UNIVERSITÄT BERN

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BERN UNIVERSITY HOSPITAL

Berner Fachhochschule

Bern Biomedical Engineering Network

Annual Report 2013/14

CONTENTS

Biomedical Engineering Research at other Institutes of the University of Bern

Bern University of Applied Sciences

Networking

Academic Education and Teaching

EDITORIAL

It is our pleasure to present the Annual Report 2013/14 of the Bern Biomedical Engineering Network (BBN). The BBN stands in the tradition of Theodor Kocher, Fritz de Quervain, Hans Goldmann and Maurice E. Müller, former chairmen at the Bern Faculty of Medicine, known not only for their many discoveries and innovations, but also for their vision that only a close collaboration between clinicians, scientists, engineers, and industrialists will allow sustainable progress in the field.

Today the BBN is a multi-disciplinary, inter-divisional and inter-institutional activity, forming a large collaborative research network between the research departments of the Inselspital, Bern University Hospital; laboratories and research institutes of the University of Bern and the Bern University of Applied Sciences; and various external partners.

The mission of the multidisciplinary team of the BBN is to advance understanding of human health, by improving existing as well as developing and validating novel diagnostic and therapeutic approaches through:

- internationally recognized research, discovery, and invention in the area of Biomedical Engineering
- the translation of research results from the lab to the clinic for the improvement of patient care
- the transfer of scientific discoveries and biomedical technology through national and international industrial collaborations
- an outstanding post-graduate biomedical engineering education and training program.

The BBN supports these efforts by encouraging a novel partnership between clinicians, laboratory scientists and engineers and aims to: cultivate new translational research projects based on clinical practice needs, identify and support promising biomedical engineering collaborative research projects, and rapidly translate biomedical engineering research into the clinic by fully utilizing the resources for technology transfer.

In training undergraduates, graduate students, and postdoctoral fellows, the BBN educates and develops the next generation of leaders in health care technology. Since 2006 our Master of Science in biomedical engineering program (www.BIOENG.Master.unibe.ch) and our interdisciplinary biomedical science doctoral program of the Graduate School for Cellular and Biomedical Sciences (www.gcb.unibe.ch) continue to attract students nationally and internationally.

Of the many people who have contributed to our success, we must single out the deans, rectors and managing directors of our schools and the Inselspital hospital management for their visions and excellent leadership. We are also grateful for the continuous support of the Swiss and international medical technology industry, many related NGOs and national and international funding agencies. Special thanks must also be given to the many research teams and collaborating clinical partners whose dedication and tireless efforts made the network what it is today. At our annual Biomedical Engineering Day we showcase our activities. This event unites faculty, alumni, students, friends, and industry partners and is a unique forum for networking between our industrial partners and the Bern biomedical engineering community.

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INSTITUTIONAL OVERVIEW

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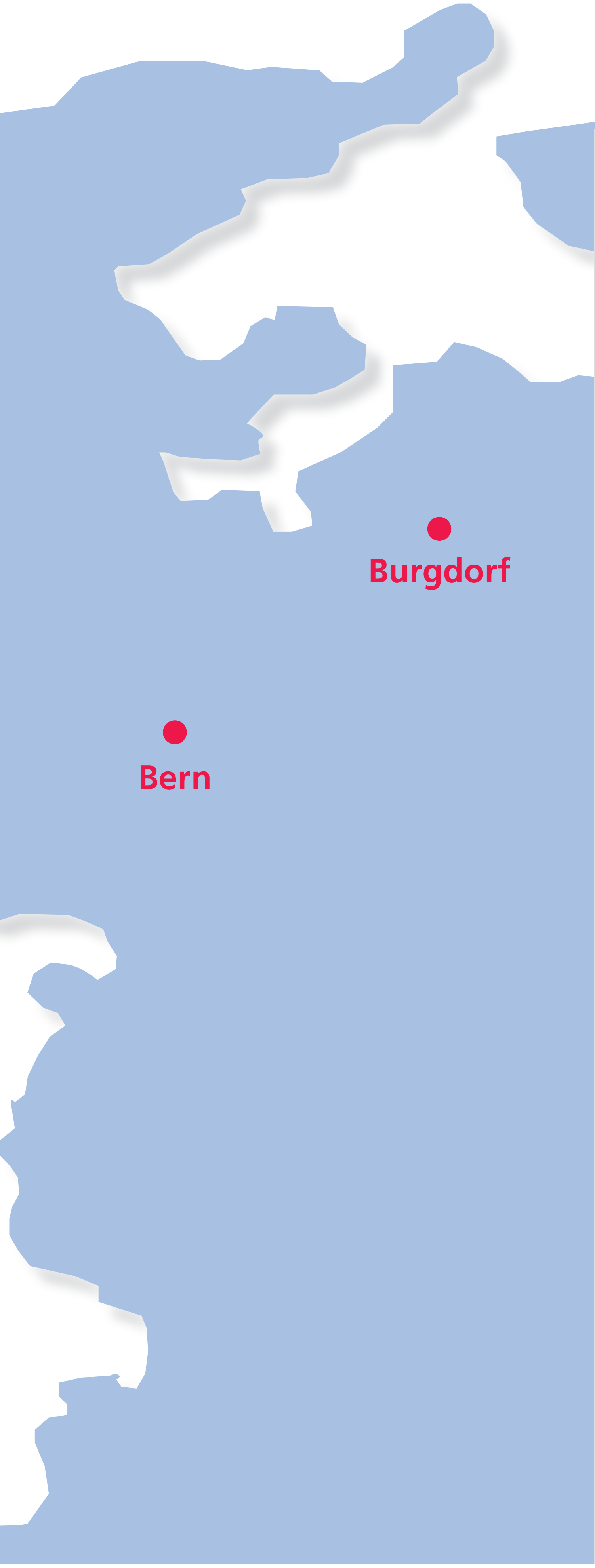

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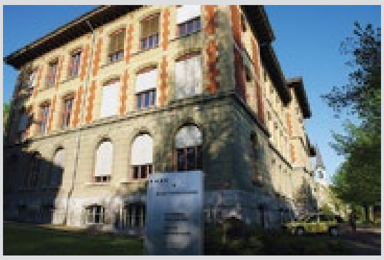

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- Institute for Print Technology

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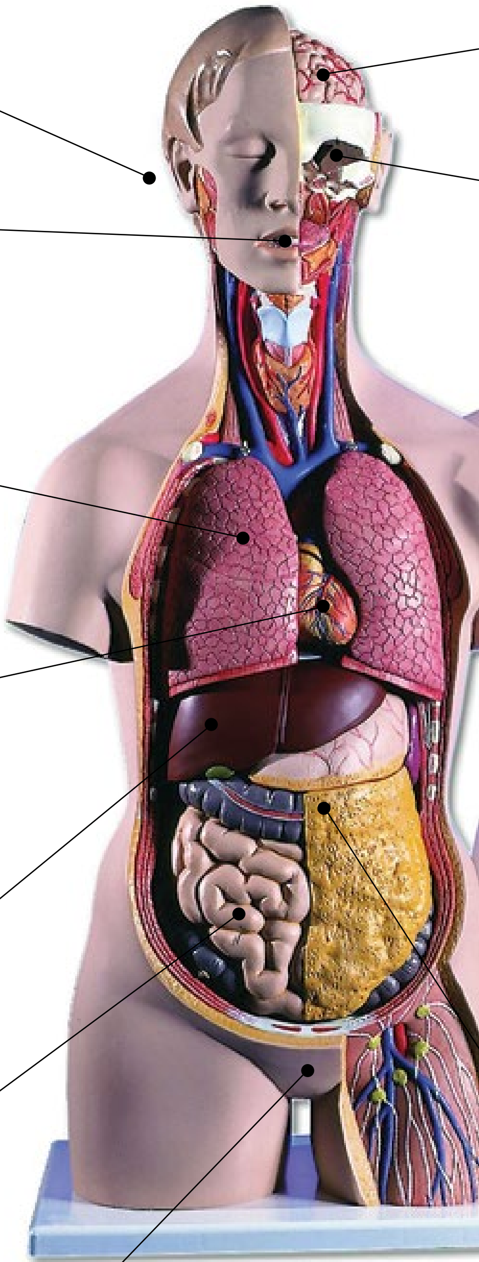
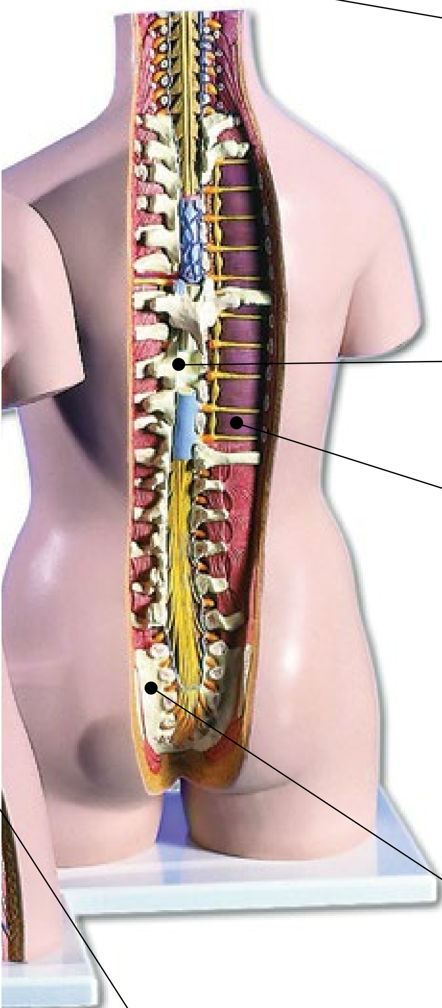
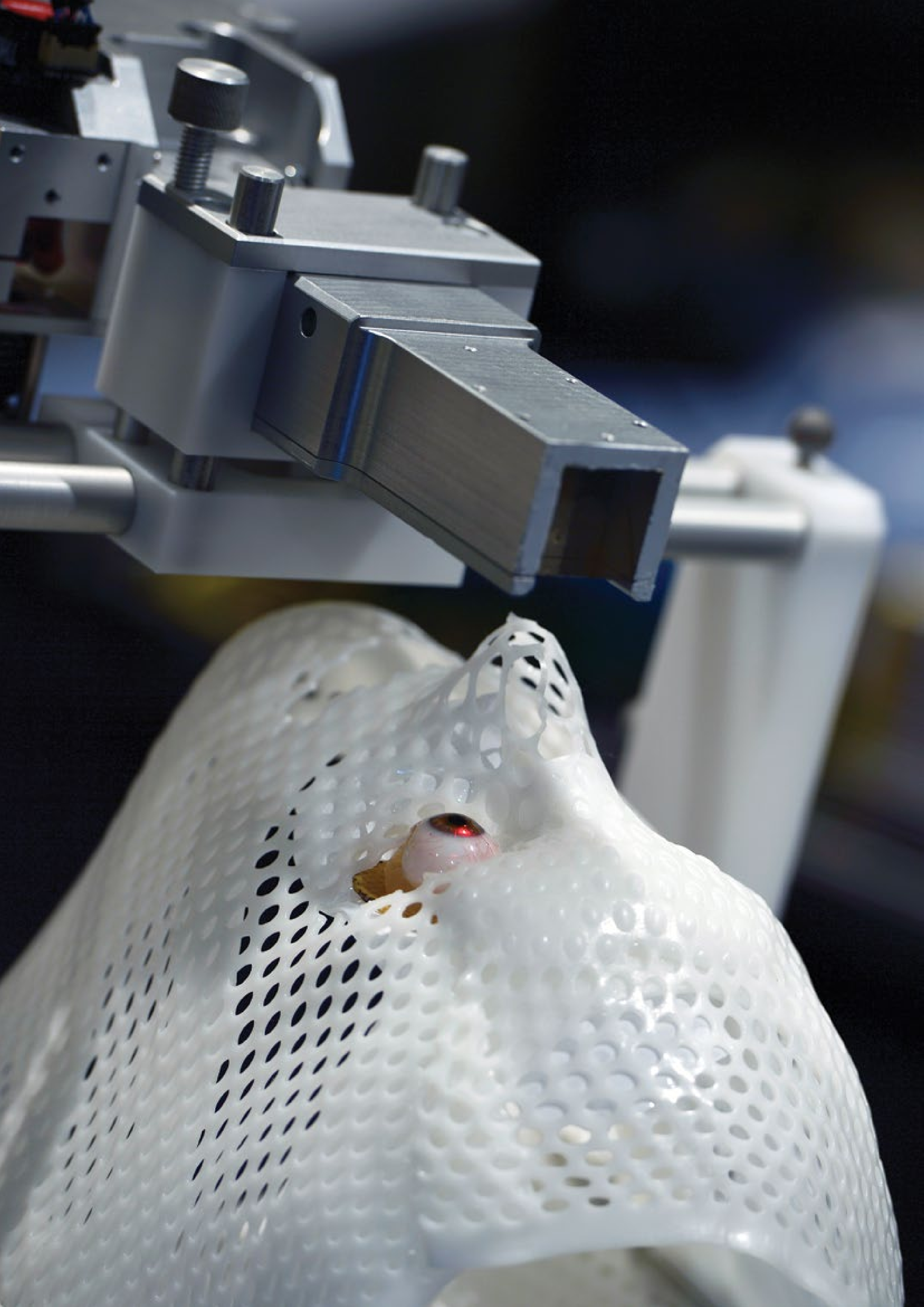
OVERVIEW OF CLINICAL SPECIALITIES







ARTORG CENTER FOR BIOMEDICAL ENGINEERING RESEARCH

The ARTORG Center, founded in 2008 brings together researchers from various biomedical engineering backgrounds and clinical departments thematically centered around specific organs and their diseases. It actively collaborates with research and development groups of the Bern University of Applied Sciences and other Swiss institutes of technology. Furthermore, knowledge and technology transfer is promoted by involving partners from the Swiss Medical Technology industry. To increase the chances of success in this kind of translational research, which refers to the transformation of scientific discoveries into practical solutions, creative teamwork across the ARTORG disciplines is promoted. The focus is on developing solutions that address particular clinical problems or unmet clinical needs.

To date, the ARTORG Center hosts eight research groups in various fields ranging from technology research for novel medical devices, simulation of biological and physiological processes to the application of nanotechnology:

- Artificial Hearing Research
- Artificial Kidney Research
- Cardiovascular Engineering
- Image Guided Therapy
- Diabetes Technology
- Gerontechnology and Rehabilitation
- Lung Regeneration Technology
- Ophthalmic Technology

Under the strategic and clinical guidance of its scientific advisory board, the ARTORG Center aims to advance healthcare by integrating education, discovery, innovation and entrepreneurship. The Center supports this effort by encouraging a new partnership between clinicians, laboratory scientists and engineers and aims to cultivate new translational research projects based on clinical practice needs, to identify and support promising biomedical engineering collaborative research projects and to rapidly translate biomedical engineering research into the clinic by fully utilizing the University of Bern resources for technology transfer.

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Artificial Hearing Research

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Research Profile

Due to an aging population, Europe is experiencing an increase in the occurrence of functional and cognitive hearing impairments. One possible and increasingly applied treatment for those who suffer from hearing loss is the implantation of a hearing device. To improve the treatment and consequently the quality of life of hearing-impaired patients, the artificial hearing research group conducts research primarily on the functionality of implantable hearing systems in addition to developing enhanced surgical implantation techniques. More specifically, fields such as audiology, signal processing, computer-assisted surgical planning, and minimally invasive surgical techniques are explored. To support the conduction of hearing research with a focus on the transfer toward clinical routine, the group includes a multidisciplinary team, which collaborates closely with industrial and clinical partners.

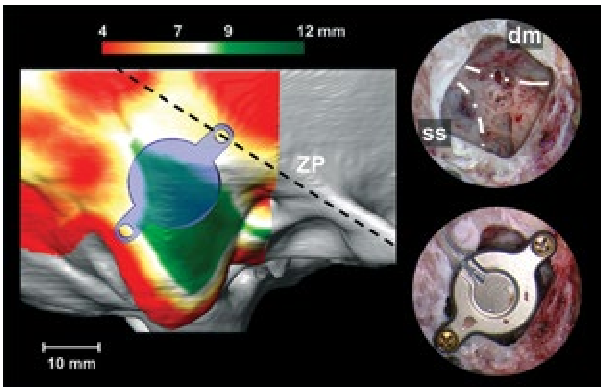
Improved Fitting Approaches for Bone Conduction Implants

Bone conduction implants (BCIs) are routinely used to treat conductive and/or mixed hearing loss, especially when conventional air conduction hearing aids cannot be used. The percutaneous BCI system consists of a retro-auricularly implanted titanium fixture, a skin-penetrating abutment, and an externally worn speech processor. The principle of the system is bone conduction. The outer and middle ear is bypassed, and sound vibrations (that are picked up by the microphone on the speech processor) travel directly to the inner ear. Improved signal processing in the new generation of digital BAHIs has seen an increase in the number of fitting parameters that can be adjusted by the audiologist to optimize sound perception. Within this research, experimental studies with experienced BAHI users are conducted to generate knowledge about improved fittings for individual patient needs.

Baha® system from Cochlear.

Bone Conduction Implantation Planning

The Bonbridge® is a transcutaneous bone conduction hearing implant that is implanted in the skull base behind the ear. The system includes a mechanical transducer (floating mass transducer, FMT), which is directly implanted under the skin and fixed to the skull bone using two self-tapping screws. The FMT, encapsulated within a cylindrical titanium casing (8.7 mm in height and 15.8 mm in diameter), has to be implanted in a region limited by critical structures, including the posterior wall of the external auditory canal, the dura mater protecting the brain, and the sigmoid sinus, a channel receiving blood from the brain. The thickness of the bone is therefore of paramount importance when planning such a surgical procedure. While current clinical planning of Bonebridge implantations is performed by manual measurements of



Topographic bone thickness map with planned implant position (blue) and corresponding intraoperative photo-documentation.

the bone thickness in separate two-dimensional axial, coronal, or sagittal computed tomography (CT) slices, optimal position finding of the FMT and screws requires complex and cumbersome tasks to be performed by the surgeon. To support surgeons prior to and during implantation, we are developing a surgical guide in the form of a bone-thickness map displaying anatomical landmarks that can be used to define a suitable implant location. The approach is currently being clinically validated, and standalone semiautomatic planning software, enabling surgeons to perform the planning efficiently in clinical routine, is being developed.

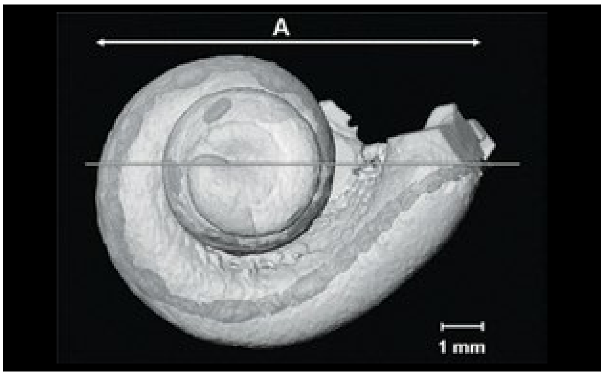
Cochlear Duct Length Estimation for Cochlear Electrode Selection

Cochlear implants are an effective treatment option for people affected by severe to profound sensorineural hearing loss. The implant consists of an electrode array that is inserted into the cochlea.

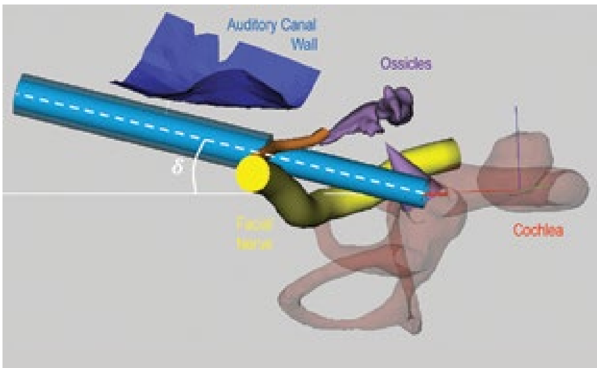
Prior to the implantation procedure, the surgeon selects a suitable electrode array length for the patient, which depends on factors such as the size of the cochlea and the presence of residual hearing obtained from audiological tests. Knowledge of patient-specific cochlear duct length (CDL) is particularly important when precise intracochlear electrode array placement is desired. In cases with no residual hearing, the surgeon aims to insert the electrode array as deeply as possible to achieve a full coverage of the sensory range. In contrast, in patients with residual hearing, electrode arrays are designed to be placed only partially within the cochlea. An electrode array inserted with the same length in two different cochleae may, however, result in a completely different insertion depth angle due to variations of the cochlear size. In this context, a preoperative estimation of the CDL could help the surgeon choose an electrode array suitable for the patient's anatomy and therefore improve outcomes of the treatment. Within this research project, the statistical correlation between the length of the CDL and the size of the cochlea, for use as a predictor of preoperative CDL estimation has been investigated. Promising findings are currently being validated in both in-vitro and in-vivo studies.

Cochlear Electrode Insertion Angle Optimization

Cochlear implants can be inserted into the cochlea through the round window membrane or via a cochleostomy. The choice of the approach depends on surgeon preference as well as on several factors, including the anatomy configuration at the level of the facial nerve and the round window. Damage to the neural elements of the cochlea, as can occur during insertion of the electrode array, may have a negative impact on residual hearing conservation. It is believed that the severity of trauma is affected by the angle of insertion relative to the plane of the cochlea basal turn. To enable the definition of a safe insertion angle for electrode insertion in minimally invasive image-guided cochlear implantation, research into the optimization of an access trajectory based on patient-specific anatomy and the insertion approach chosen by the surgeon is being undertaken. Interactive trajectory optimization and selection with insertion angle calculation and feedback is being integrated into our previously developed planning software system, and in-vitro validation of the approach is currently being conducted with clinical partners.



Cohlea size as a predictor of cochlear duct length for suitable cochlear electrode array selection.



Insertion angle calculation and feedbcak for cochlear electrode arrays.

Selected Publications

Gerber N, Bell B, Gavaghan K, Weisstanner C, Caversaccio M, Weber S (2013) Surgical planning tool for robotically assisted hearing aid implantation. Int J Comput Assist Radiol Surg 9(1):11-20

Guignard J, Stieger C, Kompis M, Caversaccio M, Arnold A (2013) Bone conduction in Thiel-embalmed cadaver heads. Hear Res 306:115-122

Guignard J, Arnold A, Weisstanner C, Caversaccio M, Stieger C (2013) A bone-thickness map as a guide for bone-anchored port implantation surgery in the temporal bone. Materials 6(11):5291-5301

Kurz A, Caversaccio M, Kompis M (2014) Hearing performance with 2 different high-power sound processors for osseointegrated auditory implants. Otol Neurotol 34(4):604-610

Krempaska S, Koval J, Schmid C, Pfiffner F, Kurz A, Kompis M (2014) Influence of directionality and maximal power output on speech understanding with bone anchored hearing implants in single sided deafness. Eur Arch Otorhinolaryngol 271(6):1395-400

Artificial Kidney Research



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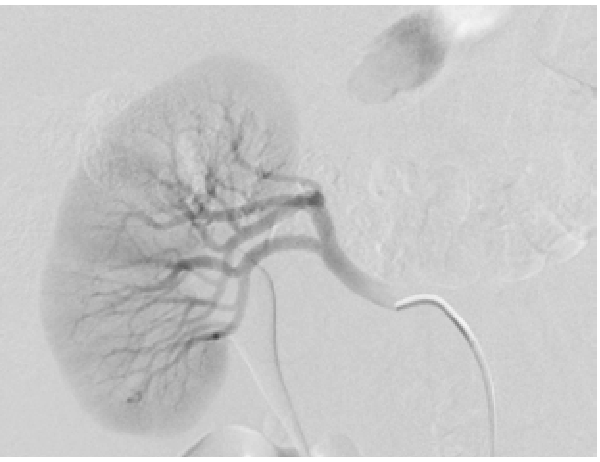
Research Profile

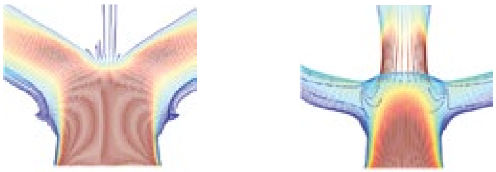
The replacement of failed renal function by dialysis is one of the most successful stories in the field of artificial solid organ replacement. While some patients have survived more than 30 years with dialysis therapy, there are still many unresolved problems; dialysis patients have a highly accelerated mortality rate and the current state-of-the-art in dialysis therapy, while highly effective during the actual treatment procedures, results in an average clearance corresponding to only about 10 to 15% of a normal renal function over a whole week.
Conventional methods to increase dialysis delivery during treatment through increased filter quality or the addition of convective transport have failed to decrease overall mortality in controlled studies. Insufficient data is available about the effectiveness of increased treatment frequency, and when combined with the high cost of hemodialysis procedures it seems unlikely that an increased number of treatments per week is an appropriate solution unless simplification of treatment practices and reduction of costs per treatment can be achieved.
The major goal of our research is to develop micro/nanofluidic devices which reflect the different functions of the kidney more precisely than current dialysis systems.



Kidney vascular system

Virtual Kidney

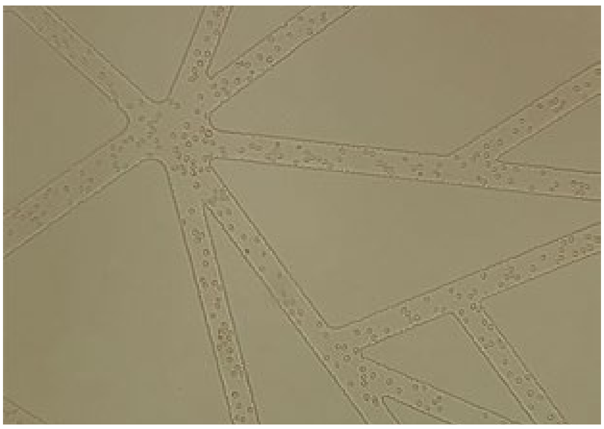
Each year half a million people undergo kidney transplantation from a deceased donor, with demand for organs significantly surpassing the number of donors. One possible solution to this challenge is through the development of an artificial kidney. The kidney can be seen as a complex filtration system which removes toxic substances from the body and retains useful ones; the kidney's basic filtration unit, called a nephron, performs multiple functions such as regulation of salt and water, electrolyte and acid base homeostasis, as well as the elimination of toxins. This project involves the recreation of fundamental kidney functions through computer simulations of complex multiphysical systems. Each function of the nephron is modelled and investigated separately as a system of micro- and nanofluidic channels with the aim of building a virtual microfluidic system capable of simulating the functions of the nephron. In the future, such a design can be validated experimentally and tested in clinical trials.



Flow streamlines in a healthy kidney (right) and in the pathological condition (left).

Optimization of Hemodialysis Process

This project aims to optimize hemodialysis performance by means of numerical analysis. There are two intermediate goals: one is to establish an understanding of blood flow behaviour in hollow fibers under the turbulence transition regime; the other is to study the influence of flow



Red Blood Cells capilliary network on the microfluidic chip.

on the separation of particles of various sizes, which are later removed. The results of such analyses can be directly applied to clinical situations. The methodology of the project is based on the usage of the Lattice Boltzmann Method to model the complex properties of fluid such as non-Newtonian effects, charges of the particles and diffusion. First, turbulence transition flows inside the hollow fiber (pipe flow) are modelled with complex multiphysics simulations; these models are then extended into the porous media application and compared with available clinical data.

Micro/Nanoparticles in Biological Environments for Patient Assistance Devices

This project involves the investigation of several aspects related to micro/nano particles in biological fluid such as blood or cell cytoplasm, with potential applications for anticoagulation devices and blood analysis systems as well as for the monitoring of the efficiency of delivered dialysis therapy. Monitoring the overall effect of intermittent renal replacement therapy over a prolonged observation period is cumbersome. It is estimated by relating the total amount of uremic toxins removed to the area under their serum concentration curve (AUC) over the whole observation period. Multiple serum samples will have to be obtained during and between treatment sessions to estimate the AUC over a full week with intermittent renal replacement therapy.

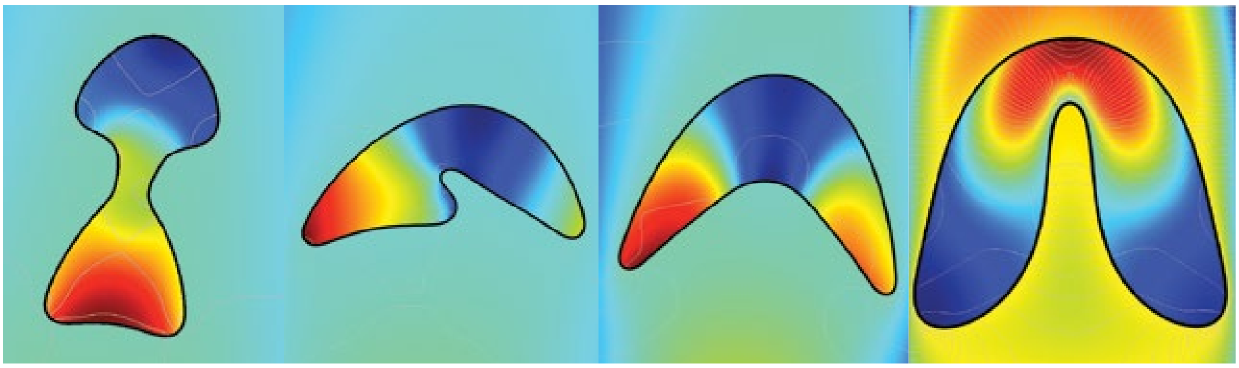
Patients completing three sessions of four hours per week at a dialysis unit are reluctant to spend additional time at the dialysis center between treatments for the additional blood samples necessary to come up with a reliable estimate of treatment efficiency over the whole observation period. Several devices have recently been developed for the continuous sampling of serum levels of various substances, with the most advanced portable devices designed for feedback controlled insulin pumps. We aim instead at simplicity in monitoring. As we are only interested in the area under the serum concentration curve, albeit over a long time period, samples can be collected and results stored for future reading at the hospital. Nevertheless, the proposed device must determine serum levels with a high accuracy due the accumulation of systemic errors when multiple values are added. Such accuracy can only be achieved on a microchip. Initial work will focus on blood urea nitrogen, phosphorus and beta-2 microglobulin.

Lifespan of the Red Blood Cells

Many patients with chronic kidney disease (CKD) suffer from anemia, i.e. an insufficient number of circulating red blood cells (RBC). Renal failure results in a decrease of renal erythropoietin (EPO) production, which is the major stimulus of RBC production in bone marrow, however, lower circulating EPO levels explain only part of the observed anemia. In addition to decreased RBC production, an increased RBC elimination is also observed in these patients. The lifespan of RBCs in uremic patients is variably decreased to about one half of the lifespan in patients with normal renal function. In CKD patients undergoing hemodialysis therapy, results are conflicting. While the improvement of the uremic milieu by renal replacement therapy should increase RBC lifespan, the cell might be destroyed by the hemodialysis procedure.

The ageing of RBCs is characterized by several factors including reduction of the elastic modes of the cell membrane, increased membrane stiffness, reduced surface area and volume, increased intracellular density and viscosity and reduced hemoglobin content.

The aim of this project therefore, is to study the aging processes of RBC and subsequently predict the lifespan of individual RBC and RBC cell populations.



Simulations of a red blood cell in a microchannel.

Selected Publications

Szwaba R, Ochrymiuk T, Lewandowski T, Czerwinska J (2013) Experimental Investigation of the Microscale Effects in Perforated Plate Aerodynamics. ASME J Fluid Eng 135:121104-121114

M'rabet Bensalah K, Uehlinger D, Kalicki R, Czerwinska J (2013) Multiscale Hemodynamic Modeling of the Intrarenal Circulation. Ann Biomed Eng 41(12):2630-2644

Czerwinska J (2013) 12th Swiss Soft Days (SSD 12). Appl. Rheol 23(6):375-376

Guignard J, Behran Terefe M, Uehlinger DE, Czerwinska J (2014) Hemodynamics and Flow Characteristics of a New Dialysis Port. ASAIO 60(1):81-89

Jebauer S, Czerwinska J (2014) Three-dimensional Vortex Structures on Heated Micro-lattice in a Gas. Int J Heat Mass Trans 70:827-834

Cardiovascular Engineering

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Research Profile

The Cardiovascular Engineering (CVE) group comprises expertise in biomedical engineering and clinical research. CVE is dedicated to finding novel solutions for the diagnostic and therapeutic management of cardiovascular diseases by developing new devices, evaluating innovative methods, and improving our understanding of basic biomedical processes. This work is based on a well-established research infrastructure and modern experimental and computational methods for the study of biomedical flow systems. CVE is integrated into the medical technology industry network in Switzerland and worldwide, ensuring a direct path to the realization of our research goals.

Energy Harvesting

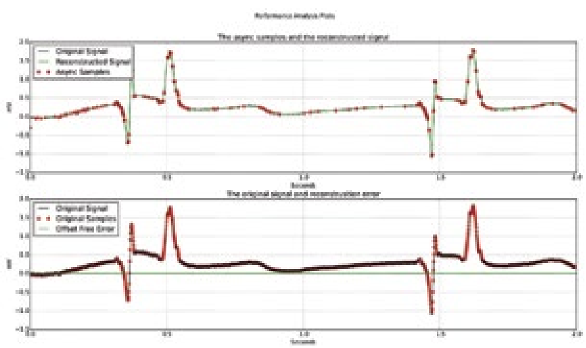
Active implants such as pacemakers, defibrillators, and neurostimulators (e.g. cochlear implants) rely on energy from batteries. Limited endurance imposes periodic device replacement, which leads to repeated interventions. Likewise, device miniaturization is restricted by battery size, motivating the search for harvestable energy sources.

Prototype of generator for energy harvesting.

One option is to collect external light in photovoltaic cells implanted directly under the skin as demonstrated in one of our projects. Another approach is to make use of intracorporeal energy sources, for example the uninterrupted mechanical motions existing in the cardiovascular system. For this purpose, we investigate the harvesting potential from arterial blood flow, vessel wall deformations as well as heart motions. Numerical simulations and bench experiments are employed before testing the in vivo feasibility.

Esophageal Electrocardiogram

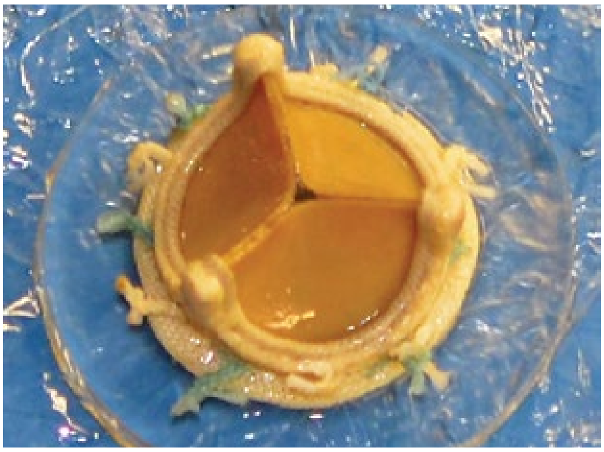
As a result of the aging population, an increasing number of patients suffer from cardiac arrhythmias. This makes long-term and high-quality ECG recording highly desirable. In close collaboration with the Bern University of Applied Sciences and the Inselspital Bern, our group is investigating an innovative esophageal ECG recorder that may improve state-of-the-art diagnostics.
A key challenge of this project is to miniaturize and integrate the recording electronics into an implantable tube. The massive amount of data generated during up to 30 days of recording needs to be compressed before storage.



Segment of esophageal ECG with non-uniform (top) and Nyquist-based sampling (bottom).

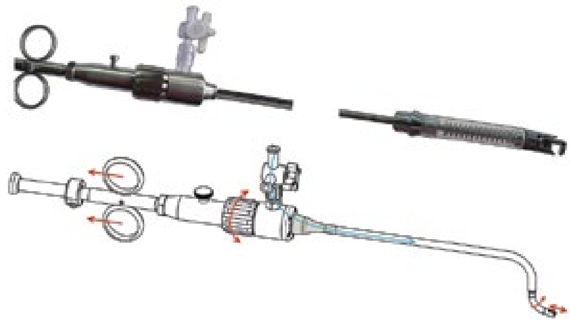
Conventional algorithms fail since they are associated with high computational effort, increasing total power consumption, i.e. the battery size. Nevertheless, the ECG signal is sparse in the time domain. Non-uniform sampling based on signal level crossing makes use of this fact. Although this novel approach does not conform to the Nyquist sampling theorem, full ECG signal reconstruction is possible using much fewer samples than in classical approaches. Memory and battery space requirements can likewise be saved.

Hemodynamics of Bioprosthetic Heart Valves
Numerous designs of aortic heart valve prostheses have been in use for more than half a century. In addition to several other factors (e.g. manufacturability, price, interventional complexity, performance etc.), the longevity of the prostheses is an important design goal, especially in an ageing society where patients want to continue their active lifestyle without the need for re-operation.
A thorough understanding of the hemodynamics of heart valves is indispensable for the design of more durable and better performing heart valves. Therefore, we are in the process of building up an experimental infrastructure for studying the hemodynamics of aortic heart valves. We are using modern optical measurement technology to quantify the complex three-dimensional blood flow interacting with the soft tissue of the bioprostheses. This enables us to qualify and compare different bioprostheses and to explore the effect of various design modifications.



Aortic valve bioprostheses.

Valve Defect Model
In order to study the mechanics of heart valve dysfunction and improve existing repair methods, there is a need to create controlled valve defects at the start of in vivo experiments. Ideally, the disturbance to normal anatomy and physiology is limited to the creation of the valve defect and should therefore be performed in a minimally invasive manner, thereby avoiding traumatic surgery. For this purpose, we have developed a steerable, catheter-based cutting tool that can be inserted via a small incision in the groin. The tool can be guided via large blood vessels into the heart and under echo guidance create the desired valve defect. After withdrawal, the animal model can be used in acute or chronic trials. It will accurately resemble a patient that presents with such a valve dysfunction, and diagnosis via imaging can be performed and the repair method to be studied (either via catheter or surgical) can then be executed under controlled circumstances.



Catheter-based tool for creating heart valve defects.

Selected Publications

Haeberlin A, Shakir S, Vogel R, Tanner H (2013) Fishing for p-waves during wide-complex tachycardia. Cardiovascular Medicine 16(9):250-253

Haeberlin A, Niederhauser T, Marisa T, Goette J, Jacomet M, Mattle D, Roten L, Fuhrer J, Tanner H, Vogel R (2013) The optimal lead insertion depth for esophageal ECG recordings with respect to atrial signal quality. J Electrocardiol 46(2):158-165

Jahren SE, Ochsner G, Shu F, Amacher R, Antaki JF, and Vandenberghe S (2013) Analysis of Pressure Head-Flow Loops of Pulsatile Rotodynamic Blood Pumps. Artif Organs doi:10.1111/aor.12139

Niederhauser T, Haeberlin A, Marisa T, Jungo M, Goette J, Jacomet M, Abächerli R, Vogel R (2013) Electrodes for Long-Term Esophageal Electrocardiography. IEEE Trans Biomed Eng 60(9):2576-84

Pfenniger A, Wickramarathna LN, Vogel R, Koch VM (2013) Design and Realization of an Energy Harvester Using Pulsating Arterial Pressure. Med Eng Phys 35(9):1256-1265

Pfenniger A, Obrist D, Stahel A, Koch VM, Vogel R (2013) Energy Harvesting through Arterial Wall Deformation: Design Considerations for a Magneto-Hydrodynamic Generator. Med Biol Eng Comput 51(7):741-55

Pfenniger A, Jonsson M, Zurbuchen A, Koch VM, Vogel R (2013) Energy harvesting from the cardiovascular system, or how to get a little help from yourself. Ann Biomed Eng 41(11):2248-2263

Pirbodaghi T, Weber A, Axiak S, Carrel T, Vandenberghe S (2013) Asymmetric speed modulation of a rotary blood pump affects ventricular unloading. Eur J Cardiothor Surg 43(2):383-388

Radu MD, Pfenniger A, Räber L, de Marchi SF, Obrist D, Kelbæk H, Windecker S, Serruys PW, Vogel R (2013) Flow disturbances in stent-related coronary evaginations: A computational fluid-dynamic simulation study. EuroIntervention, pii:20121227-03

Diabetes Technology Research

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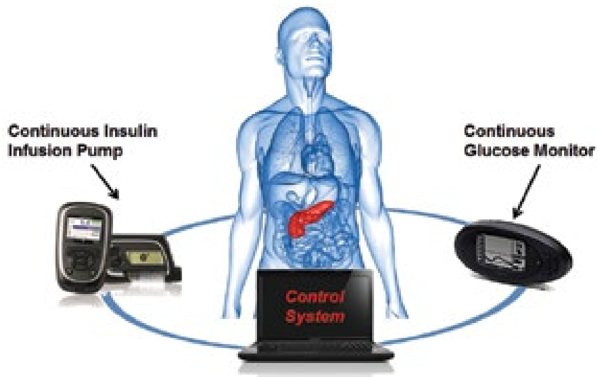
Research Profile
The Diabetes Technology Research Group (DTRG) is a collaborative research group of the ARTORG Research Center for Biomedical Engineering Research and the Department of Endocrinology, Diabetes and Clinical Nutrition at the University Hospital of Bern (Inselspital). The DTRG is a multi-national and multi-disciplinary group of scientists, engineers, clinicians and nutritionists interested in investigating novel approaches for diabetes management.
DTRG is conducting research in artificial intelligence, modeling and control, computer vision and medical informatics towards diagnosis and personalized prevention and treatment of diabetes and related chronic diseases. Backbone of the research activities is the translation of data into knowledge to enhance the diabetes management and personalize the insulin treatment.

Artificial Pancreas
The artificial pancreas is in the forefront of diabetes research since the 1970s aiming at the replacement of the role of the distorted pancreatic beta-cells by external automatic insulin infusion. The components of the artificial pancreas are a Continuous Glucose Monitor (CGM), a continuous insulin infusion pump and a control system for the estimation of optimal insulin treatment.

Reinforcement Learning for Closing the Loop
The aim of the project is to optimize and evaluate both in silico and in a clinical environment an "in house" novel control algorithm for the optimal, personalized estimation of insulin infusion, closing the loop between a CGM and insulin pump. The algorithm is based on reinforcement learning and optimal control and is being proposed for glucose regulation for the first time. The main advantage is the online adaptive ability in order to handle the high inter-/intra- patient variability occurring from the diversions of insulin sensitivity, physical activity and other environmental factors. The initialization of the algorithm is based on clinical information. The current version of the algorithm has been evaluated in silico in adults, adolescents and children showing significant improvement in glucose regulation compared to standard insulin treatment.

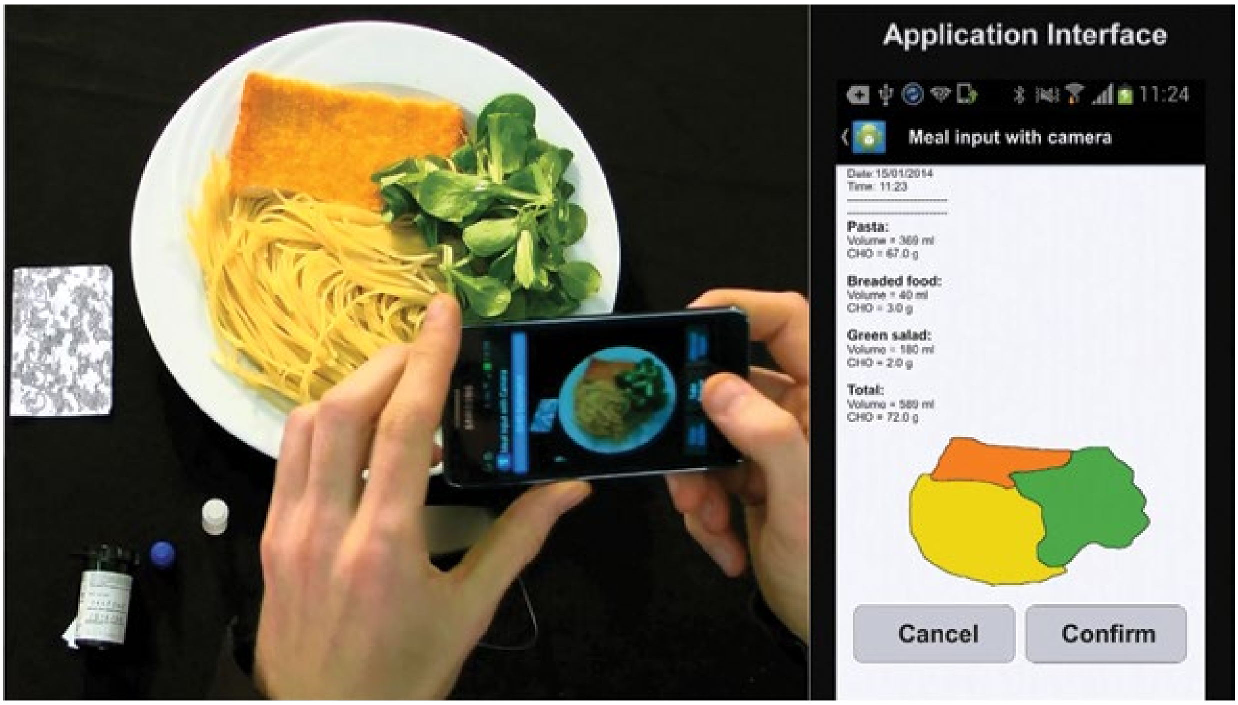
Hypoglycemia Prediction based on Data-Driven Models
Intensive insulin treatment has an inherent risk for undesired metabolic conditions. Data-driven models, based on advanced statistical and computational intelligence methods are developed for the prediction of glucose profile in the near future and the early recognition of upcoming hypo- and hyperglycemic events. The models are personalized and online adaptive in order to capture the inter-/intra- patient variability and enhance the performance and safety of the controller. So far, real time adaptive models based on auto-regression techniques and artificial intelligence methods have been developed and comparatively assessed using both in silico and real patient data. The models have been combined for the development of an early warning system against hypo- and hyperglycemic events. The results have shown that fusion of regression and artificial intelligence based models achieves prompt and accurate prediction with limited daily false alarms.



Components of an external artificial pancreas.

Carbohydrate Estimation based on Computer Vision
For the estimation of the insulin dose, the diabetic patient needs to measure the pre-meal glucose concentration and to accurately count the carbohydrates (CHO) of the anticipated meal. Imprecise counting of CHO can lead to either under- or overdosing of insulin.
The scope of this EU funded project (www.gocarb.eu) is to design, develop and evaluate a computational system which will help individuals with diabetes to automatically estimate in near real-time the grams of CHO in their meal. In a typical use scenario the individual with diabetes acquires a pair of pictures of the upcoming meal through a mobile phone camera with a reference object placed next

to the plate. Initially the dish is automatically detected, by using the edges of the plate's borders, and the different food items are localized and segmented based on local color clustering. Food type recognition follows using both color and texture features. Then, the 3D shape of the plate's content is reconstructed and the actual volume of each segmented item is estimated relying on the size of the reference object. By utilizing the estimated volume along with the recognized type and the available nutritional tables, the system computes the CHO grams of each food item. The final goal of the system is the calculation of the optimum insulin bolus given the meal's CHO content and patient specific data.
For the plate detection, an edge map is created, small edge components are discarded and then the RANSAC paradigm is applied given the ellipse-generating property of single components. The food segmentation is based on an edge preserving filter that clusters pixels relatively close in terms of color and spatial distance while a connected component analysis follows. Then, learned color histogram and Local Binary Pattern features (LBP) are computed and fed to a Support Vector Machine (SVM) that classifies each of the localized food items into one of 12 predefined food classes. For the training and evaluation of the system, two visual datasets with a broad spectrum of central European meals have been created. The first one consists of 175 meals acquired under controlled conditions while the second one contains nearly 4000 food images downloaded from the Web under different shooting conditions. For the food volume estimation, a two-view geometry approach is used. This technique allows getting a shape of an object from a set of images, obtained from different points of view. The data processing includes seven stages and involves a variety of mathematical methods. The main challenges of the 3D reconstruction are the short distances between the camera and the object, and the intense phone camera noise levels. The performances of each module separately are satisfactory considering the challenges of the problem. An average error of 7±6 grams in CHO estimation was achieved. Optimization of recognition and 3D reconstruction are still in progress. In the current implementation the application is partially running on the server side while in the final version the entire system will be integrated into the mobile phone.



The GoCARB prototype application in use. On the right, a screenshot of the application's interface provides the estimated volumes and CHO grams together with the recognition map.

Selected Publications

Anthimopoulos M, Gianola L, Scarnato L, Diem P, Mougiakakou SG (2014) A Food Recognition System for Diabetic Patients Based on an Optimized Bag-of-Features Model. IEEE J Biomed Health Inf doi:10.1109/JBHI.2014.2308928

Daskalaki E, Nørgaard K, Züger T, Prountzou A, Diem P, Mougiakakou S (2013) An Early Warning System for Hypoglycemic / Hyperglycemic Events Based on Fusion of Adaptive Prediction Models. J Diabetes Sci Technol 7(3):689-98

Daskalaki E, Diem P, Mougiakakou SG (2013) Personalized Tuning of a Reinforcement Learning Control Algorithm for Glucose Regulation. Conf Proc IEEE Eng Med Biol Soc 2013:3487-90

Patent

Shevchik S, Dehais J, Anthimopoulos M, Diem P, Mougiakakou SG, Estimation of Food Volume (Patent Application EP 13/003338.4), European Patent Office, 2013

Gerontechnology and Rehabilitation

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Research Profile

The interdisciplinary Gerontechnology and Rehabilitation Research Group is a collaborative research effort of the ARTORG Center for Biomedical Engineering Research, the Department of Old Age Psychiatry, and the Division of Cognitive and Restorative Neurology within the medical faculty at the University of Bern. The technical lead of the group is Tobias Nef. The clinical leads are Urs Mosimann and René Müri.
Gerontechnology is the study of technology and aging to promote good health, social participation, and independent living. Rehabilitation embraces the coordinated use of medical, social, professional, and technical means to improve function to allow independent participation in all areas of life with acceptable risks and good quality of life. The relevance of these fields increases with the aging of our society. In this context, the group develops and evaluates assistive and rehabilitative technologies to support elderly and disabled people to enhance autonomy and promote independent living while reducing the risks associated with daily living. Current projects aim to promote independence by enhancing in-home mobility as well as mobility and traffic-participation outdoors. Furthermore, the group develops new trainings to strengthen cognitive performance.

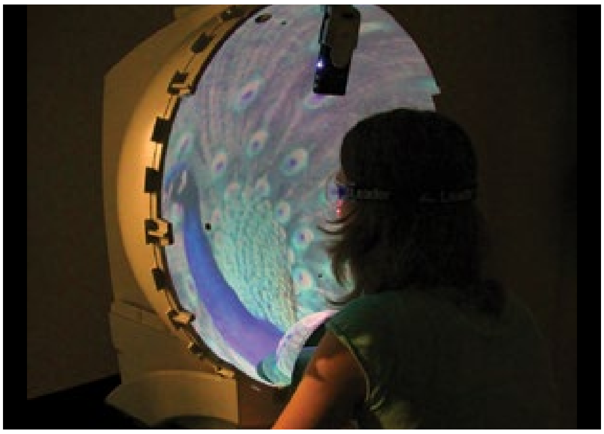
Bern Serious Games

Besides better understanding the influence of cognitive impairments on mobility and traffic participation, we also aim to develop new means to improve and maintain cognitive performance and prevent cognitive decline as long as possible. In collaboration with other European and Swiss researchers, we develop home-based cognitive and physical training based on both innovative gaming platforms (e.g. Wii and Kinect) and specifically developed serious games. Immersive "game-like" environments, also known as Serious Games, where participants use an "in-world" representation, an avatar, to engage in a variety of activities in a shared space, could play a promising role in seniors' lives, as entertainment as well as therapeutic value (McCallum, 2012; Wiemeyer & Kliem, 2012; Tarnanas et al, 2013). The theme of the Serious Games can be adapted, depending on cultural characteristics or according to the cognitive deficits of the user. The fundamental processes of cognitive training are repeating specific procedures and providing personalized guidance to seniors. Providing immediate feedback and adaptive interventions during the training could enhance the performance of the patient; lead to better results, and strengthen further the motivation of the patient to perform better, which has been proven for the real-life transfer of cognitive training and the reduction of the disease's deterioration. To this direction, the goal of this project scope is to develop novel Serious Games, which can improve, maintain, or restore mental functions. We will place a special focus on adaptive difficulty levels, allowing error-free learning that is expected to increase motivation, fun, and self-confidence.

Bern Serious Game simulation of everyday activities for early screening and adaptive cognitive stimulation.

The Age-Dependent Effect of Night Driving on Visual Performance and on Simulated Driving Behavior

Both younger and older drivers are challenged by reduced vision in low-light conditions as they occur during night driving. Contributing factors are age-related increased glare sensitivity and decreased mesopic visual acuity. We assume that the visual exploration behavior under mesopic light conditions is an important predictor of driving performance. In this project, the age-dependent influence of mesopic vision, cognition, and comorbidity are evaluated regarding their influence on visual exploration behavior and on simulated driving performance. In collaboration with the Haag-Streit AG (Köniz, Switzerland) and with the support of the Haag-Streit Foundation, we have developed a screening tool for the Octopus 900 perimeter that will support and enhance "fitness-to-drive" assessments and decisions. The results of 121 healthy test persons of all ages show age-effects in peripheral targets detection and search strategy. Older subjects actively searched for targets whereas younger subjects had a passive search strategy, which outperformed the active strategy. Current work focuses on new tests to measure higher visual functions.



Testing device of the functional visual field test. Chin rest and forehead rest are not shown.

Higher Visual Functions: How to Improve Visual Perception in Patients with Unilateral Brain Lesion

Visual perception can be defined as the integration of a series of cognitive processes, including reception, organization, and assimilation of the visual information sent to the cerebral cortex. The visual information is processed in two streams: a ventral stream for object recognition and a dorsal stream for perception of motion. A lesion in the ventral stream can cause impairment in recognition of visually presented objects (visual agnosias), deficit in reading (alexia). Lesions on the dorsal stream can lead to difficulties in perceiving visual motion (akinetopsia). These higher visual functions are of key importance for daily living activities. However, in patients with hemispheric brain lesions, impaired higher visual functions are not always detected in classical neurological examinations. Therefore, we developed a series of new tests to assess higher visual functions (i.e. visual perception of motion, size, shape, and pattern). In this study, the performances of patients with unilateral brain lesions after stroke or traumatic brain injury, as well as age-matched healthy controls are measured. We plan to use tDCS (transcranial direct current stimulation) to stimulate the impaired region of the brain to enhance the higher visual functions and, therefore, improve the level of performances at the proposed tasks.

Assistive Technology to Enhance Safety and Autonomy of Dementia Patients at Home

Most dementia patients have a strong desire to live autonomously in their known environment as long as possible. With cognitive decline, the ability to cope with activities of daily living (ADL) decreases, which leads to reduced autonomy and increased need for care. In combination with existing (i.e. Spitex) and new (i.e. ambulant old-age psychiatry) clinical and social caregiving approaches, assistive technology can help to improve care. In this project, we develop and evaluate a new assistive technology system that meets the specific needs of elderly patients with cognitive impairment. A key feature of the new system is that it works in the background and does not require active interaction between the system and the supported patient. It measures environmental data (e.g. light distribution, movement patterns) and uses this information to analyze specific behavior pattern to assess the patient's ability to cope with ADL, and to predict short- and long-term risks. After preliminary field tests in the home of healthy volunteers, the system is currently measuring dementia patients. This project is funded in part by the Bangerter-Rhyner Foundation.

An example installation of the new assistive technology system in a two bedroom flat. Environmental data are acquired by sensors distributed in the rooms. The locations of the sensors are indicated with red circles.

Selected Publications

Nef T, Müri R, Bieri R, Jäger M, Bethencourt N, Tarnanas I, Mosimann UP (2013) Can web-based computer tests predict simulated driving performance? A pilot study with healthy and cognitive impaired participants. J Med Internet Res 15(10)

Tarnanas I, Schlee W, Kolassa IT, Müri RM, Mosimann UP, Nef T (2013) Ecological validity of virtual-reality-daily-living-activities screening for early dementia: A longitudinal study. J Med Internet Res 1(2):1-14

Gruber N, Müri R, Mosimann UP, Bieri R, Aeschimann A, Zito GA, Urwyler P, Nyffeler T, Nef T (2014) Effects of age and eccentricity on visual target detection. Front Aging Neurosci 5(101)

Bieri R, Jäger M, Gruber N, Nef T, Müri R, Mosimann UP (2014) A novel computer-test to assess driving-relevant cognitive functions – a pilot study. Int Psychogeriatr 26(2):229-38

Urwyler P, Nef T, Killen A, Collerton D, Thomas A, Burn D, McKeith I, Mosimann UP (2013) Visual complaints and visual hallucinations in Parkinson's Disease. Parkinsonism Relat Disord pii:S1353-8020(13)00445-8

Nef T, Riener R, Müri R, Mosimann UP (2013) Comfort of two shoulder actuation mechanisms for arm therapy exoskeletons: a comparative study in healthy subjects. Med Biol Eng Comput 51(7):781-9

Image Guided Therapy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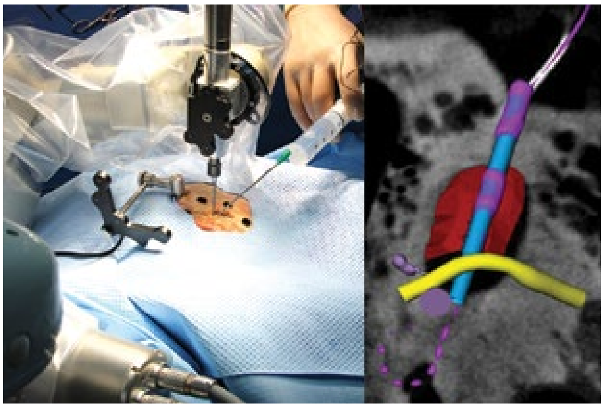
Research Profile

The Chair for Image Guided Therapy focuses on clinically related translational research in the broad area of stereotactic surgery. Research activities aim to provide novel technological solutions for diagnostic and therapeutic activities that augment the surgeon's abilities, facilitate improved surgical accuracy, reduce invasiveness, and improve clinical outcomes. Strong collaborative partnerships with clinicians at the University Hospital Bern and throughout Europe aid in the development of clinically applicable and clinically validated solutions. In order to push the boundaries of surgical image guidance, research into novel techniques in image processing, stereotactic instrument guidance, surgical robotics, and rapid prototyping is conducted.

Minimally Invasive Cochlear Implantation

Cochlear implantation, for the treatment of moderate to severe hearing loss, requires access to the inner ear for electrode insertion into the cochlea. Access is conventionally gained via a mastoidectomy in which large amounts of bone tissue are removed to enable visualization and thus, preservation of close-lying critical anatomy such as the facial nerve. The replacement of the invasive mastoidectomy with a minimally invasive tunnel requires image-guided tool positioning accuracies approximately 10 times better than is currently achievable with stereotactic image-guided surgical systems (approximately 0.2 mm) and unprecedented intraoperative safety validation techniques. Through the development of a dedicated image-guided robotic system and a high-accuracy patient-to-image registration technique, accuracies on cadaveric heads of 0.14 ± 0.08 mm have been achieved. Toward clinical trial, additional safety methods to ensure facial nerve preservation, including intraoperative registration error detection, highly specific and sensitive facial nerve monitoring, and force-density correlation tool-positioning calculations are currently being investigated.



The high accuracy image-guided robotic system for realization of a minimally invasive cochlear implantation procedure.

Stereotactic Interventional Procedures on the Liver

Minimally invasive treatment options for liver metastases such as percutaneous radiofrequency and microwave ablation are more commonly being employed with curative intent. The techniques allow small tumors to be destroyed with minimal damage to healthy liver tissue without the risks associated with open-liver surgery. The success of these procedures is, however, highly dependent on the accurate positioning of ablation needles. Conventionally, needles are positioned using repetitive acquisitions of intraoperative CT images. The development of stereotactic instrument guidance for percutaneous interventions enables accurate, time-efficient, and reproducible placement of ablation needles with considerably less radiation exposure. Within this research project, a dedicated system for percutaneous interventions is being developed in collaboration with various national and international clinical partners. Promising results have led to the transfer of the technology into other surgical domains, such as stereotactic interventions on the spine.

Stereotactic guidance for percutaneous interventions enables needles to be accurately positioned without the need for repetitive CT scans.

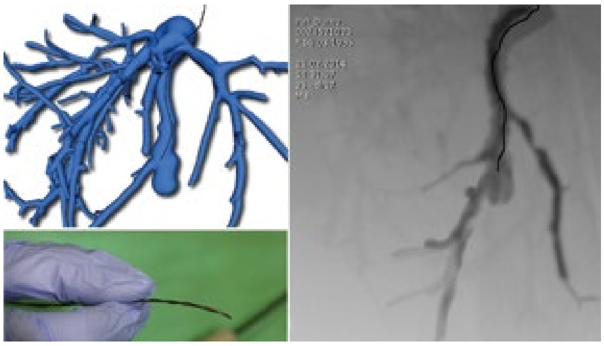
Ultrasound-Based Registration for Liver Surgery

The success of stereotactic guidance for liver surgery relies on the achievement of a sufficiently accurate patient-to-image registration on the deformable and mobile organ. Within this project, a clinically applicable solution for ultrasound-based registration in liver surgery has been successfully developed and integrated into the CAS-One Liver system (CAScination AG). The technology has been used across Europe, enabling treatment of patients with advanced liver disease, such as multi-lobar liver metastases. The project was awarded the CTI Swiss Medtech award in 2013 and adaptation of the registration approach for the facilitation of image guided laparoscopic interventions is currently being investigated.

Vascular Image-Guidance to Aid Endovascular Treatments

Minimally invasive endovascular therapy has become the treatment of choice for various vascular diseases such as arterio-venous malformation (AVM) and portal hypertension. The interventional procedure, is however, time consuming, and safe delivery of toxic sclerosants like ethanol or the placement of shunts mandate exact positioning of catheters. Sufficient accuracy in the detection, visualization, and targeting of specific vessel structures is imperative for accurate catheter placement and successful treatment. To aid such procedures, visual guidance of the catheter tip relative to pre-interventional 3D anatomical information, is envisioned. To this end, techniques for 3D vascular anatomy visualization, electromagnetic catheter tracking, and stereotactic guidance based on intraoperative fluoroscopy images are being developed.

An ultrasound-based registration algorithm has enabled more accurate stereotactic surgical procedures on the liver.



Stereotactic image-guided catheter placement based on fluoroscopic images for the treatment of endovascular to diseases.

Selected Publications

Bell B, Gerber N, Williamson T, Gavaghan K, Wimmer W, Caversaccio M, Weber S (2013) In Vitro Accuracy Evaluation of Image-Guided Robot System for Direct Cochlear Access. Otol Neurotol 34(7):1284-90

Buchs NC, Volonte F, Pugin F, Toso C, Fusaglia M, Gavaghan K, Majno PE, Peterhans M, Weber S, Morel P (2013) Augmented environments for the targeting of hepatic lesions during image-guided robotic liver surgery. J Surg Res 184(2):825-31

Gerber N, Gavaghan K, Bell B, Williamson T, Weisstanner C, Caversaccio M, Weber S (2013) High Accuracy Patient-to-Image Registration for the Facilitation of Image Guided Robotic Microsurgery on the Head. IEEE Trans Biomed Eng 60(4):960-8

Toporek G, Wallach D, Weber S, Bale R, Widmann G (2013) Cone-beam computed tomography-guided stereotactic liver punctures: a phantom study. Cardiovasc Intervent Radiol 36(6):1629-37

Wallach D, Toporek G, Weber S, Bale R, Widmann G (2014) Comparison of free-hand navigated and aiming device navigated targeting of liver lesions. Int J Med Robot 10(1):35-43

Widmann G, Wallach D, Weber S, Bale R (2013) Angiographic C-arm CT vs. MDCT guided stereotactic punctures of liver lesions: a non-rigid phantom study. AJR Am J Roentgenol 201(5):1136-40

Williamson T, Bell B, Gerber N, Salas L, Zysset P, Caversaccio M, Weber S (2013) Estimation of tool pose based on force-density correlation during robotic drilling. IEEE Trans Biomed Eng 60(4): 969-76

Lung Regeneration Technologies

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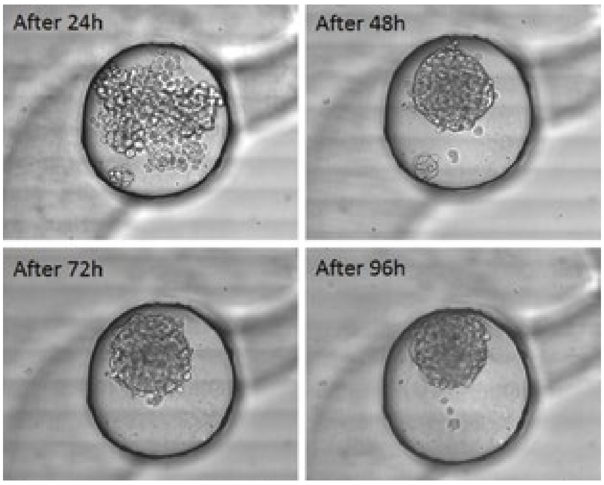
Research Profile

The Lung Regeneration Technologies Group focuses on the development of advanced in-vitro models of the lung able to recreate the cellular microenvironment of the respiratory tract. In sharp contrast to standard in-vitro models in which cells are cultured in static conditions on a hard surface, these novel systems aim at reproducing the complexity of the alveolar-capillary barrier, the gas exchanges, and the mechanical stimulation of the respiratory movements. To achieve these objectives, interdisciplinary research is performed at the interface of cell biology, lung mechanics, microtechnology, and microfluidics. Tiny microchannels and microwells with length scales that are comparable to the intrinsic dimensions of mammalian cells, can be microstructured by soft lithography and other techniques. Such microfluidic devices have the capability to accurately control the cell microenvironment.

For the future, such bioartificial lung-on-chip systems are deemed to be extremely important for the investigation of the pathophysiology of different lung diseases and the understanding of fundamental cellular or molecular mechanisms that take place in the lung. They are also intended to be implemented for personalised medicine, a new paradigm in which the treatment efficiency can be tested on such a platform with the patient's own cells in order to individualize and optimize the therapy.

Perfused Spheroids in a Microfluidic Platform

A chemoresistive microfluidic platform aimed at testing cellular aggregates of malignant pleural mesothelioma (MPM) was developed. MPM is an aggressive tumour with poor prognosis for which no treatments exist to date. The three-dimensional structure of the MPM aggregates, called spheroids, better mimic the in-vivo architecture of the tumour than two-dimensional cell cultures. On the microfluidic platform, eight MPM spheroids were trapped and continuously perfused either with cell culture medium or Cisplatin, one of the standard chemotherapeutic drugs used to treat MPM. A new method to detect the spheroid viability in function of the exposed concentration of Cisplatin was developed. This approach is based on the evaluation of the caspase activity in the supernatant sampled from the chip and tested using a microplate reader. This simple and time-saving method only requires a minimum amount of manipulations and is suited for very low numbers of cells. This feature is particularly important in view of personalised medicine applications for which the number of cells obtained from the patients is low. The 50-percent growth inhibitory concentration of perfused MPM spheroids exposed to Cisplatin was found to be twice as high as in spheroids cultured under static conditions. This chemoresistance increase might be due to the continuous support of nutrients and oxygen to the perfused spheroids. In a recent project, spheroids were formed directly on the microfluidic chip from individual cells aggregating at the bottom of microwells.

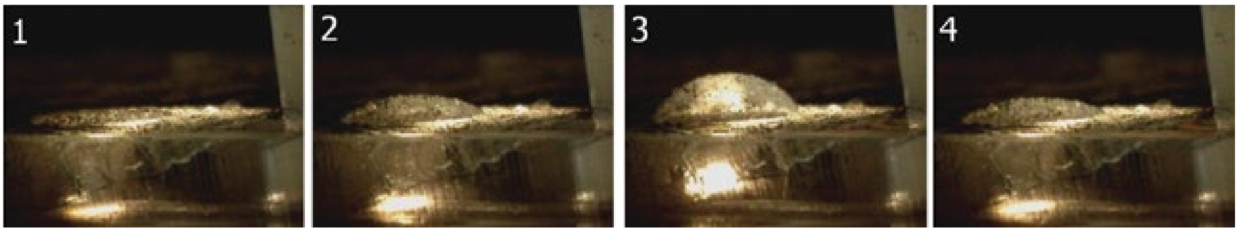


Formation of a malignant pleural mesothelioma spheroid in a 500µm diameter microwell at four different time points. The cells are continuously perfused with cell culture medium or exposed to a chemotherapeutic drug.

Breathing Lung-on-Chip

The complexity of the lung can be illustrated by its delicate tree-like architecture that ends with the alveolar sacs, where the gas exchanges take place. Oxygen and carbon dioxide diffuses through an extremely thin alveolar barrier, whose thickness is only about 0.2 to 1µm. This barrier is mainly constituted by alveolar epithelial cells, capillary endothelial cells, and of the basement membrane. The alveolar epithelium is in contact with air, while endothelial cells that formed the small vascular capillaries are in contact with blood. This whole environment is subjected to a cyclic, mechanical constraint induced by the respiratory movements. A healthy lung at rest is typically stretched by about 12 percent for a respiratory rate of 10-12 breaths per minute, while a ventilated lung is stretched up to 30 percent, often leading to acute lung injuries.

In sharp contrast to standard cell culture techniques,

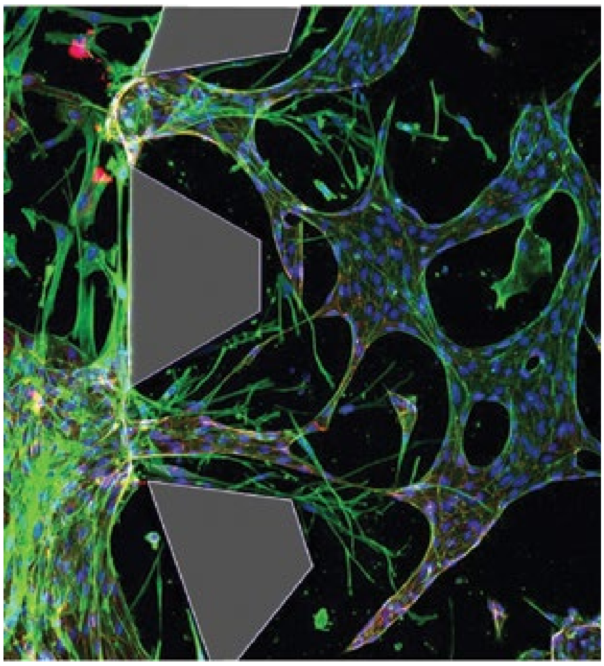


Video sequences of the cyclic (1-2-3-4-1…) stretching of a thin PDMS membrane mimicking the respiratory movements. Lung epithelial cells are cultured on such a membrane and cyclically stretched.

which poorly reproduce the complexity of the lung air-blood interface, a lung-on-chip is being developed that reproduces the thin alveolar barrier and the cyclic mechanical stress induced by the respiratory movements. Thin, flexible, and porous membranes are developed based on microfabrication technologies and integrated in a microfluidic chip. Lung epithelial cells, 16-HBE as well as A549 cells, are cultured to confluence on such a membrane and cyclically stretched (10 percent linear, 0.2Hz) for 48h. Preliminary results suggest that stretched cells express typical epithelial cells tight junctions' proteins.

Perfusable Endothelial Microcapillaries

Endothelial cells, in particular endothelial microvascular cells present in the lung parenchyma, play an important role in inflammation and the initiation of fibrogenic events in lung pathologies, such as in idiopathic pulmonary fibrosis. Nevertheless, the clear mechanism on how and if the two mechanisms are related is still unknown and requires novel models allowing to reproduce the microvasculature of the lung to investigate those mechanisms. As an example, in pulmonary fibrosis, alveolar epithelial type II cells proliferate at an abnormal rate, fibroblasts accumulate and excessively secrete extracellular matrix constituents, and microvasculature remodelling takes place. These changes lead to the disruption of normal alveolar architecture and consequently to the loss of function of the alveolar-capillary units. Such local changes cause less efficient oxygen uptake and thus shortness of breath, scarring, and, in some cases, pulmonary hypertension. In order to model the microvasculature of the lung, a new platform aiming at the creation of perfusable microvasculature that mimics the lung capillary microenvironment is currently under development. Preliminary results show the creation of perfusable microvascular networks formed in this platform within seven days. Immunostaining of endothelial and pericytes confirmed cell-cell junctions and cell alignment in vascular structures. The endothelial vessels are impermeable to 70kDa RITC-labeled dextrane. Microspheres (1 um) entered from the flow channels into the vessels, confirming patent and perfusable vessels.



Immunostaining of perfusable microvessels with endothelial cells and lung pericytes after seven days in culture in a fibrin matrix confined on a microfluidic platform. 200µm large microstructures are depicted in grey.

Selected Publications

Das T, Meunier L, Barbe L, Guenat O, Gervais T, Mes-Masson AM (2013) Empirical Chemosensitivity Testing in a Spheroid Model of Ovarian Cancer using a Microfluidics-based Multiplex Platform, Biomicrofluidics. Biomicrofluidics 7(1):011805

Ruppen J, Cortes-Dericks L, Marconi E, Karoubi G, Schmid RA, Peng R, Marti TM, Guenat OT (2014) Microfluidic platform for chemoresistive testing of multicellular pleural cancer spheroids. Lab Chip 14:1198-1205

Patent

Guenat O, Felder M, Stucki A, Stucki J, Geiser Th, EP13183063, Device for In-Vitro Modelling In-Vivo Tissues of Organs (2013)

Ophthalmic Technology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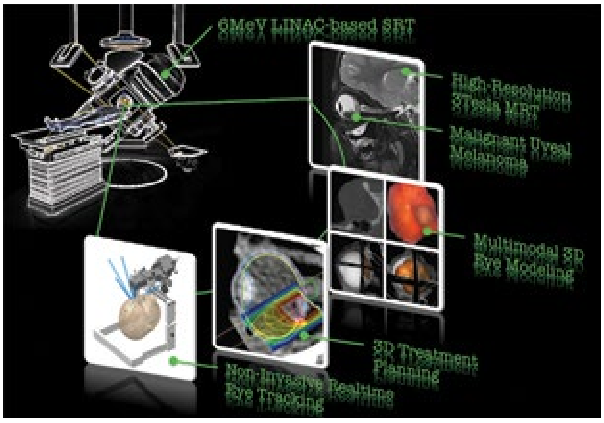
Research Profile

The Ophthalmic Technology Group is dedicated to the development of innovative diagnostic and therapeutic instruments and techniques in the area of ophthalmology. The novel engineering solutions should allow for increased treatment precision, while at the same time diminish the risks for patients and reduce the costs of the intervention. We are focused on projects that are clinically relevant and are committed to advancing project developments to a state from which potential clinical benefit can be assessed. The successful combination of applied research and development on one side and clinical implementation on the other represents the main challenge of our group. The Ophthalmic Technology Group consists of a multi-disciplinary team of engineers and clinicians. Our core competencies are in mechatronic systems design, signal processing, computer-vision, and computer-graphics. The ophthalmic technology group has strong ties to the Ophthalmology Department and the Radio Oncology of the Inselspital but also research collaborations to other institutions nationally and internationally.

External Beam Radiotherapy of Intraocular Tumor

A challenging topic in ophthalmology is the treatment of intra-ocular tumors with radiation therapy. Exact tumor shape delineation during the planning process and accurate execution of the treatment plan are vital for successful treatment outcome. External Beam Radiotherapy (EBRT), by nature, is a non-invasive treatment. However, currently there are no appropriate tracking systems available that facilitate non-invasive tracking of the tumor during the treatment. This project will help bring back the noninvasiveness of EBRT to tumor treatment in the eye. We are developing a planning system that allows the fusion of different image modalities (CT, MRI, Fundus-Photography) into one patient-specific eye model enabling us to assess tumor shape as imaged in the different modalities but in the same planning context. To guarantee optimal plan execution, we are developing a contact-free, OCT-based, tracking system to track the motion of the eye during the treatment. Tracking the anterior segments of the eye and knowing, thanks to the patient-specific eye model, the spatial relation between anterior eye structures and the posterior tumor will provide a very accurate tumor tracking.

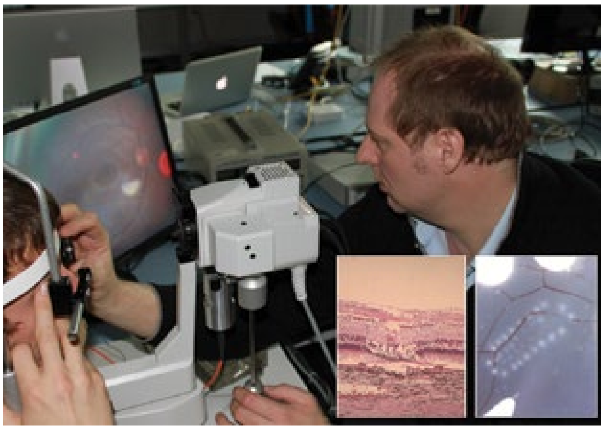


Setup of the computer-assisted photon beam therapy project, showing the LINAC therapy device and the individual parts of the planning and the treatment execution procedure.

Computer-Assisted Selective Retina Therapy

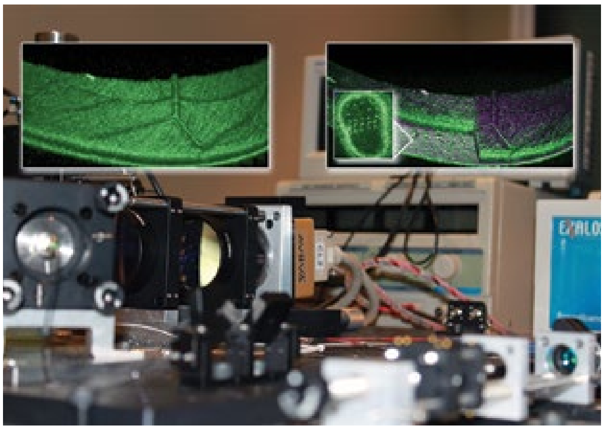
Laser photocoagulation of the retina has become an established treatment modality for many diseases, some of which have an enormous social and economic impact. The greatest limitation of conventional laser therapy is the irreversible collateral damage it causes to adjacent retinal structures such as the photoreceptor layer. With the development of the new selective retina therapy (SRT), a treatment is available that selectively destroys the retinal pigment epithelium (RPE). The RPE layer regenerates after a few days, a normal metabolism of the retina will be re-established and consequently the cause of many retinal diseases vanishes. Although highly beneficial to the patient, SRT is challenging to apply because lesions (at an optimal SRT level) are invisible. Additionally, typical laser setups using a manually steered laser slit lamp are

technically very demanding for the ophthalmologist.
To overcome these problems, we are working on a computer-assisted laser navigation system that can place laser lesions automatically. It will improve accuracy, execution time, and patient safety considerably.



Treatment setup for SRT Laser system. Treatment delivery device is shown in the middle. The operator is on the right and the patient on the left side. Lesion histology and ophthalmological representation of the laser lesions are displayed on the bottom right.

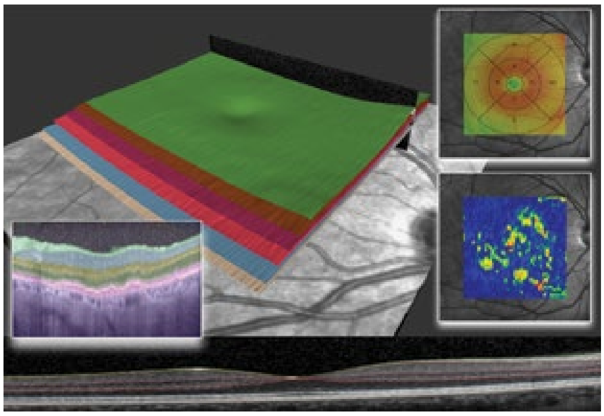
The deposition of the correct amount of laser energy for each lesion is crucial for an optimal treatment result. Therefore, we are developing a new dosimetry control for SRT using OCT. With OCT imaging, a map of the optical properties of the retinal layers is recorded and a 3D tomogram of the area under investigation is provided. Changes in reflectivity or the distortion of sample layers can thus be detected, making OCT a promising modality



Spectrometer hardware for dosimetry control together with two images showing a 3D rendering of an OCT slice stack. On the left, the original slice stack and on the right, the same slice with a segmented RPE layer and the lesions placed.

for SRT dosimetry control. OCT is completely non-invasive and operating in the near-infrared range. With OCT, it is expected that during SRT, the progress of bubble formation and cell destruction can be monitored in real-time.
A high-resolution OCT system was designed, realized, and tested, and preliminary results of ex-vivo experiments proved the ability of OCT to detect the laser lesions after the treatment. In future steps, the therapy and monitoring system will be combined to enable a real-time monitoring of the treatment including an automated detection and thresholding of the therapy laser spots as well as the option for a long-term therapy progress analysis using the same OCT system.

Automatic Quantitative Evaluation of OCT Datasets
Optical Coherence Tomography (OCT) is an interferometry based, non-invasive image modality. It is used in ophthalmology to image the retinal cell layers for diagnostic purposes, research into disease progression as well as clinical trials. To facilitate quantitative evaluation of OCT datasets, automatic methods have to be employed.
We are developing algorithms capable of automatically segmenting volumetric OCT datasets with accuracy in the order of the inter-observer variability. The methods can segment healthy eyes as well as pathologic degenerations in patient eyes with Age-related Macular Degeneration (AMD). This enables us to deploy the algorithms e.g. in AMD studies.



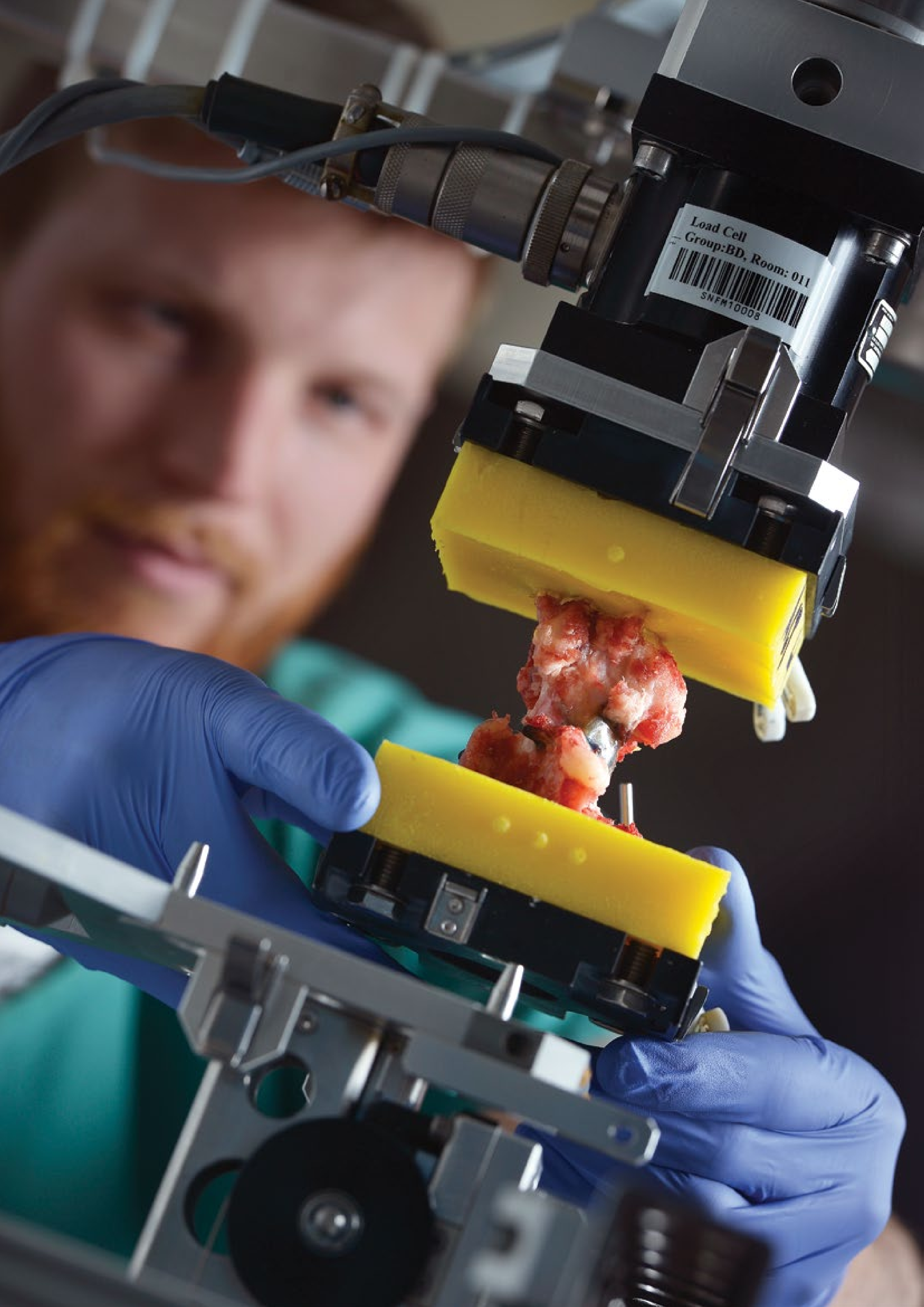
OCT segmentations of the retina from both healthy eyes (in the background) and AMD patient in lower left corner. Thickness maps of the retina are shown on the right.

To facilitate automatic OCT data processing in large-scale studies, it is indispensable to automatically assess the image quality of individual OCT data. We are working on algorithms to allow unsupervised quality control of OCT data.

Selected Publications

Abegg M, Dysli M, Wolf S, Kowal J, Dufour P, Zinkernagel M (2013) Microcystic Macular Edema : Retrograde Maculopathy Caused by Optic Neuropathy. Ophthalmology 121(1):142–149

Dysli C, Quellec G, Abegg M, Menke M, Wolf-Schnurrbusch U, Kowal J, Katayama Y, Leichtle A, Wolf S, Zinkernagel MS (2014) Quantitative analysis of fluorescence lifetime measurements of the macula using the fluorescence lifetime imaging ophthalmoscope (FLIO) in healthy subjects. Invest Ophthalmol Vis Sci 55(4):2106-13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INSTITUTE FOR SURGICAL TECHNOLOGY AND BIOMECHANICS

The Institute for Surgical Technology and Biomechanics (ISTB) was established in 2003 as part of the former Maurice E. Müller Institute for Biomechanics. The institute stands in the tradition of Maurice E. Müller, the former chairman of the Department of Orthopedics at the University of Bern. As one of the pioneers of modern orthopedic surgery, Maurice Müller is known not only for his many innovations related to devices and instruments for joint replacement and fracture treatment, but also for his vision that only a close collaboration between surgeons, scientists, engineers, and industrialists will allow sustainable progress in the field.

To date the ISTB hosts five research groups in various fields of basic and applied research for the prevention, diagnosis and treatment of disease, working from the cell level to organ systems:

- Musculoskeletal Biomechanics
- Computational Bioengineering
- Tissue and Organ Mechanobiology
- Medical Image Analysis
- Information Processing in Medical Interventions

The mission of the multidisciplinary team of the ISTB is to advance human understanding, health, and quality of life. The focus is on developing solutions that address particular clinical problems or unmet clinical needs. It supports this effort through internationally recognized research, discovery, and invention in the area of biomedical engineering, translation of research results from the lab to the clinic to improve patient care, transfer of scientific discoveries and biomedical technology through national and international industrial collaborations and a world class post-graduate biomedical engineering education program.

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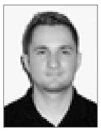
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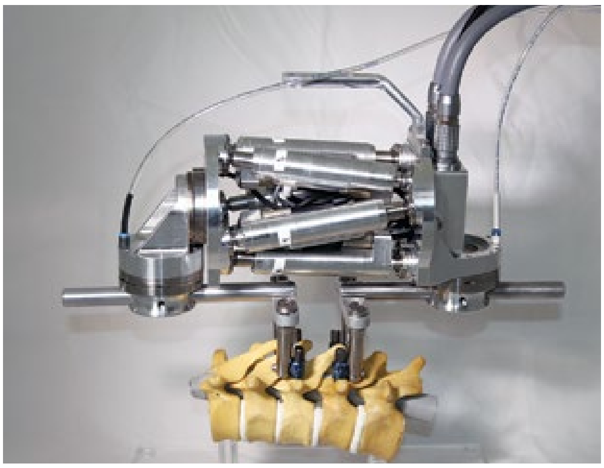
Research Profile

The Computational Bioengineering Group tackles challenges in basic and applied medical research with modern computational simulation tools. Rather than focusing on the computational methods themselves, we are concerned with their appropriate application for the resolution of practical and fundamental clinical questions. Numerical methods are combined with experimental and clinical research in order to improve the quality and extend the validity of our models.
Together with our collaborators, we constitute a strong team covering a wide spectrum of research topics ranging from direct support of surgical patient treatment to basic bone properties. Besides our core expertise in applying finite element analysis to study skeletal biomechanics, we are seeking to improve planning of computer aided interventions by developing and applying refined numerical techniques into the field of computer aided surgery. Another important research focus of the group is the development of novel statistical finite element methods for the incorporation of uncertainty in bone shape and mechanical properties into the evaluation of bone biomechanics.

Biomechanics of the Scoliotic Spine

Non-fusion operative methods for the treatment of degenerative spinal diseases have tremendous potential to increase patient quality of life. In addition to the fact that motion is preserved or restored, a natural load transfer to the adjacent segments is sustained. This is important, as clinical experience shows that fusion of motion segments frequently entails adjacent level degeneration. However, non-fusion implants are challenging, particularly for the treatment of spinal deformities, in which several segments are commonly affected. A better understanding of the mechanical properties of healthy and pathological motion segments is essential.
A parallel kinematic robot – the SpineBot – has been developed to accurately measure the three-dimensional segmental stiffness of a patient's spine in-vivo. SpineBot transmits load to individual vertebra using pedicle screws implanted as part of the corrective procedure. The six DoFs of the robot allow an arbitrary motion to be applied to adjacent vertebrae and an integrated force-torque sensor measures the corresponding mechanical response. The small, compact, and lightweight parallel kinematic construction enables the device to apply moments of over 4 Nm to a FSU with a ±10° range of motion. The SpineBot will be used to quantify the stiffness at different levels of the spine of scoliosis patients as well as to compare stiffness of lumbar spinal stenosis patients before and after decompression surgery.
Numerical models of the scoliotic spine have also been developed for the design of motion preserving non-fusion treatment to correct spinal deformities. These models are unique because they consider patient-specific geometry and mechanical properties derived from intraoperative measurements. The finite element model has been used to design a new dynamic spinal anchoring system to complement a novel growing implant. In addition, these numerical simulation tools enable the optimization of the surgical procedure on a patient-specific basis



A robotic system was developed to measure the spinal mechanical properties intra-operatively.

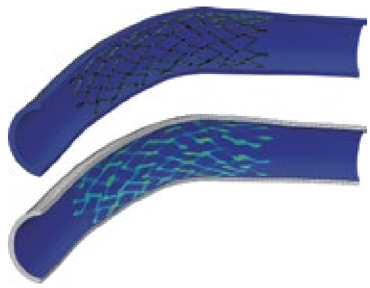
Superficial Femoral Artery

Endovascular therapy is currently considered the primary treatment modality for many patients with peripheral artery disease (PAD). Although the introduction of novel nitinol stents decreases restenosis rates compared to plain balloon angioplasty, restenosis still remains a significant problem in the peripheral arteries. In- stent restenosis, which occurs in up to 30% of the patients subsequent to bare nitinol stent placement, was reported to be associated with stent fractures and arterial wall damage. Stent failures are clearly related to the bending, torsion, and axial motion forces exerted on the femoropopliteal segment during hip and knee flexion.
To understand the causes of restenosis and to improve stent designs, an accurate characterization of this mechanical environment is necessary. Therefore, we quantified the in vivo deformations of the popliteal artery during leg flexion in subjects with clinically relevant peripheral artery disease. Rotational angiography has been used to acquire the three-dimensional arterial anatomy with the leg straight and with a flexion of 70°/20° in the knee/hip joints. Results showed that the popliteal artery of patients with symptomatic PAD is exposed to significant deformations during flexion of the knee joint. The severity of calcification directly affects arterial curvature, but not axial strain or twisting angles. These clinical observations are complemented with finite element simulations to evaluate stenting procedures.

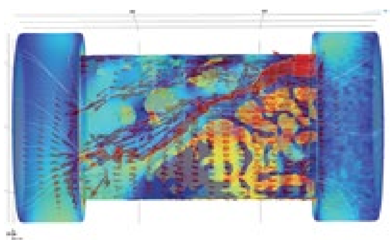
Bone Electric Conductivity

Minimally invasive cochlear implantation surgery has been proposed to replace conventional mastoidectomy for the placements of chochlear implant. To achieve this aim, a microsurgical robotic system is being developed by the group for image guided therapy of the ARTORG Centre. This system is designed to precisely drill a small tunnel through the temporal bone. However, due to the small distance between the tunnel and the facial nerve (FN) (0.3 – 0.5mm), an important challenge of this technique is the preservation of the facial nerve during the drilling procedure. Neuromonitoring is a technique widely used in surgery to locate and assess nerve function. An electrical stimulus is injected into the tissue surrounding the nerve, and electromyography is used to detect action potential elicited muscle responses. In the case of minimally invasive surgery, this technique can be used intra-operatively to monitor the distance between drill bit and the facial nerve. To detect critical distance to the FN, an electrical stimulation is sent through the drill. However, past experiments showed that it is difficult to give accurate distance predictions only based on the electric signal. For this reason, patient-specific parameters and modelling should be included to quantify the distance to the nerve. An experimental test bench has been produced to quantify the bone electric properties. The initial numerical simulations indicated that the porous network filled of marrow is mainly responsible for the flow of electric current in the tissue.

Patient-specific numerical models of the scoliotic spine have been used for the design of a motion preserving implant.



Finite element simulation of the deployment of a stent in the peripheral artery reconstructed from patients' images.



Flow of the electric current inside a bone sample.

Selected Publications

Studer HP, Riedwyl H, Amstutz CA, Hanson JVM, Büchler P (2013) Patient-specific finite-element simulation of the human cornea: A clinical validation study on cataract surgery. J Biomech 46(4):751–758

Elsheikh A, Whitford C, Hamarashid R, Kassem W, Joda A, Büchler P (2013) Stress free configuration of the human eye. Med Eng Phys 35(2):211–6

Bauer S, Lu H, May CP, Nolte L, Büchler P, Reyes M (2013) Integrated Segmentation of Brain Tumor Images For Radiotherapy and Neurosurgery. Int J Imaging Syst Technol 23(1):59–63

Gökgöl C, Diehm N, Kara L, Büchler P (2013) Quantification of Popliteal Artery Deformation During Leg Flexion in Subjects With Peripheral Artery Disease: A Pilot Study. J Endovasc Ther 20(6):828–835

Kistler M, Bonaretti S, Pfahrer M, Niklaus R, Büchler P (2013) The Virtual Skeleton Database: An Open Access Repository for Biomedical Research and Collaboration. J Med Internet Res 15(11):e245

Information Processing in Medical Interventions

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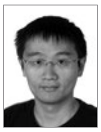
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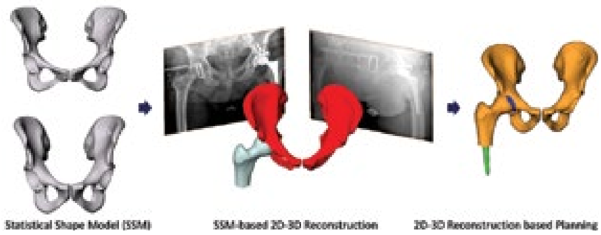
Research Profile

A large and growing family of medical interventions involve the processing of information in different stages of the intervention such as pre-operative planning, intra-operative treatment and post-operative control. Examples include the derivation of patient-specific anatomical models from pre-operative medical images, the calibration of intra-operative imaging devices and surgical instruments, the registration of medical images to patient physical space, and the measurement of treatment results from post-operative medical images. The Information Processing in Medical Interventions (IPMI) Group focuses on the development of smart information processing methods and enabling technologies to solve challenging problems in clinical routine medical interventions. In 2013 we continued our pursuit of novel information processing methodologies/systems for various applications. These include an X-ray radiography based true 3D planning and evaluation system called "iJoint" for total hip arthroplasty (THA), an X-ray radiography based true 3D planning and evaluation system called "iLeg" for lower extremity interventions, a fully automatic 2D and 3D segmentation method, and a comprehensive planning and navigation system for hip preservation surgeries.

iJoint: X-ray radiograph based true 3D planning and evaluation system for Total Hip Arthroplasty

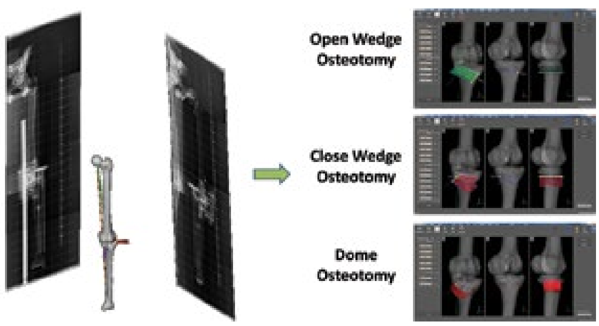
THA is considered a successful, safe and cost-effective medical intervention to restore functionality of the hip joint and to regain pain-free mobility in patients suffering from severe joint disease. Each year, about one million patients worldwide undergo THA surgery. Supported by the Commission for Technology and Innovation (CTI), we are aiming to develop an innovative framework for advancing modern total hip arthroplasty called "iJoint". Key techniques developed within this project include: a mobile and easy-to-use calibration phantom (European Patent Application No. EP2660776A1), a unique statistical shape model (SSM) based 2D-3D reconstruction method that can derive patient-specific 3D models of a hip joint from only 2D X-ray radiographs, a comprehensive planning module that supports both 2D and 3D THA planning, and a 2D-3D reconstruction based post-operative evaluation module.



2D/3D reconstruction based true 3D planning of THA surgery.

iLeg: X-ray Radiograph Based True 3D Planning and Evaluation System for Lower Extremity Interventions

Supported by the Swiss National Science Foundation (SNSF), in this project we have developed a system called "iLeg" that allows the reconstruction of patient-specific 3D models of the complete lower extremity in a weight-bearing situation from clinically available X-rays for true 3D planning and evaluation of surgical interventions of the lower extremity. Supported interventions include lower extremity osteotomy and total knee arthroplasty (TKA).



Patient-specific 3D model reconstruction and their application in planning different types of lower extremity osteotomies.

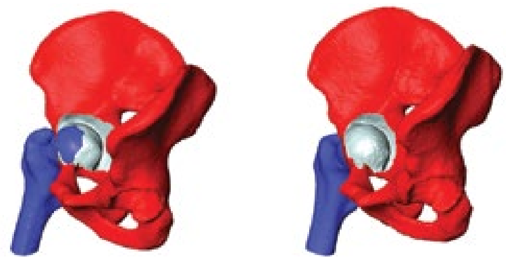
A landmark Detection Based, Fully Automatic 2D and 3D Segmentation Method

We have developed a novel method for fully-automatic landmark detection and shape segmentation in 2D X-ray and 3D CT images. To detect landmarks, we estimate the displacements from randomly sampled image patches to the (unknown) landmark positions, and then integrate these predictions via a voting scheme. Our key contribution is a new algorithm for estimating these displacements. Different from other methods in which each image patch independently predicts its displacement, we jointly estimate the displacements from all patches together in a data driven way, by considering not only the training data but also geometric constraints on the test image. Comprehensive experiments conducted on 2D X-ray images and 3D CT data demonstrated the efficacy of the developed method.

2D (top) and 3D (bottom) segmentation results obtained with our landmark detection based, fully automatic 2D and 3D segmentation method.

Articulated Statistical Shape Model-Based 2D-3D Reconstruction of a Hip Joint

Existing 2D-3D reconstruction techniques usually reconstruct a patient-specific model of a single anatomical structure without considering the relationship to its neighboring structures. Thus, when applied to the reconstruction of patient-specific hip joint models, the reconstructed models may penetrate each other and hence may not represent a true hip joint of the patient. To address this problem, we have developed a novel 2D-3D reconstruction framework using an articulated statistical shape model (aSSM). Our novel method has the advantage of preserving the hip joint structure and no model penetration can be found.



Comparison of the result obtained from an existing 2D-3D reconstruction method and that from our articulated statistical shape model-based 2D-3D reconstruction.

A Comprehensive Planning and Navigation Toolkit for Hip Preservation Surgeries

Hip preservation surgeries such as periacetabular osteotomy (PAO) and femoroacetabular impingement (FAI) treatment are efficient treatment options for younger patients with debilitating hip pain and dysfunction. However, these procedures are technically demanding and require detailed 3D information for diagnosis and intervention. To address this challenge, we have developed a comprehensive planning and navigation toolkit for hip preservation surgeries. Our comprehensive toolkit supports planning and navigation of both PAO and FAI treatment.

Selected Publications

Chen C, Xie W, Franke J, Grützner PA, Nolte LP, Zheng G (2013) Fully automatic X-ray image segmentation via joint estimation of image displacements. Med Image Comput Comput Assist Interv 2013, LNCS 8151:227 16(3):227-34

Chen C, Zheng G (2013) Fully Automatic Segmentation of AP Pelvis X-rays via Random Forest Regression and Hierarchical Sparse Shape Composition. Computer Analysis of Images and Patterns 2013 (Pt I), LNCS 8047:335–343

Murphy WS, Klingenstein G, Murphy SB, and Zheng G (2013) Pelvic tilt is minimally changed by total hip arthroplasty. Clin Orthop Relat Res 471(2):417–421

Schumann S, Nolte LP, Zheng G (2013) Comparison of partial least squares regression and principal component regression for pelvic shape prediction. J Biomech 46(1):197–199

Schumann S, Liu L, Tannast M, Bergmann M, Nolte LP, Zheng G, (2013) An integrated system for 3D hip joint reconstruction from 2D X-rays: a preliminary validation study. Ann Biomed Eng 41(10):2077-2087

Zheng G (2013) 3D volumetric intensity reconstruction from 2D x-ray images using partial least squares regression. Biomedical Imaging (ISBI), 2013 IEEE 10th International Symposium 1268-1271

Zheng G (2013) Expectation Conditional Maximization-Based Deformable Shape Registration. Computer Analysis of Images and Patterns, LNCS 8047:548–555

Edited Books

Liao H., Linte C.A., Masamune K., Peters T.A., Zheng G. (eds): Augmented reality environment for medical imaging and computer-assisted intervention - 6th International Workshop, MIAR 2013 and 8th International Workshop, AE-CAI 2013, held in conjunction with MICCAI 2013, Nagoya, Japan, Sep. 22, 2014. Proceedings, LNCS 8090, Springer 2013, ISBN 978-3-642-40842-7

Patents

Zheng G and Zhang X. Method and devices for computer assisted distal locking of intramedullary nails (a single image-based method). Patent No. US8444645

Zheng G and Schumann S. Image distortion correction and robust phantom detection. European Patent Application No. EP2660776A1

Medical Image Analysis

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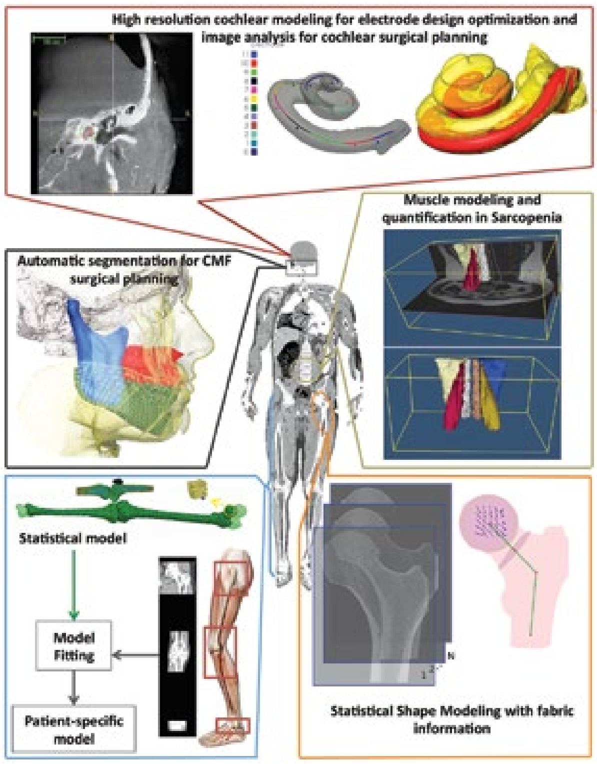
Research Profile

The Medical Image Analysis group conducts theoretical and applied research in image processing, computer vision, and artificial intelligence for the analysis of medical image datasets. The focus of our research relies on the paradigm of evidence-based image modeling and personalized medicine, which aims on the one hand to understand the natural anatomical and physiological variability encountered in a population and, on the other hand, to use this understanding to overcome imaging limitations hindering patient treatment. During the last years our group has focused on three major questions that align with the paradigm of evidence-based modeling and personalized-medicine:

- How to effectively combine Magnetic Resonance Imaging information for a comprehensive spatial and temporal characterization of brain tumors?
- How to design planning and post-operative simulation algorithms and systems to assist plastic and cranio-maxillofacial surgeons?
- How to effectively encompass anatomical and physiological variability for the understanding of musculo-skeletal diseases, the design of orthopedic devices, and less invasive, yet more effective orthopedic surgical approaches?

Computational Anatomy for Orthopedic Research

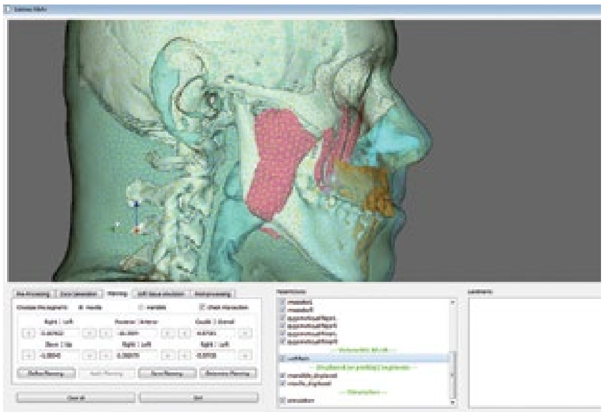
Computational anatomy enables analysis of biological variability throughout a population. Using statistical mathematical techniques, models can be built to represent the typical shape of an anatomical structure and its predominant patterns of variability across a given population. During 2013 we have used these techniques to propose population-based implant design for mandibular plates, where bone shape and bone mineral density are considered within an optimization process, as well for bone allograft selection from bone databanks. Similarly, through national and international projects we aim to use computational anatomy concepts to improve the design of cochlear electrodes, used to reestablish hearing on patients suffering from moderate to severe hearing loss, as well as to support the complex surgical planning procedure. Our research also supports the efforts in prediction of bone fractures by developing methodologies to segment and model bone microstructure and algorithms to quantify complexity and organization of biological tissues.



Modeling anatomical variability and its application to clinical applications such as cranio-maxillofacial surgery, cochlear surgery, bone fracture prediction and sarcopenia.

Oral and Cranio-Maxillofacial Surgery

Our group develops algorithms and systems to perform prediction of soft-tissue deformations after cranio-maxillofacial surgery. The algorithms have been developed with a strong emphasis on its clinical usability (i.e. compliance to imaging protocol, computation speed and usability). The simulation framework features high accuracy by incorporating non-homogeneous and anisotropic tissue properties as well as sliding contact considerations. During 2013 we focused on developing a dedicated software for soft tissue simulation in CMF interventions, termed Sotirios MxFx (Soft Tissue Reconstruction for Intra-Operative Simulation - Maxillofacial). The software is currently being evaluated in a multicenter study. On the basic research side, we have presented, along with our partners, an innovative approach termed inverse planning for CMF that allows the user to directly define the desired surgical facial outcome and obtain the corresponding surgical plan. In this way, trial and error planning can be avoided and the planning process made more effective. In addition, our developments jointly incorporate functional and anatomical considerations, such as dental occlusion and desired aesthetic outcome.



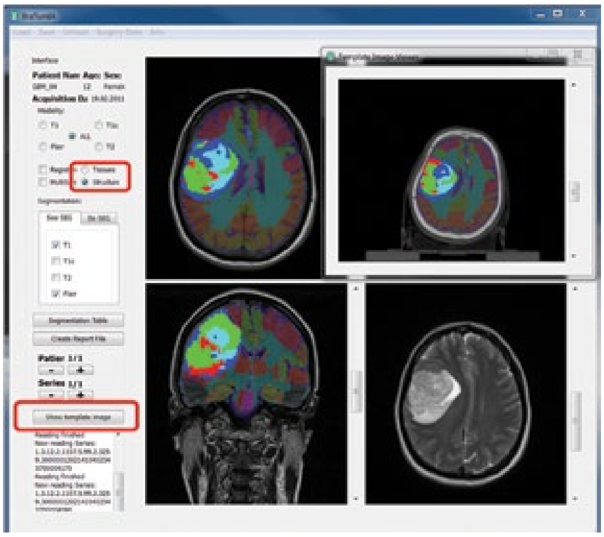
Sotirios MxFx Software: "Soft Tissue Reconstruction for IntraOperative Simulation - Maxilofacial". Sotirios enables a fast and accurate simulation of postoperative skin deformation for CMF surgery.

Brain Image Analysis

Magnetic Resonance Imaging (MRI) and its variants are a powerful imaging modality that encompasses rich anatomical and physiological information at a high resolution. In neuroscience, these modalities have become a standard in clinical practice. However the interpretation of the images requires the combined use of different modalities, which leads to the need for computer-assisted technologies. The group has developed several methodologies to analyze MRI images with a focus on fast multimodal non-rigid image registration and multimodal image segmentation for brain image tumor analysis studies. These developments are driven by clinical requirements such as computation speed, robustness, and use of standard clinical imaging protocols.

During 2013 we have further developed algorithms to automatically segment glioblastomas grade III and IV from multimodal images (i.e. T1, T1c, T2, FLAIR) and for longitudinal studies. The algorithms are based on supervised and unsupervised classification techniques tailored to the clinical scenario. Through this research, our group was awarded the 2nd prize in the international competition for brain tumor segmentation, held at Miccai 2013, Nagoya, France.

We have performed technology transfer to our clinical collaborators and deployed a software for multimodal brain tumor image analysis, termed BraTumIA (Brain Tumor Image Analysis). BraTumIA is currently being clinically evaluated and extended to consider other types of brain lesions.



Brain Tumor Image Analysis - BraTumIA. BraTumIA is a software tool that enables full segmentation of glioblastomas from multimodal images and stems from our research in multimodal brain tumor segmentation.

Selected Publications

Shahim K, Cattin P, Jürgens P, Nolte LP, Reyes M (2013) Prediction of Cranio-Maxilofacial Surgical Planning using an Inverse Soft Tissue Modelling Approach. Med Image Comput Comput Assist Interv 16(1):18-25

Bou-Sleiman H, Paul L, Nolte LP, Reyes M (2013) Comparative Evaluation of Pelvic Allograft Selection Methods. Ann Biomed Eng 41(5):931-938

Lu H, Beisteiner R, Nolte LP, Reyes M (2013) Hierarchical segmentation-assisted multimodal registration for MR brain images. Comput Med Imaging Graph 37(3):234-244

Bou-Sleiman H, Iizuka T, Nolte LP, Reyes M (2013) Population-Based Design of Mandibular Fixation Plates with Bone Quality and Morphology Considerations. Ann Biomed Eng 41(2):377-384

Bauer S, Wiest R, Nolte LP, Reyes M (2013) A survey of MRI-based medical image analysis for brain tumor studies. Phys Med Biol 58(13):97-129

Kim BR, Oh KM, Cevidanes LHS, Park JE, Sim HS, Seo SK, Reyes M, Kim YJ, Park YH (2013) Analysis of 3D Soft Tissue Changes After 1-and 2-Jaw Orthognathic Surgery in Mandibular Prognathism Patients. J Oral Maxillofac Surg 71(1):151-161

Musculoskeletal Biomechanics

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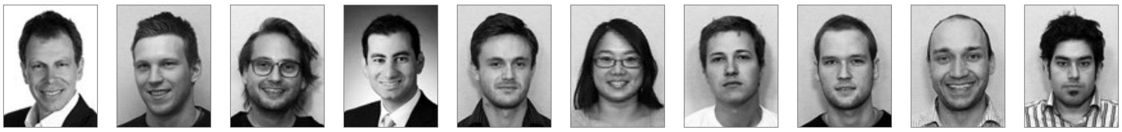

Philippe Zysset | Alexander Bürki | Arne Feldmann | Hadi Hosseini | Ghislain Maquer | Jarunan Panyasantisuk | Matthew Ruder | Jakob Schwiedrzik | Uwe Wolfram | Mohamadjavad Mirzaalimazandarani

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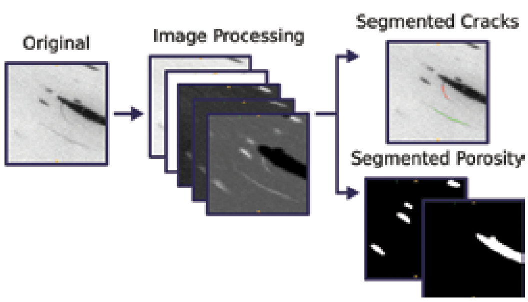
Matthias Zumstein and Beat Moor, Division of Orthopedic Surgery and Traumatology, Inselspital, Bern University Hospital

Research Profile

Motivated by prevention, diagnosis, treatment and follow-up of degenerative diseases the research of the musculoskeletal biomechanics group focuses on multi-scale structure-function relationships of bone and intervertebral disc tissue from the extracellular matrix to the organ level. A combined theoretical, experimental, and numerical approach is applied to model, validate and simulate the mechanical behavior of musculoskeletal tissues in the course of growth, aging, disease and treatment. The group also provides specialized biomechanical testing services and cooperates with local, national as well as international partners from academia, hospitals and industry to help reduce the burden of osteoporosis and other degenerative diseases.

Bone Damage

The risk of undergoing a bone fracture due to trauma may be increased by previous damage, i.e. micro-cracks initiated and accumulated under repeated physiological loading conditions. Accordingly, this research aims at exploring the loading mode dependent damage accumulation in bone tissue and its role in femoral fracture risk. The launched experimental program funded by the AO foundation was extended for image acquisition and image processing of cement lines, i.e. the interfaces where microcracks are most likely occurring. One sub-project focused on the development of cement line staining protocols and segmentation techniques, while another sub-project was devoted to the development of ITK-based segmentation algorithms. The latter were used to identify microcrack distributions from SRμCT datasets obtained at the European Synchrotron Radiation Facility. Besides the experimental efforts aiming at relating the occurrence of microcracks in cortical bone to the induced loads, the development of a constitutive model including plasticity and damage that accounts for these microcrack developments was initiated.



Automated segmentation algorithm to detect microcracks in a bone sample scanned with high resolution synchrotron radiation micro-computer tomography.

Indentation of Bone Extracellular Matrix

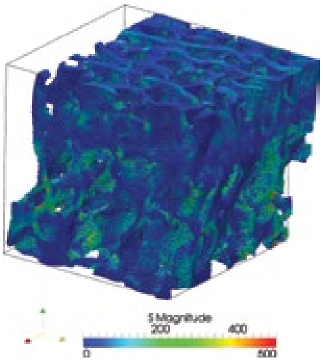
Quality of the bone extracellular matrix is a hidden variable in the diagnosis of metabolic diseases. Indentation at the micro- and nano- scale represents a powerful method to assess mechanical properties with a high spatial resolution. A protocol was developed that allows the sample to be kept in a physiological, hydrated state throughout the whole preparation process. Viscoelastic constitutive models for bone tissue were fitted to the experimental force-displacement data in order to identify the influence of hydration on the time-dependent response of the bone matrix. In a second step, the influence of the constitutive behavior of bone was assessed by means of a numerical study. An elastoplastic constitutive model was also developed and the influence of yield surface shape and maximum damage on indentation properties was explored. The ultimate goal of this research is to assess the role of tissue quality in bone fracture risk relative to aging and disease.

Finite Element Analysis of the Proximal Femur

Finite element analysis is becoming a new standard to predict bone stiffness and strength when QCT scans are available. Funded by the Swiss National Science Foundation, this research aims at establishing a novel standard QCT-based patient-specific finite element analysis of the proximal femur by including a distinct cortical bone phase and trabecular orientation into the current volumetric bone mineral density. In a first stage, linear homogenization analysis of femoral trabecular bone with mixed boundary conditions was realized in cooperation with Dieter Pahr at the Vienna University of Technology.

Clinical Applications of FEA – EuroGIOPS

Glucocorticoid-induced osteoporosis (GIO) causes rapid bone loss and impaired bone architecture leading to a reduction in bone strength, an essential determinant of vertebral fracture risk. The standard technique for diagnosis of GIO, dual energy X-ray absorptiometry, is not a satisfactory surrogate for bone strength as it accounts neither for geometry nor for spatial distribution of the bone tissue. Quantitative computed tomography (QCT) based



Shear loading on a femoral trabecular bone cube using mixed boundary conditions.

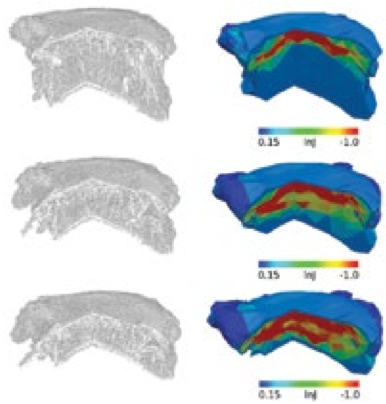
finite element analysis (FEA) can estimate patient-specific structural properties (stiffness, strength) of the vertebral body for various loading cases (e.g. compression, bending and torsion). The elastoplastic damage model developed to simulate the mechanical behavior of bone accounts for the stiffness reduction due to cracks accumulated during the post-yield loading history. Such models were used in the clinical trial EuroGIOPS to follow-up the status of patients with GIO, treated during 18 months with risedronate (antiresorptive) or teriparatide (anabolic drug).

Spine Research

In the frame of the Marie Curie Initial Training Network SpineFX supported by the EU, the aim of the spine research was to validate our recently developed constitutive model of trabecular bone for the prediction of strain localization and densification in human vertebral body subjected to large compressive deformation. Osteoporotic vertebral fractures can often only be diagnosed after a substantial deformation history of the vertebral body. Therefore, it remains a challenge for clinicians to distinguish between stable and progressive potentially harmful fractures. In order to analyze the collapse of the vertebral body under compression, a novel experimental setup based on stepwise loading of human vertebral bodies inside a high resolution peripheral quantitative computed tomography machine was designed and manufactured at the ISTB. On the one hand, the experiments helped us better understand the deformation and collapse of the vertebral body during compression. On the other hand, they served to validate our continuum finite element (FE) model of bone to simulate high compaction of trabecular bone with up to 65% strain. A fair qualitative correspondence of the strain localization zone between the experiment and finite element analysis was obtained. These encouraging preliminary results towards the prediction of extended vertebral collapse may help in assessing fracture stability in future clinical work.

Biomechanical Testing

Biomechanical experiments were performed for industrial contract research, clinical projects and internal research. For instance, measurements of the mechanical properties of dental abutments for dental reconstructions according to industrial testing standards were conducted. Regarding clinical applications, the comparison of a novel technique versus established methods of olecranon osteotomies, devised by the department of Orthopaedics and Traumatology at the University Hospital Bern, was performed. In a further study, an investigations were performed on the primary stability of cervical canine spine implants designed by the VetSuisse faculty.



Collapse of a vertebral body: experiment and simulation.

Selected Publications

Kersh M, Zysset P, Pahr DH, Wolfram U, Larsson D, Pandy MG (2013) Measurement of structural anisotropy in bone using clinical-resolution CT images. J Biomech 46(15):2659-2666

Spiesz E, Reisinger A, Pahr D, Zysset P (2013) Computational and experimental methodology for site-matched investigations of the influence of mineral mass fraction and collagen orientation on the axial indentation modulus of lamellar bone. J Mech Behav Biomed Mater 28:195-205

Zysset P, Dall'Ara E, Varga P, Pahr D (2013) Finite element analysis for prediction of bone strength. Bonekey Rep 2:386

Schwiedrzik J, Wolfram U, Zysset P (2013) A generalized anisotropic quadric yield criterion and its application to bone tissue at multiple length scales. Biomech Model Mechanobiol 12(6):1155-1168

Engelke K, Libanati C, Fuerst T, Zysset P, Genant HK (2013) Advanced CT based in vivo methods for the assessment of bone density, structure and strength. Curr Osteoporos Rep 11(3):246-255

Glüer C-C, Marin F, Ringe JD, Hawkins F, Möricke R, Papaioannu N, Farahmand P, Minisola S, Martínez G, Nolla JM, Niedhart C, Guañabens N, Nuti R, Martín-Mola E, Thomasius F, Kapetanos G, Peña J, Graeff C, Petto H, Sanz B, Reisinger A, Zysset PK (2013) Comparative effects of Teriparatide and Risedronate in glucocorticoid-induced osteoporosis in men: 18-month results of the EuroGIOPs trial. J Bone Miner Res 28(6):1355-1368

Kinzl M, Schwiedrzik J, Zysset P, Pahr D (2013) Experimentally validated finite element method for augmented vertebral bodies. Clin Biomech 28(1):15-22

Gross T, Pahr D, Zysset P (2013) Morphology-elasticity relationships with decreasing fabric information of human trabecular bone in three major anatomical location. Biomech Model Mechanobiol 12(4):793-800

Schwiedrzik J, Zysset P (2013) An anisotropic elastic visco-plastic damage model for bone tissue. Biomech Model Mechanobiol 12(2):201-213

Tissue and Organ Mechanobiology

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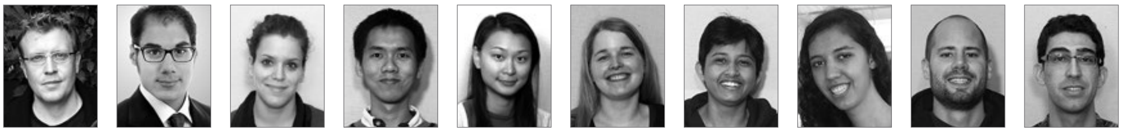

Benjamin Gantenbein, Sufian Ahmad, Elena Calandriello, Wai Hon Chooi, Samantha Chan, Daniela Frauchiger, Neha Gadhari, Rachel Horovitz, Thomas Studer, Mohammad Javad Shamsollahi

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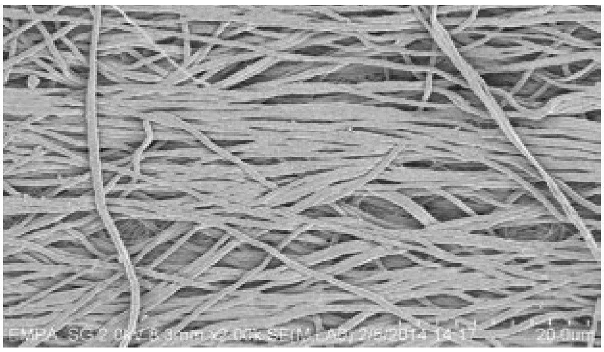
Sandro Kohl, Department for Orthopedic Surgery, Inselspital, Bern University Hospital
René Rossi, Swiss Federal Laboratories for Material Science and Technology, EMPA, Zurich
Klaus Siebenrock, Department for Orthopedic Surgery, Inselspital, Bern University Hospital
Jivko Stoyanov, Swiss Paraplegic Research, Nottwil
Karin Wuertz, Institute for Biomechanics, ETH, Zurich

Research Profile

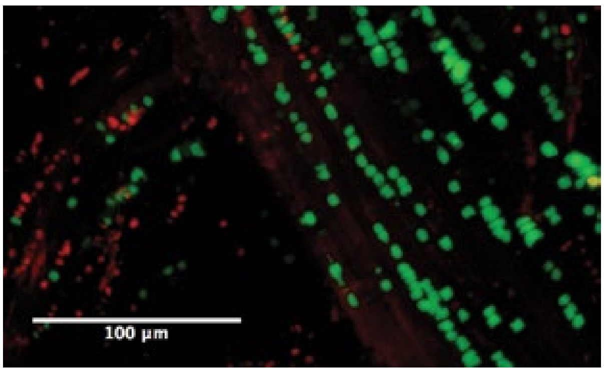
The Tissue and Organ Mechanobiology (TOM) Group of the Institute for Surgical Technology and Biomechanics (ISTB), University of Bern, conducts translational research in the intersection of tissue engineering, biology and applied clinical research. The group's primary aim is to understand the cellular response to biomechanical stimuli and how cellular communities are affected in situ using 3D tissue and organ culture models. Our research can be divided into two main foci: investigation of the causes of lower back pain due to intervertebral disc (IVD) degeneration and identification of cell-based solutions for non-healing or delayed ruptures of the anterior cruciate ligament (ACL). The common focus of the TOM group is to develop in vitro organ culture models which closely match conditions within the human body and where regenerative therapy strategies, such as novel biomaterials and cells, can be tested in a realistic in vitro set-up.



Electro-spun silk fiber scaffold, spun at 30Hz on a rotating Mandrill. The alignment should be highly cyto-compatible for annulus fibrosus cells to grow.

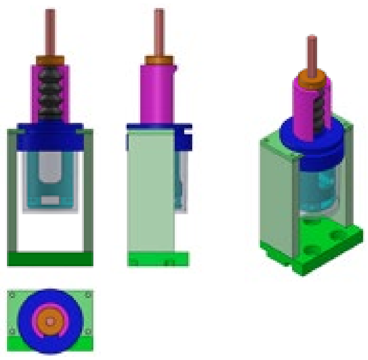
Intervertebral Disc Degeneration and Lower Back Pain

2013 has been a year of exploration of the new two degree of freedom bioreactor to test the importance of complex loading. The TOM group advanced further into the understanding the effects of complex forces such as compression and torsion on intervertebral disc (IVD) cells in situ in organ culture. Furthermore, the group explored non-viral gene therapy as an option for IVD regeneration using growth and differentiation factor 5 (GDF5) as a primary target for differentiating human mesenchymal stem cells towards IVD-like precursor cells. The group developed a strong ex-vivo model using bovine IVD organ culture. This model has been used to explore fast and reliable models for disc degeneration using non-clinically relevant enzymes such as papain or clinically relevant enzymes such as metallo-proteinases and high-temperature requirement A serine peptidase 1 (HTRA1). Furthermore, the group received an exchange fellow, Wai Hon Chooi from Barbara Chan's group at the University of Hong Kong to develop a novel collagen annulus fibrosus (AF) "plug" to repair the IVD. This exchange became possible through the achievement of a competitive AOSpine International Scientific Research Network grant. The project investigated the mechano-biological properties of the AF plug to seal the IVD. The AF is the outer fibrous part of an IVD which has very poor self-healing capacities if ruptured causing leakage of the inner more gel-like material, the nucleus pulposus (NP). This pathology is known as disc herniation. Thus, a "plug" consisting of photochemically crosslinked collagen to seal such a rupture has to fulfill a



Projection of ~200µm stack of confocal laser scanning microscope image. Live dead stain (green cells are alive and red cells are dead) of human Anterior Cruciate Ligament (ACL) cultured in standard culture medium supplemented with 10% fetal calf serum after 7 days.

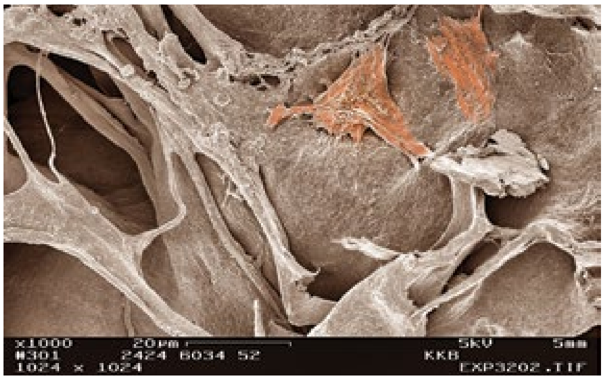
demanding task list as well as withstanding the complex loading of the human spine. To test these properties and to monitor leakage of the plug the group applied fluorescent electromagnetic beads mimicking disc or stem cells and used magnet resonance imaging to monitor possible leakage prior to and after mechanical loading. Leakage and retention of beads was determined by measuring the total fluorescence and the number of beads in the culture medium and inside the IVD, respectively. The maximal force that the annulus plug could resist in the organ culture model was also investigated.
Silk is a very old and interesting biomaterial with high elastic properties and low allergenic potential if the amino acid sericin has been removed. Here, the TOM group started to investigate into new growth-factor-enriched silk, which is produced from genetically transducted silk worms (*Bombyx mori*), which covalently link the growth factor of interest directly into the silk. The new biomaterial will be tested in-vitro on disc and mesenchymal stem cells but also in our 3D organ culture model and the complex loading bioreactor.



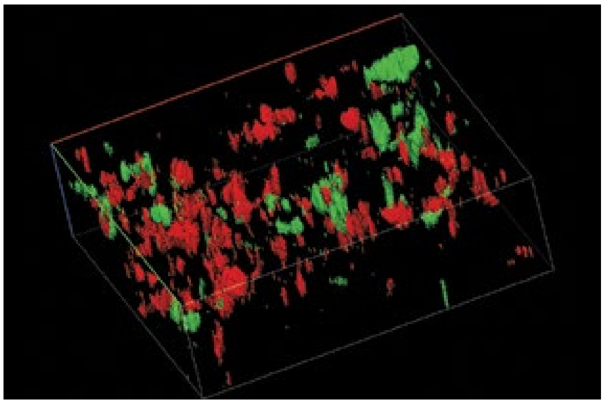
CAD Image of a new bioreactor device to culture ACL in 3D and to connect the ACL in the mechanical testing machine set-up for strain-controlled dynamic loading.

Application of Collagen Matrixes and Mesenchymal Stem Cells to accelerate Healing of the ruptured Anterior Cruciate Ligament

Anterior cruciate ligament (ACL) injuries are very common; in Switzerland the incidence of ACL rupture is estimated at 32 per 100,000 in the general population while this rate more than doubles in the sports community. The current gold standard for anterior cruciate ligament repair is reconstruction using an autograft. However, this approach has been shown to have a number of limitations. A new method has been heralded by the Knee Team at the Bern University Hospital and the Sonnenhof clinic called Dynamic Intraligamentary Stabilization (DIS) which keeps ACL remnants in place in order to promote biological healing and makes use of a dynamic screw system. Here, cell-based approaches using collagen patches or application of platelet derived plasma (PRP) are of interest. The aim of this research is to investigate the use of collagen patches in combination with DIS to support regeneration of the ACL.



Scanning electron microscope image of two mesenchymal stem cells (MSC) grown on Novocart® collagen patches (B.Braun) for 7 days to test their cyto-compatibility for the application of repair of the anterior cruciate ligament of the knee joint.



3D reconstruction of a ~200µm stack based on a series of images taken with confocal laser scanning microscopy through a 1:1 cell mix of human mesenchymal stem cells (MSC, green labelled) and human tenocytes of the anterior cruciate ligament (ACL) taken at a 10x magnification. The cells were seeded on Novocart collagen matrix (B.Braun) for 24h.

Selected Publications

Bucher C, Gazdhar A, Benneker LM, Geiser T, Gantenbein-Ritter B (2013) Nonviral Gene Delivery of Growth and Differentiation Factor 5 to Human Mesenchymal Stem Cells Injected into a 3D Bovine Intervertebral Disc Organ Culture System. Stem Cells Int 2013:326828. doi:10.1155/2013/326828

Chan SC, Bürki A, Bonél HM, Benneker LM, Gantenbein-Ritter B (2013) Papain-induced in vitro disc degeneration model for the study of injectable nucleus pulposus therapy. Spine J 13(3):273-283

Chan SCW, Walser J, Käppeli P, Shamsollahi MJ, Ferguson SJ, Gantenbein-Ritter B (2013) Region Specific Response of Intervertebral Disc Cells to Complex Dynamic Loading: An Organ Culture Study Using a Dynamic Torsion-Compression Bioreactor. PLoS ONE 8(8):e72489

Furtwängler T, Chan SC, Bahrenberg G, Richards PJ, Gantenbein-Ritter B (2013) Assessment of the Matrix Degenerative Effects of MMP-3, ADAMTS-4 and HTRA1 injected into a bovine Intervertebral Disc Organ Culture Model. Spine 38(22):E1377-E1387

Malonzo C, Chan SCW, Kabiri A, Eglin D, Grad S, Bonél M, Benneker M, Gantenbein-Ritter B (2013) A papain-induced disc degeneration model for the assessment of thermo-reversible hydrogel-cells therapeutic approach. J Tissue Eng Regen Med Jan 9 doi:10.1002/term.1667

Mechanical Design and Production

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Group Profile

The primary function of the Mechanical Design and Production (MDP) group is the co-development and manufacturing of mechanical and electro-mechanical components related to the research pursuits of the ISTB and ARTORG. The MDP group supports all levels of the design and manufacturing process from concept to production. This includes computer assisted design (CAD) modelling, prototyping and production with technical drawings, standard tooling, computer assisted manufacturing (CAM), a CNC-milling-machine and a CNC-lathe. We also support industrial and academic external research collaborators with their mechanical design and production needs.

Training and Education

The MDP group has a secondary role in training. This training encompasses the skills required to safely and proficiently operate machine shop tooling and equipment, the knowledge required to achieve the best results with a variety of materials and the skills needed to efficiently manage the design and production workflow. Trial apprenticeships are used as a means to evaluate candidates for a full apprenticeship in the MDP group. This year, we performed one course and we selected Julien Meister as our next apprentice; he will begin his training in August of 2014 as a polymechanic apprentice.

Research Equipment Design and Manufacturing (ISTB)

As expected, the requirements of a machine shop supporting research in the biomedical engineering field are as diverse as the research field itself. The variety of subjects researched in the ISTB yield a number of diverse design and production requests from prototype clinical and surgical tooling to fixtures for mechanical, biological and kinematic testing, as well as imaging system accessories and calibration equipment. The following illustrations highlight a few of this year's projects.

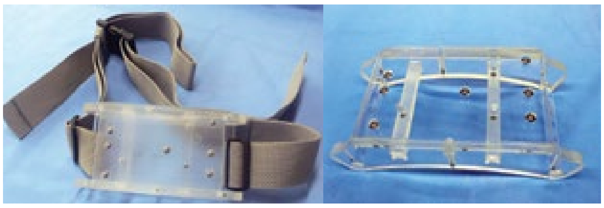
Extensometer Clamp and Indent Testing Device

The musculoskeletal biomechanics group required several different devices for a number of force and bone indent tests. The design and manufacture of these devices was supported by the MDP group. After manufacturing, the indent device was tested on the Synchrotron Radiation Micro-Computer Tomography machine in Grenoble. During experiments on the materials testing machine it can be difficult to accurately fix the measurement lever of the extensometer onto the thin bone samples. Subsequently, we have constructed a guide unit in collaboration with the musculoskeletal biomechanics group.

Custom extensometer clamp, constructed to ensure accurate fixation to thin bone samples.

Improved Acrylic Calibration Phantom

In previous years we have developed a large, universally applicable, calibration phantom for the IPMI group. Based on the measurement results with the large phantom we could now produce a phantom made of acrylic glass of a size which can be used directly on the patient.



Acrylic calibration phantom.

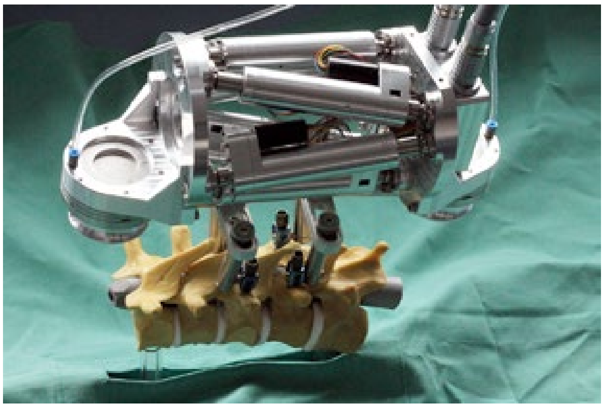
Periacetabular Osteotomy Chisel Calibration

In 2010 the MDP group developed a PAO chisel, capable of being navigated, for the Orthopedic Department at the Bern University Hospital. In a continuation of this project, we have designed an attachment for a new multi-calibration tool and constructed a prototype.

Navigated PAO chisel with calibration device.

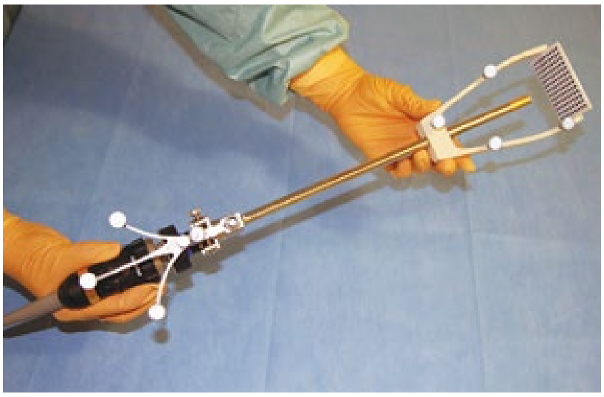
Research Equipment Design and Manufacturing (ARTORG)
The workshop at the ARTORG Center is managed by Ronald Ramseier, a former polymechanic in the ISTB MDP-group. This year the machine shop at the ARTORG Center supported a number of different projects for the IGT and Computational Bioengineering Groups, including design and manufacturing.
As the ARTORG workshop pursues many of the same aims as the MDP group at the ISTB, and as much of the production equipment is located at the MDP. The partnership between the two groups was further consolidated this year, and is still growing. Some highlights of this year's projects are shown below.

Spine Hexapod
The spine hexapod project of the Computational Bioengineering Group at the ISTB and the ARTORG Center was outfitted with new motors; this process required a number of adjustments and changes to the housing. In this embodiment, the gearbox is flange-mounted directly to the motor, leading to less power loss and vibration during operation than was observed in the initial version. Additionally, a new coupling and quick-release system was developed.



Hexapod robot for measurement of forces on the spine. A new prototype was developed with less power loss and vibration.

Endoscope Calibration Tool
With the integration of endoscopic imaging into the existing surgical navigation system of the ARTORG Center and CAScination AG, a simple and robust method of endoscope calibration was required. In order to achieve this aim, a calibration device, in the form of a stapes, was designed and manufactured.



An endoscope calibration device was developed for minimally invasive surgery.

Titanium High Accuracy Tracking Markers
The new patient and tool reference trackers for the high-precision robotic system of the IGT group were, for the first time, manufactured from medical grade titanium. This has a number of advantages; the new markers are light as aluminum but much more dimensionally stable. Surface treatment of the markers enhances the robustness and longevity of the tool while reducing the effects of reflections on measurement error. Increased viewing angle is enabled through the use of a countersunk illumination mask.

High accuracy tracking markers, constructed from titanium, allow measurement and control of a robotic system for minimally invasive cochlear implantation.


INSELSPITAL
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INSELSPITAL, BERN UNIVERSITY HOSPITAL

Interdisciplinarity and trans-professional research in the domain of biomedical engineering is firmly anchored at the Inselspital. Clinical specialists work closely together with engineers, computer scientists and scientists to develop and implement new ideas for diagnosis and treatment approaches as well as for the conduction of clinical trials. Together, they participate in national and international research projects and maintain contact with leading research institutions and scientists not only in Bern and Switzerland but throughout the world. Innovations from scientific research help the Inselspital to further develop its high standards in diagnosis, treatment and care.

Within a clinical environment, biomedical engineering research at the Inselspital, focuses on both long term and short term research objectives. The provision of joint research platforms and core infrastructure, enabled through support of the Inselspital, provides support for effective fundamental and translational biomedical engineering research for a great number of academic research groups and industrial partners in the canton of Bern.

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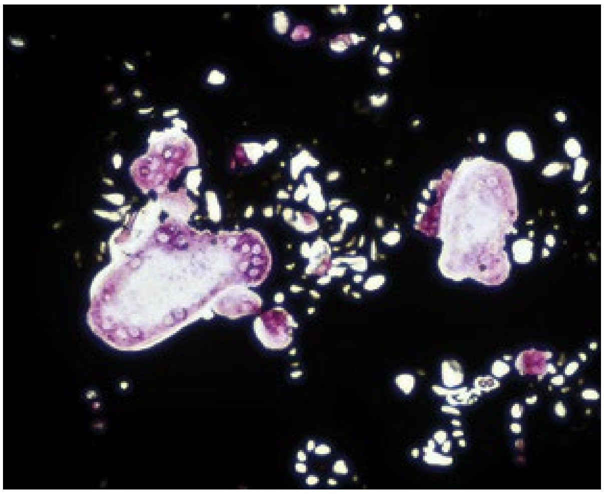
Hans-Jörg Sebald, theSpinecenter, Thun

Research Profile

The research of the Group for Bone Biology and Orthopedic Research, which is part of the Department of Clinical Research of the Medical Faculty, focuses on the biology of bone cell lineages and on the regeneration of skeletal tissues. Many of the pertinent questions have been developed in close discussions with our clinical partners and presently we focus on the following areas: (I) Together with the RIA, we investigate aspects of the cross-talk of inflammatory processes and bone metabolism. These studies include cell and molecular biology studies as well as patient – oriented research. (II) Bone healing is a complex multistep process, starting with an inflammatory phase and ending with remodelling of the primary woven bone. In between there are numerous steps involving recruitment, differentiation and activation of immune and mesenchymal cells. We have set up animal models that allow the investigation of the repair processes in dependence of the mechanical stability and of the composition of the fracture microenvironment. (III) Cartilage repair is an unsolved but pressing issue. To set up *in vitro* models suitable to predict *in vivo* behaviour, a bioreactor has been constructed allowing the execution of complex biomechanical protocols.

Osteoclastogenesis in Inflammatory Processes

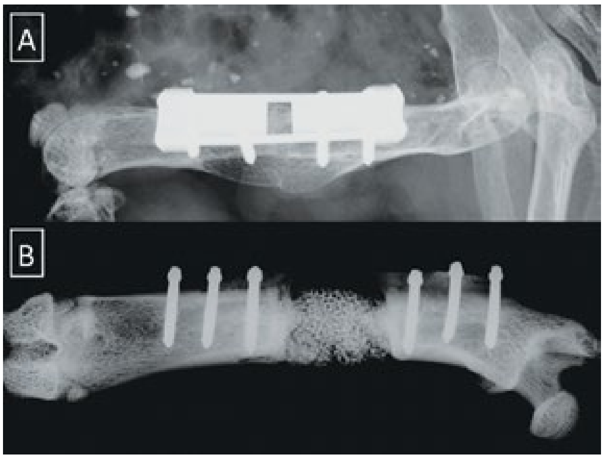
With the description of RANKL (receptor activator of NF-κB ligand) as an essential growth factor for the bone resorbing osteoclast lineage cells, the investigation of the crosstalk between immune system and bone took center stage. Indeed, inflammatory diseases of the skeleton such as Rheumatoid Arthritis cause a local subchondral and systemic bone loss. Furthermore, inflammatory cytokines like TNFα (tumor necrosis factor α) and Interleukin-1 (IL1) are potent stimulators of bone resorption. The roles of inflammatory cytokines on bone resorption, however, differ with the respective target cells. TNFα for instance stimulates osteoclastogenesis through a direct effect on osteoclast progenitors, while it inhibits the same process by inducing the release of the haematopoietic growth factor GM-CSF (granulocyte – macrophage colony stimulating factor), when acting on osteoblast lineage cells. Knowledge on the roles of inflammatory mediators in modulating bone metabolism will lead to the identification of potential therapeutic target molecules and processes and eventually will impact on the development of new and more efficient, because better targeted, therapies. Within this area, we investigate the effects on osteoclastogenesis induced by inflammatory cytokines such as TNFα and IL17. Furthermore, animal models of inducible arthritis are used to study the onset and the progress of the disease.



Mouse osteoclasts on CaP substrate resorb mineral *in vitro*. Cells are stained for TRAP. (Image: Silvia Dolder)

Bone Repair and Osseointegration

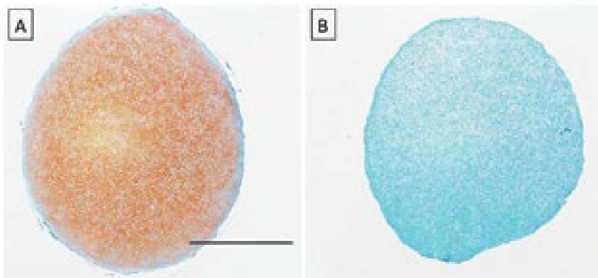
Questions of the repair of small and large bone defect are of high relevance in orthopedic surgery. In a low percentage of patients, fractures do not heal adequately, leading to delayed healing processes or even the formation of a cartilaginous pseudoarthrosis. Furthermore, the repair of large bone defects that occur for instance through trauma or tumor resection is still a problem awaiting an optimal solution. And lastly, if prosthetic implants are necessary, be it in orthopedic or in dental surgery, the integration into bone, i.e. osseointegration, is of upmost relevance. For the study of the events controlling bone repair, small animal models are required. In our group, we use the MouseFix® and RatFix® Systems that were developed by the Arbeitsgemeinschaft Osteosynthese (AO, Davos, CH) to investigate repair of small defect osteotomies (mouse) and critical size defects (rat). Using the FlexiPlate® system, which allows for the non-rigid fixation of femoral osteotomies in mice, we found the antagonists of bone morphogenetic proteins (BMP) to be highly expressed during the healing process, suggesting that endogenous or exogenously added BMP might become more efficient, when the endogenous inhibitors would be blocked. Indeed, subsequent experiments demonstrated an improvement of osseointegration and turnover of CaP based biomaterials, when a genetically modified BMP analogue that binds and inactivates the antagonists but does not elicit a cellular signal by itself, was added. These animal models will be used to investigate the efficacy of biomolecules in bone repair and material turnover. Moreover, since the availability of the compounds (concentration, time) may be crucial for their biological effects, different modes of application of the compounds will be employed.



Mouse and rat models to investigate bone repair. The MouseFix® system (A), developed by the AO (Davos, CH) allows for rigid and non-rigid fixation of small osteotomies. The RatFix® system (B), as well from the AO, allows the investigation of the repair of femoral critical size defects.

Cartilage Repair and Tissue Engineering

Cell based cartilage repair strategies, aiming to prevent progression of an initial defect in cartilage to osteoarthritis, depend on the availability of a large number of cells with the competence to produce a cartilaginous repair tissue on a carrier material placed within a defect site. To obtain the required cell numbers, articular chondrocytes, which are the cells used for cartilage repair, need to be amplified, a process which is accompanied by a loss of this competence to form a cartilage – like tissue. We aim to identify factors, which govern the potential of amplified cells to form a cartilaginous tissue, with a particular focus on the TGFβ signaling pathway and on collagen type II. To set up cell culture systems allowing the prediction of the behaviour of these cells grown on a carrier matrix *in vivo*, we developed a bioreactor which allows the recapitulation of an environment similar to articular joints with respect to chemical composition and mechanical load. This bioreactor will be used to investigate the effects of mechanical stimulation and of low oxygen tension on the development of cartilage - like tissues *in vitro*.



Expression of collagen II in high density pellet cultures of chondrocyte lineage cells grown with TGFβ (A) and TGFβ/SB-505124 (TGFβ2R kinase inhibitor) (B). The data demonstrates the necessity of functional TGFβ signaling for the development of cartilage-like tissue. Bar = 1 mm.

Selected Publications

Gengenbacher MG, Sebald HJ, Villiger PM, Hofstetter W, Seitz M (2008) Infliximab inhibits bone resorption by circulating osteoclast precursors in patients with Rheumatoid Arthritis and Ankylosing Spondylitis. Annals of the Rheumatic Diseases 67:620-4

Atanga E, Dolder S, Dauwalder T, Wetterwald A, Hofstetter W (2011) TNFα inhibits the development of osteoclasts through osteoblast – derived GM-CSF. Bone 49:1090-100

Albers CE, Hofstetter W, Sebald HJ, Siebenrock KA, Klenke FM (2012) L51P – a BMP2 variant with osteoinductive activity via inhibition of Noggin. Bone 51:401-6

Sebald HJ, Klenke FM, Siegrist M, Albers CE, Sebald W. Hofstetter W (2012) Inhibition of endogenous antagonists with an engineered BMP-2 variant increases BMP-2 efficacy in rat femoral defect healing. Acta Biomaterialia 8:3816-20

Balani D, Aeberli D, Hofstetter W, Seitz M (2013) Interleukin-17A stimulates GM-CSF release by osteoblasts and inhibits osteoclast development in vitro. Arth Rheum 65:436-46

Montjovent MO, Siegrist M, Klenke F, Wetterwald A, Dolder S, Hofstetter W (2013) Expression of antagonists of WNT and BMP signalling after non-rigid fixation of osteotomies. Bone 53:79-86

Experimental Hip Surgery

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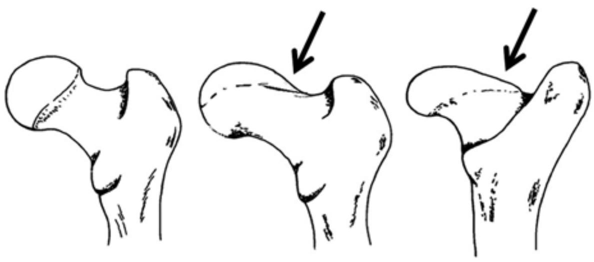
Research Profile

The project of the Experimental Hip Surgery Group is funded by a Swiss National Science Professorship grant which was awarded to the group head Moritz Tannast in 2013. The project started in October 2013 and will last 4 years with a budget covering more than 1.2 million Swiss Francs. The project is a partner collaboration between the Department of Orthopaedic Surgery at the Inselspital/University of Bern and the Musculoskeletal Research Unit of the Vetsuisse Faculty University of Zurich.
The project investigates the development, radiographic monitoring and surgical treatment of hip osteoarthritis due to femoroacetabular impingement. This pathological condition has been recently described in human beings as an important precursor of hip osteoarthritis. Although patients can benefit significantly from corrective surgery for femoroacetabular impingement, it is unknown if the progression of osteoarthritis can effectively be stopped in the long term. With an established animal model in sheep, its possible reversibility with surgical treatment, and the effect of novel cartilage therapies can be assessed. Results of this project can be directly applied to clinical patient care.

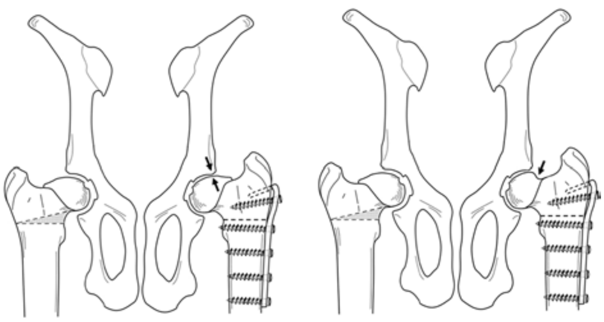
An Animal Model

Femoroacetabular impingement can be caused by an aspherical femoral head in human beings. Swiss alpine sheep have by nature an aspherical femoral head which resembles the pathological human hip morphology. By performing a surgical intervention (closed wedge intertrochanteric osteotomy), a femoroacetabular impingement conflict can experimentally be induced. The resulting hip joint lesions of this established experimental ovine femoroacetabular impingement model are very similar to the labral and chondral degenerations observed in human beings. A pilot study could show that these structural changes of the cartilage can be monitored by modern biochemical MRI sequences.



The normal human femur (left) is spherical. Patients with a cam-type deformity have an aspherical femoral head (mid). Sheep have by nature an aspherical femoral head portion.

A five arm experimental, prospective, randomized, controlled study will be performed. Based on thorough pilot experiments and power analysis, 50 sheep will undergo surgical induction of femoroacetabular impingement. A staged correction of the deformity will be performed at pre-defined time points. In addition, a novel cartilage therapy will be applied. The cartilage degeneration will be monitored with novel biochemical magnetic resonance imaging (MRI) sequences compared to the actual histological damage after euthanasia.



By performing a closed-wedge intertrochanteric osteotomy (left) in a sheep hip, a femoroacetabular impingment conflict can be produced. Similar to the surgical therapy in human beings, the aspherical portion will be removed.

Ovine Femoral Head Blood Supply

In a first step, the femoral head blood supply in the sheep hip will be anatomically described in detail. This includes information from in digital in vivo angiography studies in sheep, vascular corrosion and injection casting techniques. This information will allow for a safe surgical correction of the deformity of the sheep femur.

Virtual Simulation of Impingement Zones

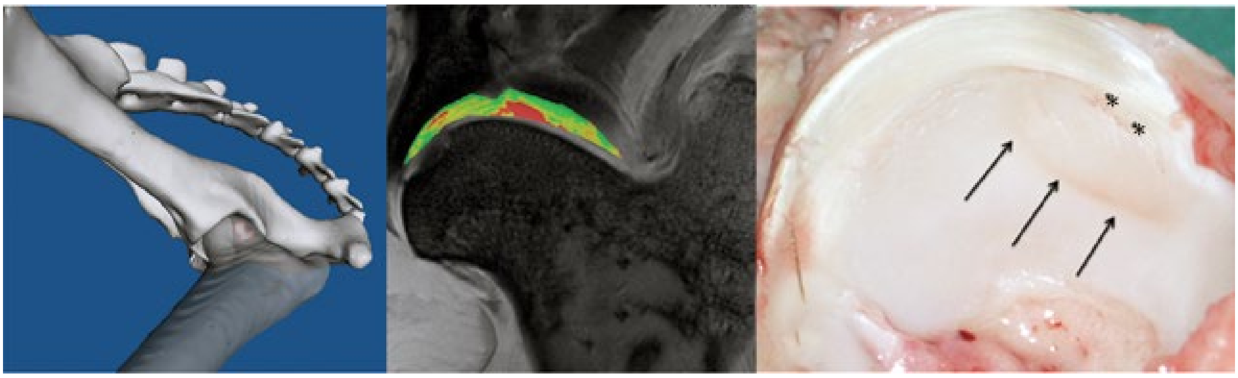
Due to the quadrupedal gait and the more horizontally oriented pelvis in sheep, the impingement location differs from human hip joints. All ovine hips will undergo virtual surgery by means of specific software, which has originally been designed and validated. This allows a 'four-dimensional' (including motion) analysis of the potential impingement zones in FAI hips. By implementing a more sophisticated motion algorithm, this software precisely predicts the area of impingement even in presence of an irregular hip morphology such as that seen in sheep hips. Based on this virtual analysis, the impingement location will be correlated with the actual histological damage. In addition, the impingement lesion could be resected with a mean accuracy of less than one millimeter with the help of an optical tracking system.

Magnetic Resonance Imaging

In the past decade, quantitative magnetic resonance imaging (MRI) techniques have increasingly been used to noninvasively assess the quality and degeneration of the articular cartilage of the hip. With these techniques, early osteoarthritic changes can be detected that may not be evident on conventional MR images and radiographs. Gadolinium enhanced-magnetic resonance imaging of cartilage (dGEMRIC), T2-relaxation time mapping, and T1ρ are currently the most promising techniques for quantitative cartilage imaging of the hip. Each of these three techniques uses a different methodology for color coding the articular cartilage. To date, we do not know which of the three MRI techniques is the best to show early degenerative – and potentially reversible – changes of the articular cartilage. All three modalities will be used and compared to the actual histological changes after euthanasia.

Clinical Relevance

The project will provide the scientific community with validated data to establish new guidelines in joint-preserving hip surgery. Data from ovine 3T MRI studies with biochemical sequences can be used as a basis for prospective randomized controlled trials using human patients. The animal model developed for this study can easily be adapted for the study of other congenital and developmental hip disorders such as developmental pathologies of the epiphysis in lambs. The imaging techniques which this study aims to validate can also be used in any future projects developed with the intention of testing the efficacy of a chondroprotective therapeutic agent or surgical cartilage repair technique.



The experimentally-induced impingement conflict can be visualized using a virtual three-dimensional computer simulation. Mid: The resulting damage can be visualized using modern biochemical MRI-sequences. Right: The resulting labral and chondral damage of the ovine hip joint is very similar to the lesions seen in human beings.

Selected Publications

Siebenrock KA, Fiechter R, Tannast M, Mamisch TC, von Rechenberg B (2013) Experimentally-induced cam impingement in the sheep hip. J Orthop Res 31(4):580-7

Inner Ear Research

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Research Profile

The Inner Ear Research Laboratory seeks to improve current and explore future therapies for hearing loss through regenerative medicine approaches. Sound perception relies on the function of specialized sensory cells in the cochlea, the so-called hair cells, transducing sound waves to the auditory nerve and further to the brain. Loss of functional sensory cells is the leading cause of deafness worldwide.

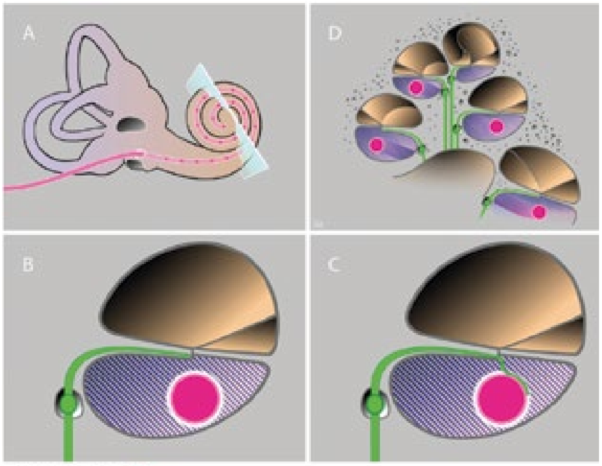
The current treatments for hearing loss consist of conventional hearing aids, for mild to moderate forms of hearing impairment, and cochlear implants (CIs), for severe forms and deafness. These devices improve hearing in the majority of recipients, however, they are not a causal therapy and are not suitable for all hearing impaired individuals. Birds, amphibians and fish can regenerate lost inner ear cell types from tissue resident stem cells and recover hearing to a normal degree from complete deafness. Translation of regenerative principles from lower vertebrates to humans is a promising way to find new and hopefully better hearing loss therapies in the future. The mammalian inner ear lacks spontaneous regenerative capacity, however, stem cells can be isolated from different inner ear organs and cultured in vitro.

Using complementary methods we address the possibility of using stem cells for tissue regeneration in the context of transplantation, drug screening and improving the interaction with cochlear implants.

NANOCI – Improving Current Cochlear Implant Systems

NANOCI (www.nanoci.org) is an EU FP7-funded programme, coordinated by Pascal Senn, aiming at improving current CI technology. Advanced methods of regenerative medicine based on human inner ear stem cells, nanotechnology and bioengineering are used in concert in an international, interdisciplinary project.

Cochlear implants (CIs) are effective neuroprosthetic devices to restore hearing in the majority of deaf individuals. However, some limitations remain. The bottleneck for optimal stimulation is caused by the anatomical gap between the electrode array and the auditory neurons in the inner ear which degrades acoustical resolution and increases energy consumption. NANOCI aims at developing a neuroprosthesis with a gapless interface (C) to the auditory nerve fibres. If successful, this may lead to improved cochlear implant systems in the future.

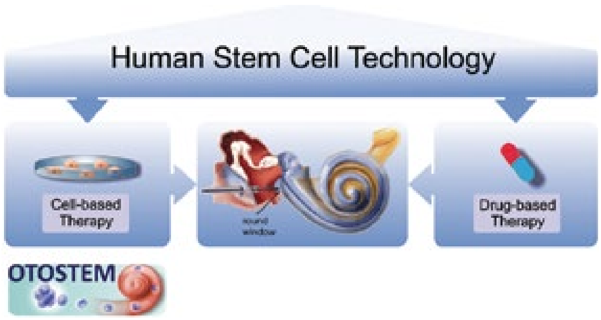


Schematic representation of the NANOCI project. A) Cochlear implant (pink) inserted in a human cochlea. B) Nerve fibers of the auditory nerve (green) are not in direct contact with electrode array of the CI (pink). By providing a bioengineered matrix (purple) we aim at recruiting the nerve fibers to the electrode (C).

OTOSTEM – Human Stem Cells for Future Hearing Loss Therapies

The lack of human otic cell models represents a significant roadblock that has hampered the development of drug-based or cell-based therapies for the treatment of hearing loss.

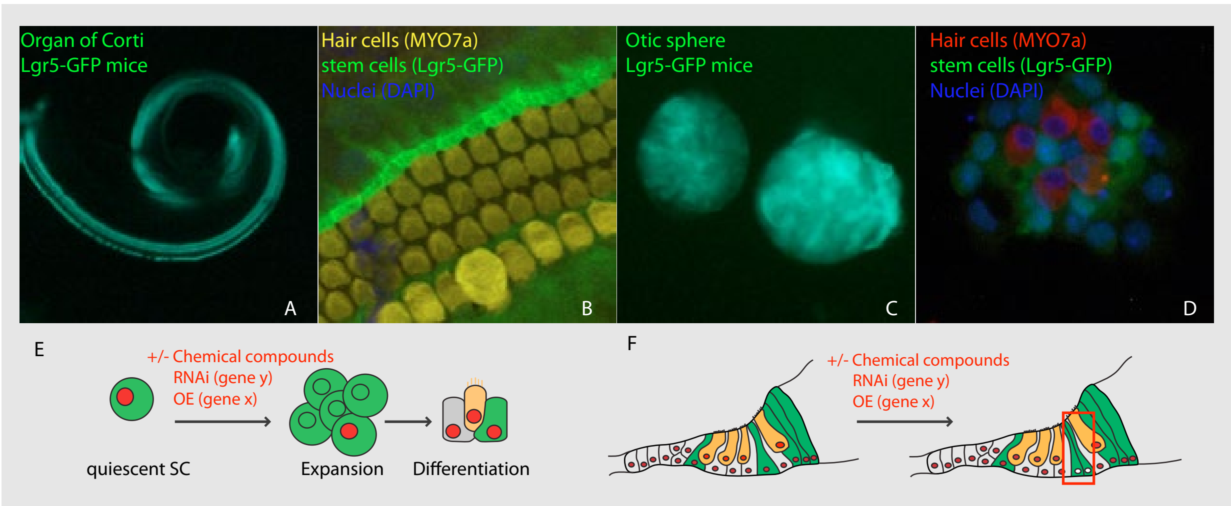
The aim of this international collaborative EU FP7-funded project (www.otostem.org) is to analyze the potential of inner ear stem cell sources (somatic and pluripotent) in three different contests: 1) to establish novel screening platforms to identify toxic or protective compounds for hair cells in pre-clinical phases, 2) to discover novel compounds triggering endogenous regeneration and 3) to establish stem cell transplantation protocols to restore hearing function. Consortium partners have already devised guidance protocols for somatic, embryonic and reprogrammed stem cells towards inner ear cell types that make use of principles of early germ layer formation and otic induction. Purification techniques for human otic progenitors will allow the development of novel bioassays, drug screens and cell transplantation studies in in vivo animal models. Our laboratory is involved in developing strategies to test the efficacy or stem cell based transplantation approaches. The innovative meningitic deafness model, pioneered by the group of Stephen Leib at the IFIK, will be used to address stem cell transplantation into a realistic disease-based hearing loss model. In addition, new hit compounds identified from screening efforts will be tested and validated further in established organ culture models. The identification of relevant candidate compounds will be further developed as lead drug candidates in noise and ototoxic drug induced in vivo models. If successful, OTOSTEM may eventually translate into preclinical trial aiming at curing hearing loss.



Schematic overview of the approach pursued by Otostem: stem cell-based therapy and drug-based therapy to restore hearing function.

Cell Cycle Reactivation of Dormant Hair Cell Progenitors

The auditory epithelium, or Organ of Corti, contains a mosaic of sensory hair cells and non-sensory support cells. The latter have been recognized as hair cell progenitors. The in vivo regenerative potential of mammalian hair cells through stem cell activity is poor and only documented in very early postnatal stages. The mammalian Organ of Corti is a post-mitotic organ, however, under specific experimental conditions, it has been possible to induce regeneration to some extent.
The aim of this project is to identify novel approaches to induce endogenous stem cell activity, by reactivating the cell cycle in quiescent progenitor cells. Transgenic animal models that allow in depth analysis of cell cycle progression and stemness are used for this purpose. We aim at identifying druggable pathways to induce stem cell activity. Small molecule compounds applied locally to the inner ear do represent an appealing therapy to target specific cases of sensory organ degeneration.
In depth knowledge of basic principles of stem cell biology and the close interaction of the laboratory of Inner Ear Research with the clinical Department of ENT and other clinicians allows for the tailoring of research projects to the needs of patients and health care professionals working with them.



A) Organ of Corti from Lgr5 GFP transgenic mice. Lgr5 labels the stem cell compartment in the OC. B) higher magnification of Lgr5GFP OC. Immunostaining for MyoVIIa shows the location of the hair cells (yellow). C) Dissociated cells from Lgr5 GFP OC can be grown in suspension as otic spheres and further differentiated in vitro (D). E) Schematic representation of our approach: genes or small molecule compound targeting to induce stem cell activity in vitro in sphere assay, organotypic cultures and eventually in vivo (F).

Selected Publications

Roccio M, Schmitter D, Knobloch M, Okawa Y, Sage D, Lutolf MP (2013) Predicting stem cell fate-changes by differential cell cycle progression patterns. Development 140(2):459-70

Di Santo S, Mina A, Ducray A, Widmer HR and Senn P (2014) Creatine supports propagation and promotes neuronal differentiation of inner ear progenitor cells. Neuroreport 25(7):446-51

Magnetic Resonance Spectroscopy and Methodology

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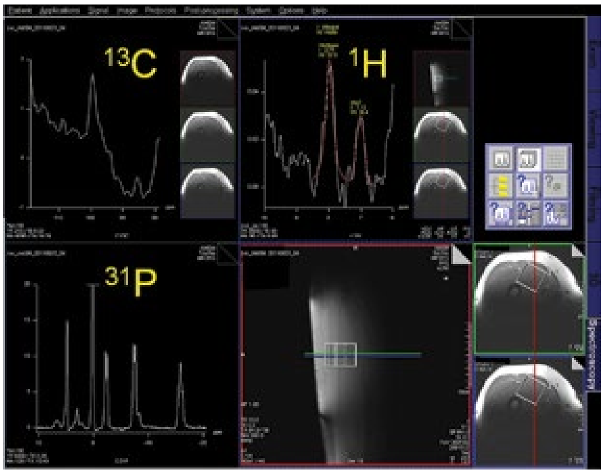
Research Profile

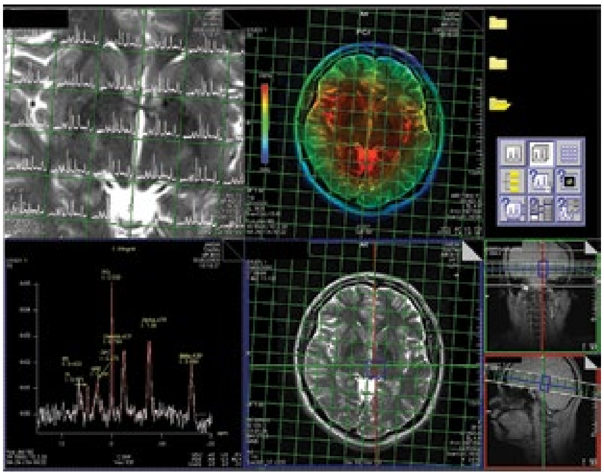
Magnetic resonance imaging (MRI) and spectroscopy (MRS) are powerful and extremely versatile methods for non-invasive studies and diagnostic examinations in humans. Our group is using these MRI, and especially MRS methods, in close collaboration with clinical partners primarily in prospective studies of different organs. The combination of methodological development and applied knowledge allows the study of physiology and pathology, together with the underlying mechanisms behind these, in situ. Currently most MRI and MRS studies are performed in muscle, liver, kidney, brain, and heart tissue. Three SNF grants with PIs in our group (one recently renewed in December 2013), six SNF grants in collaboration with other groups, and one EU-funded FP7-PEOPLE Marie Curie Initial Training Network define the direction of our research.

Insulin Resistance

One SNF grant on insulin resistance ended in November 2013 and was successfully renewed, starting in December. Insulin resistance has been a major research topic within our group for over a decade. Since insulin resistance is a major cause of cardiovascular diseases such as stroke and myocardial infarction, better understanding of this phenomenon will help us to prevent these acute diseases. We study the effects of chronic and acute exercise as well as different kinds of carbohydrates, lipids, and amino acids on muscle and liver metabolism. Several strong collaborations are based on this research topic: internally with the endocrinology, diabetology, hepatology groups at the Inselspital and externally with the preclinical institutes at the University of Bern, and with partners in Lausanne (CH), Pittsburgh (US), Lyon (FR), and Tübingen (DE).



MR spectra acquired with a 1H-13C-31P-triple tuned surface coil in the thigh muscle.


31P-MR chemical shift image of the human brain.

Brain Physiology

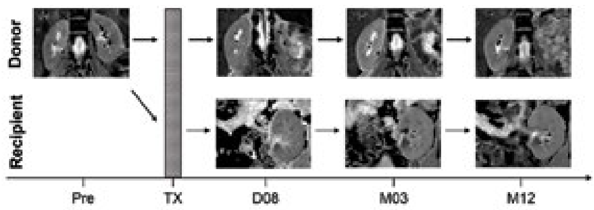
"Magnetic Resonance Techniques to Investigate Human Brain Physiology" is a second SNF grant that aims at the development of MR methods and synergistic post-processing methods that are tailored to the observation of brain metabolism, yet are also transferable to other organs. In collaboration with the ETH and University of Zurich, exchange processes between amide protons and water were recently studied in human brain and skeletal muscle. General acquisition parameters for MRS of neurotransmitters (glutamate and GABA) have been optimized using a general error estimation technique.

TRANSACT

TRANSACT (TRAnsforming Magnetic Resonance Spectroscopy into A Clinical Tool) is an EU-funded Marie Curie Initial Training Network (http://www.transact-itn.eu), which aims at improving and automating MRS methods and post-processing tools such that the clinical use of MRS becomes more robust and widespread. The specific aim of our sub-project is the definition and automatic recognition of spectral quality and clinical usability such that radiologists without specific methodological knowledge should be better able to use MRS in their routine.

Renal Function

Renal function in native and transplanted kidneys is investigated by multi-modal MRI and MRS in a third SNF project. Renal function deteriorates after kidney transplantation for multiple reasons. The functional MR modalities differ in terms of sensitivity for cortical or medullary renal tissue and in their assessed determinants. We aim to achieve better perception of the physiologic basis behind functional MR-parameters and why they may change with renal disease. Reproducibility and comparability studies have been performed employing several functional MR



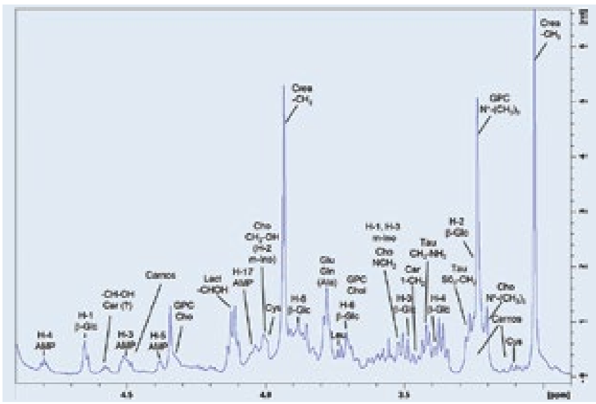
Time schedule for measurements in living donors and recipients with example ADC maps generated from DW-MR images (Pre=before transplantation, D08=8 days, M03=3 months, M12=12 months after living donation.

methods, such as diffusion weighted imaging, arterial spin labelling, and oxygen dependent MRI. In collaborations with the ISTB, image post processing was developed to minimize respiratory motion related problems of the MR acquisition. This may allow the exclusion of respiratory triggering and thus accelerate the acquisitions. For detection of renal ectopic lipids, MRS and MRI methods have been optimized. In a clinical study, living renal allograft donors and their corresponding recipients were longitudinally followed by diffusion-weighted MR Imaging.

High-Resolution Magic Angle Spinning NMR

As MR spectra in vivo have a limited spectral resolution, high-resolution magic angle spinning (HR-MAS) NMR techniques are currently being developed in order to correlate spectra of tissue in vivo and in vitro. HR-MAS makes NMR spectroscopy applicable to semi-solid materials including biological tissues or cell cultures, which under static conditions yield only poorly resolved NMR spectra with very broad lines providing only little information. Fast spinning around an axis inclined at an angle of 54.7°, the so-called "magic angle", with respect to the axis of the external magnetic field (B0) can average orientation dependent effects close to zero, thereby significantly reducing the linewidth and increasing both the spectral resolution and sensitivity.

HR-MAS allows to metabolically characterize tissue types like brain, muscle (see Fig), prostate, breast, liver, or kidney. Several HR-MAS studies have been performed on biopsies like muscle or sheep brain and analyzed by statistical "metabonomical" methods.



Excerpt of a HR-MAS NMR spectrum of a human muscle biopsy (approximately 2µl of muscle tissue) with metabolite assignments.

Selected Publications

Lecoultre V, Carrel G, Egli L, Binnert C, Boss A, MacMillan EL, Kreis R, Boesch C, Darimont C, Tappy L (2014) Coffee consumption attenuates short-term fructose-induced liver insulin resistance in healthy men. Am J Clin Nutr 99:268-275

Ulbrich EJ, Anon J, Hodler J, Busato A, Zimmermann H, Sturzenegger M, Anderson SE, Boesch C (2014) Does normalized signal intensity of discs on T2 weighted images change in whiplash patients? Injury 45:784–791

Brandejsky V, Boesch C, Kreis R (2014) Proton diffusion tensor spectroscopy of metabolites in human muscle in vivo. Magn Reson Med doi:10.1002/mrm.25139

Eisenberger U, Binser T, Thoeny HC, Boesch C, Frey FJ, Vermathen P (2013) Living Renal Allograft Transplantation: Diffusion-weighted MR Imaging in Longitudinal Follow-up of the Donated and the Remaining Kidney. Radiology doi:10.1148/radiol.13122588

Bolliger CS, Boesch C, Kreis R (2013) On the Use of Cramer-Rao Minimum Variance Bounds for the Design of Magnetic Resonance Spectroscopy Experiments. Neuroimage 83:1031-1040

MacMillan E, Boesch C, Kreis R (2013) Magnetization exchange observed in human skeletal muscle by non-water-suppressed proton magnetic resonance spectroscopy. Magn Reson Med 70:916-924

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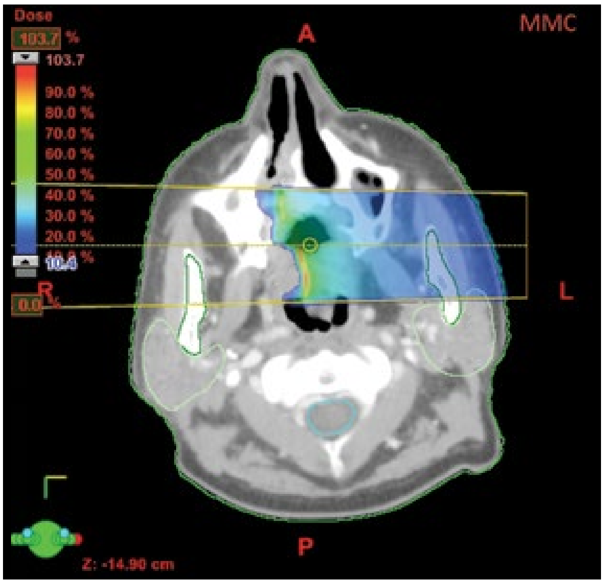
Research Profile

The Division of Medical Radiation Physics is part of the Department of Radiation Oncology and is active in clinical services as well as in research projects and education. Medical physics is an interdisciplinary field and combines physics with medicine. Traditionally, medical physics is related to medical radiation physics and addresses aspects like dosimetry, treatment planning, quality assurance, and radiation protection. Next to the implementation of new methods in radiation therapy, research activities cover more fundamental research in medical radiation physics. In order to accomplish the high accuracy needed in radiation therapy, sophisticated methods have to be established and validated before being used in clinical routine. The research performed at our division has not only proven to be of interest on a national and international level, but has also been transferred to commercial products and clinical applications.

Accurate and Efficient Dose Calculation Methods for External Beam Radiation Therapy

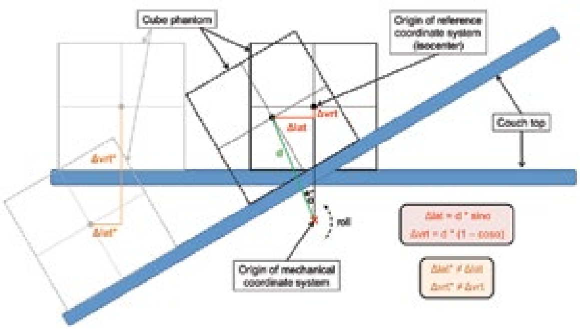
Treatment planning is a key process in radiation therapy and the calculation of dose distributions is one critical aspect for which dedicated methods are needed. The Monte Carlo (MC) method is generally known as the most accurate method in order to perform dose calculations. It is based on the statistical nature of particle interactions and thus, the MC method is performed by particle transport simulation on a computer. One major drawback of this statistical approach, however, is the enormous computation time needed. For this reason, currently, MC based dose calculation algorithms are only used in dedicated situations. Our group is actively working on efficiency improvements for MC based algorithms. For this purpose, not only the dose calculation engine but also beam models have to be adapted such that efficiency gain can be realized without any compromises in accuracy. In recent years, by collaboration with industrial partners, the Macro Monte Carlo (MMC) method has been developed and validated for clinically relevant situations. By this means, not only photon and electron beams, but also proton beams can be managed.



Dose distribution of a proton beam calculated by Macro Monte Carlo.

6DoF Couches for Stereotactic Radiosurgery and Radiation Therapy

Nowadays, image guided radiation therapy (IGRT) is often used for stereotactic radiosurgery and radiation therapy. It allows for an improvement in the accuracy of patient setup and results in a potential reduction of the required safety margins. The importance of margin reduction is given by the fact that it leads to better normal tissue sparing such that toxicity risks may be reduced. IGRT means also that the acquired images have to be converted into corresponding setup shifts. It has been shown that the clinically obtained shifts require a six degrees of freedom (6DoF) couch. In collaboration with industry, our group has evaluated a new 6DoF couch for radiation therapy.



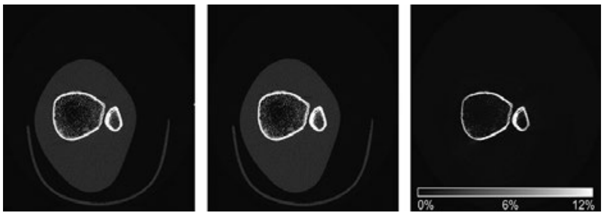
Schematic illustration of the evaluation tests for a new 6DoF couch.

Modulated Electron Radiation Therapy

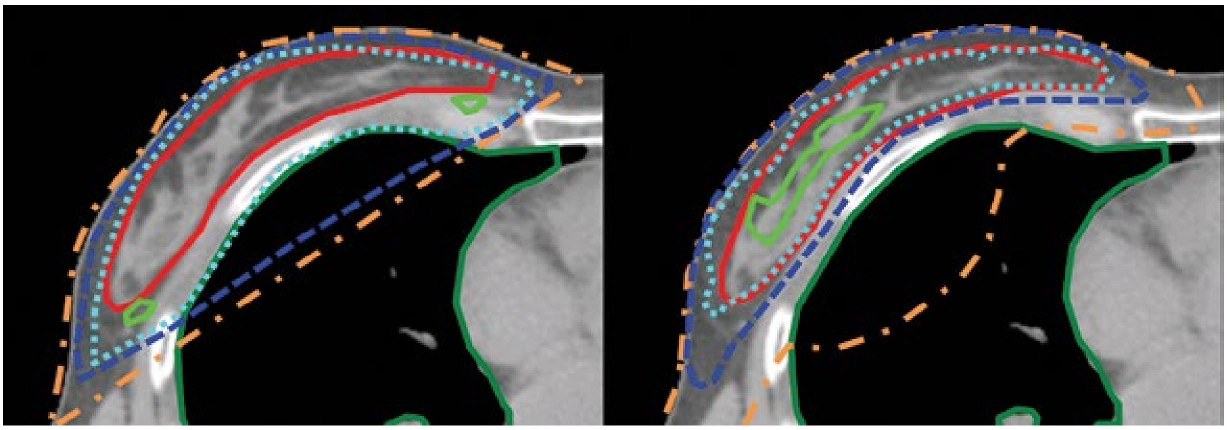
In order to treat superficial tumors, electron beams are well suited. Moreover, due to the high sensitivity of the dose distribution to the energy of the electron beam, modulated electron radiation therapy (MERT) has gained more and more interest over the last years. In our research activities, MERT is combined with a photon multileaf collimator such that the delivery can be performed efficiently and safely. A Monte Carlo framework has been developed in order to be able to characterize the electron beam and to enable optimization of the electron beam intensities. In addition, efficient verification procedures need to be established so that the method has the potential to be used in clinical routine. For this purpose, an electronic portal imaging device has been evaluated with respect to its dosimetric behavior for electron beams.

Scatter Reduction Methods for Micro-CBCT

Cone beam CT (CBCT) is a commonly used image acquisition technique and, as an example, it enables high resolution 3D imaging of bony anatomies. However, CBCT suffers from scatter radiation and spectral effects such as beam hardening. This causes some image artefacts and can lead to problems in a quantitative assessment of reconstructed images. In order to solve this problem, Monte Carlo simulations are used to characterize in detail the signals in commercial micro-CBCT scanner models. Moreover, an iterative reconstruction algorithm has been developed to correct for the beam hardening and the scatter issues.



Comparison of the reconstructed CT-slice using the original algorithm (left), the new beam hardening and scatter correction algorithm (middle) and the difference plot (right).



Comparison of dose distributions based on tangential photon fields (left) or modulated electron fields (right).

Selected Publications

Fix MK, Frei D, Volken W, Born EJ, Aebersold DM, Manser P (2013) Macro Monte Carlo for dose calculation of proton beams. Phys Med Biol 58(7): 2027-2044

Schmidhalter D, Fix MK, Wyss M, Schaer N, Munro P, Scheib S, Kunz P, Manser P (2013) Evaluation of a new six degrees of freedom couch for radiation therapy. Med Phys 40(11):111710

Chatelain C, Vetterli D, Henzen D, Favre P, Morf D, Scheib S, Fix MK, Manser P (2013) Dosimetric properties of an amorphous silicon EPID for verification of modulated electron radiotherapy. Med. Phys 40(6):061710

Henzen D, Manser P, Frei D, Volken W, Neuenschwander H, Born EJ, Vetterli D, Chatelain C, Stampanoni MFM, Fix MK (2014) Monte Carlo based beam model using a photon MLC for modulated electron radiotherapy. Med Phys 41(2):021714

Department of Neurosurgery

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Research Profile

The research activities of the Neurosurgery Department are focused on intraoperative technologies and knowledge management. The aim is to improve surgical radicality, but at the same time patient safety. Novel applications are exploited, tested and integrated in the operative and clinical workflow.
Current scientific projects include new techniques of brain mapping, intracranial aneurysm navigation, navigation and registration of functional areas, awake surgery for speech testing, monitoring of visual areas and intraoperative salvage registration strategies.

Intraoperative Ultrasound

Together with BrainLab in Feldkirchen, Germany, we are working on intraoperative three-dimensional ultrasound for resection control. The aim is to develop protocols for combined 3D Ultrasound with neuronavigation and high quality functional and DTI (diffusion tensor imaging) MRI data. The main subject is shift correction that occurs during brain surgery.

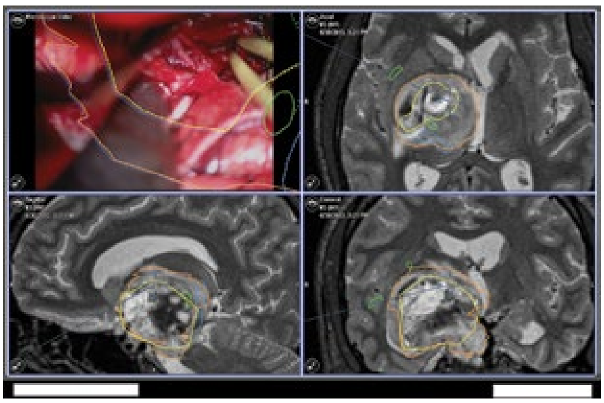
Aneurysm Navigation

Three-dimensional rotational angiography is the standard tool for diagnosing intracranial aneurysms and for aiding the decision of an optimal treatment modality. It provides high-resolution, quality 3D imaging data that is acquired during the normal diagnostic workup. Image guidance via 3D-RA may be helpful during aneurysm surgery, but the problem of patient registration using the 3D-RA has yet to be resolved. Within our scientific work we are examining the following points: 1) newly developed perspective-registration techniques that allow the use of 3D-RA volume data in surgical navigation systems; 2) the accuracy of the perspective registration technique; and 3) the clinical value of 3D-RA guidance in aneurysm surgery. The spatial relationship between the aneurysm and the parent and branching arteries in the 3D-RA–based navigation demonstrated good correspondence with the intraoperative vascular anatomy.

Probes eye view of computer guided frameless stereotactic aneurysm navigation.

Navigation and Resection of Functional Areas with Co-registration of Functional Imaging; Diffusion Tensor Imaging and Visualization of Image Data in the View of the Operating Microscope

The use of neuronavigation is standard in our department. After positioning, the patient head is registered and the surface is matched. We are working on the integration of intraoperative functional and anatomical structure data into the operating field of view. The scientific aims are to further improve surgical accuracy and to provide more detailed anatomical information to the surgeon within a single view.

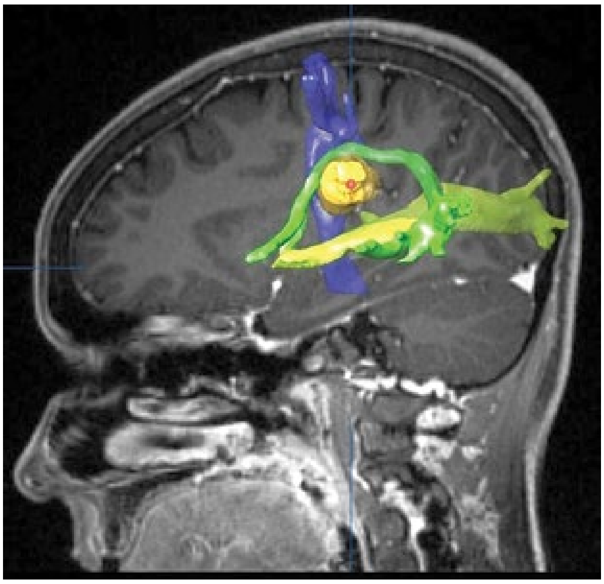


Intraoperative view of a right central lesion with diffusion tensor imaging (DTI-Tractography); the orange and yellow circles indicate the lesion-border; the green line highlights a part of the arcuate fascicle; the blue line indicates the corticospinal tract; the upper left picture shows an implemented view of all structures into the OR microscope.

Awake Surgery for Speech Testing and Monitoring of Visual Areas

Making invisible structures visible requires the intraoperative use of functional MRI data and dynamic localisation of eloquent structures with the help of dynamic physiological monitoring.

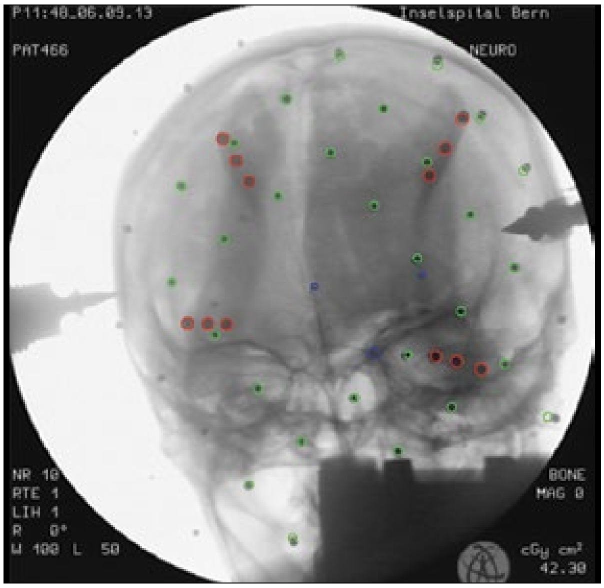
Intraoperative monitoring of functional areas is an important clinical field as well as a scientific focus. With new high resolution mapping techniques a resection of eloquent tumor in functional cortical and subcortical areas is feasible. A current research focus is the localization of primary language areas through accurate fascicle fiber tracking. Tractography of the accurate fascicle without prior knowledge of the localization of the superior temporal gyrus and inferior temporal gyrus is feasible. In cases with functional magnetic resonance imaging, the activation maps matched the tractography results. Using new imaging technologies and intraoperative mapping/monitoring, we can achieve a higher rate of complete resection of enhancing tumor and an increased rate of gross total resection.



Intraoperative view of stereotactic frameless navigation with preoperative acquired image data and diffusion tensor imaging (DTI-Tractography); the orange structure represents the lesion; green - the arcuate fascicle; yellow - the optic tract; blue - the corticospinal tract.

Intraoperative "Salvage" Registration

Another scientific focus of our department is intraoperative rescue navigation, also called "salvage" registration. Our aim is to develop an intraoperative fusion algorithm for registration of the patients head without visible anatomical structures of the patient's head. The registration technique represents an alternative to the surface matching which is only possible prior to draping of the patients head. The aim is intraoperative re-registration using ultrasound or fluoroscopy image data. Together with BrainLAB (BrainLab Feldkirchen, Germany) we are testing the workflow in real life conditions.



Software fusion algorithm of „salvage" registration for fusion of fluoroscopy and CT data.

Knowledge Management

Another main research project is the development of new software that enables physicians to catalogue, search and find documents that are considered of long term interest. In clinical practice it is common to encounter various valuable medical information from different sources such as textbooks, images, PDFs, journal articles and so on. From the beginning of the medical course, the medical knowledge is built up layer by layer, continuing with residency and subspecialty training. In most medical subjects, the knowledge needs to be available long term. The current practice of physicians is to either create a physical library of textbooks and printed PDFs or hard copies or increasingly to build up a digital file archive. However, with increasing amount of documents and progressing time, these systems fail. Another need is the sharing of either documents or commented documents between persons of their choice within such a system. Our aim is to provide a software solution that can be used in most medical subspecialties.

Selected Publications

Stieglitz LH, Fichtner J, Andres R, Schucht P, Krähenbühl AK, Raabe A, Beck J (2013) The silent loss of neuronavigation accuracy: a systematic retrospective analysis of factors influencing the mismatch of frameless stereotactic systems in cranial neurosurgery. Neurosurgery 72(5):796-807

Schucht P, Moritz-Gasser S, Herbet G, Raabe A, Duffau H (2013) Subcortical electrostimulation to identify network subserving motor control. Human brain mapping 34:3023-30

Schucht P, Murek M, Jilch A, Seidel K, Hewer E, Wiest R, Raabe A, Beck J (2013) Early re-do surgery for glioblastoma is a feasible and safe strategy to achieve complete resection of enhancing tumor. PLoS One 8(11):e79846

Seidel K, Beck J, Stieglitz L, Schucht P, Raabe A (2013) The warning-sign hierarchy between quantitative subcortical motor mapping and continuous motor evoked potential monitoring during resection of supratentorial brain tumors. J Neurosurg 118(2):287-296

Interventional Neurovascular Research

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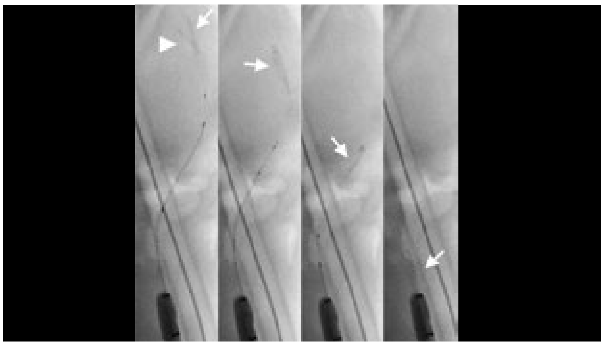
Research Profile

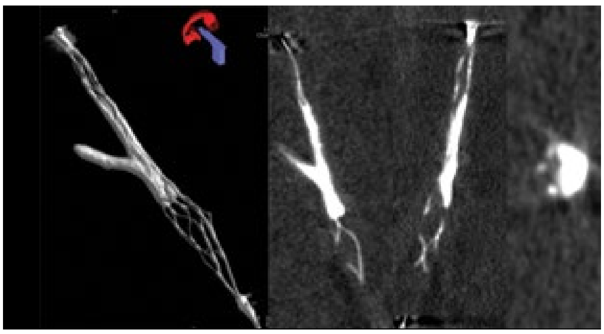
In recent years, endovascular neuro-interventional techniques have evolved significantly, with an increasing spectrum of indications, to include minimally invasive endovascular treatment procedures for acute ischemic stroke, intracranial aneurysms and other cerebrovascular diseases such as arterio-venous malformations and fistulas, as well as stenosis of brain supplying vessels. The Interventional Neurovascular Research Group (INRG) is focused on the pre-clinical experimental evaluation of novel treatment approaches and the development of devices for endovascular treatment of neurovascular diseases. Furthermore, the improvement and development of pre-interventional neuroimaging and image-guided treatment monitoring are crucial components in the management of complex cerebrovascular diseases.

Acute Stroke Treatment

Acute ischemic stroke is a major cause of death and disability in industrialized countries. The management, diagnosis and treatment approaches for acute ischemic stroke have changed enormously in the past decades. Stroke management initially consisted only of prevention, treatment of complications and symptoms, and rehabilitation; today, various different thrombolytic drugs and endovascular treatment approaches are available. The most significant modifiable factors influencing the clinical outcome of patients are time between symptom onset and revascularization, recanalization and reperfusion rate and the occurrence of secondary complications such as symptomatic intracranial hemorrhage. Of those, recanalization has been shown to be the most crucial modifiable prognostic factor. The INRG has developed an in-vivo animal model for the pre-clinical evaluation and development of mechanical thrombectomy devices for the treatment of acute ischemic stroke. This model allows for a reliable evaluation of efficacy and safety as well as improvement of thrombectomy devices prior to their introduction into clinical use. Numerous experimental studies have paved the way for the transfer of the latest generation of mechanical thrombectomy devices, so called stent retrievers, into clinical practice locally and internationally. Furthermore, the model has gained international acceptance as an educational training model for mechanical thrombectomy device handling. This model is utilized in a number of international training courses on acute ischemic stroke treatment organized by the Institute of Diagnostic and Interventional Neuroradiology in collaboration with several neurological and neuro-radiological European societies.



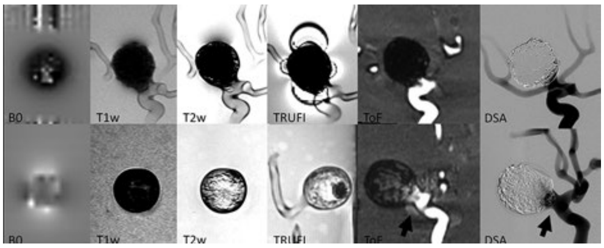
Successful retrieval of a bifurcation thrombus in the animal model using opacified thrombi and a stent retriever device. Note retrieval of the side branch portion (arrow head) and the straight position of the thrombus during mobilization and retrieval (arrow).



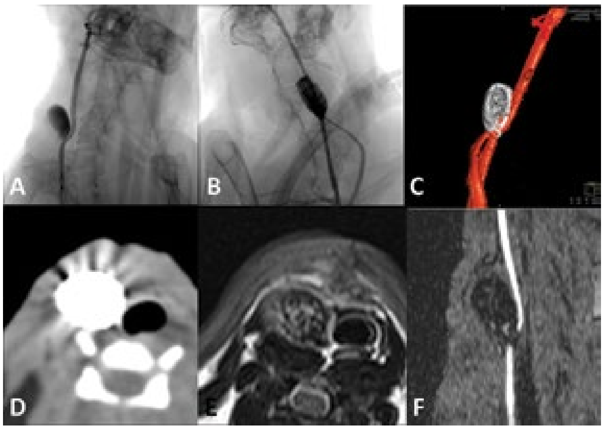
Flat panel CT 3D volume reconstruction, maximum intensity projection (MIP) and multiplanar reconstruction of a thrombus. Note the typical appearance of the opacified thrombus with thrombus material in- and outside in relation to the stent struts.

Aneurysm Treatment

A common indication for endovascular intervention is the treatment of unruptured and ruptured intracranial aneurysms. Since the ISAT-Trial (International Subarachnoid Aneurysm Trial), the majority of these aneurysms, around 50’000 annually worldwide, are treated endovascularly. The standard for endovascular treatment involves the occlusion of the aneurysms through the deployment of platinum coils. New polymer-based endovascular devices (polymer strands, "plastic coils") are currently under development as an adjunctive tool to platinum-based standard coils for endovascular aneurysm treatment. Conventional platinum coils cause imaging artifacts, reducing image quality and impairing interpretation on intra-procedural or non-invasive follow-up imaging. The results of in-vitro and in-vivo evaluation at different packing densities of polymer strands showed significant reduction of imaging artifacts in fluoroscopy, CT and MRI when compared to standard platinum coils; this may be advantageous for improved detection of complications intra-operatively and during follow-up imaging. Furthermore, the applicability of the device under fluoroscopic guidance has been demonstrated in-vivo in a dedicated aneurysm model in rabbits, developed in collaboration with the Department of Neurosurgery. Further research involves the development of in-vitro aneurysm models, in collaboration with the ARTORG Center, for measurements of different aspects of flow dynamics and their role in aneurysm formation and growth, as well as for hands-on training for endovascular aneurysm treatment.



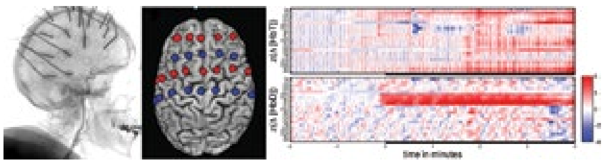
MR images and corresponding DSA of standard platinum coils (upper row) and polymeric coils (lower row) in-vitro. Less magnetic field distortion and artefact production are seen with polymeric coils.



DSA demonstrating the aneurysm model in a rabbit (A). Post-treatment DSA and 3D rotational angiography (B, C) showing complete occlusion of the aneurysm. Note the persisting beam hardening artefact on CT (D). MR images demonstrating visibility of individual coil loops (E) and lack of intra-aneurysmal flow (F).

Neuroimaging of Vascular Disorders

The diagnosis and treatment of vascular disorders is one of the most challenging fields in neuroradiological practice today. Neuroimaging and accurate post-processing are prerequisites for appropriate decision making ahead of endovascular therapy. The major goal of stroke imaging is to predict potentially salveagable tissue without losing critical treatment time. The most important prognostic factors associated with prolonged survival of hypoxic neurons are excellent collateral flow, small infarct cores and sucessful recanalization. Semi-automated volumetry of the infarct core and critically hypoperfused tissue has been analyzed in more than 400 stroke cases; a software was developed in-house to this end. Imaging characteristics of occlusive thrombembolic disease have been further studied by means of susceptibility weighted MRI, providing additional evidence that thrombus length can be reliably detected by non-invasive imaging to estimate the success of recanalization. Using multichannel continuous-wave near-infrared spectrosopy (NIRS), we investigated oxygenation changes during occlusive endovascular neuroradiologic interventions, as this technology provides valuable human reference data on oxygenation changes as they typically occur during acute stroke. In coperation with the SCAN workgroup, funding was obtained for research on cerebral perfusion and vascular reserve capacity in patients with carotid stenosis using a non-invasive MRI technique, so-called arterial spin labelling (ASL). The chronic cerebral hypoperfusion state documented by ASL was correlated with neuropsychological deficits. Volumetric measurements of the global brain, including white and grey matter volumes, were obtained to look for focal areas of atrophy in such patients. Beyond clinical studies, our field of research encompasses advanced computer simulation analysis of flow in the cerebral vascular tree to better understand the vascular flow dynamics and relate them to clinical indications, e.g. wall shear stresses in aneurysms.



NIRS during balloon occlusion of a carotid artery indicates changes in total haemoglobin and haemoglobin difference. The method is under evaluation for monitoring of neuro-interventions.

Selected Publications

Mordasini P, Brekenfeld C, Byrne JV, Fischer U, Arnold M, Jung S, Schroth G, Gralla J (2013) Experimental evaluation of immediate recanalization effect and recanalization efficacy of a new thrombus retriever for acute stroke treatment in-vivo. AJNR Am J Neuroradiol 34:153-158

Mordasini P, Kraehenbuehl AK, Byrne JV, Vandenberghe S, Reinert M, Hoppe H, Gralla J (2013) In vitro and in vivo imaging characteristics assessment of polymeric coils compared with standard platinum coils for the treatment of intracranial aneurysms. AJNR Am J Neuroradiol 34(11):2177-2183

Jung S, Gilgen M, Slotboom J, El-Koussy M, Zubler C, Kiefer C, Luedi R, Mono ML, Heldner MR, Weck A, Mordasini P, Schroth G, Mattle HP, Arnold M, Gralla J, Fischer U (2013) Factors that determine penumbral tissue loss in acute ischaemic stroke. Brain 136:3554-60

Support Center for Advanced Neuroimaging

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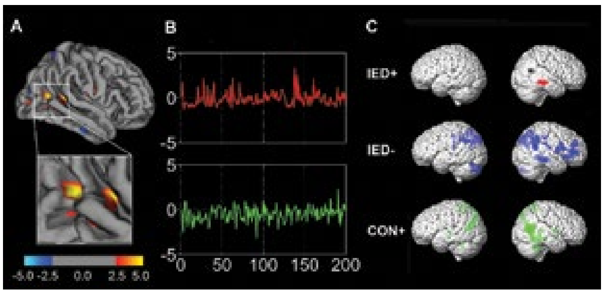
Research Profile

The Support Center for Advanced Neuroimaging (SCAN) is a multidisciplinary imaging laboratory that hosts MR-physicists, computer engineers, neuroradiologists, neurologists and psychologists who focus on sequence development, postprocessing and clinical validation of advanced and functional neuroimaging technologies at the Neurocenter of the Inselspital. Long standing cooperation with the University of Bern has been established with the Division of Psychiatric Neurophysiology (T. Dierks, A. Federspiel), the Department of Psychology (K. Henke, P. Wirtz) and the Institute for Surgical Technology and Biomechanics (M. Reyes). Main clinical foci of the research group encompass non-invasive imaging-based methods (in combination with neurophysiology) to determine the epileptic zone in candidates for resective surgery, the clinical application of imaging techniques to estimate the tissue at risk in patients with ischemic stroke (using MRI and near-infrared spectroscopy), to determine the volume and composition of brain tumor tissue in patients with brain tumors (using perfusion MRI and MR-Spectroscopy) and to develop novel MR-based methodologies to quantify macromolecule compositions in progressive neurodegenerative disorders (e.g. Chorea Huntington). In addition, the SCAN performs clinical neuroimaging, especially functional MRI studies in cooperation with our clinical partners and the research groups of the University Bern. Our overarching goal is to improve patient care through non-invasive neuroimaging technologies.

Neuroimaging of Epilepsy

The combined, simultaneous acquisition of electroencephalography and functional magnetic resonance imaging (simultaneous EEG-fMRI) bridges a gap between neurophysiology and neuroradiology. It extends the application of clinical fMRI – as it is frequently used now for presurgical brain mapping – from externally driven task-related protocols to a neurophysiologically driven prediction of hemodynamic responses. Simultaneous EEG-fMRI thus has an immediate impact in clinical epileptology, where it serves as an additional diagnostic tool during the pre-surgical work-up of patients considered for epilepsy surgery, and remains under intensive practical and theoretical development. This work is currently funded by the SNF SPUM framework and addresses two major fields of human epilepsy research: i) investigation of BOLD correlates of epileptiform EEG-signals in clinically well-defined epilepsy syndromes such as absence epilepsy or mesial temporal lobe epilepsy with hippocampal sclerosis. The aim of this line of investigation is not only to achieve a more complete syndromic description, but to unravel pathophysiological mechanisms that could lead to a deeper understanding of epileptogenesis and perhaps even to a more refined, evidence-based classification of the epilepsies as disorders that affect the whole brain rather than only a circumscribed area in the brain. ii) Localization of epileptogenic foci during the pre-surgical work-up of pediatric and adult patients that suffer from pharmacoresistant epilepsies. Here, the focus is on localization of the seizure-onset zone, and simultaneous EEG-fMRI has proven valuable even if no epileptogenic lesion can be detected by conventional MRI protocols. EEG-fMRI provided evidence

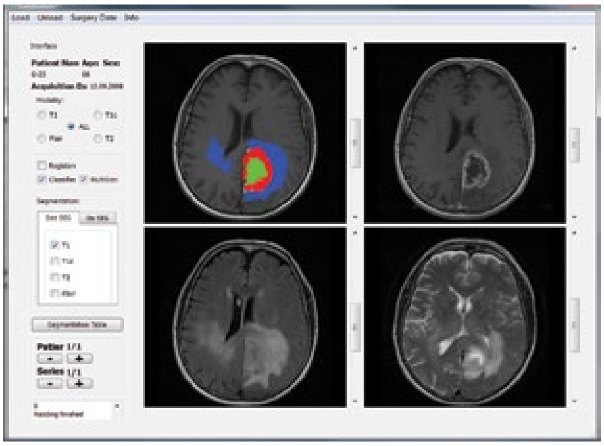


Cortical thickness analysis and fMRI responses to epileptic discharges during simultaneous EEG recordings indicate the area of epileptic activity.

that focal interictal epileptiform discharges are correlated with functional activation and deactivation in specific large-scale networks that span a number of cortical and subcortical nodes. Better understanding of altered network characteristics in epilepsy may pave a novel way for the development of biomarkers and new, less invasive treatment of epilepsy.

Neuroimaging of Brain Tumors

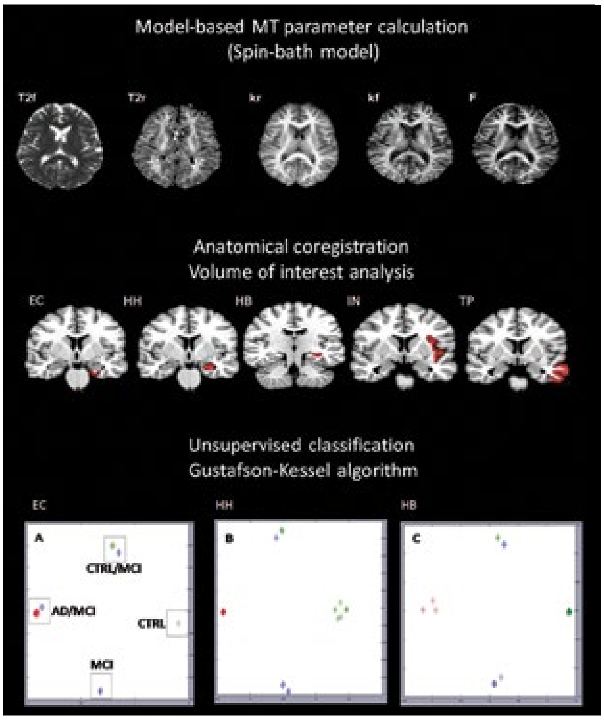
Our research focuses on a multi-parametric and quantitative classification of pseudoprogression (i.e. therapy-associated growth) and pseudoresponse (i.e. decrease of enhancement in the presence of tumor growth) using feature analysis. This work is currently funded by the SNF and aims to identify MRI/MR-Spectroscopy parameters that are complementary indicators of tumor progression, adding functional properties to the currently proposed criteria. In this field of research, the SCAN is currently a full partner in the EU-funded FP7-PEOPLE Marie Curie Initial Training Network (ITN) TRANSACT running from 2013 to 2017. The aim is to transform Magnetic Resonance Spectroscopy into a Clinical Tool. TRANSACT links 10 academic and 4 industrial partners with complementary expertise in basic science, clinical research and information technology. A third focus of research in neuroimaging of brain tumors is automated delineation of brain tumor boundaries from magnetic resonance images, in close collaboration with the medical imaging analysis group of the ISTB. Bauer et al. from ISTB have presented a fully automatic technique to segregate multi-modal images into necrosis, enhancing tumors, edema and solid parts of the tumor. The automated segmentation tool for brain tumor image analysis (BRATUMIA) reproduces 2-D diameter-based criteria for brain tumor assessment and 3-D volumetric measures and is currently evaluated together with the Departments of Neurosurgery and Radiation Oncology at the Inselspital Bern with grant supports of the Bernese and Swiss Cancer League and serves as a prerequisite for the multi-parametric classification as described above.



Automated subcompartment volumetry of cerebral gliomas indicate necrotic tissue (green), enhancing tumor (red) and edema (blue).

Neuroimaging of degenerative CNS Disorders

Neurodegenerative diseases are one of most central medical, social and economic challenges of the 21st century. The efforts of the SCAN focus on the development and validation of new MRI approaches in order to characterize typical early indicators for the onset of neurodegenerative disorders. New methods under investigation are magnetization transfer (MT) and quantitative susceptibility mapping (QSM). Both techniques allow to evaluate the MR data on the base of physical models and to derive new parameters that characterize the disease related macromolecular pool within a typical imaging volume element. Our research in this field focuses on imaging based detection of aberrant molecules as inert biochemical markers of a degenerative disorder and its progression. We have devised a new and clinically feasible, standardized, non-invasive method for the assessment of disease related parameter values which express the interaction of the abnormal proteins with the immediate environment (free water in the brain) and their concentration.



Model based magnetization transfer imaging (mMT) reflects the exchange of magnetization between molecules of water and molecules of more-solid structural components. The figure indicates the imaging based pre-classification of patients with mild cognitive impairment, Alzheimer`s disease and healthy controls. Using mMT, the automated classification segregates the cohorts with an accuracy of 0.92 based on their individual macromolecular depositions in the mid-temporal cortex.

Selected Publications

Wiest R, Estermann L, Scheidegger O, Rummel C, Jann K, Seeck M, Schindler K, Hauf M (2013) Widespread grey matter changes and hemodynamic correlates to interictal epileptiform discharges in pharmacoresistant mesial temporal epilepsy. J Neurol 260:1601-10

Bauer S, Wiest R, Nolte LP, Reyes M (2013) A survey of MRI-based medical image analysis for brain tumor studies. Phys Med Biol 7(58):R97-129

Wiest R., Burren Y, Hauf M., Schroth G., Pruesner J, Zbinden M., Cattapan-Ludewig C, Kiefer C (2013) Classification of Mild Cognitive Impairment and Alzheimer Disease Using Model-based MR and Magnetization Transfer Imaging. AJNR 34:740-6

Visceral Surgery

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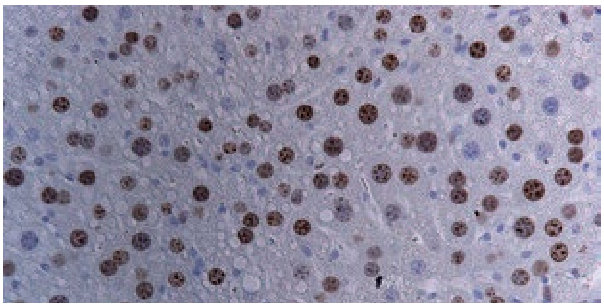
Research Profile

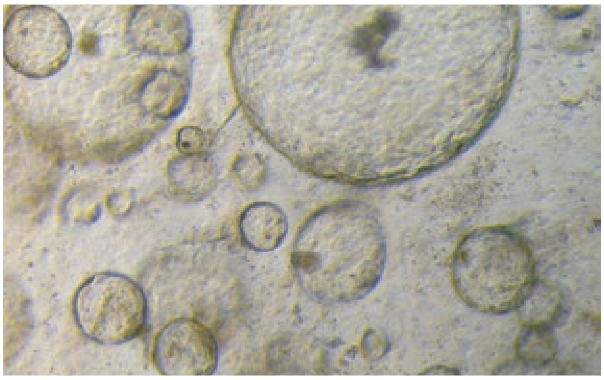
The research interests of the Department of Visceral Surgery and Medicine include regenerative medicine and the image guidance of surgical procedures. Specific topics of interest within regenerative medicine include the molecular basis of liver regeneration and sphincter muscle augmentation and regeneration. Furthermore, we introduce novel developments in image-guided technology into the context of computer-assisted liver surgery. Also, novel approaches for augmented reality in minimally invasive surgery such as tools enhancing the visible field displayed during laparoscopic surgery, are currently developed. Using variable approaches, our research activities aim at improving common standards in order to establish well-founded clinical treatment strategies within the broad field of visceral surgery. A dedicated team of over 50 members performs investigations and experiments, some of which are shown in further detail below.

Regenerative Medicine in the Liver

Our group is studying regenerative medicine in the liver following two different approaches. Firstly, the liver is able to sense and respond to damage and regenerate itself by its major parenchymal cell type, the hepatocyte, re-entering the cell cycle to proliferate and restore the damaged or lost tissue mass. We are investigating this unique ability by focusing on novel pathways in order to define new targets to promote liver function and hepatocyte proliferation during regeneration of diseased livers. In a second approach we are isolating and expanding liver-derived progenitor cells in vitro. Liver progenitor cells have the potential to assist the regenerative capacity of diseased livers and may also offer an expandable cell source to support extracorporeal bio-artificial liver systems.



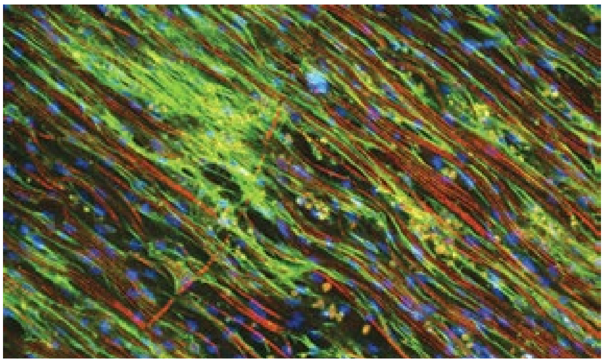
Photomicrograph taken at 200x magnification of mouse liver tissue 48 hours after 67% hepatectomy. Brown reactions are the nuclei of hepatocytes stained positive for the proliferation marker Ki67 indicating a robust proliferative response throughout the liver tissue.



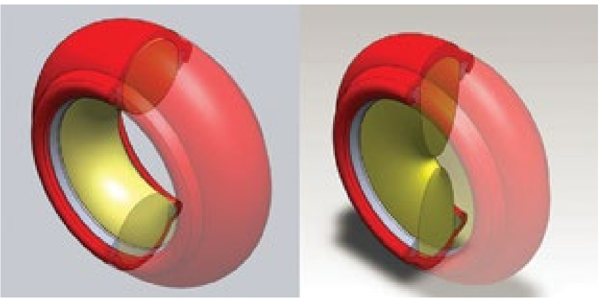
Photomicrograph taken at 50x magnification of liver progenitor cells isolated from a human gall bladder and cultured in vitro for 8 passages.

Novel Technologies for Pelvic Floor Disorders

This research focuses on development of novel technologies for the treatment of pelvic floor disorders such as fecal incontinence or outlet obstruction. These diseases have a prevalence of up to 15% and concomitant economic consequences are therefore relevant. A defect of the anal sphincter following vaginal delivery or oncologic surgery, and degenerative muscular atrophy as a consequence of age or neurological diseases, are the most common causes. Current conservative and surgical therapeutic options are associated with a limited success rate and explantation rates for artificial sphincter devices are high due to technical problems, erosion and infection. Our research activities aim at providing novel technologies for therapy; to this end, we are currently involved in two projects, separately evaluating biological and technical approaches. Concerning the biological approach, we test cellular based therapies and tissue engineering for augmentation or replacement of the continence organ (muscle and intestine). Technical solutions are investigated as part of a multidisciplinary consortium consisting of representatives ranging from clinical medicine via micro-electronics towards biomaterial science. The aims of this project include the development of implantable prototype devices acting as artificial continence muscles using established shape memory alloys (SMAs) or low-voltage electrically activated polymers (EAPs) controlled by implemented pressure sensors and the patient.



Engineered muscle in vitro with muscle cells (cells green, nuclei blue) aligned along a biomaterial matrix (red).



Potential design of an implantable device replacing the sphincter muscle based on electrically activated polymers (red) deforming a silicon inlay (yellow).

Computer-Assisted Navigation in Liver Surgery

Computer-Assisted Liver Surgery (CALS) is an established means to enable accurate and fast navigation as well as targeting of intrahepatic lesions during liver surgery. Used in surgical treatment of metastatic liver disease and primary liver tumors, this is of interest especially in the setting of multiple bilobed lesions localized deeply within the liver tissue, where the use of standard resection or ultrasound-controlled ablation techniques are limited. A challenging key point to enable Computer-assisted navigation is to match preoperatively gained 3D images (based on 3-phase CT reconstructions) with the real-time intraoperative situation and liver position. In the past year we further developed this process called registration, developing a method using a navigated ultrasound probe for acquisition of high density key points along intrahepatic vessel walls. Thereby augmenting accuracy for navigation, consecutive targeting and microwave ablation of intrahepatic lesions can be done safer and faster. Overall, 71 patients have been safely treated with CALS-directed ablation in our clinic so far. The close collaboration between engineers and surgeons enables ongoing development of new technologies with direct clinical testing in order to establish high quality tools for a use in the clinical routine.

Ultrasound-based registration as used in the operating room.

Augmented Reality in Laparoscopic Surgery

The use of laparoscopy has developed rapidly over the last two decades and is now widely adopted in daily clinical practice. Currently, new indications for such minimally invasive approaches are being developed for surgery on the liver, however navigation within the organ is limited due to the lack of tactile feedback and limited exposure of the various vessels. Therefore we are developing novel approaches that aim at displaying the arteries, veins and bile ducts lying within the liver parenchyma on a screen, thereby giving the surgeon a roadmap to safely and accurately perform the dissection. Some hepatic lesions, tumors or metastases may be difficult to identify during the operation as they may be visible on CT but not intraoperative ultrasound. Through the use of augmented reality, the precise location of the tumor to be resected may be shown on the screen in an intuitive manner.

Selected Publications

Graubardt N, Fahrner R, Trochsler M, Keogh A, Breu K, Furer C, Stroka D, Robson SC, Slack E, Candinas D, Beldi G (2013) Promotion of liver regeneration by natural killer cells in a murine model is dependent on extracellular adenosine triphosphate phosphohydrolysis. Hepatology 57(5):1969-79

Kurmann A, Visth E, Candinas D, Beldi G (2011) Long-term follow-up of open and laparoscopic repair of large incisional hernias. World J Surg 35(2):297-301

Banz V, Tinguely P, Worni M, Müller P, Inderbitzin D, Ribes D, Peterhans M, Weber S, Candinas D (2014) Indications for stereotactic liver surgery: Findings from a single center study over 4 years. SGC Swiss Surgical Congress Bern 2014

Department of Osteoporosis

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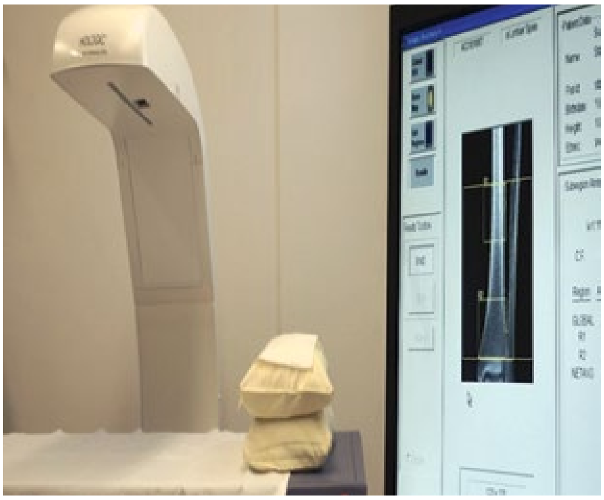
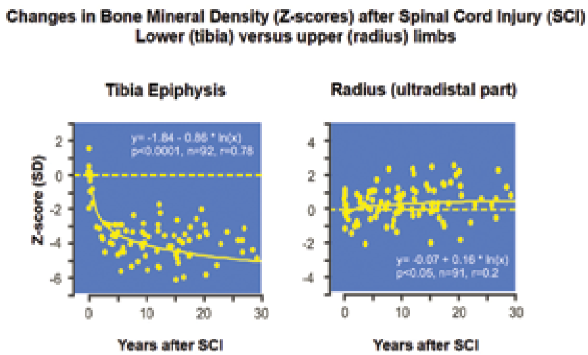
Research Profile

The research activities of the Department of Osteoporosis cover a broad range of aspects within the field of metabolic bone diseases and include clinical and experimental basic/translational projects. The clinical research side comprises a number of focus areas, including the epidemiology and socioeconomic burden of osteoporotic fractures and the refinement of fracture risk prediction through the development of novel general and local osteoporotic diagnostics, including the establishment and evaluation of new bone-densitometry sites and techniques such as the prediction of bone strength using high-resolution peripheral quantitative Xtreme CT in the distal tibia and the femur. Other foci include the development of the fracture-risk assessment tool FRAX® for clinical fracture-risk assessment, in co-operation with the WHO Collaborating Centre for Metabolic Bone Diseases, studies relating to the loss of bone incurred after paraplegia, in the context of microgravity; secondary osteoporosis in various populations, including patients with renal stones, tubular acidosis, HIV-infections or primary hyperparathyroidism, as well as in transsexuals and in men undergoing opioid-substitution therapy; and various phase II and III trials relating to the pharmacological treatment of primary and secondary osteoporosis in men and women.
The projects of the experimental / translational research arm of the department are supervised by Ernst B. Hunziker (Department of Clinical Research) and focus on the targeted stimulation of bone anabolism through local therapeutic intervention (a combination of internal medicine and orthopedic surgery) at high risk topographic sites, the assessment of bone strength in the vertebrae for transpedicular fixation and novel injectables for the treatment of lumbar vertebral and hip fractures, including the development of release systems for osteogenic compounds and of implants for osteoporotic patients in orthopedics and dentistry.

DXA of the Distal Tibia

The measurement of bone mineral density (BMD) measurements by dual-energy X-ray absorptiometry (DXA) is a standard technique to identify patients with low BMD and to monitor changes in this parameter during therapy with bone-active substances. Low BMD-values are predictive of individual fracture risk. However, whilst this circumstance has been unequivocally established for central measurement sites of the skeleton, the hip, the lumbar spine and, to some extent, the one-third radius, the situation is less clear with regard to other peripheral sites, such as the tibia. The tibia is a weight-bearing bone, which is readily accessible to peripheral BMD-measurements in the distal third. Peripheral BMD-measurements are of particular


DXA of the distal tibia.



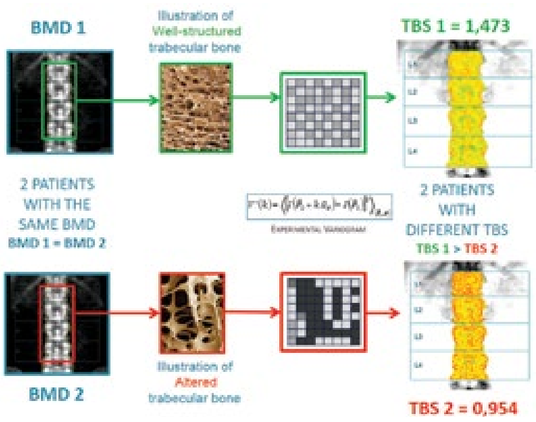
BMD in paraplegic patients (upper vs. lower limbs).

interest in elderly patients in whom conditions such as osteoarthritis may preempt the diagnosis of low bone mass in central skeletal locations. They are also of interest in patients with metabolic bone diseases or in those with specific forms of osteoporosis that affect the weight-bearing bones, such as immobilization osteoporosis in paraplegics. We have developed and established a technique to measure by DXA the BMD in the distal tibia and have validated it for fracture-risk prediction.

Trabecular Bone Score (TBS) of the Lumbar Spine: Clinical Validation of a Novel Tool to Measure Vertebral Bone Microarchitectonic Texture in Osteoporotic Patient Populations Before and During Treatment.

The microarchitecture of trabecular bone is an important determinant of bone strength, complementary to bone density. The trabecular bone score (TBS) is a novel grey-level texture measurement. It is based on the analysis of two-dimensional (2D) projections of DXA-images. The TBS is capable of differentiating between two three-dimensional (3D) microarchitectures of cancellous bone that exhibit the same bone density but different trabecular characteristics. TBS-values, as evaluated from 2D- projections of DXA-images correlate closely with the 3D-microarchitectonic characteristics of trabecular bone, independently of BMD. A low TBS-value has been shown to be associated with a poor bone microarchitecture, including low connectivity, high trabecular spacing, and a reduced number of trabeculae. Hence, high TBS-values are indicative of a strong, fracture-resistant microarchitecture, whereas low ones reflect a weak, fracture-prone microarchitecture. The primary asset of TBS-measurements is that they may be specifically used to assess some dimensions of vertebral bone microarchitectonic texture, which is recognized to be an important BMD-independent determinant of bone strength. In collaboration with Didier Hans we have shown for the first time in a randomized controlled trial that in postmenopausal osteoporotic women, an annual intravenous injection of zoledronate significantly increases the BMD of the lumbar spine compared to that in placebo-treated individuals over a 3-year period, and the TBS over 2 years.

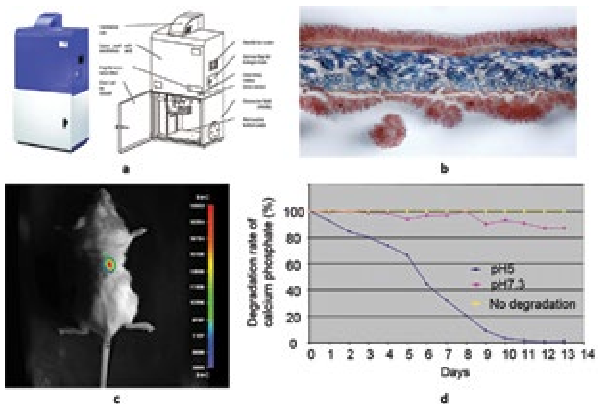
Furthermore, in a second clinical trial, differential effects on BMD- and TBS-values in the lumbar spine were revealed after a 2-year treatment course with either the bone anabolic substance teriparatide or the anti-resorptive drug ibandronate.



Principle of TBS-measurement in the lumbar spine.

In-vivo tracking of the degradation of a calcium-phosphate layer that has been deposited on a collagenous membrane

Collagenous membranes are widely and successfully used in clinical practice, particularly in dentistry as a barrier for guided bone regeneration. However, they suffer from the drawback of often being too rapidly degraded for some indications, such as guided bone regeneration in osteoporosis. We hypothesize that the degradation rate of collagenous membranes can be modulated by coating them with a fine layer of calcium phosphate of adjustable thickness. Initially, we wish to quantify the rate of degradation of calcium-phosphate layers of different thicknesses in an in vivo mouse model. Subsequently, the influence of a calcium-phosphate layer on the mechanism of degradation of the underlying collageneous membrane itself was evaluated. In order to achieve this, the calcium-phosphate layers are labelled with a fluorescent probe, and the degradation of the tagged calcium-phosphate layers is monitored using an in-vivo imaging system (NightOWL II in-vivo imaging system). We have confirmed that the degradation rate of a calcium-phosphate layer can be tracked by an in-vivo imaging system using a CCD-camera. In addition, we have established an in-vitro assay that simulates the in-vivo degradation of the coating.We are currently monitoring the temporal course of degradation of calcium-phosphate layers in vivo.



The NightOWL II in-vivo imaging system (a). Preliminary results demonstrating the deposition of the calcium-phosphate layer on the collagenous membrane (b), the imaging of a calcium-phosphate-coated collagenous membrane, implanted within a Balb/c mouse (c), and the subsequent rate of degradation of a calcium-phosphate layer under in-vitro conditions that simulate the process in-vivo (d).

Selected Publications

Popp AW, Guler S, Lamy O, Senn C, Buffat H, Perrelet R, Hans D, Lippuner K (2013) Effects of zoledronate versus placebo on spine bone mineral density and microarchitecture assessed by the trabecular bone score in postmenopausal women with osteoporosis: a three-year study. J Bone Miner Res 28(3):449-54

Popp AW, Buffat H, Cavelti A, Windolf M, Perrelet R, Senn C, Lippuner K (2014) Cortical bone loss at the tibia in postmenopausal women with osteoporosis is associated with incident non-vertebral fractures: Results of a randomized controlled ancillary study of HORIZON. Maturitas 77(3):287-93

Invasive Cardiology Research

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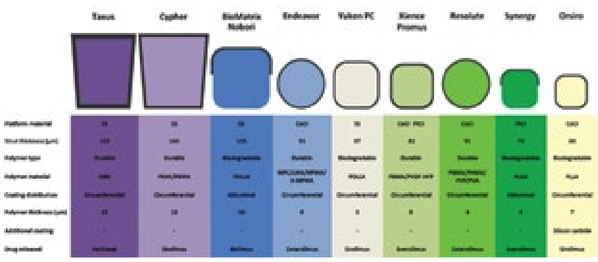
Research Profile

The Head of Invasive Cardiology at Bern University Hospital has a long-standing research focus on cardiac devices for the minimal-invasive treatment of coronary artery disease and structural heart diseases. Research activities encompass studies with focus on pathophysiological mechanisms, preclinical and clinical evaluation of novel intracoronary stents and transcatheter heart valve technologies as well as large scale, multicenter, international, randomized clinical trials. The research group has well established national and international partnerships across Europe and the United States.

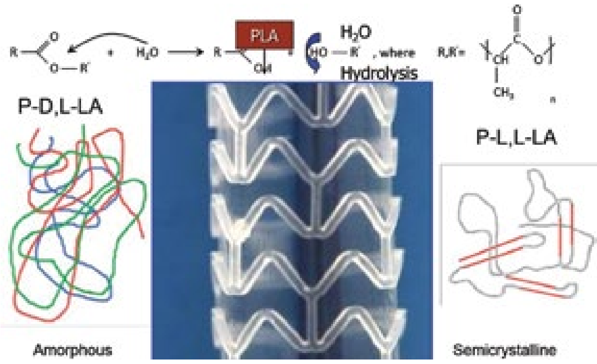
Coronary Artery Stents and Scaffolds

Coronary artery stents are metallic prostheses which restore the flow of blocked coronary arteries and have been shown life-saving particularly in the setting of acute myocardial infarction. A breakthrough of stent technology has been the advent of drug-eluting stents with controlled release of anti-proliferative drugs from surface polymers in order to effectively prevent recurrent events. Our group has been actively involved in the development and systematic clinical evaluation of new generation devices with the use of biodegradable polymers for anti-proliferative drug release, particularly among patients with acute myocardial infarction. Currently, one randomized trial investigates a novel biodegradable polymer based DES against a durable polymer based DES in more than 2000 patients and results have been accepted for publication in the Lancet later this year.



Progress in metallic DES Technology.

The latest development in the field of intracoronary devices are fully bioresorbable scaffolds, which release anti-proliferative drugs and subsequently undergo complete bioresorption within 1-2 years after implantation. These devices have the potential to restore a vessel to normal function in terms of vasomotion, lumen patency and atherosclerosis regression. Currently, our group investigates the arterial healing pattern of fully bioresorbable scaffolds compared with metallic drug-eluting stents in patients with acute myocardial infarction.



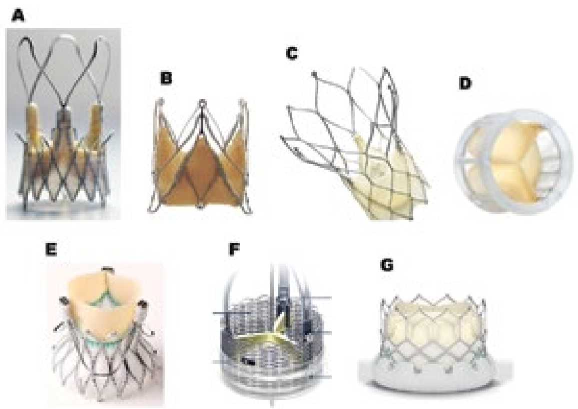
Bioresorbable Coronary Scaffolds and Polylactide Degradation Mechanism.

Intracoronary Imaging

The arterial healing process after stent implantation can be monitored by high resolution intravascular imaging methods. Specifically, optical coherence tomography (OCT) is a light based intracoronary imaging device, which allows the visualization of stents and the adjacent coronary vessel wall with a resolution of 10 µm. Long-term monitoring of the healing response provides information on the biological compatibility of coronary artery stents. The healing profile may substantially differ depending on stent type and underlying lesion morphology.
Atherosclerosis is a chronic inflammatory disease, which is complicated by acute coronary syndromes due to vulnerable plaque rupture or erosion. This sudden manifestation is not always preceded by clinical symptoms. OCT is considered ideal to assess plaque micro-characteristics such as the fibrous cap overlying vulnerable plaques, macrophage accumulations, thrombus formation or atherosclerosis related microchannels. Virtual histology ultravascular ultrasound (IVUS-VH) is a sound based technology which uses the radiofrequency signal of ultrasound to detect the composition of atherosclerotic plaques. The combined use of both OCT and IVUS-VH has, so far, not been tested with respect to the accuracy when detecting high risk plaques and the prediction of future cardiovascular events. Our research team conducted a serial, intracoronary multimodality imaging study, which will provide important insights into atherosclerosis progression over time and anti-inflammatory therapies.

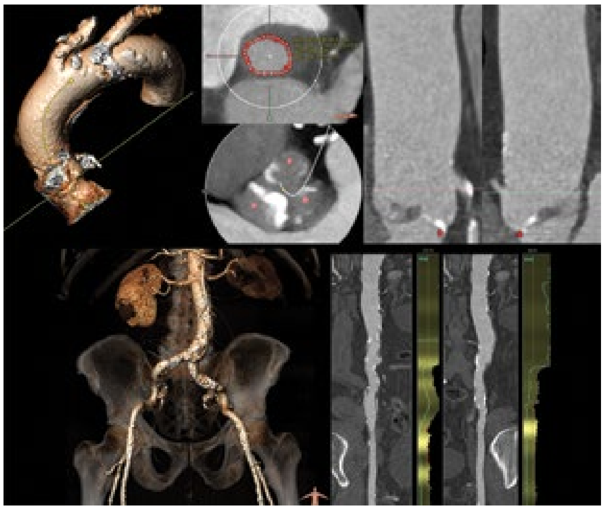
Minimal Invasive Treatment of Degenerative Aortic Valve Stenosis and Three-Dimensional Imaging Algorithms

Degenerative aortic valve stenosis is the clinically most relevant valvular heart disease. Although surgical aortic valve replacement has been the standard of care until recently, up to one third of affected patients have not been referred as they were deemed inoperable or at high surgical risk owing to frequent comorbidities. Transcatheter aortic valve implantation (TAVI) is a novel catheter based, minimally-invasive treatment of severe aortic stenosis, which can be performed under local anesthesia and without the need for cardiopulmonary hemodynamic support. TAVI has shown results superior to medical therapy, and provides similar clinical outcomes as surgical aortic valve replacement in high-risk patients. Currently, nine different TAVI prostheses are in clinical use. Our group is actively involved in the evaluation of new generation devices and delivery systems which focus on even smaller prosthesis and delivery catheter profiles in order to further reduce access-related adverse events, enhance device implantation and placement, and eliminate paravalvular leaks and conduction disturbances.



New generation TAVI prosthesis: A Symetis Acurate TA, B JenaValve, C St. Jude Portico, D Direct Flow Medical, E Medtronic Engager, F Boston Scientific Lotus Valve, G Edwards Sapien 3.

A detailed assessment of the aortic root and peripheral vasculature is required in patients undergoing TAVI in order to select the appropriate device and access route. Conventional echocardiographic or angiographic imaging do not fully disclose anatomic details of the aortic annulus and the aortic root as they provide only two-dimensional information for three-dimensional structures. Sophisticated algorithms using three-dimensional reconstruction of CT images have been developed to reliably reconstruct the aortic root and peripheral vasculature and provide detailed information on the dimension, the eccentricity and calcification of the aortic annulus, which is essential in the simulation of a TAVI procedure and the selection of the appropriate prosthesis design and dimension. Ongoing study protocols aim to further refine the optimal patient and device selection to further improve long-term clinical outcomes.



Pre-procedural anatomy evaluation using computed tomography imaging and 3D reconstruction of the aortic root and the peripheral vasculature.

Changes in Myocardial Structure and Function after TAVI

Degenerative aortic stenosis results in left ventricular outflow obstruction, followed by structural changes of the myocardium as a response to the progressive pressure overload. Adaptive changes in myocardium and substantial gains in myocardial mass are the result of long lasting ventricular pressure overload, leading to left ventricular hypertrophy and diastolic dysfunction. As TAVI is a minimal-invasive technique that is performed during a beating heart procedure immediate changes of left ventricular function can be assessed under physiological conditions. Our group currently correlates histopathological structural changes with hemodynamic systolic and diastolic parameters to elucidate the immediate and long-lasting myocardial effects after aortic valve replacement. Information from non-invasive imaging using MRI as well as invasive parameters from conductance catheter measurement of the pressure-volume relationship will improve our understanding of pathophysiological changes related to aortic stenosis and provide insights into myocardial recovery after successful treatment.

Selected Publications

Büllesfeld L, Stortecky S, Kalesan B, Gloekler S, Khattab A, Nietlispach F, Delfine V, Huber C, Eberle B, Meier B, Wenaweser P, Windecker S (2013) Aortic root dimensions among patients with severe aortic stenosis undergoing transcatheter aortic valve replacement. JACC Cardiovasc Interv 6(1):72-83

Wenaweser P, Stortecky S, Schwander S, Heg D, Huber C, Pilgrim T, Gloekler S, O'Sullivan C, Meier B, Jüni P, Carrel T, Windecker S (2013) Clinical outcomes of patients with estimated low or intermediate surgical risk undergoing transcatheter aortic valve implantation. Eur Heart J 34(25):1894-905

Pilgrim, T, Heg D, Roffi M, Tüller D, Muller O, Vuillomenet A, Cook S, Weilenman D, Kaiser C, Jamshidi P, Fahrni T, Moschovitis A, Noble S, Eberli FR, Wenaweser P, Jüni P, Windecker S. Ultrathin strut biodegradable polymer sirolimus-eluting stent versus durable polymer everolimus-eluting stent for percutaneous coronary revascularization (BIOSCIENCE): a randomised, multicentre, non-inferiority trial. Lancet 2014, in press

BIOMEDICAL ENGINEERING RESEARCH AT OTHER INSTITUTES OF THE UNIVERSITY OF BERN

Supplementary to the previously mentioned institutions concerned with biomedical engineering research, a number of additional research institutions of the University of Bern, active in vastly different domains of science, also conduct specific research activities in biomedical engineering.

While the research interests of the institutes lie in differing domains, biomedical engineering research, with its interdisciplinary nature, benefits greatly from the specific expertise that these technological and scientific institutes provide.

Clinical Trials Unit Bern

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Cochrane Haematological Malignancies Group
Bundesamt für Gesundheit
SwissTransplant
ARTORG Center, University of Bern
Schweizerische Pädiatrische Onkologie Gruppe

Research Profile

Cllinical Trials Unit (CTU) Bern was formally founded at the end of 2007 with initial funding by the Swiss National Science Foundation (SNF). As of today, CTU Bern is one of nine core facilities of the Department of Clinical Research of the University of Bern.
The aims of the CTU are to support and collaborate in clinical trials, epidemiological studies and meta-analyses in any clinical field to strengthen and expand the evidence base for health care nationally and internationally. The CTU offers the scientific, technical and computing expertise needed to support patient-oriented clinical research at all stages, from conception to completion and dissemination. Relevant expertise is provided within the unit itself, or by facilitating and coordinating contact with outside experts. Services are provided in a modular fashion and range from advice and general support to full development of the design and conduct of clinical studies. CTU Bern works according to established scientific standards and the services offered by the unit enable clinical researchers to comply with legal and regulatory requirements.
CTU Bern is organized into five workflows: Statistics & Methodology, Data Management, Project Coordination, Quality Assurance & Monitoring, and Clinical Investigation. These workflows provide a range of services from methodological consulting, to GCP-compliant data management solutions, central/on-site monitoring, and statistical analysis. Although the primary focus of CTU Bern lies on late phase clinical studies it has some expertise on early phase clinical trials including exploratory clinical trials.

Statistics & Methodology

Initiating and conducting a clinical study according to scientific and international standards is becoming more complex and time consuming. Several issues have to be considered before initiating a study, including the relevance and potential impact, methodology, feasibility, and costs. CTU Bern provides an open access consultancy service covering all relevant aspects of study design, management and analysis. This includes power analysis and sample size estimation depending on objective, study design and other relevant aspects.

Systematic Reviews and Meta-Analysis
Decisions in health care should be informed by as high a proportion as possible of all the reliable evidence relevant to particular questions. The results of new studies should therefore be presented and interpreted within the context of previous research summarized in systematic reviews and meta-analyses.

Statistical Analysis
Data of a clinical study can be analyzed in many ways, some of which may be inappropriate in a particular situation. It is essential to pre-specify which statistical procedure will be used for each analysis, including a distinction between primary and secondary analyses and an explicit description of methods and software used for the analysis. An analysis plan has to ensure the coherent and appropriate use of study design and analysis to address the objectives of the study. The analysis has to provide coherent and relevant information while realistically acknowledging its uncertainty.

Write-Up of Scientific Reports
Particularly for inexperienced clinical researchers it may be difficult to determine a successful strategy for write-up and publication of clinical study reports. Support may be required in understanding the implicit rules and dynamics of scientific publishing.

Data Management

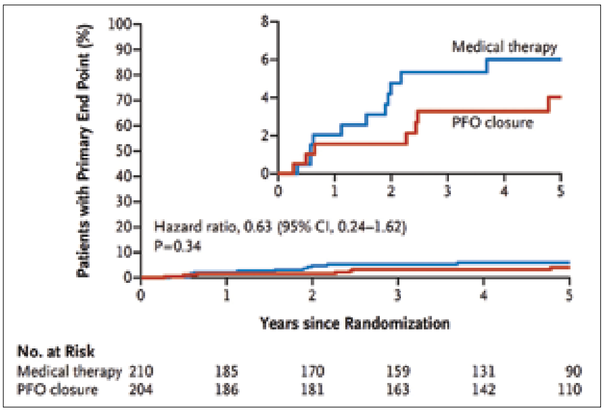
CTU Bern provides and maintains a secure and up-to-date IT infrastructure. The servers hosting the study databases are stored in a dedicated server facility. We have a 24x7 maintenance agreement with its hardware supplier in order to reduce downtime in case of hardware breakdowns. CTU Bern Data Management ensures that all software required to run the servers is regularly updated. Backups of all study- and meta-data are made regularly according to a detailed back-up plan. The plan defines internal back-ups several times per day and daily back-ups on external disks. Our security measures have been checked by the "Datenschutzaufsichtsstelle des Kantons Bern".The workflow Data Management (DM) at CTU Bern offers two different models of services and support during the setup of a clinical study database or register:

Entire setup of a study database done by CTU Bern
Based on paper case report forms (CRFs) or on study specifications (list of CRFs, variables etc.), CTU Bern will do the complete setup of the database (eCRFs, edit-checks, visit structure) using one of its two web-based Electronic Data Capturing (EDC) solutions.

Collaborative Setup
If an investigator wants to setup the study database mostly by her-/himself, we can introduce she/he to our EDC system REDCap, where studies can be set-up independently (eCRFs, edit-checks, visit structure). CTU Bern will give as much support as requested. At the end, CTU Bern will

review the implementation and put it productive, so that data-entry can start.

Electronic Data Capturing (EDC) Solutions
All EDC systems used at CTU Bern are web-based i.e. authorized users can access the study database via any computer with internet connection (and web-browser installed). Secure Sockets Layer (SSL) encryption is used to ensure a secure internet connection.
Depending on the complexity of the study design and the needs of the investigator, CTU Bern offers different GCP-compliant EDC solutions



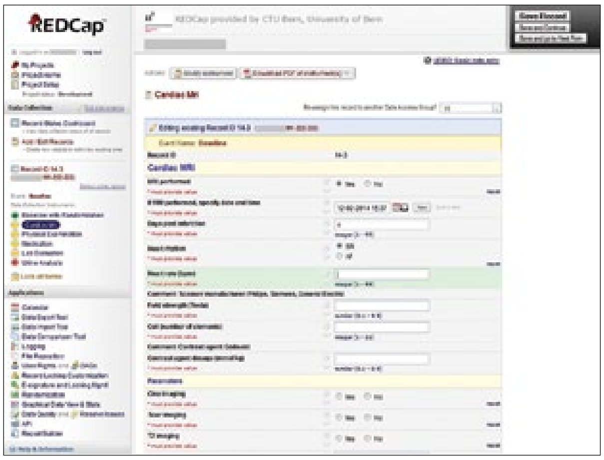
Kaplan-Meier cumulative estimates of the rate of the primary composite outcome of death, stroke, transient ischemic attack, or peripheral embolism in the PC trial.

Quality Assurance & Monitoring

CTU Bern offers quality control services (monitoring) to sponsors including sponsor-investigators working at Inselspital Bern or other interested parties for single-center or multi-center clinical studies. We offer two interrelated services to support you in ensuring a high-quality study conduct:

On-site monitoring
The on-site monitor provides support for clinical studies in terms of quality control and quality assurance. He or she visits study sites at regular intervals during the study to ensure that the study is conducted in accordance with the protocol, applicable Standard Operating Procedures (SOPs), International Conference on Harmonization Good Clinical Practice (ICH-GCP) guidelines, and regulatory requirements. For multi-center studies, the monitor is also an important point of contact between the sponsor and the center.

Central data monitoring
Central data monitoring is concerned with centralized checks of the accumulating study data. These checks are usually done on a regular basis during study conduct and include range, plausibility, and consistency checks. Because some of these measures are based on statistical techniques there is a close collaboration between the Quality Assurance & Monitoring workflow and the Statistics & Methodology workflow. There is also a close link to on-site monitoring because findings identified during central data monitoring might trigger on-site visits and vice versa.



CTU REDCap clinical trial recording software.

Clinical Investigation

The Clinical Investigation workflow is a service unit within the CTU Bern that offers professional services to investigators working at Inselspital Bern or to other interested parties engaged in single-center or multi-center clinical studies. These services include logistic support, planning, coordination and execution of clinical studies from phases I to IV as well as observational studies.

Selected Publications

Meier B, Kalesan B, Mattle HP, Khattab AA, Hildick-Smith D, Dudek D, Andersen G, Ibrahim R, Schuler G, Walton AS, Wahl A, Windecker S, Juni P (2013) Percutaneous closure of patent foramen ovale in cryptogenic embolism. N Engl J Med 368:1083-1091

Visser JA, Hokken-Koelega AC, Zandwijken GR, Limacher A, Ranke MB, Fluck CE (2013) Anti-Mullerian hormone levels in girls and adolescents with Turner syndrome are related to karyotype, pubertal development and growth hormone treatment. Hum Reprod 28:1899-1907

Scherz N, Mean M, Limacher A, Righini M, Jaeger K, Beer HJ, Frauchiger B, Osterwalder J, Kucher N, Matter CM, Banyai M, Angelillo-Scherrer A, Lammle B, Husmann M, Egloff M, Aschwanden M, Bounameaux H, Cornuz J, Rodondi N, Aujesky D (2013) Prospective, multicenter validation of prediction scores for major bleeding in elderly patients with venous thromboembolism. J Thromb Haemost 11:435-443

Leunig M, Juni P, Werlen S, Limacher A, Nuesch E, Pfirrmann CW, Trelle S, Odermatt A, Hofstetter W, Ganz R, Reichenbach S (2013) Prevalence of cam and pincer-type deformities on hip MRI in an asymptomatic young Swiss female population: a cross-sectional study. Osteoarthritis Cartilage 21:544-550

Skoetz N, Trelle S, Rancea M, Haverkamp H, Diehl V, Engert A, Borchmann P (2013) Effect of initial treatment strategy on survival of patients with advanced-stage Hodgkin's lymphoma: a systematic review and network meta-analysis. Lancet Oncol 14:943-952

Nuesch E, Hauser W, Bernardy K, Barth J, Juni P (2013): Comparative efficacy of pharmacological and non-pharmacological interventions in fibromyalgia syndrome: network meta-analysis. Ann Rheum Dis 72:955-962

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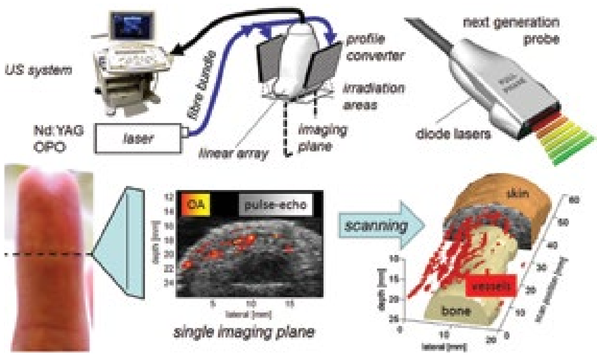
Walter Inäbnit, Haag-Streit, Liebefeld
Bernhard Nussbaumer, Pantec Engineering AG, Ruggell, Liechtenstein
NFP64 – Project partners "Opportunities and Risks of Nanomaterials ", www.nfp64.ch
SwissTransMed – Project partners ONIRIUS "Non-invasive multimodal high resolution optical acoustic imager for early hypoxia detection in neonatal brain", www.swisstransmed.ch
EU-FP7 Projectpartners FULLPHASE "Fully integrated real time multi-color photoacoustics for early disease detection", www.fullphase-fp7.eu

Research Profile

The research of the department is focused upon the investigation of various possibilities to employ pulsed infrared lasers in new medical disciplines and the optimization of the clinical outcome in fields the laser is already being used. Emphasis is placed upon four interdependent fields: (1) The study of the physical processes underlying the light propagation in tissue and the interaction of laser radiation with soft and hard tissues, (2) laser-induced reversible and irreversible changes in optical properties of tissue response and the consequence of these changes on thermal damage and ablation, (3) the development of laser and fiber delivery systems optimized for specific medical applications; and (4) the development of novel biomedical optical and ultrasound imaging techniques. In particular, we concentrate on the development of optoacoustic imaging techniques, a research area which is gaining increasing interest in medicine due to its ability to image tissue structures and function and its potential in patient-tailored tumor therapy. Questions to be addressed are of applied and fundamental science character: (i) What limits the image depth and resolution, (ii) How does laser light interact with gold nanoparticles that were taken up by cells for contrast enhancement, and (iii) How to improve multimodal optoacoustic devices for clinical use by simultaneously measuring echo and Doppler ultrasound, tissue elastography, speed of sound and optoacoustics. Further primary topics are two-photon imaging and interactions of ultrashort near infrared laser pulses with biological soft matter as well as laser-induced tissue soldering using nanoparticle scaffolds.

Optoacoustic Imaging

Optoacoustic (OA) imaging allows the display of optical contrast inside tissue based on the detection of thermoelastically generated ultrasound after tissue irradiation using short nanosecond pulsed lasers. In combination with pulse-echo ultrasound, OA is promising to improve diagnostic accuracy via the display of small blood vessels and the local blood oxygenation level within the anatomical context. An important requirement for such a combination is a clinically useful OA imaging depth of several centimeters. This has been difficult to achieve in the past owing to clutter signals originating from the site of tissue irradiation. We have combined a fiber coupled tunable laser source and a research ultrasound system, which allows real time imaging and freehand clinical scanning

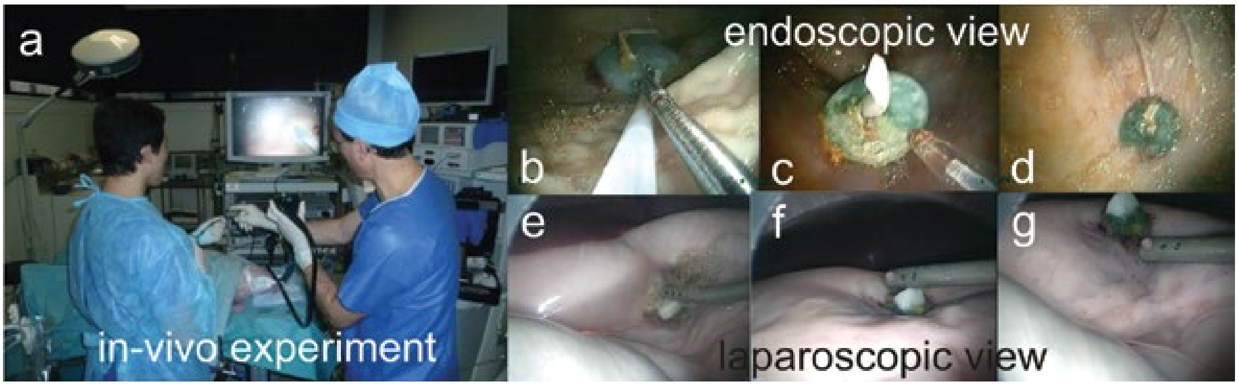


Combined ultrasound and optoacoustic imaging as a first step towards a multimodal diagnostic system able to simultaneously provide structural and functional tissue information such as micro-vasculature of the finger tip.

of humans. Sound speed as a diagnostic marker has been of interest for many years due to the fact that sound speed can reveal structural changes of tissue that come along with diseases such as cancer, cirrhosis, fibrosis, and fatty liver disease. In addition, knowledge of the spatial distribution of sound speed benefits ultrasound imaging in general: image reconstruction conventionally assumes a homogeneous sound speed, which leads to blurring and inaccurate display of tissue anatomy in the presence of acoustic aberrations. We are developing a technique with which spatially resolved detection of sound speed is achieved using conventional pulse-echo ultrasound. This technique is promising as an addition to conventional ultrasound, as well as for improving spatial resolution and contrast of all ultrasound-based modalities including OA imaging. Our reserach is directed towards the development of a multimodal diagnostic imaging system combining classical echo and Doppler ultasound with elastography, optoacoustic and speed of sound measurements.

Laser-Tissue Soldering

The purpose of our research is to provide a new minimally invasive sutureless laser-assisted tissue soldering technique applicable to both cylindrical and planar geometries such as i.e. vessel anasthomosis or sealing of the stomach wall after incision during NOTES (Natural Orifice Transluminal Endoscopic Surgery) procedures. The aforementioned geometries permit foreseeable medical needs such as urological applications, gastrointestinal, vascular anastomoses, and neurosurgical applications to be addressed. The goal is to find a new method, in advanced interventional endoscopic surgery (NOTES), to functionally connect tissue, particularly where there is no existing solution to the problem and to displace standard tissue connection techniques, which will revolutionize minimal invasive surgery. The clinical need for sutureless tissue fusion technologies stems from a trend towards minimally invasive surgery and the prolonged inflammatory response associated with traditional micro-suturing. The ability to provide a strong, liquid-tight seal in a short period of time cannot be achieved using traditional approaches. Tissue soldering is a kind of tissue fusion that is based on a heat denaturation process of proteins, providing the necessary tissue strength and liquid-tight seals; therefore it is applicable to all tissues containing proteins. The novelty of our approach in relation to existing techniques is the use of a special electrospun scaffold containing nano particles (NP) specially designed and optimized for the soldering procedure. The NPs are based on solid silica spheres covered with ICG-doped polycaprolactone. In collaboration with the Institut de Recherche contre les Cancers de l'Appareil Digestif (IRCAD) in Strasbourg we studied the long-term effect after endoscopic laser soldering gastrotomy. Essential to the success of the project is an efficient delivery system for the tissue soldering matrix and an associated intelligent light application platform developed by KARL STORZ. The platform provides inherent endoscopic visualization so that the whole procedure can be done with complete visual control. The whole closing procedure can be done in 10 - 15 min. None of the animal cases showed any signs of problems, with a total closure of the stomach already observed after one week.



Images showing the in-vivo experiments performed at the IRCAD in Strasbourg. (a) Overview of the operation field showing the handling of the endoscopic instrumentation used. (b-d) snapshots from a movie taken during the soldering procedure, (b) forceps and guiding instrument to place the plug into the gastric incision, (c) half of the plug is already soldered visualized by a clear change in the surface structure of the plug, (d) soldered plug. (e-g) snapshots taken through an additionally performed laparoscopic incision. (e) showing the water tightness of the closure (no air bubbles can be seen leaking out of the insufflated stomach), (f) picture showing the strong fixation of the soldered plug – it was not possible to mechanically push it back into the stomach, (g) final view of the soldered plug.

Selected Publications

Schönbächler A, Glaied O, Huwyler J, Frenz M, Pielesa U (2013) Indocyanine Green Loaded Biocompatible Nanoparticles: Stabilisation of Indocyanine Green (ICG) Using Biocompatible Silica-Poly (ε-Caprolactone) Grafted Nanocomposites. Journal of Photochemistry and Photobiology A: Chemistry 261:12-19

Jaeger M, Bamber J, Frenz M (2013) Clutter elimination for deep clinical optoacoustic imaging using localised vibration tagging (LOVIT). Photoacoustics 1(2):19-29

Akarçay G, Preisser S, Frenz M, Rička J (2012) Determining the optical properties of a gelatin-TiO2 phantom at 780nm. Biomed Opt Express 3(3):418-434

Peeters S, Kitz M, Preisser S, Wetterwald A, Rothen-Rutishauser B, Thalmann GN, Brandenberger C, Bailey A, Frenz M (2012) Mechanisms of nanoparticle-mediated photomechanical cell damage. Biomed Opt Express 3(3):435-46

Bogni S, Ortner M, Vajtai I, Jost C, Reinert M, Dallemagne B, Frenz M (2012) New laser soldering based closures: a promising method in natural orifices transluminal endoscopic surgery. Gastrointest Endosc 76(1):151-8

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Michel Milinkovitch, Department of Genetics and Evolution, University of Geneva, Geneva
Laurent Müller, 3D Impact Media, Bern

Research Profile

The Computer Graphics Group is part of the Institute of Computer Science and Applied Mathematics at the Faculty of Science. The field of computer graphics provides basic technologies for a wide range of application areas from the entertainment industry, communication technologies, medical visualization and scientific applications to everyday tools like digital maps. The Computer Graphics Group performs fundamental research in a broad area of topics in computer graphics, including realistic image synthesis, 3D geometry representation and processing, novel display technologies, and image and light field processing. The focus of the research group is on developing advanced algorithmic and numerical tools to provide the underlying technology for novel solutions and applications in these areas. In addition, the group is actively seeking opportunities for interdisciplinary research and is involved in an ongoing collaboration with biologists at the University of Geneva, where custom computer graphics tools are used to investigate fundamental biological questions. The research group maintains strong partnerships with national and international collaborators in academia as well as in industrial research labs. The Computer Graphics Group is actively involved in the biomedical research community through the mentoring of PhD students in the Graduate School for Cellular and Biomedical Sciences and teaching contributions to the Master of Science in Biomedical Engineering.

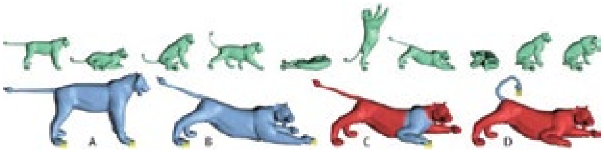
Realistic Image Synthesis

Realistic image synthesis is the problem of computing images of digital 3D environments as they would be seen by a virtual camera placed in the environment. The physical model underlying realistic rendering algorithms captures the most significant properties of light transport that are relevant to human perception, while still being computationally tractable for large, complex 3D scenes. The physical model essentially describes the light at each 3D point as the integral of the light that is transported to this point via all possible paths that connect the point to a light source. Practical rendering algorithms strive to compute approximate solutions of this integral using numerical methods, of which probably the most widely used is Monte Carlo integration. Monte Carlo methods approximate the integral by randomly sampling light paths and adding up the contributions of each path. Errors introduced by this process, however, can be visually distracting, and a large number of samples typically needs to be drawn. Even on modern CPUs, pure Monte Carlo algorithms require minutes to hours of computation time to produce acceptable results. Since computation time is roughly proportional to the number of samples drawn, the efficiency of rendering algorithms is largely determined by two factors: the ability to generate first, samples that reduce image error most; and the ability to make maximum use of the information that is contained in the generated samples to compute the final image. The Computer Graphics Group develops novel numerical algorithms to improve the efficiency of rendering algorithms. We are currently focusing on image space adaptive sampling and reconstruction methods, and Markov Chain Monte Carlo sampling techniques.

Monte Carlo rendering of a complex virtual scene may take several hours (left). With computation time limited to one minute, conventional approaches lead to noisy results (middle). With the same time budget, our image based adaptive sampling and reconstruction algorithm renders an image with few artifacts (right).

3D Geometry Representation and Processing

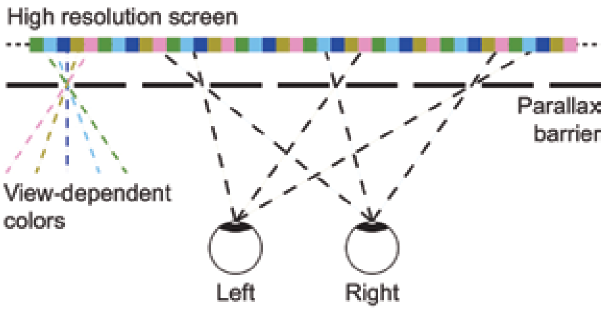
3D geometry processing is the technology to represent, process, and edit virtual 3D objects. It has applications in 3D computer graphics content production, computer aided design and manufacturing, 3D printing, and computer simulation. Research topics include 3D geometry representations, surface reconstruction from scanned 3D data, algorithms for 3D surface processing such as smoothing and parameterization, and algorithms for interactive 3D object editing. The Computer Graphics Group has pioneered novel point-sampled representations for geometry processing and interactive editing. Current research focuses on data-driven modeling, where the idea is that 3D content creators access databases of existing material to browse, retrieve, edit, enhance, or combine 3D content, thereby creating the desired result. The success of this paradigm hinges first on the availability of suitable data, and second on data representations and user interfaces to perform the desired operations. A main objective of ongoing work is to develop novel methods to scan 3D geometry and automatically build representations that can be interactively edited and manipulated by a user in an intuitive way.



An example of data-driven modeling for three-dimensional shapes. Top row: A database of ten lion example poses. Bottom row: A user generates a novel pose (D) using a sequence of simple interactions (A-C).

Novel Display Technologies

Novel display technologies such as multi-view 3D displays offer viewing of high-resolution stereoscopic images from arbitrary positions without special glasses. Conceptually, these displays consist of view-dependent pixels that reveal a different color to the observer based on the viewing angle. View-dependent pixels can be implemented using conventional high-resolution displays and parallax-barriers, integral lens sheets, or holographic screens. Although the basic optical principles of multi-view auto-stereoscopy have been known for over a century only recently such displays have become practical. Today, various manufacturers offer multi-view displays based on parallax barriers, lenticular sheets, or multi-projector systems. Multi-view displays feature a number of advantages over competing autostereoscopic display technologies, such as stereo-projection systems using shuttered or polarized glasses. Most importantly, multi-view displays do not require users to wear any special glasses, which leads to a more natural and unrestricted viewing experience. They also do not require head tracking to provide motion parallax; instead, they provide accurate perspective views from any point inside a viewing frustum simultaneously. They are truly multi-user capable, since none of the display parameters needs to be adjusted to a specific individual user. As a disadvantage, multi-view displays suffer from inferior image quality compared to many active stereo systems using shuttered or polarized glasses. With current technology, their spatial resolution and the amount of depth that they can represent is more limited than in active stereo systems. The Computer Graphics Group recently proposed a multi-dimensional signal processing framework to address these issues. Using this framework, the objective is to develop techniques to pre-process image data for multi-view 3D displays to optimize image quality. The framework includes a concise model to describe sampling and reconstruction on such displays, making it possible to take into account and compensate for the physical properties of the display and significantly improve image quality.



A multiview autostereoscopic display implementing pixels with view dependent colors created by a parallax barrier.

Image and Light Field Processing

The Computer Graphics Group also investigates basic algorithms for image and light field processing. Light fields can be interpreted as an extension of conventional 2D images to a 4D spatio-angular representation of light rays. Light fields have proven a useful representation for image based rendering and computational photography, enabling applications such as digital refocusing. We have recently developed a dual-domain image filter that operates in both the spatial and frequency domain. The filter obtains state-of-the-art performance for image denoising and compression artefact removal. We are currently extending this filter to light fields, where we also investigate its use for depth reconstruction. Based on this framework, we are developing a hand-held light field photography technique that will allow casual users to capture and process light fields, and perform advanced computational photography operations such as 3D reconstruction, refocusing, and image inpainting.

Selected Publications

Rousselle F, Manzi M, Zwicker M (2013) Robust Denoising using Feature and Color Information. Computer Graphics Forum 32(7):121-130

Knaus C, Zwicker M (2013) Dual-Domain Image Denoising. In Proc of 20th IEEE International Conference on Image Processing (ICIP):440-444

Donatsch D, Färber N, Zwicker M (2013) 3DTV-Conference: The True Vision-Capture, Transmission and Display of 3D Video (3DTV-CON):7-8

Institute for Evaluative Research in Medicine

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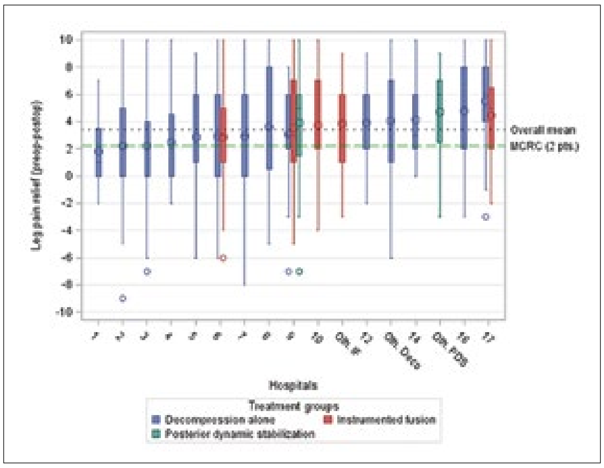
Research Profile

The Institute for Evaluative Research in Medicine has defined its mission as a dedicated academic research institute in the field of health service and outcome research at the interface of quality assurance in medicine and delivery of care. It has become an interdisciplinary think tank between surgeons, physicians, epidemiologists, computer scientists and experts from other disciplines involved in health care. Their input is crucial to IEFM's overall mission of contributing to the advancement of the rapidly changing health care environment. IEFM is active in various areas of evaluative medicine. Traditional clinical trials research is expanded on by including national and international registries, and designing and developing IT systems for the collection, archiving and distribution of medical data. In a cooperation of the group for Evaluative Clinical Research and the Medical Informatics and Documentation group, national and international projects are implemented on the institute`s proprietary MEMdoc documentation platform. Thanks to the sophisticated concept of distributed national satellite servers, data privacy and protection regulations are fulfilled in the participating countries while the central database and application are housed at the University of Bern. Capture of clinical, implant and image data from routine clinical settings are the specialty of MEMdoc. User needs regarding data recording, data usage, and data reporting are constantly considered and integrated. The institute`s clinical researchers consult in content development and structuring of case report forms, choice of outcome forms for patients, data



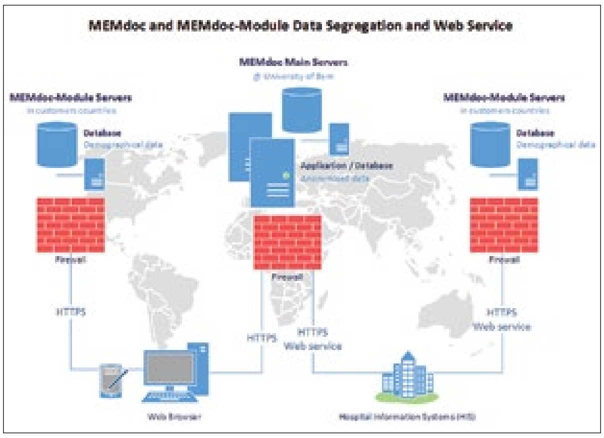
Leg pain relief per hospital and treatment in patients with lumbar spinal stenosis (based on Spine Tango registry data).

collection modes, different language versions, and finally take on the task of data evaluation and reporting, be it as an integrated online function or as more comprehensive offline reports and publications. The applied statistical methods account for the known challenges regarding bias and internal validity of observational study designs.

Medical Informatics and Documentation

One of the major challenges in developing software for medical environments is creating an effective communication chain between IT developers and the clinical staff in the hospitals. At IEFM the development team is under the same roof as the medical research and customer support teams. This organization expedites the communication channels and provides the development team with timely and valuable feedback about the needs of the end users. Over the years IEFM has established an in-house competence with regards to the requirements and usability of software within the current clinical work flow. The end result, MEMdoc, is a system that facilitates the documentation process for clinicians and improves the quantity and quality of the collected data. Data privacy protection has always been a primary concern for users and IEFM. Patients whose medical information is stored in MEMdoc and their health care providers must be informed and confident that the privacy of the data is secured and that its handling and storage meets all local and national regulations. Since most data protection agencies do not issue general certificates of compliance for specific platforms like MEMdoc, each project must be examined and validated individually. Several studies on MEMdoc have been approved by agencies from Germany, France, Switzerland and the Canton of Bern. Through each project our understanding of the matter has deepened and our technical solutions have improved. The current Release 4 of the MEMdoc Portal has been in live mode since 2011 and has undergone many changes and improvements. New tools have been developed for easier handling of users, patients and studies while existing tools have been enhanced to meet the ever growing needs of the user community. Application flow and features, although much appreciated by users, are secondary to easy and flexible data collection methods. With this in mind the MEMdoc application has expanded data collection facilities for all forms of medical data including image and implant data. OMR (optical mark recognition), a proven technology for data collection, has long been a staple of the MEMdoc application and has been expanded and simplified in Release 4 with support for both Windows and Mac users from all popular web browsers. Image capture has been extended with a redesigned image upload function that allows multiple uploads for a single case as well as simplified image retrieval for subsequent analysis and presentations. The SEDICO (secure data integration concept) implant capture tool, previously only available to users documenting on the MEMdoc central server, is now available to MEMdoc-Module users. Users who do not use the SEDICO interface can now use an inexpensive handheld barcode reader to scan implant barcodes directly into the recorded questionnaires. Finally, access to the ever growing list of online suppliers and products has been enhanced with a faster search engine and the ability to segregate products by category (e.g. cups, heads, stems, liners, etc.) and anatomical location of use.

While one of the major advantages of the MEMdoc system lies in its web-based access allowing contributions from users around the world to create a global data pool, IEFM is aware that MEMdoc is not the only documentation solution available. Users of other systems, however, may still want to contribute to a nationally endorsed data pool like Spine Tango housed exclusively on MEMdoc. To this end IEFM developed the MEMdoc Web Service. This tool provides an interface that can be integrated into existing hospital information systems (HIS) and virtually any third-party data collection system to facilitate data entry, reduce physician workload and decrease data entry errors. Through our web service, applications can request the latest version of the definition of our data collection forms along with the complete set of validation rules. It is then up to the third-party application to collect the data and apply the rules. Once the data is collected it can then be contributed to the MEMdoc central repository. We developed such a system to ensure that the data received from external sources was of the same quality as that recorded directly on MEMdoc. Hence, redundant data entry is reduced while the value of the collected information is increased via silent synchronization of local data with a central instance. Such an interface between commercial systems and an academic documentation portal is unique and the combination of the advantages of both approaches goes beyond the current state of art of medical documentation.



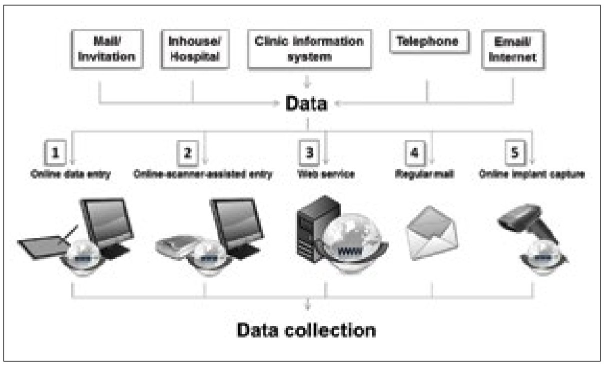
MEMdoc and MEMdoc-module data segregation principle to protect sensitive data.

Evaluative Clinical Research

The group for Evaluative Clinical Research focusses on analyses of large observational datasets collected with the MEMdoc portal. Also, data from public databases like those of the Swiss Federal Statistical Office or similar foreign databases are evaluated. Specific analytical models are used to maximize the evidence that can be gathered from the data, and cross registry benchmarking is used if, for instance, a clinical comparator is missing in one project but present in another. The group closely interacts with the group for Medical Informatics and Documentation by composing project specific statistical scripts for ready-made reports that are periodically uploaded to the users` accounts on MEMdoc. That way, a direct return of their documentation efforts can be presented to the MEMdoc users that often go beyond their capabilities of analyzing their data. Moreover, the group offers statistical and methodological support to all MEMdoc users regarding formulation of study designs, research protocols, data evaluation for hypothesis based research going beyond the standard reports, creation of slides for presentations and writing up scientific manuscripts. Most of the institute`s project partners make use of the complete evaluative cycle that our team offers, and we firmly believe that database design, project execution and data evaluation should be in one and the same expert hands.

SIRIS, the Swiss Implant Registry

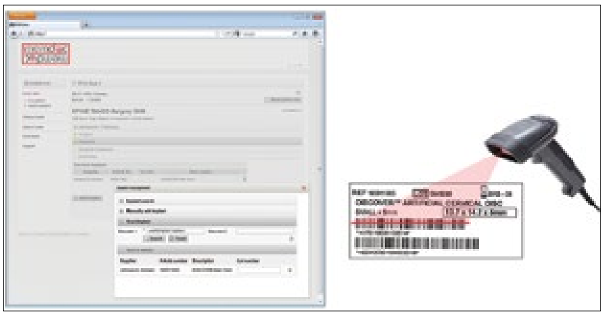
It took 10 years from terminating the traditional Maurice E. Müller European IDES hip and knee registries until the Swiss Implant Registry SIRIS could officially be launched in September 2013. Representing the core competence of the IEFM, all our expertise of medical informatics, project management and support, methodological ground work and data evaluation is demanded by this, our largest endeavor. Within a few months, close to 150 Swiss hospitals and around 1500 registered users have started entering their 36`000 annual hip and knee prosthesis implantations. Thanks to our previous analytical work with the French Hip Registry of SOFCOT, which we have been hosting since 2006, and our collaboration with the Australian joint registry, we are looking forward to providing the international orthopaedic community with results from SIRIS about quality and survival of the numerous implant types used on the Swiss market. An essential ingredient of SIRIS and any other implant registry is precise, yet time and resource efficient capture of implant data. This is put into practice with the MEMdoc barcode scanner technology and our partner GHX, a medical data logistics house, which uses the reordering process of implants to route this data set to MEMdoc and match it with the respective clinical data set. There are plans to integrate other orthopaedic and eventually even non-orthopaedic implants into the SIRIS project, which would make it the central turntable of implant post-market surveillance and quality assurance in Switzerland.



Data collection modes in MEMdoc.

Spine Tango and SWISSspine – the spine registries

Spine Tango, the international spine registry of Eurospine, the Spine Society of Europe, is the only international spine registry to date and represents the most comprehensive developmental and evaluative efforts of IEFM. Since its initiation in 2000, five generations of surgical case report forms have been developed, the only registry form for non-surgical spinal treatments, often still the therapeutical gold standard in spinal diseases, and the new add-on forms for adult degenerative deformity and adolescent scoliosis form the battery of physician based documentation instruments of Spine Tango. In addition, a multitude of patients based questionnaires, the so called PROMs (patient reported outcome measures), are available. Thanks to its meanwhile global dimensions, Spine Tango is a multi-lingual registry that serves about 70 hospitals in all parts of the world, from Europe, to North and South America and Australia. The distributed server concept was originally developed for the Tango, which is now put into practice with satellite servers in Germany, Italy, Great Britain, Belgium, Poland, Austria, the USA and Australia. A clone of Spine Tango has been implemented for DWG, the German Spine Society. Despite being a separate project, the Swiss governmentally mandated HTA registry SWISSspine, has been collecting data about total disc arthroplasty, balloon kyphoplasty, interspinous spacers and posterior dynamic stabilization devices since 2005. Unique knowledge about the performance and safety of these therapies in day-to-day clinical settings has been generated, and in the years 2014-2016 we will conduct the first national ten-year follow-up of total disc arthroplasty in the world. The evidence derived from SWISSspine decides about permanent reimbursement of the concerned therapies by the Swiss basic health insurance, making it a model for cooperation between industry, the specialist society, and academia.



Standardized implant capture using bar-code reader technology.

Swissnoso – surveillance of nosocomial infections in Switzerland

Swissnoso in collaboration with ANQ (National Association for Quality Control in hospitals and clinics in Switzerland) has designed a national registry for the surveillance of surgical site infections (surgical wound infections) based on an existing program in Western and Southern Switzerland. This registry now documents surgical site infections for 15 different intervention types and for each participating hospital and allows anonymous benchmarking between them, while adjusting for case mix. These data are provided in the form of annually published reports for each hospital. It was started in June 2009 and currently includes around 145 hospitals and departments.

DGU registry on pelvic trauma

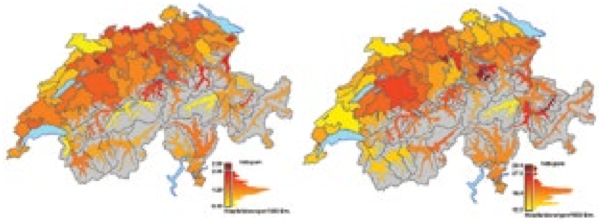
The German Trauma Society`s (DGU) registry on pelvic fractures was moved onto the MEMdoc platform in 2004 and is meanwhile used by 39 participating hospitals in Germany and Belgium, which came along with an English version of the documentation forms introduced in 2011. Further expansion of the registry to other European and non-European countries is desired and expected in the upcoming years. In 2013 the registry reached the mark of 10'000 documented pelvic trauma cases. The data on pelvic fractures are being extensively used for research. The analyses in the registry have already resulted in over 20 peer-reviewed publications in English- and German-speaking journals. Regular meetings and scientific collaborations with this group underline the close and fruitful partnership with our data center and resulted in a multitude of new publications and the development of the first follow-up form of this project which was implemented in late 2009 and is increasingly being used among the participants.

Spitex - Home Care Data

Home Care Data is the data pool of the Spitex association of Switzerland. Spitex is a nationwide organization for support, health care and nursing outside hospitals and nursing homes. Spitex uses the RAI-Home-Care for the surveillance of the home care demand, which is an international instrument for documentation of data from home-care area adapted for Switzerland. Numerous applications for data acquisition were developed by several licensed IT companies and are in use at hundreds of locations in Switzerland. In 2013 all these IT companies were mandated to develop an interface to the MEMdoc platform that should enable a periodical transfer of anonymised data. Thus, MEMdoc serves as a central data pool and monitoring tool for the collected national data.

Health Services Research

Public databases can provide a lot of meaningful information that can mostly not be generated otherwise. Data analyses and comparisons in international contexts can be even more interesting and allow conclusions that may be relevant for a complete healthcare system. Specialized statistical methods allow the creation of maps of health care utilization. So called health service areas help visualize the spatio-temporal variation of health care usage between regions and correlate this variation with the density of healthcare providers or hospitals. Also, patient flows in and out of health service areas can be quantified and visualized. Applying such approaches onto registry data and linking it with public data is the next generation of health services research that is enabled by IEFM`s cooperation with OBSAN and its registry activities.



Swiss regional variations in performed total knee arthroplasties in the years 2002-2003.

Selected Publications

Aghayev E, Bärlocher C, Sgier F, Hasdemir M, Steinsiepe KF, Wernli F, Porchet F, Hausmann O, Ramadan A, Maestretti G, Ebeling U, Neukamp M, Röder C (2013) Five-year results of cervical disc prostheses in the SWISSspine registry. Eur Spine J 22(8):1723-30

Aghayev E, Elfering A, Schizas C, Mannion AF; SWISSspine Registry Group (2013) Factor analysis of the North American Spine Society outcome assessment instrument: a study based on a spine registry of patients treated with lumbar and cervical disc arthroplasty. Spine J doi:10.1016/j.spinee.2013.07.446

Aghayev E, Teuscher R, Neukamp M, Lee EJ, Melloh M, Eggli S, Röder C (2013) The course of radiographic loosening, pain and functional outcome around the first revision of a total hip arthroplasty. BMC Musculoskelet Disord 14(1):167

Burkhardt M, Nienaber U, Holstein JH, Culemann U, Bouillon B, Aghayev E, Paffrath T, Maegele M, Pohlemann T, Lefering R; TraumaRegister DGU(®); Pelvic Injury Register of the German Trauma Society (2013) Trauma registry record linkage: methodological approach to benefit from complementary data using the example of the German Pelvic Injury Register and the TraumaRegister DGU(®). BMC Med Res Methodol 13:30

Hübschle L, Borgström F, Olafsson G, Röder C, Moulin P, Popp AW, Külling F, Aghayev E; the SWISSspine Registry Group (2013) Real-life results of balloon kyphoplasty for vertebral compression fractures from the SWISSspine registry. Spine J doi:10.1016/j.spinee.2013.12.019

Pizanis A, Pohlemann T, Burkhardt M, Aghayev E, Holstein JH (2013) Emergency stabilization of the pelvic ring: Clinical comparison between three different techniques. Injury 44(12):1760-4

Röder C, Boszczyk B, Perler G, Aghayev E, Külling F, Maestretti G (2013) Cement volume is the most important modifiable predictor for pain relief in BKP: results from SWISSspine, a nationwide registry. Eur Spine J 22(10):2241-8

Spross C, Aghayev E, Kocher R, Röder C, Forster T, Kuelling FA (2013) Incidence and risk factors for early adjacent vertebral fractures after balloon kyphoplasty for osteoporotic fractures: analysis of the SWISSspine registry. Eur Spine J Oct 2 [Epub ahead of print]

Zwingmann J, Südkamp NP, König B, Culemann U, Pohlemann T, Aghayev E, Schmal H (2013) Intra- and postoperative complications of navigated and conventional techniques in percutaneous iliosacral screw fixation after pelvic fractures: Results from the German Pelvic Trauma Registry. Injury 44(12):1765-72

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Research Profile

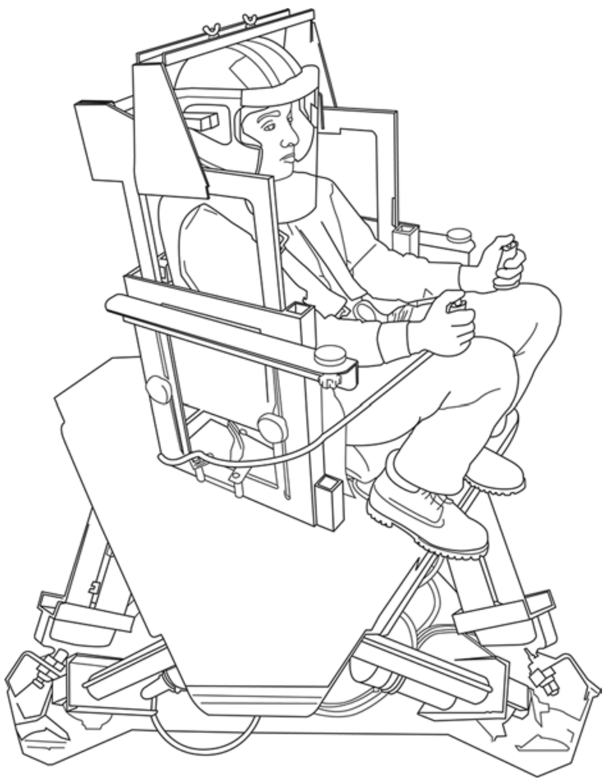
We investigate the basic mechanisms that underlie cognitive functions like perception, mental imagery, learning, decisions and spatial orientation. Our laboratories are equipped with virtual reality technology, a MOOG motion platform, eye tracking facilities, EEG, GVS, and CVS. The members of the group are experienced with various psychophysical methods, advanced statistical data analysis, and computational modelling. We are responsible for introductory and advanced statistics courses in the Psychology curriculum. As well as being strongly involved in basic research projects, we are keen on implementing our findings in clinical research. Promoting cognitive performance will become a main challenge for the future of society as life expectancy has increased rapidly, while, at the same time, knowledge decays faster and faster. We frequently collaborate locally with partners from ENT, Neurology, Psychiatry, and Pathology and we are engaged in several international collaborations.

Mental Imagery: Seeing with the Mind's Eye

Mental imagery is a core cognitive ability, which aids problem solving, memory, planning, and creativity. We investigate the neuro-cognitive mechanisms that underlie mental imagery, develop tools to measure individual differences, explore new ways to use mental imagery in cognitive training, and investigate how mental images interact with sensory processing from other modalities. We were able to demonstrate that mental imagery training improves performance in visual perception tasks. The perceptual threshold was reduced in the same manner as expected after perceptual learning with real stimuli. Previous models on perceptual learning all require a physical stimulus whereas our experiments revealed that perceptual learning - the most basic form of learning - can result from imagery training (funded by SNF). Moreover, recent research from our group shows that there are systematic eye movements during mental imagery even though there is no perceptual input to be processed. The eyes tend to revisit the location where stimuli have been encoded when the information needs to be retrieved at a later point in time. We are currently examining in more detail the non-sensory role eye fixations during memory retrieval, mental image construction and mental image scanning, including patient groups (e.g., patients with abducens paresis) and with the use of TMS and MEPs.

Virtual reality set-up for immersion in realistic scenes and interaction with avatars. The head mounted display is equipped for eye tracking.

Once we know more about the functional role of eye movements in memory and imagery we can design interventions to promote cognitive performance.



Moog motion platform (six degrees of freedom) used for psycho-physics of self-motion perception.

Spatial Cognition and the Vestibular Sense

Several projects focus on the processing of gravito-inertial information, and we use Bayesian statistics for modelling and to analysing mechanisms of perception (e.g., subjective visual vertical). In several experimental studies we were able to demonstrate that vestibular information is involved in high-level cognitive tasks such as mental body transformations, numerical cognition, affective processes, empathy and decisions. In collaboration with the ENT Department we are currently developing cognitive rehabilitation tools for unilateral and bilateral vestibular patients suffering from chronic symptoms (e.g., vertigo). Using an extended training regime we aim to activate via top-down processes cortico-fugal vestibular projections in order to counteract the asymmetry in brainstem vestibular nuclei as they result from unilateral loss (funded by SNF).

Decisions in Diagnostics and Neuroeconomy

More recently, we started to investigate decisions in purchase situations and in medical diagnostics. We analysed how pathologists take decisions, and how decisions are influenced by prior exposure to low magnification samples. We investigate when biases in judgment start to emerge and what can be done to counteract the bias. This could be implemented in professional education. Cognitive psychology has a lot to offer, and its use in the clinical context is by far not exploited.

Selected Publications

Martarelli CS, Mast FW (2013) Eye movements during long-term pictorial recall. Psychol Res 77(3):303-309

Preuss N, Mast FW, Hasler G (2014): Purchase decision-making is modulated by vestibular stimulation. Front Behav Neurosci 8:51

Preuss N, Hasler G, Mast FW (2014). Caloric vestibular stimulation modulates affective control and mood. Brain Stimulation 7(1):133-40

School of Dental Medicine: Translational Biomaterials Research in Implant Dentistry and Periodontology

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Research Profile

Biomaterials play an important role in implant therapy and regenerative techniques in dental medicine. Initiated in the early 1970's by André Schroeder, the School of Dental Medicine has a long-standing tradition of more than 40 years in translational research to examine new biomaterials in implant dentistry and periodontology with the aim to develop new or improve existing surgical techniques for the benefit of patients. Our successful concept is based on a multidisciplinary approach linking the two departments with global players in the dental Medtech industry located in Switzerland. This mutually beneficial interplay is reflected in the fact that we are recognized as a world leading institution in the field. Besides our high-end clinical expertise and research, two laboratories for preclinical research make significant contributions to our reputation and success.

The first laboratory was established in 1996 when Robert Schenk moved to the School of Dental Medicine. In 2005, this lab was merged with another histology laboratory and was later renamed "Robert K. Schenk Laboratory of Oral Histology". The lab has been since headed by Dieter Bosshardt and has state-of-the-art equipment. Significant investments, particularly in digital microscopy and image analysis, were made in 2008 and 2013 to maintain the reputation of a world-leading laboratory in oral histology.

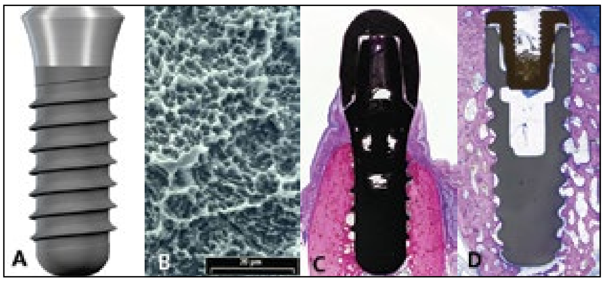
The second lab is the Laboratory of Oral Cell Biology. It was established in 2009 and is currently headed by Reinhard Gruber.

The Robert K. Schenk Laboratory of Oral Histology is equiped with state-of-the-art digital microscopy and image analysis.

Surface and Material Research of Dental Implants

The examination of bone integration of titanium implants with a micro-porous TPS coating was the first preclinical study done by André Schroeder in the early 1970's. In the mid 1980's, preclinical research started to focus on surface characteristics of titanium implants to improve osseointegration. In the late 1990's, preclinical and clinical studies demonstrated that a microrough titanium surface produced by sandblasting and acid-etching (SLA) allowed faster osseointegration, and hence much shorter healing periods. Further progress was made in the mid 2000's with a hydrophilic SLA surface, which allowed a further reduction of the healing period for patients.

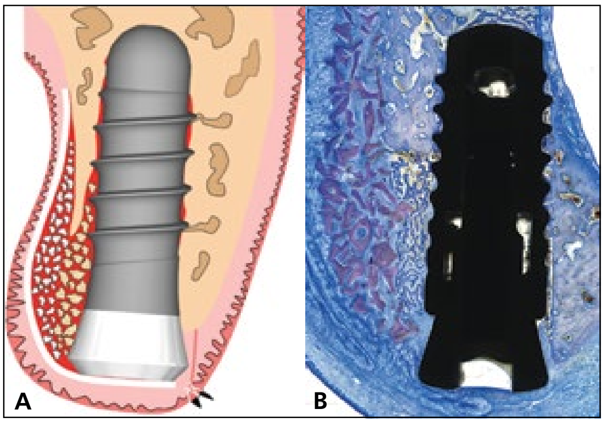
In the past 5 years, the research focus changed to the examination of alternative implant materials, such as titanium-zirconia alloys or pure zirconia implants. With both materials, bone integration and the influence of surface characteristics on the speed and percentage of bone apposition, are examined.



(A-C) Surface modifications like gritblasting and acid-etching (SLA) produce a microrough surface that accelerates osseointegration of titanium implants with much shorter healing periods. (D) Zirconia implants still undergo surface modifications to accelerate osseointegration.

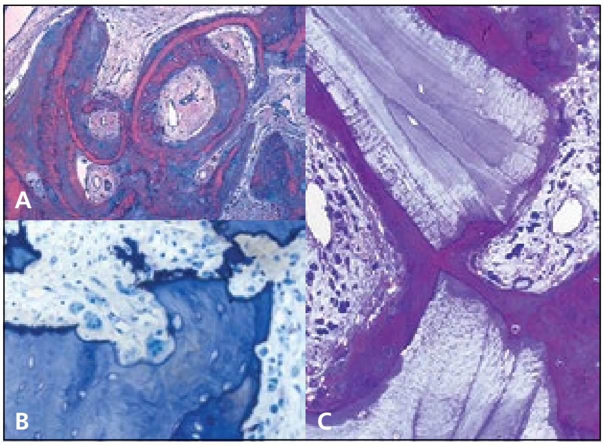
Biomaterials for Bone Augmentation in Implant Dentistry

A prerequisite for achieving and maintaining successful osseointegration of dental implants is the presence of a sufficient bone volume at the recipient site. Guided bone regeneration (GBR) is a technique widely used to augment bony defects in the alveolar ridge. While a barrier membrane shields off the soft connective tissue from the underlying bone defect, autologous bone and various bone substitute materials are used to support the barrier membrane and act as a scaffold to promote bone ingrowth. The long-term success of dental implants in GBR-generated bone depends on the volume stability of soft and hard tissues. Autologous bone grafts are considered the gold standard for bone augmentation, since they have osteogenic properties, yet resorption is high. One branch of our research investigates the impact of paracrine signals of molecules released from bone chips on mesenchymal cell differentiation. To overcome the disadvantage of fast resorption, autologous bone is mixed with CaP-based bone substitutes with a low substitution rate. Thus, unraveling the mechanism behind the slow resorption pattern of these biomaterials is another clinically relevant research topic.



Schematic drawing (A) and histology after 4 weeks of healing (B) of a GBR procedure using autologous bone, a slow-resorption bone substitute material and a collagen barrier membranes for lateral ridge augmentation.

Biomaterials for Periodontal Regenerative Therapy
Periodontitis is one of the most common chronic bacterial infections in humans. Untreated periodontitis eventually results in tooth loss. Guided tissue regeneration (GTR) is a technique used to regenerate lost periodontal tissues around teeth. The rationale behind GTR is to use a physical barrier membrane to selectively guide cell proliferation and tissue expansion of cells from the periodontal ligament and alveolar bone into the periodontal defect. Autologous bone and bone substitute materials are all used with the aim of achieving periodontal regeneration, but the regeneration of four tissues (i.e., bone, periodontal ligament, cementum, gingiva) is challenging. Our group is evaluating the effects of combinations of biologically active molecules with bone substitute materials on downstream cellular pathways such as cell attachment, proliferation, and differentiation of mesenchymal cells.



Autologous bone is regarded as the gold standard for bone augmentation because of its osteoconductive, osteoinductive and osteogenic properties. Although autologous bone accelerates early bone formation (A), bone resorption is pronounced (B). (C) Bone substitute materials like this xenogeneic material also show good osteoconduction, but resorption is minimal and they stay in place for a long time.

Biomaterials for Gingival Recession Coverage
Gingival recession is defined as the exposure of the root surface and affects many adults. Root coverage procedures not only aim to obtain complete root coverage and to improve esthetics, but also to increase the thickness of the soft tissue covering the recession. Various types of periodontal surgical procedures with and without soft tissue grafting and/or biologic agents are in use. Soft tissue grafts are usually harvested from the palate as connective tissue graft (CTG). Our group is evaluating the effects of biologically active molecules (enamel matrix derivative) on the attachment, proliferation, and differentiation of palatal or gingival connective tissue cells. Recent findings from our laboratory suggest that TGF-βRI kinase activity is necessary to mediate the effects of enamel matrix derivative on gene expression in vitro. However, since CTG harvesting is associated with increased morbidity and prolonged surgical time, our group is testing new biomaterials in clinical and preclinical studies.

Selected Publications

Aroca S, Molnár B, Windisch P, Gera I, Salvi GE, Nikolidakis D, Sculean A (2013) Treatment of multiple adjacent Miller class I and II gingival recessions with a modified coronally advanced tunnel (MCAT) technique and a collagen matrix or palatal connective tissue graft: a randomized, controlled clinical trial. J Clin Periodontol 40:713-720

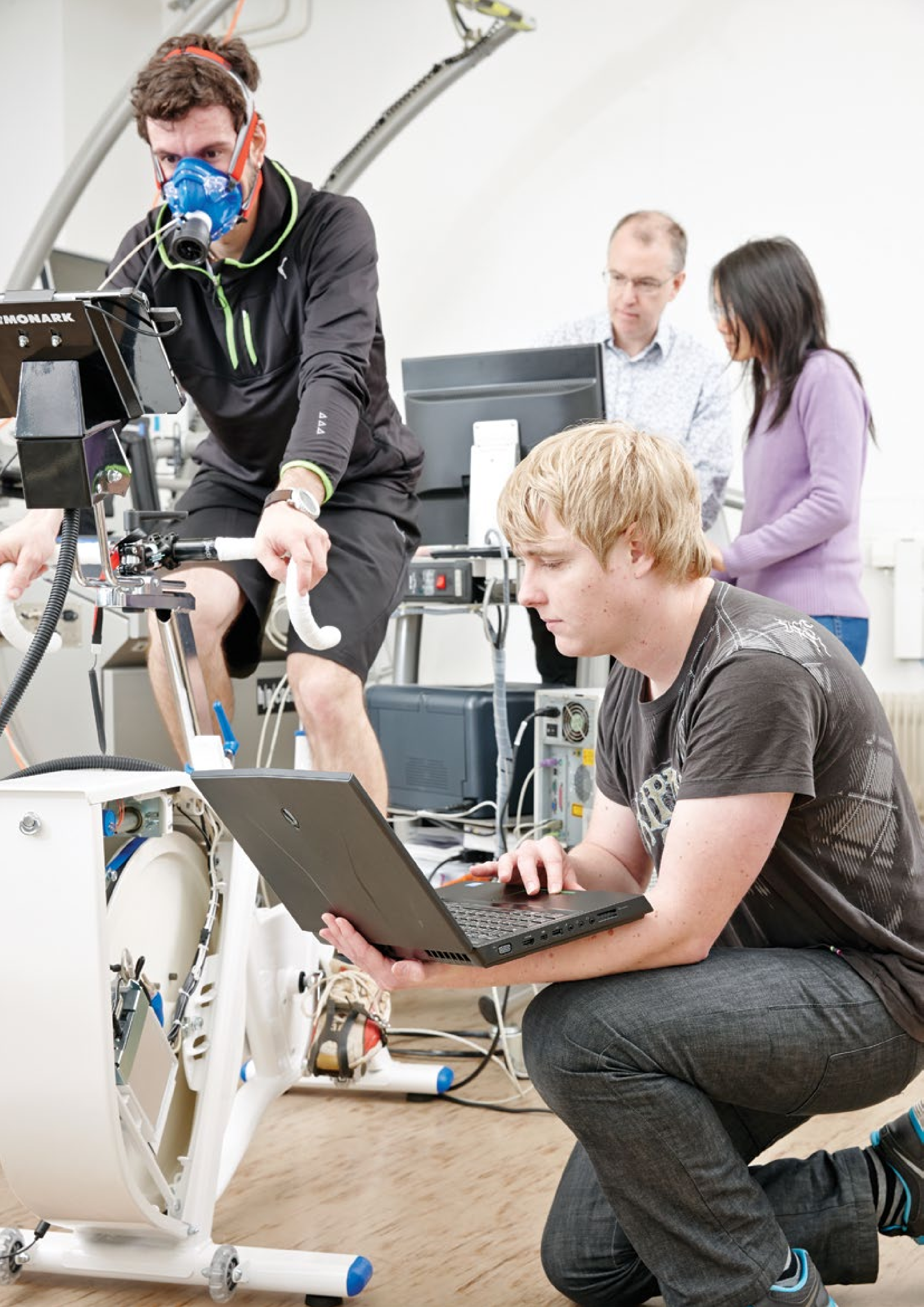
Buser D, Chappuis V, Kuchler U, Bornstein MM, Wittneben JG, Buser R, Cavusoglu Y, Belser US (2013) Long-term stabilty of early implant placement with contour augmentation. J Dent Res 92:176S-182S

Chappuis V, Engel O, Reyes M, Shahim K, Nolte LP, Buser D(2013) Ridge alterations post-extraction in the esthetic zone: A 3D analysis with CBCT. J Dent Res 92:195S-201S

Gruber R, Bosshardt DD, Miron RJ, Gemperli AC, Buser D, Sculean A (2013) Enamel matrix derivative inhibits adipocyte differentiation of 3T3-L1 cells via activation of TGF-βRI kinase activity. PLoS One 12(8):e71046

Miron RJ, Gruber R, Hedbom E, Saulacic N, Zhang Y, Sculean A, Bosshardt DD, Buser D (2013) Osteogenic and osteoclastic growth factor release from autogenous bone grafts. Clin Impl Dent Rel Res 15:481-89

Saulacic N, Hug C, Bosshardt DD, Schaller B, Buser D, Haeniwa H, Iizuka T (2013) Relative Contributions of Osteogenic Tissues to new bone formation in periosteal distraction osteogenesis: Histological and histomorphological evaluation in a rat calvaria. Clin Implant Dent Relat Res 15:692-706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BERN UNIVERSITY OF APPLIED SCIENCES

Companies in the sector of Biomedical technology are extremely innovative, experience strong growth, and are faced with the constant challenge of acquiring qualified professional employees. Who have to possess a profoundly technical knowledge and who are to act in an application-oriented and interdisciplinary conduct. The Bern University of Applied Sciences makes a crucial contribution to the success and competitiveness of this sector and the Canton of Bern. It provides customised services in education and further training, in applied research and development as well as in the transfer of technological knowledge. Profound, technical and application-oriented.

With the Bachelor of Science in Medical Informatics, the Bachelor of Science in Micro- and Medical Technology and the Masters of Advanced Studies in Medical Informatics and Medical Technology, it promotes the qualifications of professional employees onto the appropriate levels. Due to the close link between research and teaching, new knowledge and developments are rapidly incorporated in tuition, resulting in high-quality and practically based teaching. In the autumn of 2014, the first cohort of highly-coveted Bachelors of Science in Medical Information Technology trained in Switzerland will join the professional world. As the result of the cooperation with the University of Bern, the Bern University of Applied Sciences exerts its technical expertise into the Master of Science in Biomedical Engineering. Graduates of Universities of Applied Sciences of appropriate scientific/technical subject areas study on an interdisciplinary basis together with co-students from different specialist- and cultural backgrounds. Successful graduates are enabled access to a doctorate with the aim of graduating with a PhD.

But also the research institutes of the Bern University of Applied Sciences are destined to develop innovative solutions together with partners. They base their practical research on the needs of the industry and society as well as generate valuable and profound research results. They are efficiently networked and combine expertise from various different disciplines. In this manner, they can advance developments in close collaboration with companies and other educational and research institutions and transform them into marketable or socially relevant innovations.

Bern University of Applied Sciences: A partnership that is worth it!

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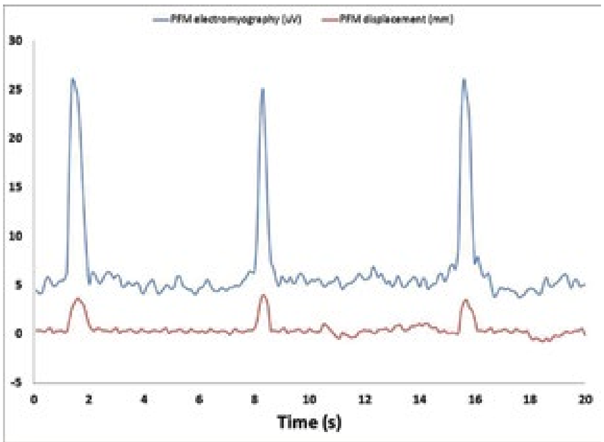
Research Profile

The Applied Research and Development Physiotherapy unit of the Health Department at the Bern University of Applied Sciences focuses on the functional analysis of human movement in relevant, daily life, activities. The movement laboratory is equipped with essential kinematic, kinetic and neuromuscular analysis methods to provide an excellent environment for movement science research. In addition to general facilities necessary for teaching physiotherapy bachelor or master students, the profile of the lab has a number of foci: one research group investigates pelvic floor muscle characteristics and develops diagnostic tools and therapeutic concepts to enhance incontinence therapy. The investigation of postural control and movement patterns in elderly people, as well as other musculoskeletal complaints, through the use of stochastic resonance whole body vibration training interventions is a second focus area. A third focus is placed on neuromuscular and biomechanical adaptations of the lower extremity to training and therapy interventions. Studies on hypermobile women, adaptations of running gait pattern or current research on therapy adaptions in pes planovalgus associated complaints underline this focus.

Stress Urinary Incontinence Physiotherapy

Stress urinary incontinence (SUI) is a condition which is often found in women and affects and impairs the physical, psychosocial, social and economic well-being of affected individuals. SUI continues to remain a taboo, with only a minority of incontinent women consulting a physician about their problem due to shame and embarrassment, lack of information about their treatment options, fear of surgery and the misconception that incontinence is an inevitable consequence of age or giving birth.
SUI physiotherapy aiming at pelvic floor muscles (PFM) functioning is the most commonly used treatment, and has been shown to be effective and recommended as a first-line therapy. But the optimal and standardized training protocol especially for involuntary, reflexive PFM contractions remains unknown. So far, no light has been shed on the reflexive type of contraction and displacement during impact loading on the PFM, as in coughing, running or jumping activities that typically provoke incontinence. PFM displacement can be recorded with an electromagnetic tracking system, complemented by vaginal surface electromyography that displays concurrent electrical activity of the PFM during functional activities (Figure 1). Our work aims at a deeper understanding of PFM kinematics and activity during impact and therefore helps to elucidate PFM action related to incontinence pathophysiology. The relevant outcomes would instantly benefit the PFM diagnosis and development of specific training programs.



PFM activity and cranial-caudal displacement during reflexive PFM contractions.

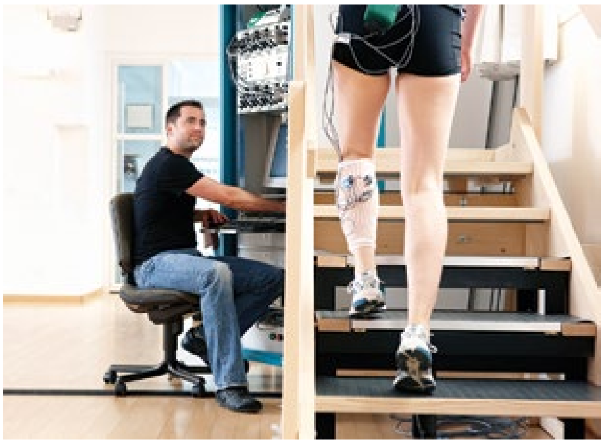
Functional Adaptations to Stochastic Resonance Interventions

There are two types of whole body vibration: sinusoidal (S-WBV) and stochastic resonance whole body vibration (SR-WBV). During S-WBV, the platform vibrates vertically or seesawing with a frequency of 20–50Hz and an amplitude of 2–6mm. This stimulates muscle spindles, which activate alpha motor neurons resulting in muscle contractions, comparable to the tonic vibration reflex. The SR-WBV applies 1 to 12 Hz through two independently vibrating platforms. Due to the continuously changing frequency and unpredictable applied "noise", the nerve-muscle system learns to respond effectively to these disorders as habituation to stochastic stimuli is hardly possible. Improvement in everyday movements is also possible due to enhanced reactivity. We focus on SR-WBV due its stochastic character. Not only could we show that SR-WBV is an appropriate and economic method for skilling up, the technique has proven to create only a slight strain and is well accepted in the elderly or patients after stroke or severe brain injury. The effects on balance, strength, power, muscle activity or gait are currently under investigation, however SR-WBV seems to be an efficient option for the prevention of musculoskeletal complaints and falls at work. Further studies are needed to ascertain the influence of muscle activity on musculoskeletal complaints and to explore how SR-WBV can be used as low intensity core stabilization training or sensorimotor exercise for the back.

Measuring back muscles activity during stochastic whole body vibration.

Lower Extremity Neuromuscular Adaptations to Training and Therapy Interventions

Lower extremity function plays a key role in human mobility. Mobility impairment by pathologic conditions is not only directly relevant for human locomotion but can also result in several negative psycho-social side effects. This research aims at providing more insight into functional adaptations of the lower extremity due to pathologic changes. This analysis provides the possibility to generate diagnostic parameters that can differentiate between pathologic and asymptomatic movement. The identification of selective quantities and the proof of their validity and reliability make it possible to apply those quantities in clinical intervention studies where training or therapy interventions, or orthopedic devices, are tested in clinical trials. A current project on pes planovalgus associated complaints works directly along this paradigm: pes planovalguis is a common foot deformity and early stages are thought to be treated with non-surgical therapy options like foot orthoses (relief of tendon stress by mechanical unloading of the arch) or strengthening exercises. Beside clinical effects, no study to date has evaluated functional changes pre-post in dynamic movements of daily life like gait or stair climbing. The widespread use of several non-surgical treatment strategies has lead to extensive health care expenses, while an optimized therapeutic strategy could eventually lead to more efficient health care expenditures.



Analysis of lower extremity function.

Selected Publications

Elfering A, Arnold S, Schade V, Burger C, Radlinger L (2013) Stochastic resonance whole-body vibration, musculoskeletal complaints and body balance: A worksite training study. Saf Health Work 4(3):149-155

König N, Reschke A, Wolter M, Müller S, Mayer F, Baur H (2013). Plantar pressure trigger for reliable nerve stimulus application during dynamic H-reflex measurements. Gait Posture 37(4):637-639

Luginbuehl H, Greter C, Gruenenfelder D, Bayens JP, Kuhn A, Radlinger L (2013) Intra-session test-retest reliability of pelvic floor muscle electromyography during running. Int Urogynecol J 24(9):1515-1522

Institute for Human Centered Engineering

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The Institute for Human Centered Engineering is additionally comprised of approximately 60 research engineers, not cited here by name.

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Hubert Käslin, Microelectronics Design Center, ETH, Zurich
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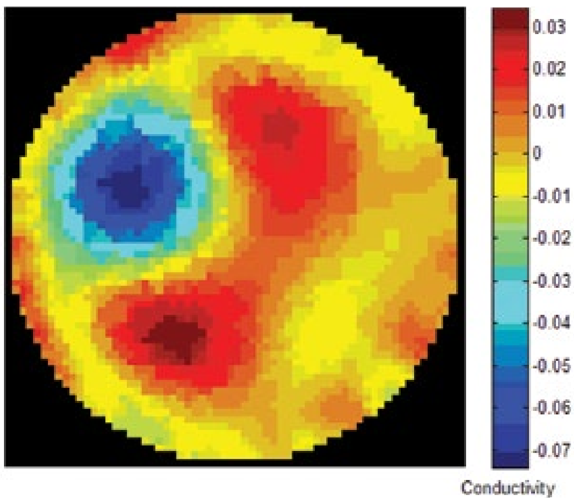
Research Profile

The Institute for Human Centered Engineering (HuCE) combines its know-how acquired from research projects in various fields with engineering technologies in an interdisciplinary way to develop new products for industry and clinics. The focus is on strong engineering technology core competences. Our practical problem solving approach together with our clinical partnerships provides a basis for innovative products. The engineering core competences in our six research laboratories are medical instrumentation, electronic implants, optical instruments for diagnosis, imaging in medical technology, optical coherence tomography, haptic feedback systems, sensors and sensor networks, signal processing and control, low-power microelectronics and high-speed hardware algorithms in combination with biomedical engineering applications. HuCE is currently involved in three SNF and a dozen CTI-funded research projects, several medtec and industrial engineering projects, and has been the incubator for multiple spin-off companies.

Research Area: Medical Imaging in Diagnosis

Electrical Impedance Tomography

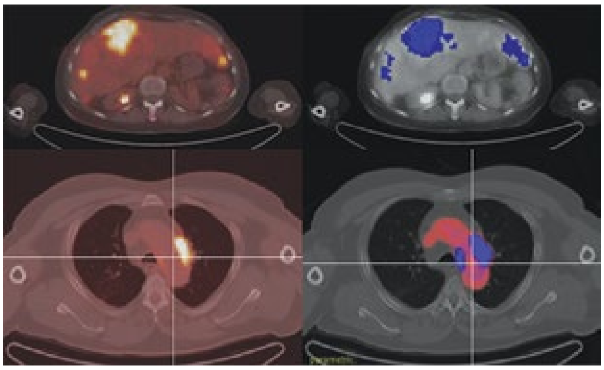
HuCE-BME Lab: Electrical impedance tomography (EIT) calculates an image of the spatial distribution of electrical conductivity inside the body. It is based on electrical stimulations and voltage measurements performed on the body's surface. The EIT technique is very attractive because it enables the acquisition of tomographic images without having to resort to ionizing radiation such as X-rays. Currently, the main potential application for EIT in the medical domain is the monitoring of respiratory and cardiac functions of patients.



An EIT image.

Computer Aided Diagnostics on PET/CT Images

HuCE-cpvrLab: In several student projects it was shown that diagnostics based on PET/CT (Positron Emission Tomography in combination with Computed Tomography) could be improved by evaluating available time-activity data from the PET scanner. In PET studies a radioactively labelled tracer (18F-fluordesoxyglucose) is injected an hour before the PET scanner measures its accumulation in body tissues. In the resulting PET images some tissues or organs and cancer with high glucose consumption appear bright. To apply the new method, the patient is also scanned during the one-hour tracer accumulation phase and the additional data is used to improve the classification of the PET images. It can be shown, that the different organs and tumor tissues show differing tracer accumulation patterns over time. These patterns can be used to differentiate tumors or metastases from other tissues. Application of the new tissue classification methods to different patients was made possible by accurate normalization of the time-activity measurements according to image derived blood pool activities.

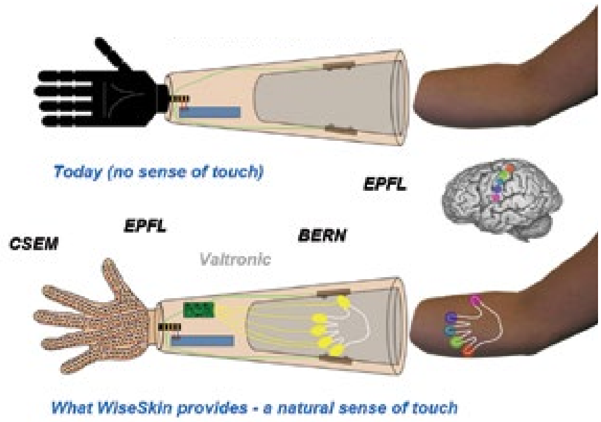


Images to support diagnostics:
Top left: Standard PET-CT image showing liver with a tumor on top, the kidney below and two metastases on the sides. Top right: The blue overlay from the new classification methods clearly identifies and delineates tumor tissue and metastases including conspicuous tissue while omitting activity within the kidney as non-tumor tissue.
Images to support radiotherapy planning:
Bottom left: Standard PET-CT image showing a lung tumor around the aorta. Bottom right: The new classification algorithms allows for more precise delineation of the tumor (blue) as well the aorta (red).

Research Area: Medical Instrumentation

WiseSkin – A Prosthesis with Sensor Skin

HuCE-BME Lab: Amputation of a hand or limb is a catastrophic event affecting life quality. The WiseSkin project aims at developing a prosthesis with a sensor skin, which would allow for the feeling of pressure, shear, and temperature. The project is sponsored by NanoTera and SNSF, with three partners: CSEM, EPFL and BFH. The WiseSkin concept is based on miniature, soft-MEMS sensors embedded into a silicone "skin". Wireless communication is used to transfer data to the actuators. The novel, stretchable powering subsystem also serves as a waveguide for the wireless communication. Our work involves the investigation of non-invasive sensory substitution system using phantom maps, system design, as well as final integration and development of a functional prototype.



The prospective of WiseSkin project and the work distribution of partners. (Source: C. Antfolk, "On sensory feedback in hand prostheses". PhD thesis. Lund University, 2012).

VoiSee - A Portable Electronic Visual Aid for Macular Degeneration

HuCE-BME Lab: Age-related macular degeneration (AMD) is the most frequent cause of visual impairment in developed countries, with 1-3% of the population suffering from this disease. It is marked by the degeneration of photoreceptors in the macular region of the retina leading to opacities, distortions, total visual field failures (scotoma) in the center of the visual field (the macula) and may even result in blindness. As currently there is no cure for AMD, the only effective aid for people affected by this disease are magnifying devices. While there are numerous stationary viewing aids, surprisingly few portable ones exist. Existing portable devices are marked by either a reduced field of view (yielding e.g. a limited number of magnified letters) or by large proportions and heavy weights so that they can hardly be carried around, especially considering the elevated average age of AMD patients. We thus, conceived a device that will fill this gap and consequently help AMD patients to be mobile and active again in their everyday life. The VoiSee project comprises the development of a novel portable electronic viewing aid for AMD patients and the testing thereof under realistic conditions. It combines high resolution digital image acquisition with electronic and optical magnification and image processing and enhancement to produce a large image on an

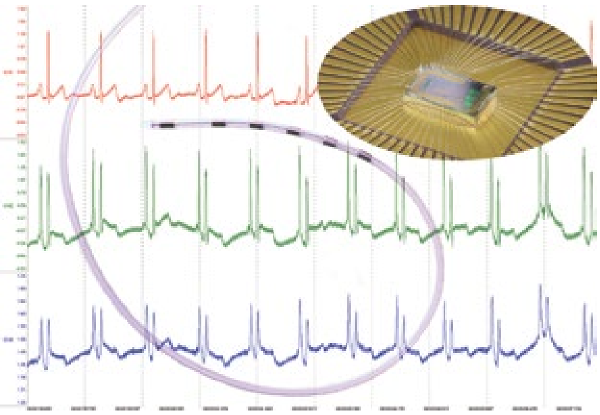
Mobile despite strong visual impairment. Texts from far and near are magnified on the VoiSee display and enhanced so that people suffering from age-related macular degeneration can recognize them in their peripheral visual field. (Image: Eva Schmassmann).

optimized near-to-eye display. Intelligent integration of the different components results in a device that provides a very large field of view of more than 68° (equal to a 53”-screen at a 1 m distance) while still remaining fairly light-weight and small, so that it easily fits into handbags. Employing simple to use and intuitive control elements, patients can adjust the desired magnification while various other patient specific image parameters can be fine-tuned by medical professionals. Within the framework of this project a CTI-project is conducted in collaboration with Reber Informatik+Engineering GmbH, Münsingen which has been nominated for the CTI Medtech award 2013.

Research Area: Diagnostic Devices - Implants

Esophageal ECG Recording Device

HuCE-microLab: Cardiac arrhythmia are often accompanied by palpitation which a patient may not interpret as a rhythm disorder. To detect such arrhythmia, cardiologists need a long-term capturing device for ECG signals. In our research we are developing an esophageal ECG recording device, which is completely integrated into an esophageal catheter. The technology challenges are broad and thus, the engineering activities include various fields of research: new electrochemical / electromechanical sensor principles for reduced esophageal ECG signal baseline wander; novel ECG signal-capturing principles for compression of the measured data directly within its capturing stage; new approaches in low-power microelectronics, including very recent approaches in asynchronous logic design, concepts for reduced power consumption and thus reduced overall volume needed for implanting the complete device electronics into the catheter. Ongoing clinical research by cardiologists and rhythmologists leads to new interpretation of the additional features that can be extracted from esophagueal ECG signals.

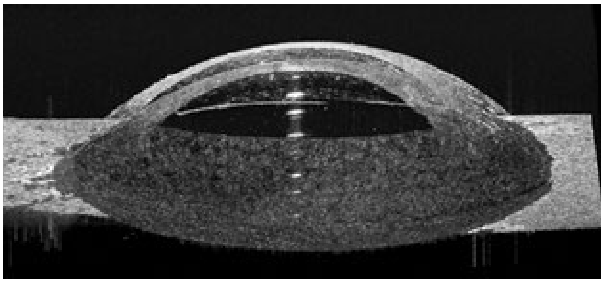


Compared to the surface ECG (top), it can clearly be seen that the other two esophagus ECG signals captured by our new device show a much more pronounced P-wave.
This improved signal quality is due to the closeness of the sensor catheter to atrium of the heart.
Esophagus ECG test circuitry on a first chip (top right), directly to be bonded inside the catheter. In the near future the complete electronics will be placed inside the catheter (middle).

Research Area: Ophthalmology

Cornea Power Measurements

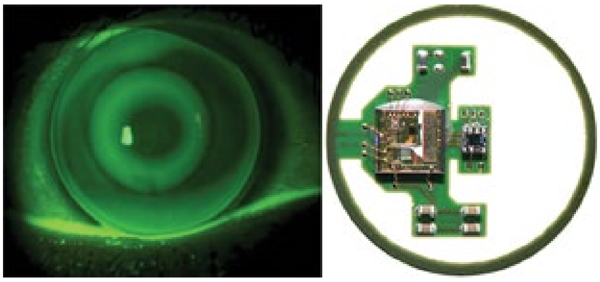
HuCE-microLab: An essential step in the planning of a large number of ophthalmologic interventsions is the determination of the corneal refractive power. Current biometric devices determine tpower solely on the basis of measurements of the cornea front surface. The goal of the present research project (CTI 16077) is to measure both, the corneal power of the front as well as that of the back surfaces by 3D optical imaging. Uncontrollable eye movements, like saccades, happen several times per second, and ask thus, for a very high-speed image-capturing system to prevent image blurring by eye movement. In our approach we research for near redundancy-free 3D imaging and try, at the same time, to increase the speed of the image capturing optics and the post-processing by implementing the needed signal-processing tasks directly in hardware algorithms.



3D image capturing with processing in real-time with high-speed hardware algorithms.

Dynamic contour tonometer lens

HuCE-microLab: Glaucoma is an eye disease that is the second most common cause of blindness. An elevation of the intraocular pressure (IOP) is the highest risk factor for this disease. The decrease of IOP by medication is currently the only possibility to counteract glaucoma progression. Measuring the IOP is therefore crucial. State-of-the-art medical examination uses selective pressure measurements for a few seconds only, which, unfortunately, are insufficient to continuously capture the strongly varying IOPs during day and night (diurnal IOP). Diurnal IOP curves may show IOP peaks and trends (fluctuations), which would hopefully provide a better indication. Goal of the

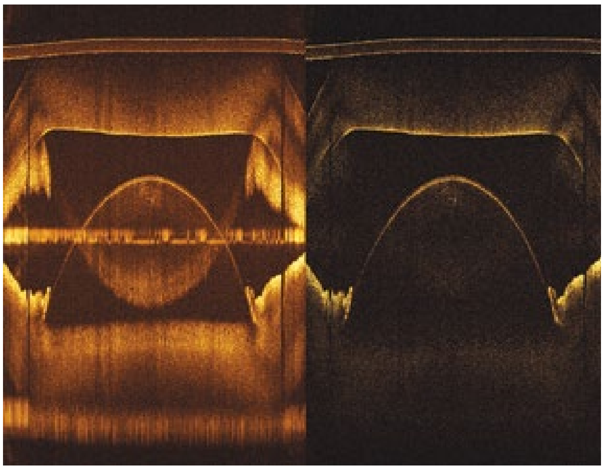


Dedicated lens for IOP measuring (left), miniaturized RFID lens electronics with pressure sensor element and antenna (diameter 10 mm), ready to be integrated into the lens (right).

present research project is to develop a diurnal pressure measuring system and thus help to improve glaucoma therapy. Based on our industrial partner's patent, we have developed the complete electronics for IOP measuring, including the RFID sensing electronics for integration into the lens and a miniaturized, low power data logger controlling the lens (CTI 14076). First experiments have shown that given a minimal sensor sampling rate, even the heart rate can be extracted from the IOP measurements by our system.

Seeing Surgical Laser

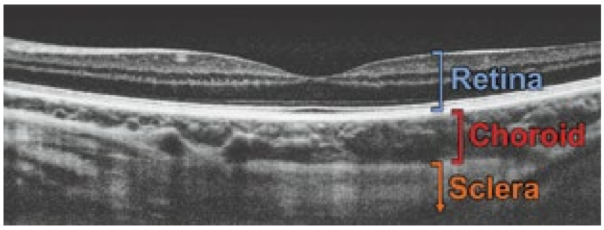
HuCE-optoLab: In a CTI project (CTI 12984.1) we have developed a visualization device as add-on to an existing femtosecond laser system for surgery of the anterior segment of the eye. The 3D imaging system is based on OCT and allows for detailed visualization and measurement of the surgery region during the operation. The SD-OCT is tailored to the application and fully integrated in the femtosecond laser system. Major design goals were high resolution and extended measurement range without compromising the cutting performance of the femtosecond laser system. Additional challenges were system stability and compactness. State of the art technologies where implemented to allow surgeries to be performed successfully. In order to enlarge the restricted measurement depth of SD-OCT we applied a novel algorithm based on optical dispersion mismatch in the OCT interferometer. This technique doubles the measuring depth and enables the imaging of the whole anterior segment including the posterior surface of the crystalline lens.



Pig-eye scan recorded with the developed system and processed with the implemented Full Range algorithm. An enlargement of the restricted measurement depth is shown.

Characterizing Myopic Changes of the Choroid

HuCE-optoLab: Myopia, as a continuously spreading disease, is found in an increasing number of young patients and involves an imbalance of the eyes growth control mechanisms. In cooperation with Chinese partner universities the project (SNF 320030_146021) develops a multi-light source ophthalmic optical coherence tomography and eye-tracking confocal laser scanner system that enables generation of high resolution images with high contrast even at the deeper ophthalmic layers. Specialized software utilizes this device to monitor a cohort of young subjects at micrometer resolution while they are presented with optical stimuli that can influence the axial eye growth of the retina, choroid and sclera. The goal is to precisely and positively influence the eye shape and suppress or even reverse the progress of myopia before the eye shape becomes inalterably deformed.



The ~250 µm thick human retina is held at its optimum position on the choroid and sclera by mechanisms that are currently only partially understood. These control the thickness of the supporting choroid and sclera and are also triggered by optical stimuli that reach the peripheral visual field. Supressing excessive elongation stops the development of strong myopia and related diseases.

Selected Publications

Mamatjan Y, Grychtol B, Gaggero P, Justiz J, Koch VM, Adler A, (2013) Evaluation and Real-Time Monitoring of Data Quality in Electrical Impedance Tomography. IEEE Transactions on Medical Imaging 32(11):1998-2007

Bandi V, Goette J, Jacomet M, Niederhäusern T, Bachmann A, Duelk M (2013) FPGA-Based Real-Time Swept-Source OCT System for B-Scan Live-Streaming of Volumetric Imaging. Proc. SPIE 8571 Optical Coherence Tomography and Coherence Domain Optical Methods in Biomedicine 2013

Unterhuber A, Považay B, Müller A, Jensen OB, Duelk M, Le T, Petersen PM, Velez C, Esmaeelpour M, Andersen PE, Drexler W (2013) Simultaneous dual wavelength eye-tracked ultrahigh resolution retinal and choroidal optical coherence tomography. Opt Lett 38(21):4312-5

Täschler D, Ernst D, Bachofner K, Bachmann AH, Duelk M, Meier Ch (2013) MEMS-based scanning head with variable focus for retinal and vitreous imaging. OSA European Conferences on Biomedical Optics (ECBO), May 2013

Rakhmatullina E, Bossen A, Bachofner KK, Meier C, Lussi A (2013) Optical pen-size reflectometer for the monitoring of early dental erosion in native and polished enamel. J Biomed Opt 18(11):117009

Pfenniger A, Wickramarathna LN, Vogel R, Koch VM (2013) Design and Realization of an Energy Harvester Using Pulsating Arterial Pressure. Med Eng Phys 35(9):1256-1265

Institute for Print Technology

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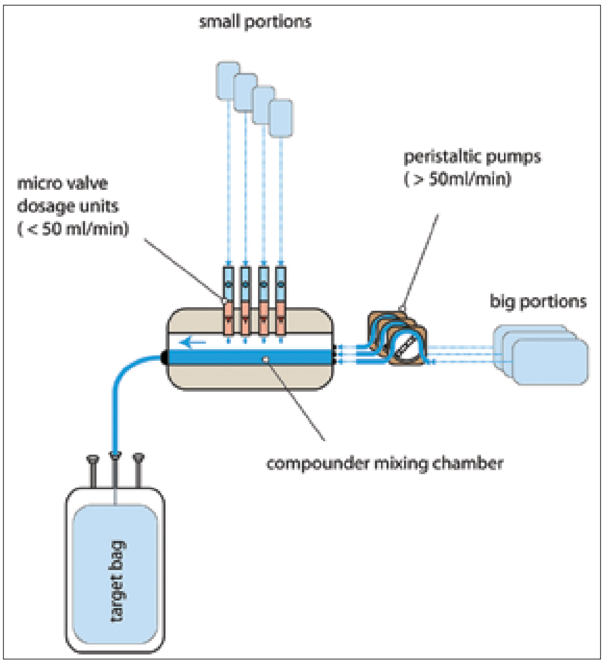
Research Profile

The Institute of Print Technology (IDT) is involved with fluid handling systems in the pico- to milliliter range. In addition to research and development of unique inkjet and micro-fluidic systems, the IDT develops process technologies and measurement techniques for specialty applications. The demand for Single-Use-Systems (SUS) for the cell culture and research industry has been growing for years. Nutrient dosing-systems featuring integrated process control and ready for use in SUS bioreactor systems from various manufacturers are being actively developed by the IDT. The ultimate goal is an inexpensive SUS unit with an exact measurement system, enabling simultaneous precision process control and monitoring. The applications for such feed systems are not limited to cell culturing in bioreactors; dosing of medications or nutrients to intensive care patients is another area of suitability. Using digital print techniques, in development at the IDT, it is possible to optimize and functionalize surface properties for specific use cases in many industries. Such surface preparations can create homogenous or structured surface layers, change coefficients of friction or alter surface energies. Additionally, surfaces can be prepared for specific functionality by printing with hydrophobic or hydrophilic materials, conductive inks or aggressive etching chemicals. Measurement systems for viscosity, dissolved oxygen, pH value and micro-flow for biotech process control and monitoring are being developed by the IDT within several projects. Automated measurement systems, suitable for long term studies, are being developed to analyse drop formation in pico- and nano- dosing installations.
Often, during feasibility studies, the IDT will develop system components into functional examples which can be used independently by industrial clients in their own tests.

Multi-Channel TPN Compounder

Prescription of total parenteral nutrition (TPN) bags or ready-to-use intravenous preparations is currently declared in amounts or moles of ingredients per volume. However, only a few compounders are commercially available. Major drawbacks are their expensive price, a big scale orientation by 24 channels, a not readily available support in some countries, and their dosing of ingredients in a gravimetric mode. As a result, densities taken from specifications, and periodically determined flow factors must be used to run these machines. Volume dosing in pharmaceutical preparation is an understudied problem. Evaluation of the suitability of printing technology devices in pharmaceutical applications and of the feasibility of a low-cost multi-channel compounder has been done. The team was evaluating a dosing unit developed for its applicability and practicability in pharmaceutical preparation processes such as total parenteral nutrition bags and/or further mixtures prescribed for individual pharmacotherapy.



TPN multi cannel Compounder scheme.

Features of a novel modularly assembled multi-channel dosing-unit, formerly designed for inkjet printing, were assessed for and found to be suitable for resolving dosing problems in the course of compounding. The core of the dosing unit consists of multiple autoclavable, chemically resistant, highly precise volumetric dispensing valves and integrated flow rate sensors measuring differential pressures. Thus, dosing is independent of temperature and viscosity (patent WO2013030034). The pressure above the valve amounts to 500+/-5 mbar. An electronic valve-driver controls the valves to microseconds. Media are transferred as single drops of 0.5 µl by a feeder into a mixing chamber. Exact dosing is warranted on a wide range of µl to dl. The option of nano-dosing as well as the integration of valve and sensors is currently being developed. A prototype (patent CH702769A2) for preparation of all-in-one-TPN-bags is currently under construction, together with an electronic interface to patient and administration databases.

Single Use Dosing System

Over the past decades, changes in bioreactor system design have mainly focused on the software and control side. Over the past years the single-use revolution has also changed the bioreactor design and enabled the miniaturization of bioreactor systems for high throughput applications. New technologies for sensors, for example optical measurement methods, are cheaply available but miniaturized dosing systems have been missing. The challenge is to add precisely small amounts of liquids. This is particularly important when working with continuous additions of media, control liquids or nutritions. Adding a droplet of concentrated medium on a 3-litre scale does not influence the culture, but a droplet on a 50-ml volume has a significant influence to the running culture. This gap was closed by the development of a new dosing system based on micro-valve technology by the IDT and ReseaChem GmbH. To keep the system easy to use and uninfluenced by the dosed liquid itself, a special single use injection valve in combination with a new single use mass flow controller was developed.

Single Use Bioreactor with Dosing unit and control unit.

Single use Dosing System with integrated flow meter.

This combination allows droplets of liquid to be added to the culture on a continuous basis on a nanoliter scale. This allows smooth additions under direct controlled condition of (highly concentrated) liquids into the bioreactor by measuring the volume of each dosed droplet. To be able to measure within an error of 5%, the mass flow controller passed on measuring different pressure differences needs to have an ultra short response time (less than 1 µs) and a sampling rate higher than 20 kHz.

Autoclavable Micro-Dosing Unit

Pressure put on biotech laboratories to generate more results, in less time, using less costly liquids led to the development of mini bioreactors with typical reactor volumes smaller than 1000 ml. An observed weakness of these bioreactors was the inability to dose amounts of liquids in the nl range. A research project was undertaken to develop an autoclavable micro-dosing unit appropriate for use in mini bioreactors. Dosing is accomplished using inkjet valves, which were adapted for biotech application. A driver controls the switching of the micro-valves to within microsecond precision, enabling constant, linear or exponential feeding strategies. The micro-dosing unit allows mini bioreactors to operate in fed-batch mode, based on time intervals or measured characteristics, such as pH, or dissolved oxygen. Liquids are fed as single droplets into the bioreactor, with each droplet possessing a volume of roughly 500 nl. Feed rates from 200 to 5000 µl at a dosing accuracy repeatability of 5% were achieved. The dosing unit was successfully field-tested, ensuring that sterility could be maintained throughout experiments. At the conclusion of the project, a patent was awarded for the developed dosing technology and associated procedure.

Autoclavable micro dosing unit on a mini bioreactor head plate.

Patent

Berger S, Zumbrunnen S, Marmet P, Haslebacher P, Schär M (2013) Flow Sensor, WO2013030034

Institute for Rehabilitation and Performance Technology

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Research Profile

The Institute for Rehabilitation and Performance Technology (IRPT) uses methods and technologies from sports and exercise physiology to improve the rehabilitation process after accidents or illnesses. Core competencies are cardiopulmonary and neurological rehabilitation after stroke or spinal injury, feedback systems as well as automation and control of training equipment. The IRPT develops its procedures and systems in collaboration with Swiss rehabilitation clinics, and can thus ensure that they can be quickly and directly used by patients. A growing number of CTI- and SNF-funded projects supports the transfer of knowledge into industry and application to concrete products. Currently around 20 people are members of the IRPT. The team consists of several research associates, PhD students, postdocs, and a group of Bachelor and Master students with backgrounds in electrical, mechanical and bio-mechanical engineering, human movement sciences, physiotherapy and rehabilitation medicine. The IRPT is located in Burgdorf (Bern) on the campus of the Engineering and Information Technology department of Bern University of Applied Sciences.

Rehabilitation Engineering

The interdisciplinary research of the Rehabilitation Engineering group focuses on neural control of movement in clinical populations with neurological deficits resulting from spinal cord injury, stroke and other causes. Combining rehabilitation technology and cognitive performance feedbacks the group's goal is to reinforce the patient's volitional drive and to exploit the central nervous system's lifelong capacity for plasticity, regeneration and repair. This approach promotes cardiopulmonary and musculoskeletal health and supports an environment in which positive neurological adaptations can occur. The work harnesses multidisciplinary expertise in engineering, neurosciences, sports and exercise science and medicine to address prevention and management of the progressive secondary complications of spinal cord injury and stroke and a wide range of further neurological conditions and to promote neurological recovery for improved motor control, sensation and autonomic function.

The Rehabilitation Engineering group develops new technical devices and extends the functionality of existing products. New developments include novel rehabilitation tricycles for adults and children with neurological impairment. This new generation of tricycles combines novel drivetrain technology using electric drives with functional electrical stimulation (FES) of paralysed muscle groups. The functionality of existing robotics-assisted rehabilitation devices, including treadmills and tilt tables, has been extended to cover application for cardiopulmonary rehabilitation. This involves biofeedback of patient effort, volitional control of mechanical work rate, together with automatic feedback control of physiological outcome variables including heart rate, oxygen uptake and metabolic work rate. A key feature of the group's work is the employment of methods and protocols from sports and exercise physiology and the adaptation of these to the rehabilitation setting. These approaches are applied in the clinic for rehabilitation of people with various neurological problems including stroke and spinal cord injury.

The IRPT's dedicated research lab within the Reha Rheinfelden: The Lokomat has been enhanced for cardiopulmonary rehabilitation of stroke patients.

The following selection of research and clinical projects gives an overview of the spectrum of research activities of the Rehabilitation Engineering group:

- Cardiopulmonary rehabilitation of stroke patients using

robotics-assisted treadmill exercise (RATE)
- Active control and neurological stimulation of the ankle joint during RATE
- Cardiopulmonary rehabilitation of patients with incomplete spinal cord injury or stroke using a robotics-assisted tilt table
- Rehabilitation tricycle incorporating FES and motorized assistance
- Physiological responses to µ-vibration of the foot soles during gait-like motion

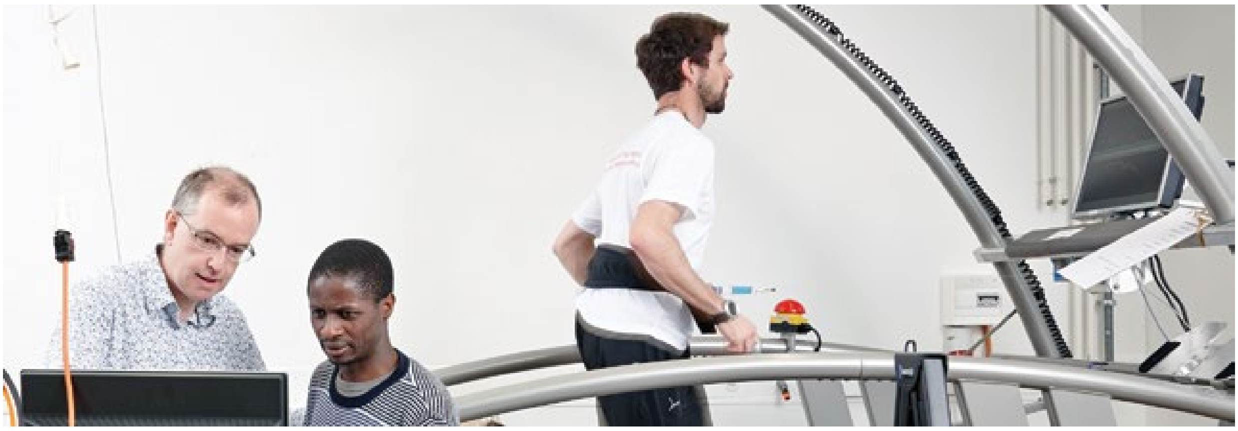
The IRPT has an excellent infrastructure for research including a dedicated research lab within the Reha Rheinfelden. Robotics-assisted devices include a treadmill (Lokomat) and tilt table (Erigo) by Hocoma. The institute also has modern cardio-respiratory monitoring systems. Initial research and development work is carried out in the labs in Burgdorf.

Sports Engineering

The Sports Engineering group focuses on interdisciplinary research on advanced feedback control methods for treadmill automation. The work builds on multidisciplinary expertise in engineering and sports and exercise science. The work deals mainly with high-end performance, but many of the methods have also been translated successfully into activities of the Rehabilitation Engineering group. The group has developed feedback control algorithms that allow exercise intensity to be specified for training and testing via automatic regulation of heart rate, oxygen uptake, or metabolic work rate. In each case, a target profile for the controlled variable is selected. During the exercise, treadmill speed and slope are automatically adjusted so that the target response is achieved. Also, high-precision positioning algorithms have been developed. This allows users to select their own walking or running speed, while the feedback control continuously adjusts treadmill speed to maintain a reference position. These applications are available for walking, running and cycling on a treadmill.

The following selection of research and development projects gives an overview of the spectrum of research activities of the Sports Engineering group:
- Feedback control of heart rate, oxygen uptake or metabolic work rate during treadmill exercise
- Automatic position control for walking and running
- Automatic control of position and physiological variables while cycling on a treadmill

The IRPT labs in Burgdorf are equipped with a high-performance treadmill (Venus by h/p/cosmos). Various position monitoring sensors, including ultrasound and laser and a real-time communication protocol give complete control over the treadmill through a computer. The institute also has modern cardio-respiratory monitoring systems for on-line breath-by-breath recording.



A high-performance treadmill enhanced with digital position control and bio-feedback developed at the IRPT.

Selected Publications

Saengsuwan J, Laubacher M, Nef T, Hunt KJ (2014) Cardiopulmonary performance testing using a robotics-assisted tilt table: feasibility assessment in able-bodied subjects. Technol Health Care Feb 27 [Epub ahead of print]

Stoller O, Schindelholz M, Bichsel L, Hunt KJ (2014) Cardiopulmonary responses to robotic end-effector-based walking and stair climbing. Med Eng Phys 36(4):425-31

Stoller O, de Bruin ED, Schuster-Amft C, Schindelholz M, de Bie RA, Hunt KJ (2013) Cardiovascular rehabilitation soon after stroke using feedback-controlled robotics-assisted treadmill exercise: study protocol of a randomised controlled pilot trial. Trials 14:304

Hunt KJ, Hosmann D, Grob M, Saengsuwan J (2013) Metabolic efficiency of volitional and electrically-stimulated cycling in able-bodied subjects. Med Eng Phys 35: 919-925.

Stoller O, Schindelholz M, Bichsel L, Schuster C, de Bie RA, de Bruin ED, Hunt KJ (2013) Feedback-controlled robotics-assisted treadmill exercise to assess and influence aerobic capacity early after stroke: a proof-of-concept study. Disabil Rehabil Assist Technol April 18 [Epub ahead of print]

Schindelholz M, Stoller O, Hunt KJ (2013) A software module for cardiovascular rehabilitation in robotics-assisted treadmill exercise. Biomed Signal Process Control 10:296-307

Institute of ICT-Based Management, Medical Informatics

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Research Partners
BAG coordination body eHealth Switzerland, Bern
GS1 Switzerland, Bern
The Swiss Hospital Association, Bern
Hospital Centre, Biel
Swiss Post Solutions, Bern
Economiesuisse, Zurich

Research Profile
The Health Care Informatics Research Group is focusing on the interoperable networking of medical and administrative data in the field of health care. At the same time, the group considers the processes as a whole, while taking into account the data flow, the specific ICT and their interactions with the user. The research assistants have obtained extensive experience in these fields and managed large-scale IT projects and compiled and implemented specifications both on the inside and outside of hospitals over many years.

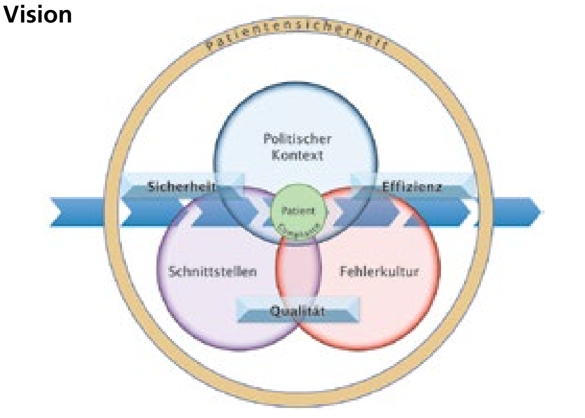
Current projects are focusing on patient safety in terms of the medication process, evaluation of eHealth projects in Switzerland, advice on conceptual design and introductory support for large-scale IT projects in Swiss hospitals, participation in professional associations and expert groups as well as the compiling of expert opinions.

Hospital of the Future
The "Hospital of the Future" project together with GS1 and Economiesuisse clearly demonstrates how Medical Informatics and Medical Technology interact: MedTec supplies data directly or indirectly. They are then analyzed taking the whole process into consideration using the appropriate tools with regards to data flow, user requirements (usability) and content interpretation. Subsequent improvements of the ICT data flow process generate significant added value by optimizing the ICT value-added chain.
Swiss health care is a complex sector involving a wide range of different participants and their various fields of activity. What all stakeholders have in common is their interest in the most effective and appropriate care of patients in the context of an economical approach. This also includes accurate documentation of services provided for the benefit of patients. Even though this requirement is largely met in terms of treatment procedures, fact is that logistically relevant information regarding dispensed medication or materials, which would enable a continuous supply chain, is often missing in the documentation generated. At the same time it is imminent that the traceability of problems or of product piracy is essential in the context of patient safety. Closer analysis of the flow of electronic information in health care also indicates that knowledge of patients in various different locations frequently leads to isolated existence of data. The "Hospital of the Future" study, which is accompanied by a multi-stakeholder advisory board, starts at this point in order to establish why the flow of information regarding patients in health care is being interrupted. The patient-perspective is of central significance in this project. The patient pathways and accompanying processes between admission to and discharge from hospital were analyzed during the first part of the project.

Interface Crossculture Process Analysis Tool
A practical generic process analysis tool was developed to identify interruptions in the information flow ("Interface Crossculture Process Analysis Tool" - "IXPRA") which was then validated in the context of a test hospital. The processes to be analyzed are represented in a matrix which enables each sub-stage of a process to be depicted in terms of the services rendered during this stage (use cases), the ICT involved as well as the participants (interaction stratum). This procedure quickly clarifies the process component during which the flow of information is interrupted, and in which participants and software are involved. The validation phase in the test hospital shows that the tool is easy to understand and quickly generates a common understanding of the visualized process situation. It also demonstrates that it is extremely suitable as a basis of discussion regarding measures to be derived. IXPRA makes it possible to identify the staff involved and the additional stakeholders in each process stage and for advisory boards to formulate measures designed to eliminate interruptions in the flow of information.
In particular, the medication process was analyzed more closely during the study. Practically the complete supply chain can be demonstrated on the basis of this example process. In addition, the patient is strongly involved in this process - he or she is directly involved within the scope of diagnosis, therapy planning and implementation, and his or her behavior has an impact on the result. The error and learning culture of those in charge of treatment as well as any opportunities for political influence were taken into account as they have a direct impact on the central theme of patient safety.
Analysis with the IXPRA model highlighted the fact that the complex activities surrounding the medication process take center stage: the parallel sub-processes all intersect directly with the patient at the time when medication is administered. This implies that the provision of information during this stage of treatment and the passing on of information for preceding and subsequent process stages are especially critical. At the same time, the dispensing of medication is particularly susceptible to errors and thus represents a hazard in terms of patient safety. For this reason, an introductory account of patient safety has also been included in the study: How can (near) errors be handled constructively, and how can policy have a possibly positive impact on patient safety?
We can conclude that it is essential to implement a continuous flow of information in Swiss health care in the

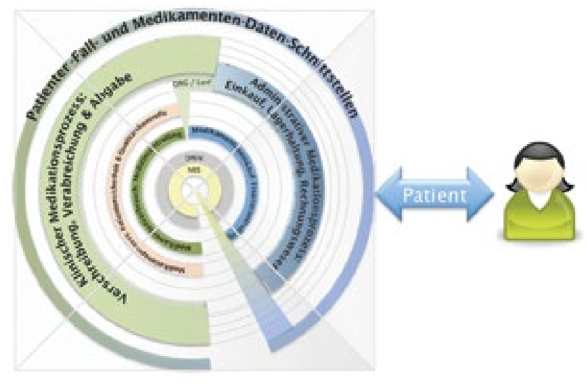
interests of patient safety as well as of economic efficiency. Factors such as the various technical and cultural interfaces, the handling of errors within the framework of a learning culture, and possible political guidelines all impact on patient safety. Fault-free interaction of these components increases the quality of treatment, the efficiency of processes and the safety of patients. But patients themselves make an important contribution to the success of treatment: Compliance, i.e. "therapy loyalty", is an essential pre-requisite of health care in terms of patients. However, this also presupposes the possibility of open dialogue between patients and those in charge of treatment. Finally, politicians need to make all participants aware of the importance of patient safety. This could be implemented on the basis of targeted training, open communication, professional moderation of the necessary discussion and/or with the aid of central coordination of the various initiatives in terms of patient safety: all in the interests of a future "medicina sicura".

Vision



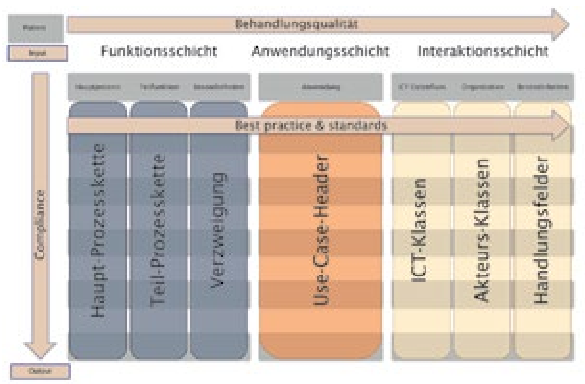
The patient located in the center expects the health care system to provide efficient processes along with high-quality and safe treatment.

Analysis



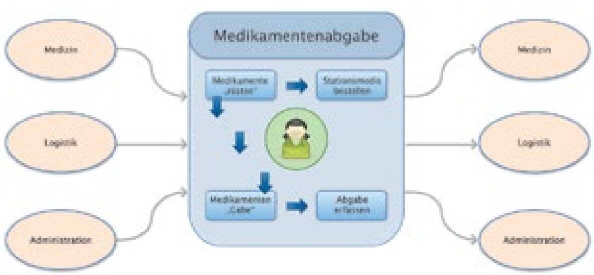
The various parallel sub-processes of the medication process. Medical field shown in green, administrative/logistical field shown in blue, quality management, controlling and management processes depicted in the center.

Vision



The generic process analysis tool which can clearly show the services provided during each process stage as well as the software and participants involved (technical and cultural interfaces).

Implementation and improvement



The various sub-processes of the medication process and the patient intersect during the “medication dispensing” work step.

Selected Publications

Kohlhof H, Hartel MJ, Holm J, Jejina N, Eggli S (2007) eMed™: Computerised physician drug order entry optimises patient safety. Swiss Medical Informatics 62:40-42

Holm J, Gasenzer R, Dubois J-P (2010) Resultate zur Umfrage über die Ausbildung von Medizininformatikern in der Schweiz. Swiss Medical Informatics 70:3-12

Holm J (2011) eHealth auf gesundem Wege. Aktuelle Technik 12:48-50,

Lehmann M, Holm J (2012) Semantische Interoperabilität im Gesundheitswesen. Aktuelle Technik 11:02-04

Holm J, Lehmann M (2013) ePatientendossier – Pragmatische und wirkungsvolle Umsetzung im Spital. Arzt/ Spital / Pflege 1, 16-17

Holm J, Lehmann M, Gasenzer R (2013) Das Spitalinformationssystem als Erfolgsfaktor im Wettbewerb. Competence 5:12-13

Holm J, Lehmann M, Nüssli S (2013) Empfehlungslandschaft eHealth Schweiz: den Überblick behalten. Clinicum 5-13, 01-03

NETWORKING

The Competence Center for Medical Technology, CCMT serves as a liaison between the key medical innovators as well as academic research and development service providers in Bern and the medtech industry in Switzerland and abroad. It actively seeks and brings together those people and institutions who will realize the next generations of medical technology.

One of the key events for the biomedical engineering community in and beyond the region is the annual Biomedical Engineering Day in Bern. The BME Day is a mayor networking venue for companies from the medtech and lifescience industry and young talent from academia.

At the Biomedical Engineering Day, the alumni organization Biomedical Enginering Club of the University of Bern and the Bern University of Applied Sciences holds its annual general assembly.

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Lukas Rohr

Stefan Weber

Stake Holders

Medical Cluster
University of Bern
Bern University of Applied Sciences
Economic Development Agency of the Canton Bern

Research and Development

The foundation Competence Center for Medical Technology (CCMT) serves as a knowledge and technology transfer platform between academic service providers and the medical technology industry in Switzerland and abroad. The CCMT is supported by its founders the University of Bern, the Bern University of Applied Sciences, and the Medical Cluster as well as the Economic Development Agency of the Canton Bern.

The foundation provides internal and external communication services and serves as a networking hub for the initiation of collaborations between researchers and industry as well as between the different research groups of the founding institutions.

The CCMT contacts and visits potential industry partners on a regular basis in order to communicate the competences of its academic partners, and initiate project collaborations. It is an explicit goal of the CCMT to initiate, enable and support CTI projects. Special consideration is also given to all aspects of intellectual property rights and contracting (in close collaboration with the official KTT offices of the academic partners).

Free Lunch Event

In order to present innovative new technologies to the research and medical community of its partner institutions, the CCMT organizes so called Free Lunch events on a regular basis. In 2013, the main event held at the Haus der Universität on 28. March focused on 3D bio-printing that enables researchers to explore the potential of biological tissue engineering trough 3D-printed parts.

regenHU CEO Marc Thurner demonstrated the creation of tissue and organ models with BioInk®, a set of biomaterials supporting cellular growth, in combination with the company's 3D Discovery® instrument that is capable of generating three-dimensional constructs of cells, proteins, and extracellular matrix components. regenHu's technology is enabling researchers to print complex organ models for automated tissue-based in vitro assays for clinical diagnostics, drug discovery, and drug toxicity tests as well as complex in vitro models of human diseases.

Also presenting the potential of 3D-printing for clinical research at the event was Dobrila Nesic of the Department of Clinical Research of the Inselspital, Bern University Hospital.

New, cost-effective 3D bio-printing platforms enable researchers to explore the potential of biological tissue engineering through 3D-printed parts.

At the CCMT's Free Lunch Event, hosted at the Haus der Universität Bern, participants could observe a live demo of a 3DDiscovery® instrument printing biological material.

Knowledge and Technology Transfer

Knowledge and technology transfer between clinics, research institutions and the medtech industry has always been the main focus of the CCMT. In 2013 several long-term projects, that had been assisted and accompanied by the foundation, came to fruitition and to high honors.

The evolution of the electronic visual aid VoiSee™ had been supported by the CCMT since 2008. The mobile device, was developed by the Bern University of Applied Sciences, Engineering and Information Technology and the Reber Informatik + Engineering GmbH in Münsingen with support from the ARTORG Center of the University of Bern. VoiSee™ is a visual aid providing larger pictures and better contrasts, in particular for patients with macular degeneration.

At the CTI MedTech Event 2013 in Bern, VoiSee™ was one of three finalists for the annual CTI MedTech prize. It was edged only by CAScination AG, a spin-off of the University of Bern, that was also promoted by the CCMT on its way to market success. The makers of VoiSee™ received a standing ovation though at the World Medtech Forum Lucern in September of 2013 where the presentation of the first small series production of the device was celebrated by an international gathering.

Success in KTT hinges on the possibility to quickly access a large and diverse network of competent potential partners. In order to maintain and improve its network, the CCMT participates in regional, national and international seminars, conferences, exhibitions and other networking events on a regular basis.

VoiSee™ is a portable electronic visual aid for larger pictures and better contrasts, in particular for patients with macular degeneration. The device was developed by the Bern University of Applied Sciences, Engineering and Information Technology and the Reber Informatik + Engineering GmbH. For more Information see page 81 of this report.

Selected Events and Achievements

Free Lunch Event 3D Bio-Printing for researchers
Presentation of the 3D Discovery Machine of RegenHU for participants from the University of Bern, the Inselspital, Bern University Hospital, the Department for Clinical Research and the Bern University of Applied Sciences

Innovationsforum Medtech Switzerland - Germany in Erlangen
The CCMT accompanied a delegation of 40 Swiss representatives from industry and medical research to the Innovationsforum Medtech which was visited by Swiss Federal Chancellor Schneider-Ammann

2nd Congress of the European Academy of ORL and Head and Neck Surgery, Nice, France
Support with systematic expert interviews for the University of Bern spin-off CAScination AG at the 2nd Congress of the European Academy of ORL and Head and Neck Surgery in Nice

Representation of the University of Bern (medical technology) at the LUGA Exhibition in Lucerne
Presentation of the medical technology R and D-excellence (ORL robot) of the University of Bern and the Inselspital, Bern University Hospital

CTI MedTech-Event
For the first time, two projects that had been initiated and/or supported by the CCMT were among the three finalists for the CTI MedTech-Prize: CAScination and VoiSee™. CAScination is the winner of the CTI MedTech Prize 2013

World Medtech Forum Lucerne
Special event hosted by the CCMT in celebration of the first small series production of the successful CTI project VoiSee™ of Bern University of Applied Sciences, Engineering and Information Technology, the University of Bern and the Reber Informatik + Engineering GmbH at the WMTF in Lucerne

R and D project Sensogram
Successful networking of the newly, with the help of the CCMT implanted US-company Sensogram Technologie AG with the ARTORG Center of the University of Bern. Initiation of a clinical study with the Cardiology Department of the Inselspital, Bern University Hospital, ARTORG and the CTU

Transfer Services

26 companies visited, 4 CTI project applications supported

Biomedical Engineering Day

Since 2009 the industry, medical doctors, and engineers meet for the Biomedical Engineering Day at the Inselspital in Bern with great success.

The Biomedical Engineering Day takes place every year in May in the auditorium Ettore Rossi at the Inselspital in Bern.

The Master in Biomedical Engineering program of the University of Bern organized this event in 2014 for the sixth time. The event is an efficient platform in Switzerland for networking of Master and PhD graduates and Swiss and international medical technology companies. In 2013 the companies introduced themselves through oral presentations and gave insight into their commercial activities and their company philosophies as well as showed their demands on junior employees. Students thus had the opportunity to get to know potential future employers and contact them directly. This was made possible between the sessions in personal conversations and at the exhibitors' booths.

The BME Day offered great opportunities for the Bernese biomedical researchers, too. The ARTORG Center for Biomedical Engineering Research and the Institute for Surgical Technology and Biomechanics as well as the Bern University of Applied Sciences, a partner within the Master program, used the possibility of presenting current research projects to more than 250 participants. Interestingly, Master and PhD students play an important role in many of these projects. Thereby, this event was a demonstration of scientific achievements, too. Besides company representatives, scientists, researchers, and young academics, many medical doctors participated in this year's event as they had the chance for intensive communication with the biomedical engineers.
One highlight of the day was the successful live liver surgery by Daniel Candinas, Head of the Department of Visceral Surgery and Medicine, Inselspital Bern. Illustrative explanations in the auditorium were given by Stefan Weber, head of the ARTORG Center for Biomedical Engineering Research, and a close scientific collaborator of Daniel Candinas.

Attentive participants in the auditorium.

A student from the Lung Regeneration Technology Group at the ARTORG Center describes the principle of a microfluidic lung-on-chip to a BFH student.

Two UniBe students discuss the latest BME newsletter.

Lunch time: a great networking opportunity.

Biomedical Engineering Day: Awards
The three institutions Medical Cluster, Competence Center for Medical Technology CCMT and the Swiss Institute for Computer Assisted Surgery SICAS are alternately sponsoring awards for excellent academic achievements in the field of Biomedical Engineering at the University of Bern. In 2013 the proud sponsor was SICAS. Bernhard Reber, director of the SICAS Foundation, congratulated the three winners.

Juan Ansó received the SICAS Award 2013 for the best Master thesis in the Biomedical Engineering Program of the University of Bern. His work is titled: Integrated Facial Nerve Monitoring for Functional Control of Robotic Assisted Drilling in the Mastoid.

Samantha Chan received the SICAS Award 2013 for the best PhD thesis in the field of Medical Engineering with the title: Evolution of in Vitro Organ Culture Models for the Intervertebral Disc.

Patrick Steiner was the winner of the SICAS Poster Award 2013 for his poster: Image Enhancement Algorithms for OCT Imaging of Subthreshold SRT Laser Lesions.

Acknowledgments
We thank our sponsors and exhibitors

- Amgen
- AO Foundation
- BME Club
- Cellek Biotek
- CCMT
- Congrex
- Credit Suisse
- CSEM
- Haag-Streit
- Institut Straumann
- Maxon Motor
- Medical Cluster
- NCCR Co-Me
- Nobel Biocare
- RMS Foundation
- SICAS Foundation
- Stryker Trauma
- Ziemer Ophthalmic Systems

The Biomedical Engineering Club

The BME Club and Its Mission

The BME Club is an alumni club with the mission to provide and promote networking among its interdisciplinary members. Our members represent a growing network of biomedical engineers, scientists, past and present students and medical technology corporates who all desire to bring together the principles of engineering, biology, and clinical medicine. BME club accomplishes these goals by hosting events such as information sessions on the latest cutting-edge research in different fields of biomedical engineering, by facilitating attendance of international conferences and by organizing touring visits of various industrial plants and laboratories. The BME club is recognized as an official alumni association of the University of Bern under the umbrella organization – Alumni UniBe. A dedicated executive committee follows the principles of our constitution.

We are an enthusiastic and versatile group with diverse activities:
- bi-monthly "Stammtisch" in a local restaurant as an amiable platform to network, brainstorm or simply chat
- visits to Swiss medical and engineering companies
- providing information on career opportunities (including job offers)
- organizing annual welcome event for new students of the BME Master program
- organizing an annual alumni gathering
- participating in the annual BME day (co-organized with Master Study Coordination)
- publishing annual BME Newsletter
- rewarding two students each year with student travel award
- providing access to the Medical Cluster events
- joint membership with SSBE (Swiss Society for Biomedical Engineering)

BME alumni who join us will automatically become a member of Alumni UniBe, the alumni association of the University of Bern. Among other benefits this includes receiving a lifelong UniBe email address.

In short, the BME club represents a unique platform for professional, lifelong communication and networking. For further details look up our website at http://www.bmeclub.ch.

How to Join

Becoming a member is easy! Simply sign up at any BME Club event or visit us at http://www.bmeclub.ch. We are looking forward to seeing you!

The BME Club Board in 2013/2014

Prabitha Urwyler
President

Matteo Fusaglia
PhD Students

Dobrila Nesic
Faculty

Tom de Bruyne
Vice President

Tobias Imfeld
Webmaster

Hanieh Mohammadi
Master Students

Julia Spyra
Secretary, Back Office

Christian Güder
Treasurer

Lukas Bösch
Alumni

Rudolf Sidler
Job Market

A group of BME Club members after their visit to MPS AG in April 2013.

The BME Club team at the Grand Prix in Bern, May 2013. Top from left to right: Christian Gueder, Jorge Sague, Gregor Spreiter, Constanze Hofmann, Juan Anso, Andreas Vollenweider, Tom De Bruyne.
Bottom from left to right: Matthias Peterhans, Jochen Walser, Lukas Kohler, Andreas Renggli.

The BME Master alumni meet for the already legendary annual barbeque on the top floor terrace of Murtenstrasse 50 in August 2013.

BME Club members have lunch at the World Medtech Forum in Lucerne in September 2013. The event was co-sponsored by the Precision Cluster and the Bern University of Applied Sciences for celebrating the success of VoiSee, a viewing aid for elderly patients with age-related macular degradation (AMD).

BME Club Stammtisch at Restaurant Beaulieu in fall 2013.

A group of BME Club members is enjoying a hot Glühwein at the traditional Bernese Onion Market in November 2013.


Kramme
Medizintechnik
3. Auflage
· Verfahren
· Systeme
· Informations-
verarbeitung
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ACADEMIC EDUCATION AND TEACHING

Academic education is a cornerstone of the Bern Biomedical Engineering Network. At the master level, a joint program in Biomedical Engineering (BME) was established by the Medical Faculty of the University of Bern and the department of Engineering and Information Technology of the University of Applied Sciences of Bern with the aim of training multidisciplinary engineers to deliver scientifically founded and cost-effective solutions for biomedical problems in research and industry.

For Graduates of the MSc in Biomedical Engineering and other candidates from related areas who are interested in an in-depth training in experimental and computational research and/or who aim for an academic career, a corresponding doctoral degree (PhD in Biomedical Engineering) can be attained at the interfaculty Graduate School for Cellular and Biomedical Sciences (GCB) of the University of Bern. The GCB is jointly administered by the Faculties of Medicine, Science and Vetsuisse and offers tailored structured training programs at an international level.

At Bern University of Applied Sciences the Medical Information Laboratory for example enables the processes of the Swiss health care system to be visualised on a 1:1 basis. Students of the Medical Informatics learn and work with the new laboratory infrastructure on realistic questions and projects which have been developed in conjunction with partners from hospitals, industry and public authorities.

Philippe Zysset
Program Director Master of Biomedical Engineering
University of Bern

Marlene Wolf
Coordinator Graduate School for Cellular and Biomedical Sciences
University of Bern

Lukas Rohr
Head of Departement
Bern University of Applied Sciences
Engineering and Information Technology

Master of Science in Biomedical Engineering

The Curriculum
Since the start of the Master's Program Biomedical Engineering in March 2006, the constant effort to improve the quality of our curriculum has resulted in substantial changes of the course structure over the past years. The first curriculum consisted of a number of individual courses that were either mandatory or elective, but their coherence with regards to contents was in most cases not expressed by a defined structure. However, two major modules (formerly called "focus areas") already existed.

As of Fall Semester 2009, all courses were grouped in a strictly modular way in order to enhance the clarity and reduce the complexity of the curricular structure. A main idea was to guide the students through their studies in a better way by adding an elective part to the major modules, which formerly had consisted exclusively of mandatory courses. Besides, the curriculum was expanded by a number of new specialized courses as well as an additional major module called "Image-Guided Therapy".

Adaptations in the legal framework of the master's program are now offering more flexibility in the design of courses and modules, thus providing the basis for a se-cond fundamental restructuration of the curriculum as of Fall Semester 2013. In particular, a new module called "Complementary Skills" is replacing the former module "Unrestricted Electives". In addition, the list of mandatory courses in both basic and major modules was revised.

Duration of Studies and Part-Time Professional Occupation
The full-time study program takes 4 semesters, which corresponds to 120 ECTS points, one ECTS point being defined as 25-30 hours of student workload. It can be extended to a maximum of 6 semesters. When a student decides to complete the studies in parallel to a part-time professional occupation, further extension is possible on request. To support regular part-time work, mandatory courses take place (with rare exceptions) on only 3 days per week.

Basic Modules
The basic modules provide the students with the necessary background to be able to fully understand the highly complex subject matter in the specialized courses. All students with an engineering background (for all other students, individual study plans are set up which may contain certain variations) have to complete all courses in the Basic Modules Human Medicine, Applied Mathematics, and Biomedical Engineering. In the first semester, all courses belong to these basic modules, whereas in the second and third semester, they make up for approximately 30%.

Major Modules
The choice of one of three major modules Biomechanical Systems, Electronic Implants, or Image-Guided Therapy after the first semester constitutes the first opportunity for specialization. The former major module "Musculoskeletal System" has been adapted and renamed "Biomechanical Systems".

Approximately one third of the major modules consists of mandatory courses. In the elective part of the major module, the student is allowed to select any course from the list of courses in the master's program, giving rise to a high degree of diversity and flexibility and allowing for numerous course combinations. However, this freedom makes it somewhat difficult for the student to make reasonable choices regarding professional prospects.

This is why the responsible lecturers developed a recommended study plan to guide the students through the course selection process and to avoid organizational problems such as overlapping courses. If a student follows the recommended path, he or she can be sure to establish a sound professional profile.

Module "Complementary Skills"
Apart from the rapid development of technology itself, today's biomedical engineers are increasingly challenged by complementary issues like project planning, quality assurance and product safety, legal regulations and intellectual property rights, as well as marketing aspects. Language competence in English is of paramount importance both in an industrial and academic environment. This situation is accounted for by the introduction of a new module called "Complementary Skills" where students are required to complete two mandatory courses (Innovation Management; Regulatory Affairs and Patents) as well as 2 ECTS from the electives courses (Scientific Writing in Biomedical Engineering; Introduction to Epidemiology and Health Technology Assessment). If a student selects more than 2 ECTS from the elective part, the additional points can be credited in the student's major module.

Master's Thesis
The last semester is dedicated to a master's thesis project on an individually suited topic in an academic research group at the University of Bern or the Bern University of Applied Sciences or, for particular cases, in an industrial research and development environment. As a rule, all 90 ECTS points from the course program have to be completed, thus ensuring that the student is able to fully concentrate on the challenges imposed by exciting research activities. The master's thesis includes the thesis report, a thesis presentation and defense as well as a one-page abstract for publication in the Annual Report of the master's program.

Basic Modules (38 ECTS)

"Basics in Human Medicine" (11 ECTS)

"Applied Mathematics" (8 ECTS)

"Biomedical Engineering" (19 ECTS)

Major Module "Biomechanical Systems" (44 ECTS)

Mandatory Part (16 ECTS)

Elective Part (28 ECTS)

Major Module "Electronic Implants" (44 ECTS)

Mandatory Part (16 ECTS)

Elective Part (28 ECTS)

Major Module "Image-Guided Therapy" (44 ECTS)

Mandatory Part (16 ECTS)

Elective Part (28 ECTS)

Module "Complementary Skills" (8 ECTS)

Mandatory Courses (6 ECTS)

Elective Courses (2 ECTS)

Master Thesis (30 ECTS)

List of Courses

Biological Principles of Human Medicine
Biomaterials
Biomedical Acoustics
Biomedical Instrumentation
Biomedical Laser Applications
Biomedical Signal Processing and Analysis
BioMicrofluidics
C++
Clinical Applications of Image-Guided Therapy
Computer Assisted Surgery
Computer Graphics
Computer Vision
Cutting Edge Microscopy
Design of Biomechanical Systems
Engineering Design
Engineering Mechanics I
Engineering Mechanics II
Finite Element Analysis I
Finite Element Analysis II
Functional Anatomy and Histology
Functional Anatomy of the Locomotor Apparatus
Health Technology Assessment
Image-Guided Therapy Lab
Innovation Management
Intelligent Implants and Surgical Instruments
Introduction to Medical Statistics
Introduction to Signal and Image Processing
Machine Learning
Medical Image Analysis
Medical Image Analysis Lab
Medical Robotics
Microelectronics
Microsystems Engineering
Modeling and Simulation
Molecular Biology
Numerical Methods
Ophthalmic Technologies
Osteology
Physiology
Principles of Medical Imaging
Programming of Microcontrollers
Regulatory Affairs and Patents
Rehabilitation Technology
Scientific Writing in Biomedical Engineering
Technology and Diabetes Management
Tissue Biomechanics
Tissue Biomechanics Lab
Tissue Engineering
Tissue Engineering - Practical Course

Major Module: Biomechanical Systems

Philippe Zysset

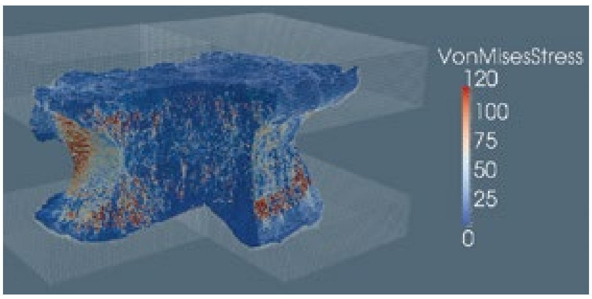
The cardiovascular and musculoskeletal systems are the transport and structural bases for our physical activities and their health have a profound influence on our quality of life. Cardiovascular diseases, musculoskeletal injuries and pathologies are the most costly ailments facing our health care systems, both in terms of direct medical costs and compensation payments related to loss-of-work.
In this module, students will gain a comprehensive understanding of the multi-scale organisation of the cardiovascular and musculoskeletal systems, combining knowledge from the cell, tissue, organ to the body level. They will learn how to apply engineering, biological and medical theory and methods to resolve complex problems in biomechanics and mechanobiology. Students will learn to draw connections between tissue morphology and mechanical response, and vice versa. Students will also gain the required expertise to apply their knowledge in relevant, practice-oriented problem solving in the fields of cardiology, vessel surgery, orthopaedics, dentistry, rehabilitation and sports sciences.

The mandatory courses in this module provide the student with fundamental knowledge of fluid and solid mechanics, tissue engineering, tissue biomechanics and finite element analysis. This provides an overview of the functional adaptation of the cardiovascular or musculoskeletal system to the demands of daily living, and the necessary conditions for its repair and regeneration. This major module requires a prior knowledge of mechanics, numerical methods and related engineering sciences, as many of the mandatory and elective courses build upon these foundations. Elective courses allow the students to extend their competence in a chosen direction, gaining knowledge in analytical methodologies, medical device design, minimally invasive surgery or rehabilitation.

Knowledge gained during the coursework highlights the multidisciplinary nature of this study focus area, encompassing the cell to body, the idea to application and the lab bench top to the hospital bedside. This knowledge is applied during the final thesis project, a project often with a link to a final diagnostic or therapeutic application. Examples of recent thesis projects include the analysis of rotodynamic blood pumps, the development of a monitoring tool for screw insertion in bone or the investigation of collagen scaffolds towards anterior cruciate ligament repair.

Career prospects are numerous. Many students proceed to further post-graduate education and research, pursuing doctoral research in the fields of biomechanics, tissue engineering or development of biomaterials. Most of the major companies in the fields of cardiovascular engineering, orthopaedics, dentistry, rehabilitation engineering and pharmaceuticals are strongly represented within the Swiss Medical Technology industry and continue to experience growth, therefore driving a demand for graduates of this major module. At the interface between biomedical engineering and clinical applications, graduates may also pursue careers related to the evaluation and validation of contemporary health technology, a cornerstone for future policies on the adoption of these new methods in the highly competitive health care domain.

A mesenchymal stem cells (MSC) grown on Novocart® collagen patches (B.Braun) for 7 days to test their cyto-compatibility for the application of repair of the anterior cruciate ligament of the knee joint. The picture shows MSCs spreaded onto the novocart collagen matrix.



Stress distribution in µCT based FEM model.

Major Module: Electronic Implants

Volker M. Koch

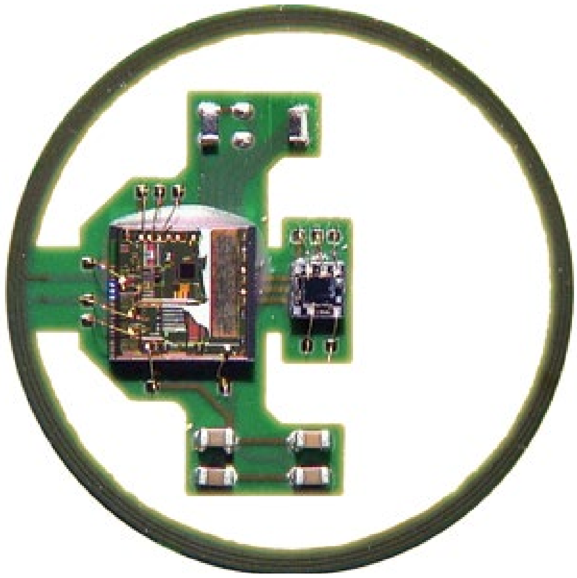
Electronic implants are devices like cardiac pacemakers and cochlear implants. Due to miniaturization and other developments, many new applications become feasible and this exciting area is growing rapidly. For example, cochlear implants provide already approximately 200’000 people a sense of sound. These people were previously profoundly deaf or severely hard of hearing. Recently, researchers demonstrated that electronic retinal implants allow the blind to read large words.

There are many more applications for electronic implants beyond treating heart problems, hearing loss or blindness. For example, there are electronic implants that treat obesity, depression, incontinence, hydrocephalus, pain, paraplegia, and joint diseases.

In this module, students will learn about the basics of electronic implants. This includes: sensor and measurement technology, signal processing and analysis, microcontroller programming, actuator technology, and miniaturization of micro-electro-mechanical systems. Application-oriented topics are also taught, e.g., cardiovascular technology and biomedical acoustics.

Since the development and manufacturing of electronic implants is highly complex and since it involves many different disciplines, it is not the goal of this major that students are able to develop an electronic implant on their own but rather to be able to work successfully in a project team that develops electronic implants.

Students may already apply their knowledge as a part-time assistant in a laboratory and/or during their master’s projects. After finishing the degree program, a wide variety of career paths are available, ranging from research and development to project and product management. Many well-known companies in Switzerland work in this field, e.g., Codman and Phonak Acoustic Implants. This list is, of course, not complete. For example, many "traditional" implants manufacturers have recently become interested in electronic implants, e.g., to measure forces in knee implants.



Glaucoma disease is normally associated with fluid pressure in the eye. The photo shows a miniaturised sensor system used for 24 hours measurements of the intra-ocular pressure and wireless RFID transmission of energy and data. The electronics, bonded on a 10 mm diameter flex print, is ready for integration into a dedicated eye lens. Photo: BFH, Institute for Human Centered Engineering - microLab, CTI project dynamic contour tonometer (industrial partner: Ziemer Ophthalmic Systems).

Major Module: Image-Guided Therapy

Stefan Weber

Image-Guided Therapy refers to the concept of guiding medical procedures and interventions through perceiving and viewing of medical image data, possibly extended by using stereotactic tracking systems. Medical imaging typically relates to a great variety of modalities ranging from 2D fluoroscopy and ultrasound to 3D computed tomography and magnet-resonance imaging, possibly extended to complex 4D time series and enhanced with functional information (PET, SPECT). Guidance is realized by various means of determination of the spatial instrument-to-patient relationship and by suitable visualizations. Image guidance is very often accompanied by other surgical technologies such as surgical robotics, sensor enhanced instrument systems as well as information and communication technology.

Students of the IGT module will be introduced to the fundamentals of the above-mentioned clinical and technical aspects of image-guided therapy. They will receive an overview of currently applied clinical standards as well as an overview of latest advancements in research (check out the recently introduced course on Clinical applications of IGT as well as the IGT Lab). Successful students will be able to develop novel clinic-technological applications for complex medical procedures as well as improve existing approaches to IGT. This will enable further careers both in the industrial and academic sector.

Mandatory courses of this module are concerned with the fundamentals of Signal and Image Processing and Medical Image Analysis. Furthermore, fundamental aspects of stereotactic image guidance, tracking, patient-to-image registration and basic clinical applications are taught in the course Computer-Assisted Surgery. Recent trends and fundamental aspects in surgical robot technology, minimally invasive procedures and its applications within IGT are introduced in the course Medical Robotics. Additional elective courses extend students competencies in related areas such as computer graphics, pattern recognition, machine learning, and regulatory affairs.

Preclinical validation of a precision robot system for cochlear implantation.

Faculty

University
Christiane Albrecht
Oliver Baum
Brett Bell
Philippe Büchler
André Busato
Samantha Chan
Roch Philippe Charles
Justyna Czerwinska Ing.
Bruno Da Costa
Marcel Egger
Paolo Favaro
Michael Fix
Martin Frenz
Benjamin Gantenbein
Marianne Geiser Kamber
Olivier Guenat
Kati Hänssgen
Ruslan Hlushchuk
Wilhelm Hofstetter
Hans Heinrich Hoppeler
Jürg Hüsler
Samuel Iff
Peter Jüni
Sonja Kleinlogel
Doris Kopp
Jens Kowal
Jan Kucera
Simon Milligan
Beatrice Minder
Stavroula Mougiakakou
Tobias Nef
Dobrila Nesic
Thomas Nevian
Ernst Niggli
Lutz Peter Nolte
Mauricio Reyes
Anne Rutjes
Johannes Schittny
Walter Martin Senn
Jürg Streit
Stefan Tschanz
Christophe Von Garnier
Daphné Wallach
Stefan Weber
Uwe Wolfram
Guoyan Zheng
Matthias Zwicker
Philippe Zysset

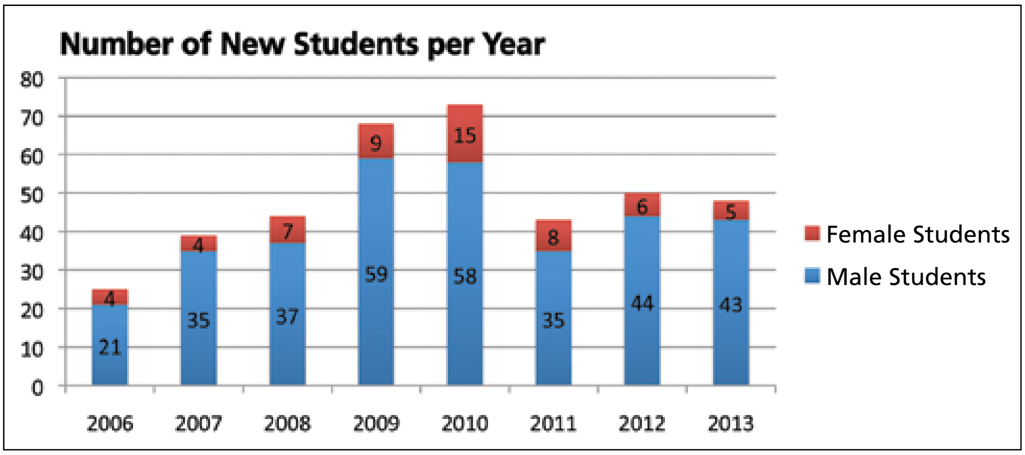
Inselspital, Bern University Hospital
Marco Domenico Caversaccio
Peter Diem
Patrick Dubach
Martin Kompis
Pascal Senn
Lennart Stieglitz
Heinz Zimmermann

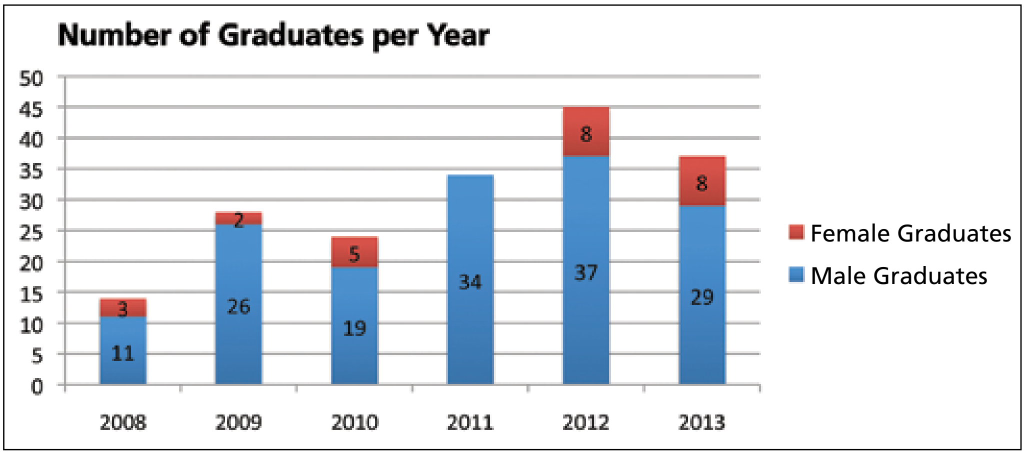
Bern University of Applied Sciences
Norman Baier
Daniel Debrunner
Bertrand Dutoit
Elham Firouzi
Josef Götte
Kenneth Hunt
Marcel Jacomet
Björn Jensen
Jörn Justiz
Theo Kluter
Volker Koch
Martin Kucera
Alexander Mack
Christoph Meier
Yves Mussard
Heinrich Schwarzenbach
Andreas Stahel
Jasmin Wandel

Research Partner Institutions and Industry
Nicolas Buchs
Jürgen Burger
Philippe Cattin
Emmanuel De Haller
Alex Dommann
David Eglin
Marie Noëlle Giraud
Daniel Haschtmann
Ulrich Hofer
Herbert Keppner
Beat Lechmann
Reto Lerf
Reto Luginbühl
Glenn Lurman
Walter Moser
Matthias Peterhans
Wolfram Petrich
Barbara Rothen Rutishauser
Birgit Schäfer
Samuel Schenk
Arnulf Staib
Jivko Stoyanov
Rolf Vogel
André Weber

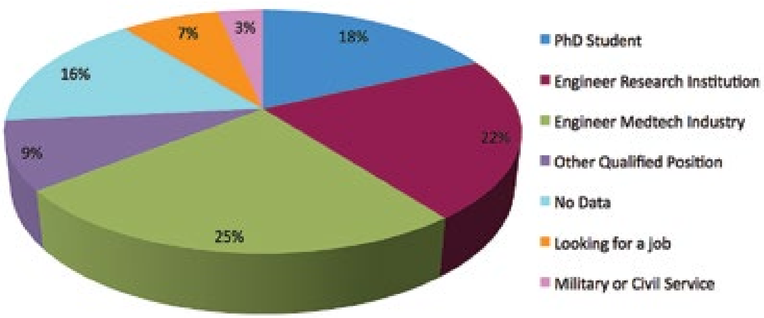
Statistics

Number of Students and Graduates per Year





BME Alumni: Career Directions
Profession after Graduation



Completed Master Theses in 2013

Salman Alaraibi
Simulation of Soft Tissue Deformation for Cranio Maxillo Facial Surgery using Cone-Beam CT Imaging and Inverse Planning Modeling
Supervisors: Kamal Shahim, Mauricio Reyes

Juan Anso
Integrated Facial Nerve Monitoring for Functional Control of Robotic Assisted Drilling in the Mastoid
Supervisors: Brett Bell, Stefan Weber

Steven Balestra
Statistical Shape Model-Based Articulated 2D-3D Reconstruction
Supervisors: Guoyan Zheng, Steffen Schumann

Stefan Brun
Development of a Portable System for Perfusion of Isolated Porcine Hearts
Supervisors: Hendrik Tevaearai, Sarah Longnus

Dawei Chen
An Integrated Head Holding Device for Robotic Assisted ENT Surgery
Supervisors: Stefan Weber, Brett Bell

Thomas Fejes
A Framework for Medical Image Analysis of Brain Tumor Studies
Supervisors: Mauricio Reyes, Stefan Bauer

Prosper Agbesi Fiave
Design of Miniaturized Electro Spray Instrument for Gene Therapeutic Treatment of Idiopathic Pulmonary Fibrosis
Supervisors: David Hradetzky, Amiq Gazdhar

Sébastien Gelin
Study of Magnetic Resonance Imaging Sequences of the Brain: Segmentation of MPRAGE and MP2RAGE in Early Degenerative Brain Diseases
Supervisor: Meritxell Bach Cuadra

Pedro Antonio González Pérez
Simulations Towards the Optimal Esophageal Lead System
Supervisors: Thomas Niederhauser, Rolf Vogel

Constanze Hofmann
User Interfaces for Automated Knee Rehabilitation
Supervisors: Agathe Koller, Kenneth James Hunt

Clément Huguenin-Dumittan
Characterization of Human Mesenchymal Stem Cell Clones for Intervertebral Disc Regeneration
Supervisor: Jivko Stoyanov

Matthias Hutter
Novel Approach for a Control Loop for Piezo Motors
Supervisors: Andreas Stahel, Josef Götte

Agnes Carmen Imhof
Use of Electrical Stimulation of Hepatic Neurons to Improve Glucose Homeostasis
Supervisor: Darleen Sandoval

Completed Master Theses in 2013

Roger Infanger
Novel Sensor Belt Connector for an Electrical Impedance Tomography Device
Supervisors: Josef X. Brunner, Pascal Olivier Gaggero

Silje Ekroll Jahren
Analysis of HQ loops of Rotodynamic Blood Pumps
Supervisors: Stijn Vandenberghe, Gregor Ochsner

Patrick Käppeli
An In-Vitro Model for the Characterization of Immiscible and Nonlinear Multiphase-Flow in Porous Media
Supervisors: Stephen Ferguson, René Widmer

Anna Khimchenko
Study of the Electrical Conductivity of Tissues and Organs for Electrical Impedance Tomography
Supervisors: Pascal Olivier Gaggero, Stephan H. Böhm

Birgit Lehretter
Simulation of Air-Guiding in a Respiration Training Device
Supervisor: Bernard Schmutz

Raphael Meier
Decision Forests for Multimodal Brain Tumor Segmentation
Supervisor: Stefan Bauer

David Morgenthaler
Laser Head Calibration
Supervisor: Philippe Cattin

Michael Muster
Foot-Stimulation Module for a Robotic Tilt -Table
Supervisors: Kenneth James Hunt, Silvio Nussbaumer

Rajankumar Parekh
Development of a new Chemoresistive Microfluidic Chip for Spheroid Formation
Supervisor: Olivier Guenat

Diana Catherine Peña Bello
p-HEMA Based Coating for Sustained Delivery of Antimicrobial Active Compounds in Orthopedic Device Associated Infection Therapies
Supervisors: Jorge Sague, Reto Luginbühl

Dominik Rey
Single-View Augmented Reality Navigation System
Supervisors: Philippe Cattin, Adrian Schneider

Michael Rieger
Model-Based Iterative Reconstruction
Supervisor: Tobias Kober

Angie Lilibeth Salas Téllez
Correlation of Bone Machining Parameters with Image Data for 3D Pose Estimation
Supervisors: Stefan Weber, Tom Williamson

Eric Schoenholzer
Development of an S100 Protein-Based Assay for Assessment of Human Articular Chondrocytes Re-differentiation in Monolayer
Supervisor: Dobrila Nesic

Ishan Dipakkumar Shah
Design of a Haptic Device Mimicking Index Finger Abduction Force
Supervisors: Nicole Wenderoth, Roger Gassert

Bergdís Ýr Sigurdardóttir
Finite Element Simulation to Optimize the Propertie Distribution of an Iso-Elasic Femoral Stem to Increase Stability after a Cementless total Hip Replacement
Supervisor: Benedikt Helgason

Marc Stadelmann
Computed Tomography Image Recycling for non-invasive Estimation of Bone Strength
Supervisor: Steven Boyd

Christoph Strub
Towards personalized medicine: homogeneous cell distribution on a microfluidic chip to form tumor-spheroids
Supervisors: Olivier Guenat, Janine Ruppen

Benedikt Julian Thelen
2D-3D Reconstruction-based Implant Migration Measurement
Supervisors: Guoyan Zheng, Steffen Schumann

Peter von Niederhäusern
Reconstruction of Optical Metamorphopsia Produced by Pathological Retinal Layers
Supervisors: Roger Cattin, Martin Schmid

Jonas Walti
NaviPen
Supervisors: Philippe Cattin, Adrian Schneider

Simon Wüest
Myoblast Differentiation under Simulated Microgravity: Long Term Cell Culture on Random Positioning Machines
Supervisors: Marcel Egli, Stéphane Richard

Thomas Wyss Balmer
GPU-Based Processing of Long-Term Oesophageal ECG
Supervisors: Thomas Niederhauser, Rolf Vogel

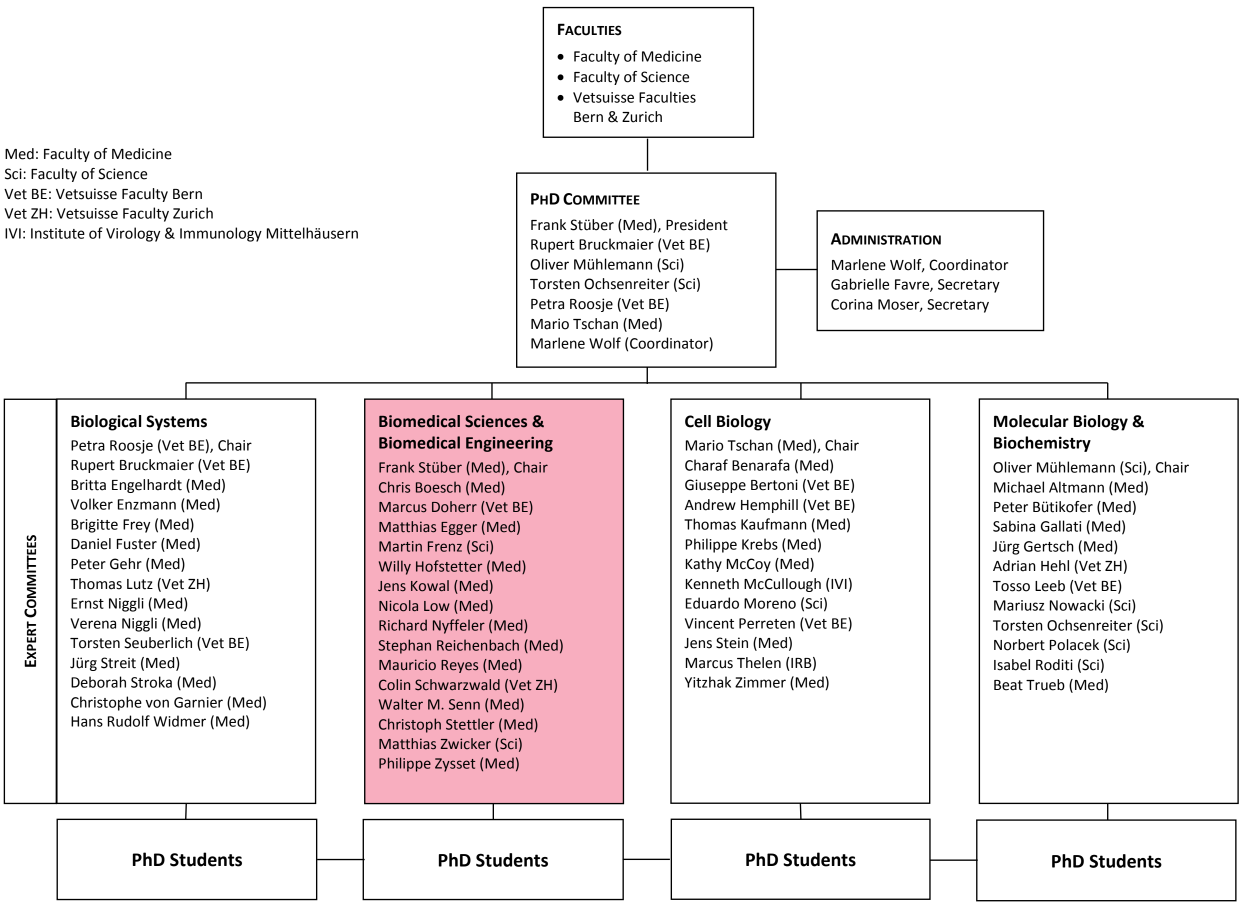
Stefan Zuber
The Dynamics of a Side-Ways Impact on the Hip
Supervisors: Benedikt Helgason, Philippe Büchler

Graduate School for Cellular and Biomedical Sciences

Organization
The GCB is headed by the PhD Committee (executive committee), which is composed of two members each of the Faculty of Medicine, the Faculty of Science, and the Vetsuisse Faculty Bern, and the Programme Coordinator. Taking turns, each faculty member acts as President.
In August 2013, Frank Stüber (Faculty of Medicine) took over the presidency from Oliver Mühlemann (Faculty of Science), who had exceptionally served as president of the GCB for three years, in order to complete certain tasks. Our warmest thanks go to Oliver's unconditional commitment and dedication to the concerns of the GCB, and we are very pleased to be able to continue the important work of the GCB under Frank's leadership.

Four Expert Committees – Molecular Biology & Biochemistry, Cell Biology, Biological Systems, and Biomedical Sciences & Biomedical Engineering – ensure that the different research fields are represented by experts in the respective areas.

In November 2013, Mira Delea resigned from her post as secretary of the GCB (50%) and moved to Lyon, France, with her family, while Corina Moser has taken over Mira's administrative responsibilities within the GCB and is currently employed in a 40% position.



Pages 116 - 121 of this report are excerpts from: Wolf M, Favre G: Annual Report 2013, Graduate School for Cellular and Biomedical Sciences, University of Bern (May 9, 2014); http://www.gcb.unibe.ch/unibe/graduateschools/gcb/content/e3529/e489632/Annual_Report_2013_WEB_eng.pdf (PDF), http://media.unibe.ch/public/gcb/jahresbericht_2013/index.html (flip book, Adobe Flash Player required).

PhD Programme
The Graduate School for Cellular and Biomedical Sciences of the University of Bern (GCB) offers structured training in experimental research in the fields of biochemistry, cell and molecular biology, immunology, biomedical sciences, epidemiology, neuroscience, and biomedical engineering, leading to a PhD, MD,PhD, or DVM,PhD degree. Its administration is jointly assured by the Faculty of Medicine, the Faculty of Science and the Vetsuisse Faculty.

By the end of 2013, 358 students were enrolled in the PhD programme. The thesis projects are carried out at laboratories of the three participating faculties or at affiliated institutions; in 2013, these included the Institute of Virology and Immunology (IVI) in Mittelhäusern (to be merged with the Institute of Veterinary Virology of the Vetsuisse Faculty on January 1, 2014), the Institute for Research in Biomedicine (IRB) in Bellinzona, and the EMPA St. Gallen.

Each student is supervised by a thesis committee consisting of the supervisor, a co-advisor and a member of the appropriate Expert Committee (mentor). The supervisor is responsible for the research project, adequate supervision, the laboratory infrastructure and the salary of the student. The co-advisor must not be affiliated with the same institute as the supervisor, but should be an expert in the research area of the thesis project. He meets with the student at least twice a year to discuss and assess progress of the thesis work, as well as advising and supporting him/her. The mentor decides, together with the student and the supervisor, on the individual training programme, taking into account the student's previous education.

The training programme requires a certain number of learning credits which can be obtained by participating in approved, project-related and interdisciplinary courses, workshops, seminars, and lectures during the doctoral training period. Prior to graduation, candidates must (i) pass the exams of the individual training programme, and (ii) in the course of the second year, present their work in a scientific seminar in the presence of the thesis committee, to document in-depth knowledge of the research field ("Mid-term Evaluation").

The GCB actively supports the participation of students in national and international conferences and in special training courses offered by recognized institutions in Switzerland and abroad, by granting a financial contribution which covers a substantial part of the costs in each case. This support is very much appreciated by both students and supervisors; accordingly, the budget for this support was completely used up in 2013.

A further aim of the structured doctoral programme of the GCB lies in the promotion of a lively scientific exchange between PhD students and senior scientists, and the stimulation of networking activities such as regular discussions with the thesis committee, exchange among peers during the annual GCB Symposium, the opportunities to attend external courses and conferences, and to invite internationally renowned scientists for a GCB seminar.

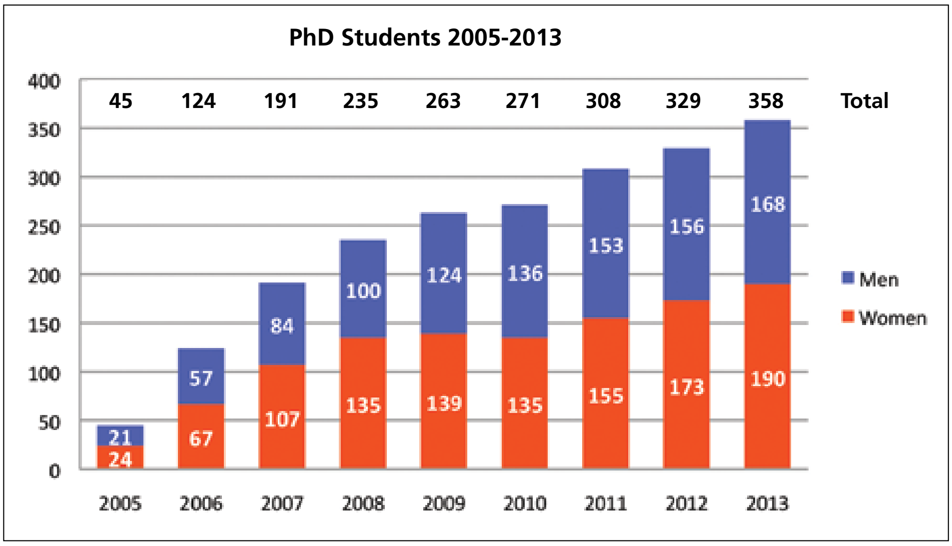
MD-PhD Programme
The MD-PhD programme is intended for medical graduates interested in experimental research and aiming at an academic career. A structured training programme within the framework of the GCB enables them to acquire a high standard of knowledge in natural sciences and physiology. According to the guidelines of the National MD-PhD Programme, candidates should already start their training in the course of their medical studies and follow relevant courses and exams in cell and molecular biology or other related fields simultaneously with their medical curriculum.

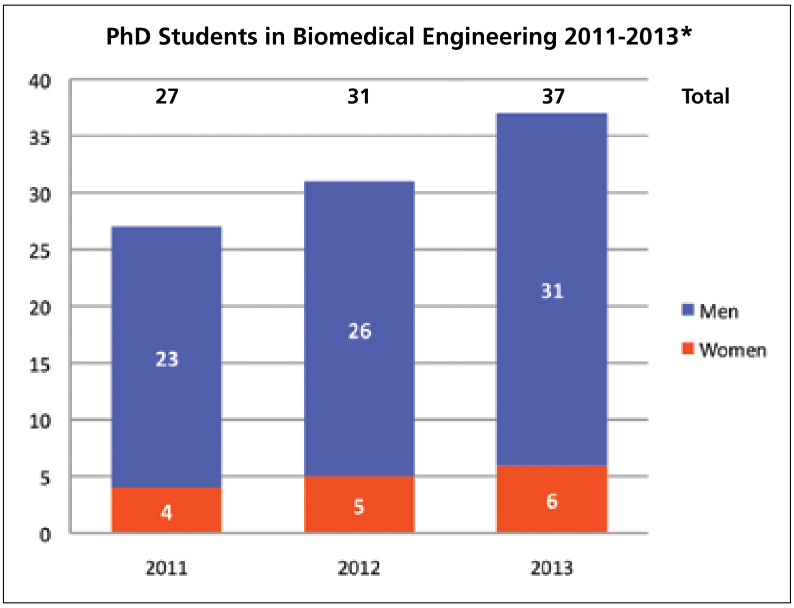
In 2013, the Coordinator Marlene Wolf interviewed and advised about 10 medical students in their second to fourth year. Four of them were interested in the MD-PhD programme, and an individual training programme was put together for each of them. They now attend basic science courses.

The National MD-PhD Programme, which is supported by the Swiss National Science Foundation (SNSF), the Swiss Academy of Medical Sciences (SAMW) and several other foundations, awards 9 to 13 fellowships every year to outstanding medical candidates (Human as well as Veterinary Medicine) studying at Swiss Universities (for information, see http://www.samw.ch/de/Forschung/MD-PhD- Programm.html).

Doctoral Students
Students can apply three times per year for admission to the Graduate School: on 15 April, 15 August, and 15 December.

The GCB is internationally oriented and represented by doctoral students with master diplomas from 38 different countries. In December 2013, 186 students (52.0%) were holding a degree from a foreign university. 53.1% of the doctoral students are women.





* surveyed separately since 2011

Courses and Seminars

The PhD programme involves theoretical training in addition to the experimental work on the research project. For each student, seminars and courses are individually selected from courses organized and supported by the GCB, from the teaching units of the faculties, and also from courses offered by other Swiss Universities, in particular by the ETHZ or the EPFL for the field of Biomedical Engineering, or by interuniversitary programmes like StarOmics (CUSO), the Doctoral Program in Population Genomics (Universities of Basel, Bern, Fribourg and Lausanne), the Forum for Genetic Research (sc | nat, Swiss Academy of Sciences), the BENEFRI Neuroscience Programme (Universities of Bern, Neuchâtel and Fribourg), or the Swiss Institute of Bioinformatics (SIB). Some students also take part in internationally organized Summer Schools which provide high quality training in specific fields.

GCB Seminar Series

The GCB Seminar Series gives PhD students the opportunity to invite internationally renowned specialists from their field of research for an interactive teaching lecture and a research seminar intended for a broad audience.

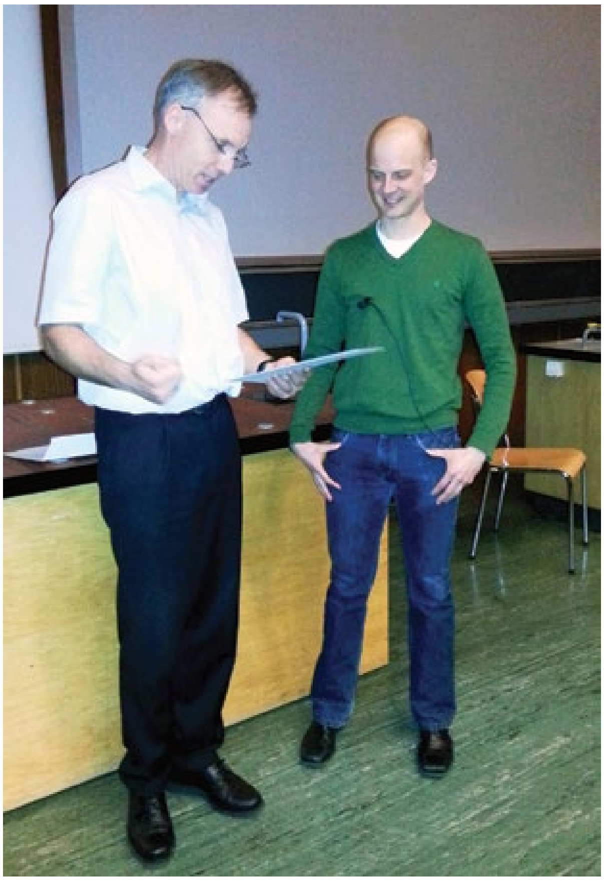
GCB Students' Symposium 2013

On 30 January 2013, the GCB Students' Symposium 2013 was held once again on the premises of the Department of Chemistry and Biochemistry. During a whole day, the different research projects of the GCB doctoral students were presented in 48 short talks in four parallel sessions and 138 posters (two sessions). The presentations illustrated the wide range of topics covered by the GCB and demonstrated the students' consistently high level of competence in the fields of cellular and biomedical sciences, epidemiology and biomedical engineering. The symposium offered an excellent opportunity for both GCB students and their supervisors to engage in a reciprocally rewarding and highly stimulating discussion on the research work going on at the GCB. The invited guest speaker, Walter J. Gehring, Biozentrum, University of Basel, gave a highly acclaimed talk on "The Evolution of Vision". The breaks were extensively used for further informal discussions and active networking, and the Symposium once more closed with an apéro during the second poster session, which gave further opportunity for lively exchange among participants.

Walter J. Gehring giving his keynote lecture on occasion of the GCB Students' Symposium 2013.

Congratulations

The 2013 GCB Award for "Best PhD Thesis" (CHF 3'000.–) was awarded to Andreas Boss, PhD, in January 2014 during the GCB Students' Symposium for his work entitled "Application of multinuclear magnetic resonance spectroscopy for the non-invasive investigation of skeletal muscle and liver metabolism". He performed his PhD work under the supervision of Chris Boesch at the Department of Clinical Research, Magnetic Resonance Spectroscopy and Methodology AMSM, University of Bern, and defended his thesis successfully on May 22, 2013.



Andreas Boss, PhD (right), receiving the "GCB Award for Best PhD Thesis" for 2013 from the hands of Frank Stüber, President of the GCB (left) on occasion of the GCB Students' Symposium 2014.

Our warmest congratulations go to Andreas Boss, for his outstanding success. After his graduation, the laureate moved to the Netherlands, where he is currently pursuing a career as a postdoctoral fellow at the Department of Radiology, Radboud University Medical Center, Nijmegen, The Netherlands.

We are very proud to report that Andreas Boss, has also received the Benoît Pochon Award 2013 for his PhD thesis.

Graduations
In the course of 2013, 67 students successfully completed the PhD programme of the GCB and obtained their doctoral degree, jointly issued by the Faculty of Medicine, the Faculty of Science, and the Vetsuisse Faculty.

Of the graduates, 35 – i.e., 52.2% – were students with a master diploma from a foreign University who joined the GCB for their PhD studies. Of the 67 dissertations completed within the PhD programme of the GCB in 2013, twelve theses focus on a Biomedical Engineering topic.

Completed Dissertations 2013

Stefan Bauer, PhD in Biomedical Engineering
Medical image analysis and image-based modeling for brain tumor studies
Supervisor: Mauricio Reyes

Christine Bolliger, PhD in Biomedical Sciences
Novel combinations of acquisition and processing methods for the quantification of brain metabolites by in vivo ^{1}H magnetic resonance spectroscopy
Supervisor: Roland Kreis

Andreas Boss, PhD
Application of multinuclear magnetic resonance spectroscopy for the non-invasive Investigation of skeletal muscle and liver metabolism
Supervisor: Chris Boesch

Vaclav Brandejsky, PhD in Biomedical Sciences
Studies of metabolism by means of ^{1}H magnetic resonance spectroscopy
Supervisor: Chris Boesch

Elena Daskalaki, PhD in Biomedical Engineering
Towards the external artificial pancreas: Design and development of a personalized control system for glucose regulation in individuals with type 1 diabetes
Supervisor: Stavroula Mougiakakou

Marcelo Elias de Oliveira, PhD in Biomedical Engineering
A non-invasive technique for assessing the spinal flexibility in adolescent idiopathic scoliosis
Supervisors: Philippe Büchler, Lutz-P. Nolte

Nicolas Gerber, PhD in Biomedical Engineering
Computer assisted planning and image guided surgery for hearing aid implantation
Supervisors: Stefan Weber, Lutz-P. Nolte

Jérémie Guignard, PhD in Biomedical Engineering
Biomedical implants in the temporal bone: Anatomy, physics, and surgical procedure aspects
Supervisor: Christof Stieger

Ghislain Maquer, PhD in Biomedical Engineering
Image-based biomechanical assessment of vertebral body and intervertebral disc in the human lumbar spine
Supervisor: Philippe Zysset

Aloïs Pfenniger, PhD in Biomedical Engineering
Intracorporeal energy harvesting with a focus on the human cardiovascular system
Supervisor: Rolf Vogel

Tohid Pirbodaghi, PhD in Biomedical Engineering
Speed modulation of rotary blood pumps: Experimental evaluation
Supervisor: Stijn Vandenberghe

Hadi Seyed Hosseini, PhD in Biomedical Engineering
Constitutive modeling of trabecular bone in large strain compression
Supervisor: Philippe Zysset

Educational Opportunities at Bern University of Applied Sciences

Bern University of Applied Sciences offers Bachelor and Master degree courses as well as extra-occupational further education in Medical Technology and Medical Informatics.

Bachelor of Science in Medical Informatics

The Bachelor of Science in Medical Informatics was designed to provide students with a sound part-time or full-time study programme to train them for the challenges of ICT (communications and information systems) in the healthcare sector. Today's highly complex, interdisciplinary healthcare informatics demands expertise in the fields of informatics, medicine and organisation/management/leadership. Bern University of Applied Sciences is the first university in Switzerland with the capacity to offer such a degree programme, and has been running it since 2011. With this Bachelor's degree, students attain a level of professionalism which enables them to assume positions of responsibility in healthcare informatics in the IT field. It also opens doors for further university studies, such as a Master's degree in Science and Promotion.

A unique 3-stage Switzerland-wide Medical Informatics Laboratory concept acts as an interface between education and research.

- It is an accurate reflection of the ICT working environments of the service providers in the Swiss healthcare sector (hospitals, family physicians, pharmacies, Spitex)
- Management in the healthcare sector (hospitals, insurance companies, public authorities)
- 2-room AAL apartment (sensor-based living)

This laboratory concept enables our students to understand correlations in the healthcare sector, provides a real-life insight into their future working environments, and is a driving force in terms of research projects.

Medical Informatics: Hugely Important for the Healthcare Sector

A study carried out by Bern University of Applied Sciences at hospitals and clinics, manufacturers of medical software and devices, insurance companies, and other key stakeholders in the healthcare sector on training requirements in the Swiss medical informatics field revealed that the Swiss healthcare sector will require an additional 700 medical informatics professionals by 2015. To date, Switzerland has recruited qualified medical informatics professionals abroad, or Swiss students have had to complete this degree programme abroad if they were interested in the course of study.

The study also revealed that specialists who are experts in both medical processes and IT are now indispensable in the day-to-day running of hospitals, clinics, institutions and medical practices. Today, there are already more than 1,200 professionals employed Switzerland-wide in the field of medical informatics. The majority are newcomers to the industry who have until now undertaken further training where possible (approx. 20%) or who have to acquire their knowledge on the job under less than ideal circumstances. Only ten per cent have a qualification in medical informatics. As there has not been any relevant qualification in Switzerland until now, qualified specialists have inevitably been recruited from nearby countries.

The participants in the above-mentioned study also commented on the requirements that these specialists must meet: In addition to a comprehensive knowledge of informatics, a basic knowledge of medicine, process and data management as well as project management skills are required.

What is Medical Informatics?
Medical informatics professionals deal primarily with the systematic compilation, preparation and processing of data and information in the medical and healthcare sectors. They provide support by setting up information systems which are linked to knowledge-based systems and map important working processes in medical diagnosis, treatment or documentation. They also develop or model information systems for hospitals, emergency centres, chemists and medical practices, and link these primary systems not only with each other but also with other stakeholders in the healthcare sector (insurance companies, public authorities). By involving patients as data holders, e-health networks are formed in which data security, protection of privacy and interoperability must be ensured.

Other task areas of medical informatics include simulations of surgical operations or image processing techniques in diagnosis (e.g. computer tomography). The extraction and processing of relevant medical performance data for medical and administrative controlling in particular and for management are also part of the aforementioned task areas. On top of this, big data and personalised medicine are new areas of research which directly affect medical informatics and must be utilised for the healthcare sector. A major trend in the field of ambient assisted living (AAL) is also perceptible. Here medical technology and medical informatics are particularly closely related. It is imperative that the data is compiled in an integrated manner using a variety of sensory technology, and interpreted medically.

All these examples show that medical informatics professionals must have an excellent understanding of processes in medicine and in the healthcare sector in addition to informatics, with professional project management skills also being required. If communication with doctors and nursing staff is not effective, their concerns cannot be fully understood and implemented. Expertise in project leadership and management are also necessary when implementing large informatics projects.

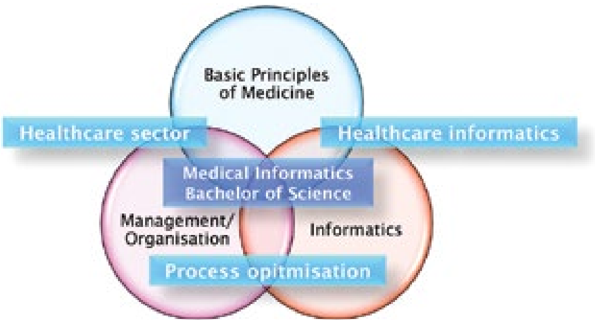
In order to keep pace with the speed of technological development, strategies are required to ensure continuous and independent acquisition of new knowledge, its presentation and implementation within your own organisation. Medical informatics students are highly qualified experts in this area with excellent professional prospects at the interface between medicine, informatics and technology.

Goals of the Degree Programme
Students will
- be prepared for project management tasks in the field of medical informatics in hospitals, public authorities and companies,
- understand all aspects of the procedures of the healthcare sector and its stakeholders from an informatics point of view,
- be familiar with the interdisciplinary and transdisciplinary workings of hospitals, their administrative and medical processes as well as collaboration between the different disciplines which derives from this,
- be able to communicate effectively with specialists from the fields of medicine, informatics, organisation, economics and law in the healthcare sector, and understand their concerns,
- be able to co-design and manage the implementation of large informatics projects both in hospitals and in trans-sector networks (eHealth),
- be able to analyse, evaluate and optimise the introduction and maintenance of ICT in the healthcare sector,
- be able to specify medical ICT in companies, design the necessary architecture and develop systems efficiently in their field of responsibility, with particular focus on intuitive software user interface design,
- be able to recognise the requirements and features of the different types of documentation of the service providers, and take this into consideration when designing the ICT,
- be able to understand the concepts of semantic interoperability and their meaning and apply them,
- be able to manage development cycles from the design phase to the prototype through to the final version as a product owner or master of agile development methods for optimal implementation of requirements,

- be familiar with object oriented programming concepts and how to apply them,
- be familiar with the architecture, design and programming of mobile applications,
- be familiar with the set-up and modelling of data for the purpose of efficient use in databases and be able to administer and evaluate these accordingly,
- be familiar with procedures during clinical studies and in the field of quality management, and be able to support corresponding projects in informatics terms in a leading role,
- be able to present informatics projects competently in companies and in research both orally and in writing, as well as chair and moderate meetings,
- be familiar with the economic aspects and correlations of the healthcare sector,
- gain a high level of awareness of quality requirements and legal provisions, and provide their services to the healthcare sector in a professional manner, and with empathy and responsibility for patients and their personal rights (e.g. data protection).

Content and Structure of the Degree Programme

The curriculum of the Bachelor degree was designed strictly in accordance with the international guidelines of the International Medical Informatics Association (IMIA) on Education in Biomedical and Health Informatics and the requirements of the Swiss healthcare sector. In the process, three main topics were identified: Basic Principles of Medicine, Informatics and Management / Organisation.



Three main topics form the basis of the Bachelor degree programme: Basic Principles of Medicine, Informatics and Organisation / Management. The complex of issues surrounding the healthcare sector, process optimisation and healthcare informatics form the interfaces between these main topics. The modules were specified according to this outline.

Medical informatics is carried out for the benefit of patients in the field of tension between medicine and economics. In the process, medical informatics professionals must always keep the legal and in particular ethical background circumstances in mind and modify their actions accordingly.

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Bachelor Studies in Micro- and Medicaltechnology

The interdisciplinary Bachelor of Science in Micro- and Medicaltechnology provides students with a broad fundamental knowledge and a solid basis for the development of innovative products. The specialisation in Medical Technology provides students with the knowledge to develop and produce micro systems (e.g. intelligent operational instruments) as well as actuators and sensors for medical devices.
They are extremely popular: over the past few years, around one quarter of the students of Micro Technology have written their final theses on a topic in this field.

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Continuing Education in Medical Technology and Medical Informatics

Bern University of Applied Sciences offers a modular structured, part-time university degree in Medical Technology Management and Medical Informatics Management which is unique in Switzerland. The coordinated modules can be scheduled to fit in with the participants' professional demands and can be completed at various levels up to the Master of Advanced Studies. The practice-oriented tuition is centred around reality-based scenarios around which the individual courses are grouped.
The courses in Medical Technology Management are primarily geared towards engineers, technical professionals and natural scientists. Students are gradually prepared for carrying out demanding projects in the development, procurement, marketing and maintenance of medical technology products, and for assuming managerial responsibilities in the field of medical technology.
The courses in Medical Informatics Management are primarily geared towards information technology professionals and medical specialists. Students are specifically prepared for interdisciplinary tasks in the field of 'eHealth'. The content focuses primarily on the introduction and support of information and communication systems in the healthcare sector, the development of strategies and concepts as well as preparation for management tasks in the field of medical informatics.

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