year – resembling a period of enormous mental stress for parents. Mothers of healthy children are interviewed as controls. Collected data serve to analyze the course of treatment and possible deficits and to estimate the care situation of affected mothers.



Assessing quality of life of mothers of children with CL/P

### Identification of genetic risk variants by molecular genetics

In order to identify risk factors for CL/P, we examine DNA samples from a broad range of patients and, if applicable, their relatives and compare them to data from control groups. In cooperation with the Institutes of Human Genetics of the university hospital of Bonn and of UK Erlangen, we perform next generation sequencing analyses enabling us to analyze large regions of DNA up to whole genomes. Our aim is always to pinpoint (possibly inherited) changes in the patient's DNA sequence that lead to the manifestation of the disease. Chromosomal regions identified in this way serve to find and characterize responsible genes. Those genes are examined in detail with regard to their biological function and how it might cause the cleft. Using the described molecular genetic methods, we also seek to identify relevant genetic loci for craniofacial dysgnathia, tooth agenesis (hypo- or oligodontia) and in future for molar incisor hypomineralization.

In further molecular genetic analyses, we seek to identify gene variants contributing to formation and progression of periodontitis. Although the impact of a genetic component is estimably 33 - 50 %, only a few risk variants have been identified up to now. In order to identify unknown genetic variants causing a higher risk for periodontitis, we perform expression quantitative trait locus (eQTL) analyses. By this innovative method, we can identify changes in the transcriptome of immune cells stimulated with periodontal virulence factors and attribute them to certain gene variants. With the same technique, we investigate on genetic factors influencing atherosclerosis and allergies against metals. For these comprehensive analyses, we cooperate with the Institute of Human Genetics and the Institute of Medical Microbiology, Immunology and Parasitology of the university hospital of Bonn and with the Department of Cardiology, Angiology and Pneumonology of the university hospital of Heidelberg and Center of Human Genetics of the university hospital of Marburg.

At best, our molecular genetic analyses lead to new diagnostic possibilities that could direct appropriate therapeutic measures in the sense of personalized medicine. The acquired knowledge might also help to develop new medication and preventive measures.

# Mechanisms of dental brace-induced immune tolerance against nickelions

In a cell biological project we focus on the fact that small amounts of nickel ions released from dental braces can desensitize the immune system. Thus, they may exert a protective effect against the development of nickel allergies. We want to elucidate the molecular mechanisms how dendritic cells as well as fibroblasts of the gingiva may contribute to immune tolerance. This might proof useful for fighting allergies in general.

# Teaching

The Chair of Dental, Oral, and Maxillofacial Medicine – especially Orofacial Orthopedics is engaged in dental medicine. Within the scope of orthodontic analysis and treatment, the curriculum comprises comprehensive clinically based material. Skills lab work enables the students to collect and evaluate diagnostic data and to control the clinical application of orthodontic devices.

In addition, MD and PhD theses are supervised, and residents are further trained to become specialized orthodontists according to the Bavarian Curriculum.

#### **Selected publications**

Ludwig KU et al. Imputation of orofacial clefting data identifies novel risk loci and sheds light on the genetic background of cleft lip  $\pm$  cleft palate and cleft palate only. Hum Mol Genet. 2017; 26:829-842

Papageorgiou SN, Kutschera E, Memmert S, Gölz L, Jäger A, Bourauel C, Eliades T. Effectiveness of early orthopaedic treatment with headgear: a systematic review and metaanalysis. Eur J Orthod. 2017; 39:176-187

Detterbeck A, Hofmeister M, Haddad D, Weber D, Schmid M, Hölzing A, Zabler S, Hofmann E, Hiller KH, Jakob P, Engel J, Hiller J, Hirschfelder U. Determination of the mesiodistal tooth width via 3D imaging techniques with and without ionizing radiation: CBCT, MSCT, and µCT versus MRI. Eur J Orthod. 2017;39(3):310-319

Grozdinska A, Hofmann E, Schmid M, Hirschfelder U. Prevalence of temporomandibular disorders in patients with Hashimoto thyroiditis. J Orofac Orthop. 2018;79(4):277-288

Böhmer AC, Gölz L, Kreusch T, Kramer FJ, Pötzsch B, Nöthen MM, Jäger A, Mangold E, Knapp M, Ludwig KU. Investigation of dominant and recessive inheritance models in genome-wide association studies data of nonsyndromic cleft lip with or without cleft palate. Birth defects research. 2018; 110:336-341

Hofmann E, Detterbeck A, Chepura T, Kirschneck C, Schmid M, Hirschfelder U. Oculoauriculovertebral spectrum and maxillary sinus volumes: CT-based comparative evaluation. J Orofac Orthop. 2018 Jul;79(4): 259-266