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ARTORG CENTER
BIOMEDICAL ENGINEERING RESEARCH

Annual Report 2011

ARTORG Center

Contents

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Introduction

2011 in Retrospect

For the research groups of the Artificial Organ (ARTORG) Center for Biomedical Engineering Research, 2011 was its third full year of operation and a beginning consolidation. Today the center comprises a multidisciplinary team of over 80 co-workers. We have settled into our new office and laboratory space on the University hospital, Inselspital campus, an ideal research environment, which we share with various groups of the Department of Clinical Research. The ARTORG Center is also closely integrated into the Institute for Surgical Technology and Biomechanics (ISTB, www.istb.unibe.ch), with two faculty members cross-appointed between the two institutions. Through participation in national and international research network programs, we have been able to continue our translational research activities in all our focus areas.

Our young teams have successfully expanded their research budgets by generating external funding through both government sources and contributions by non-governmental organizations and our industrial partners. The ARTORG Center continues to be a member of the Swiss National Center of Competence in Research CO-ME (www.co-me.ch) and hosts various subprojects that have a primary focus on computer-aided surgery around the head and soft tissue interventions. This network of excellence has now moved into its eleventh year since its inauguration in 2001.

We were proud to have our research and development efforts recognized by several awards, including the nominations for the CTI Swiss Medtech and the Swiss Technology Awards. Close collaboration with our start-up CAScination provides our laboratory direct access to highly advanced marked platforms for image guided therapy. Key collaborative projects with the Swiss MedTech industry continue to be developed through funding from KTI/CTI, which is the Innovation Promotion Agency of the Swiss Federal Office for Professional Education and Technology. In addition, major parts of our research activities are made possible through direct funding by non-governmental organizations and our industrial partners.

All ARTORG group leaders have joined the Master of Science in Biomedical Engineering program (www.bme.master.unibe.ch) as lecturers offering high level courses in their areas of specialization. This greatly helped to attract students nationally and internationally but also guest auditors from the Medtech industry. Currently, more than 150 students are enrolled in the program to become specialists in biomedical engineering. In addition, about 40 students from the ISTB and the ARTORG Center are currently enrolled in the interdisciplinary biomedical science doctoral program (www.gcb.unibe.ch).

We hereby introduce to you the third annual report of the ARTORG Center for Biomedical Engineering Research, which presents our research and educational activities and the progress made in 2011.

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Marco D. Caversaccio
Vice Director

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ARTORG Center for Biomedical Engineering Research

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S. Weidner

The ARTORG Center brings together researchers from various biomedical engineering groups and clinical departments thematically centered around its label Artificial Organs. During the past almost four years ten ARTORG research groups have been established focusing on their specific areas of research. The Center's management team consists of the Director and the Vice Director and is supported by the central services team. Strategic guidance and scientific quality of the ARTORG Center are in the hands of the Scientific Advisory Board, composed of biomedical engineering experts. The ARTORG center has defined its mission as a dedicated academic institution to advance healthcare by integrating education, discovery, innovation and entrepreneurship. The Center supports this effort by encouraging a close partnership between clinicians, laboratory scientists and engineers and aims to cultivate new translational research projects based on clinical practice needs. Through our Center for Competence in Medical Technology (www.ccmedtech.ch), knowledge and technology transfer is promoted by involving partners from the Medical Technology industry.

Organization

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Artificial Kidney Research

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Artificial Hearing Research

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Clinical Partners of Inselspital

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Research Profile

Hearing not only fulfils an important function in interpersonal relationships but also helps in orientation and in alerting danger. Approximately 10% of the general population have a hearing loss which ranges from a slight loss up to complete deafness. The university department of ENT head and neck surgery of the Inselspital has an extensive experience in hearing rehabilitation i.e. otological microsurgery, conventional hearing systems, semi- and fully implantable hearing systems and cochlear implants. The Artificial Hearing Research group investigates implantable hearing systems. Implantable hearing systems differ from conventional hearing aids in that at least one part of the device is implanted, requiring not only acoustics but considerations of implant technology as well. Therefore our research group is a network consisting of engineers, surgeons, audiologists and industrial partners.

Current Research Areas

Direct Acoustical Cochlear Stimulation (DACS) Multicenter Clinical Trial

DACS is a novel implantable hearing aid. The initial development of the DACS was driven by our ENT clinic together with an engineering company from Bern. It is designed for patients with severe to combined advanced otosclerosis. We have shown the proof of concept in a pilot clinical study with a percutaneous system. This year, after industrial fabrication the C-DACS- ID with a transcutaneous transmission was successfully implanted in 15 patients in a clinical multicenter study conducted at the Inselspital, MHH Hannover (D) and Radboud University Nijmegen (NL). Prior to surgery the patients used a conventional hearing aid. After the operation with the activated DACS the patients improved in hearing thresholds and speech understanding when compared to the preoperative situation. In the subjective evaluation patients reported that the sound with the DACS system is more natural than with conventional hearing aids.
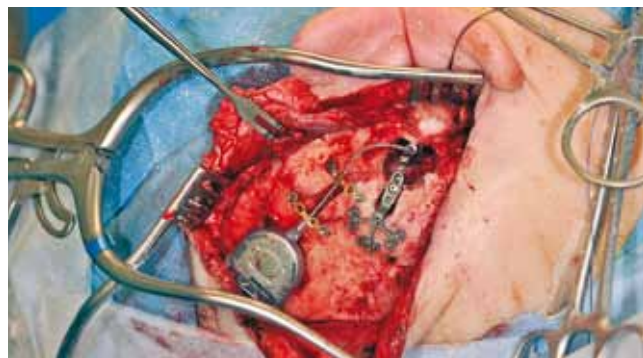
DACS implant before (left) and after (right) the Implantation.

Gesture Recognition in Spatial Hearing Tests

Localization of sound is important in different acoustical situations such as hearing approaching vehicles or for understanding speech in noise. In order to study objectively the benefit of binaural hearing, sound localization tests are beneficial. Typical

setups use speaker arrays in a half circle or a full circle. During these tests the subject has to indicate from which direction he perceives the sound. One common possibility is labeling each loudspeaker and the subject communicates his perception orally. The operator will then write down the result. We developed a new system which simplifies this process. The system works on the principle of automated gesture recognition. The patient has only to point with his hand to the loudspeaker where he perceives the sound. Our software automatically captures the gesture with a camera (Kinect Microsoft), calculates the angle based on a gesture recognition algorithm (Microsoft SDK) and stores it to a database. With this system a typical test setup (36 stimuli) can be accomplished in less than 5 minutes. This allows multiple localization tests to be integrated in study designs or even in clinical practice with only a small burden of time. Additionally, we have integrated the speech in noise tests (OLSA). The system also allows other audiological tests to be integrated, which makes it a useful tool in clinical research in audiology.

Setup for sound localization test using gesture recognition: (1) camera, (2a) color picture and (2b) depth picture from camera, (3) picture after gesture recognition (4) result seen by the operator.
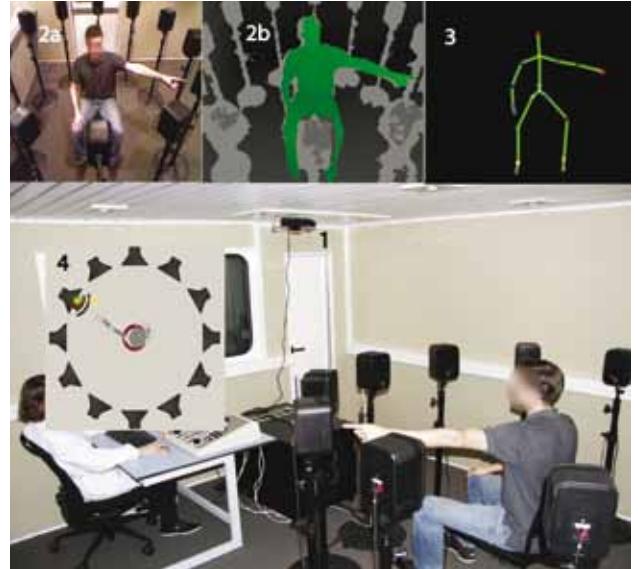
Minimally invasive Cochlear Implant Surgery (Winner of CTI Medtech Poster Award 2011)

For cochlear implants and other implantable hearing devices, surgical access to the middle ear cavity (mastoidectomy) is necessary. A navigation-controlled mechatronic system could support the surgeon, especially with a minimally invasive (keyhole) mastoidectomy. In collaboration with the CCAS (Center for Computer Aided Surgery) of ARTORG a prototype of such system was designed. A study on anatomical whole head specimens has been successfully performed (see in the section CCAS for detailed information). The efforts and progress in this ambitious project have been honored with the first prize of the CTI Medtec Poster Award.

Bone Anchored Port (Nominated for CTI Medtech Award 2011)

There is a long history of low complication for skin-perforating implants (e.g. BAHA) in the ear region. On the other hand many complications for long term vascular accesses have been reported. One reason might be that catheters are fixed in only soft tissue and therefore have continous slight movements and irritation of the surrounding tissue. The hypothesis is that a vascular access system which is anchored to the bone could be beneficial for the therapy of patients undergoing Hemodialysis. In partnership with the the University Department of Nephrology and Hypertension and an industrial partner we developed a functional prototype. During the design process a number of scientific questions have been raised. As an example we developed a 3D anatomical model of the implantation site, the temporal bone which hosts vital structures such as the facial nerve or the sigmoid sinus (a major blood vessel). These structures must not be damaged during the surgery. Therefore we implanted a prototype of the dialysis port virtually on 3D models. This model was generated with CT images of potential patients and a statistical shape model.
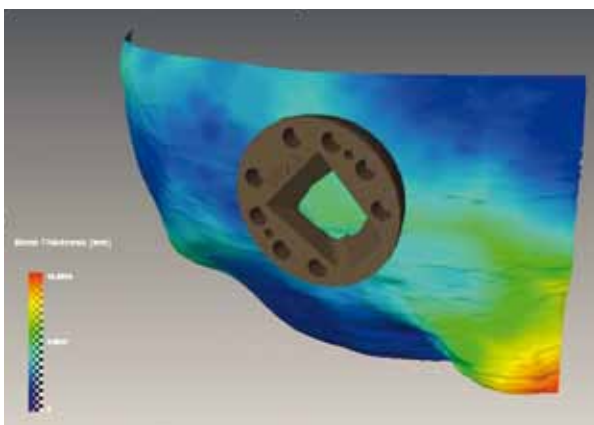
Colored map representing the thickness of bone behind the ear with fixation plate.
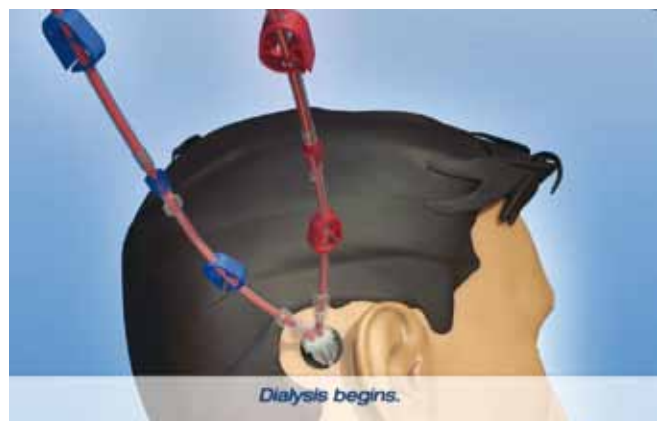
Port during hemodialysis, when connected to a hemodialysis machine (not shown).

Artificial Kidney Research

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Research Profile

The replacement of a failed renal function by dialysis is one of the most successful stories of artificial solid organ replacement. Despite the fact that some dialysis patients have survived more than 30 years with dialysis therapy, many problems are yet unresolved. Dialysis patients have a highly accelerated mortality rate. Current state-of-the-art in dialysis therapy, while highly effective during the actual treatment procedures of about 4 hours thrice weekly, results in an average clearance corresponding to only about 10 to 15% of a normal renal function over the whole week. Conventional methods to increase the amount of dialysis delivered during the treatment procedure either by increasing the quality of filters or by adding convective transport have failed to decrease overall mortality in controlled studies. The use of nightly intermittent or daily dialyses to significantly increase the total amount of dialysis delivered is tempting, but due to the low number of patients treated with this method, no outcome data are expected anytime soon. Hemodialysis is an expensive procedure. Given the current state of health care finances it is unlikely that an increased number of dialysis per week will be reimbursed, especially with no outcome data available. Research into methods resulting in an increased frequency of dialysis treatments will therefore also have to focus on simplification and reduction of costs per treatment. The main goal of the research is to obtain micro/nanofluidic devices which in more precise way address kidney functions than the current dialysis systems.

Kidney vascular system

Current Research Areas

Virtual Kidney

Each year half a million people undergo kidney transplantation from deceased donors. The demand for organs significantly surpasses the number of donors everywhere in the world. One of the solutions to that challenge is to investigate possibilities of building an artificial kidney. The kidney can be seen as a complex filtration system which removes toxic substances from the body and retains useful ones. Here, we investigate virtual designs of basic functions of the kidney by performing computer simulations of complex multiphysical systems with chemical reactions. There is a big advantage of such an approach. Numerical simulations are more efficient and offer a cheaper way to test all the possible scenarios as compared with experiments. The kidney's basic filtration unit is called nephron. It performs multiple functions such as regulation of salt and water, electrolyte and acid base homeostasis, and the elimination of toxins. Each of these functions is modelled and investigated separately as a system of micro- and nanofluidic channels. This project aims at building a virtual microfluidic system adequate to simulate the functions of the nephron. In the future, such a design can be validated experimentally and tested in clinical trials.
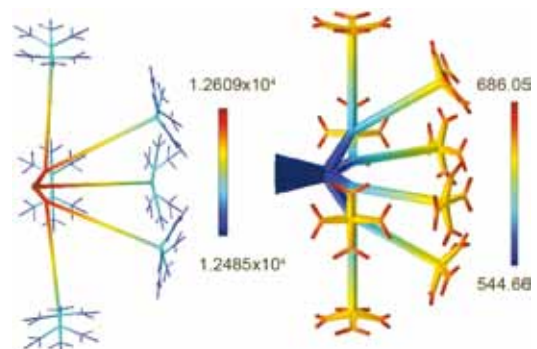
Comparison of pressure distribution in the arterial and venous trees of the renal lobule [Pa]

Optimization of Hemodialysis Process

The project aims at the optimization of hemodialysis performance by means of numerical analysis. There are two intimidate goals. One is to establish an understanding of blood flow behaviour in hollow fibers under the turbulence transition regime and the other is to study the influence of flow on the separation of various sizes of particles, which are later removed. The results of such analyses can be directly applied to the clinical situation. The methodology of the project is based on the usage
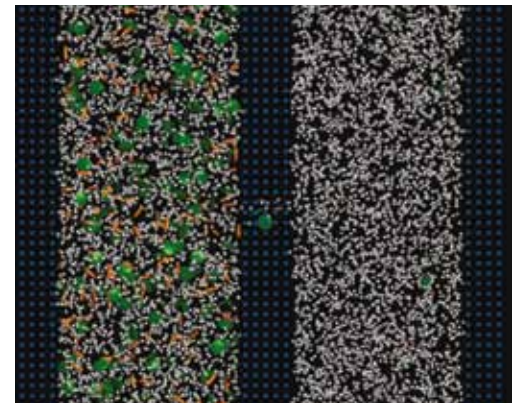
Hemodialyser

of the Lattice Boltzmann Method to model complex properties of fluid such as non-newtonian effects, charges of the particles and diffusion. The project is divided into two main steps. The first is to model turbulence transition flows inside the hollow fiber (pipe flow) with multiphysics complex phenomena and the second is to extend these models into the porous media application and compare them with available clinical data.

Micro/Nanoparticles in Biological Environment for Patient Assistance Devices

Several aspects related to micro/nano particles in biological fluid such as blood or cytoplasm are investigated. Applications include anticoagulation devices and blood analysis systems. A relevant application for dialysis patients is the monitoring of the efficacy of the dialysis therapy delivered. Monitoring the effect of intermittent renal replacement therapy over a prolonged observation period is cumbersome. Guidelines with respect to the amount of therapy delivered are traditionally given on a "per treatment" base. Weekly clearances are often used to describe the efficiency of continuous renal replacement therapies such as continuous ambulatory peritoneal dialysis (CAPD). The same measure can also be used to describe the overall efficiency of intermittent forms of renal replacement therapies by relating the total amount removed to the area under its serum concentration curve (AUC) over the whole observation period. While serum levels remain constant and the AUC is easily available during steady state conditions of continuous renal replacement therapy, 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 spending each week about 3 times 4 hours at a dialysis unit are reluctant to spend additional time at the dialysis centre between treatment sessions for the additional blood samples necessary to come up with a reliable estimate of AUC over the whole observation period of one week. Several devices have recently been developed for the continuous sampling of serum levels of various substances. Today, the most advanced portable devices for continuous sampling are developed for feedback controlled insulin pumps. Complex sophisticated sampling devices are used for insulin pumps, since single glucose levels have to be available in real-time to trigger feedback loops. In contrast to these devices we aim at simplicity. Since we are only interested in the area under the serum concentration curve, though over a long time period, samples will be collected and results of the analyses stored to be available for future reading at the hospital. Nevertheless, the proposed device needs to determine serum levels at high accuracy due the accumulation of systemic errors when multiple values are added to obtain AUCs. Such an accuracy can only be achieved on microchip. Initially we will focus on blood urea nitrogen, phosphorus and beta-2 microglobulin.

Nanoparticle transport through the membrane

Lifespan of the Red Blood Cells

The lifespan of red blood cells (RBC) in healthy human subjects is on average about 120 days. The RBC lifespan can be defined as the time period from the release of the cell from bone marrow into the circulation until its death from senescence. During that time the cell remains in the circulatory system. Many patients with chronic kidney disease (CKD) suffer from anemia, i.e. an insufficient number of circulating RBC. Renal failure results in a decrease of renal erythropoietin (EPO) production, which is the major stimulus of RBC production in the bone marrow. However, a decreased RBC production due to lower circulating EPO levels explains only part of the anemia observed in many CKD patients. In addition to a decreased RBC production, an increased RBC elimination is also observed in CKD patients. The lifespan of RBC 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 the results are conflicting. On one side the improvement of the uremic milieu by renal replacement therapy should increase RBC lifespan, on the other side part of the cell might be destructed by the hemodialysis procedure per se.
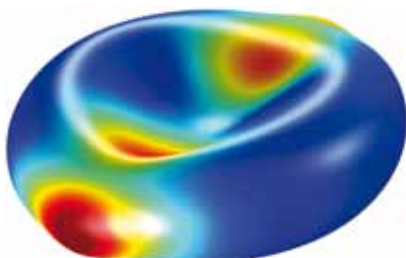
The ageing of a RBC is characterized by several factors: reduction of the elastic modes of the cell membrane, increase of the stiffness of the membrane, reduction of the surface area and volume, increase of the intracellular density and viscosity, and reduction of the hemoglobin content of the cell.

The aim of this project is to study cell ageing processes of RBC and from that to predict the lifespan of individual RBC and RBC cell populations.

Red blood cell stretched by optical tweezers

Cardiovascular Engineering

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Research Profile

ARTORG Cardiovascular Engineering (ACE) is a joint technological-clinical research organization of the University of Bern and clinical partners of the Departments of Cardiovascular Surgery and Cardiology of the Bern University Hospital (Inselspital). ACE converges expertise in biomedical engineering research, clinical research and clinical medicine in search of novel solutions for the diagnostic and therapeutic management of cardiovascular diseases. With the patient in the focus, our dedicated vision is to improve cardiovascular care by education, development, application and evaluation. To achieve this, joint ventures are formed and services rendered to lead to continuous translation of new technologies to clinical practice.

ACE is co-directed by Stijn Vandenberghe and Rolf Vogel, two experienced researchers with strong technological and clinical background, respectively, and has well established collaborative links to internal and external institutes covering the broad spectrum of multi-disciplinary research activities. ACE is well integrated into the medical technology industry network in Switzerland and worldwide, ensuring a direct path to the realization of our research goals.

Current Research Areas

The Esophageal Electrocardiogram

Heart rhythm disorders (arrhythmias) can be associated with fatal outcomes such as sudden cardiac death or cerebral apoplexy. The surface electrocardiogram (ECG) using skin electrodes attached to the chest wall and the limbs is the clinical gold-standard to detect and to characterize the type of arrhythmia. However, many patients suffer from short-lasting, rarely occurring episodes, and therefore require long-term ECG recordings in order to make the diagnosis and define the therapy. The probability to detect such paroxysmal arrhythmias increases with the recording duration. Regrettably, surface ECGs suffer from two important limitations. First, the limited sensitivity for the electrical activity of the atria, which is crucial for adequate treatment. Second, the limited suitability for long-term studies which is related to electromechanical contact problems of the skin electrodes and their potential to harm the skin.

As a promising alternative, ECG signals derived from the esophageal mucosa may be used. Due to the vicinity of the esophagus and the heart, this technique offers an optimal access to record the electrical activity of the myocardium. In collaboration with the University of Applied Sciences, Biel, and Acrostak (Schweiz) AG, Winterthur, we are developing the first dedicated long-term recording system for the esophageal ECG adapted to the space constraints and the site-typical signal interferences. The scientific challenges of the project are: characterization and selection of the electrode material, design of an ultra-low power recorder system (optimize power and memory consumption) and the characterization, processing as well as classification of the esophageal ECG signal, which requires clinical studies. Esophageal ECGs are perturbed by low frequency noise arising from esophageal peristalsis, cardiac motion and respiration. This baseline wander overlaps with esophageal ECG signal bandwidth and thus cannot be filtered real-time with conventional methods. Furthermore, the high amplitude of the baseline wander might drive the analog circuitry into saturation and makes further signal processing and delineation impractical.
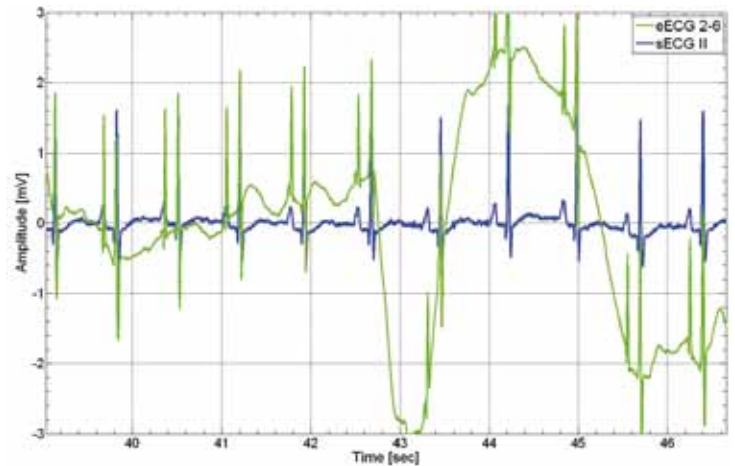
Topographical situation (left) showing two electrodes in the esophagus behind the heart. The ECG (right) derived from the esophageal mucosa (green) clearly shows better signal amplitudes compared to the standard surface lead II (blue).

To overcome the baseline wander problem we investigated a first esophageal ECG recorder design. The core of this system is a new micro-converter (ADuC7060®, Analog Devices) with a 24-bit ADC. An expanded input range was realized by reducing amplifier's gain to prevent saturation of the analog circuitry. In combination with the high resolution ADC, the recorder provides excellent signals appropriate for further digital signal interpretation using powerful workstations. New signal compression techniques will reduce the memory and finally prolong the recording time.

Tiny continuous high resolution long-term ECG recorder
The circuit board and the battery are placed in a dedicated body case. An electrode catheter with four electrodes can be connected.
The attached soft ear-frame containing a metal core adapts to patient specific ear shapes and sizes. During recording, a washable bag protects the recorder against water and guarantees hygiene and comfort.

Human Energy Harvesting

Power supply is a major restriction in the design of medical implants such as pacemakers, defibrillators, neuro-stimulators or hearing aids. Batteries often account for an important percentage of their volume and weight. Furthermore, the batteries need to be replaced periodically. Today's efforts towards devices with low power electronics and intelligent power management open new perspectives, and thus, human energy harvesting potentially becomes a sufficient power source. As an example, power consumption of the latest pacemaker generation is reported to be below 10 µW.

Human energy harvesting is defined as the process of extracting and storing energy from the human body. Various energy sources can be found in the human body such as mechanical energy (vibrations, joint motion, moving body masses), thermal energy (temperature gradient between ambience and body), chemical energy (e.g., glucose) and hydraulic energy (blood flow, pressure gradients).

Our program focuses on the harvesting of energy from the cardiovascular system. An obvious advantage of this system is that energy supply is permanently available. With three on-going projects in this field, the goal is to demonstrate the potential to harvest energy from the following cardiovascular mechanisms:
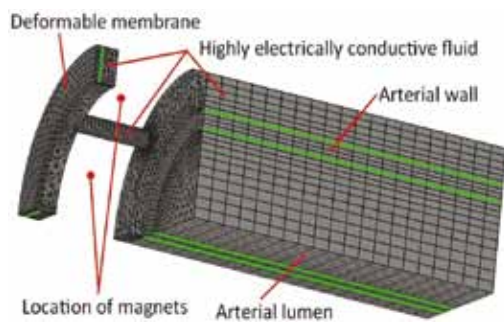
Energy Harvesting from the Beating Heart

The mass-imbalance oscillation generator, a crucial module of the Swiss watch industry, in conjunction with a micro generating system can be used to transform the energy of the mechanical motion of the heart into electrical energy. For in-vitro studies, we mounted the generator on a robot that was controlled with human cardiac wall motion data as can be obtained by magnetic resonance imaging (MRI). The energy harvested by this concept is sufficient to power a pacemaker as confirmed by an animal study. The next steps comprise design optimization using simulation studies and manufacturing of an optimized device in an industrial collaboration.
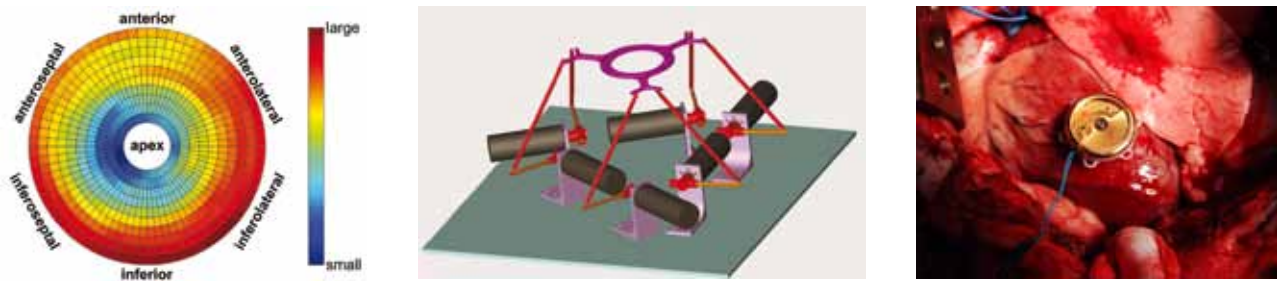
Distribution of wall motion amplitude of a left ventricle as obtained with MRI tagging (left). Purpose-built robot for accurate reproduction of cardiac wall-motion (middle). A modified ETA Autoquartz attached to the heart of a sheep (right).

Energy Harvesting from Arterial Wall Deformation Using Electro-magneto-hydrodynamics

This project is aimed at developing a generator that harvests energy from blood pressure variations by exploiting the motion of the arterial wall between the diastolic and systolic phase. The concept is to focus some of the power available in distributed, low-amplitude motions, into electro-mechanically efficient motions. This is achieved by using a highly electrically conductive fluid, which is driven by the motion of the arterial wall within a separate compartment outside the artery. A constant magnetic field is applied to part of this compartment, which allows converting the fluid's motion into electrical energy based on the principle of electro-magneto-hydrodynamics. A FEM simulation encompassing fluid-structure interactions as well as magneto- and electrostatics was developed to evaluate this concept. The setup of the simulation allows parametric studies of the geometry in order to find the optimal configuration. During 2011, a prototype has been built and tested. Performance measurements have demonstrated the feasibility of the concept.

Numerical generator model (left) and a prototype design (right).

Intravascular Turbine Generator

The objective of this project is to develop and test an intravascular turbine generator (ITG) for harvesting energy from blood flow. Our goal is to harvest 1 mW of electrical power from the approximately 1.5 W available power in the human circulation by a miniaturized hydrodynamic turbine implanted into a small, non-vital artery. Numerical flow modeling is employed in order to assess the applicability of different turbine-generator concepts for the small-scale dimensions, pulsating flow conditions and particular working fluid. One of the main design drivers is to minimize the mechanical forces that the blood cells experience inside the turbine. The numerical model allows for optimizing the design before verifying the results experimentally.

Prototype of a Tesla turbine (left) and numerical flow visualization between two turbine discs (right).
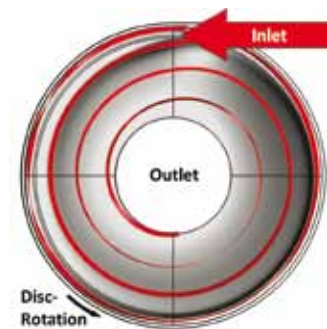
Pneumatic Driver for Ventricular Assist Devices (VAD)

Patients suffering from end-stage heart failure can be mechanically supported with blood pumps (VADs). Older versions of these are actuated with compressed air, which means that the patient always needs to be connected to a big driver console with a built-in compressor. For patient safety, changes to the device settings can only be made via special clinical consoles inside the hospital and within a small range. This limited control poses a problem for research purposes, where the optimal driving algorithm is explored. Therefore we have developed our own pneumatic driver that gives full control over the VAD and is suitable for lab use or in vivo investigation of the VAD-heart interaction.

Our driver provides alternating pulses of air pressure and vacuum to eject and fill the blood pump. Two blood pumps can be controlled simultaneously, in case the left and right heart chambers need support. Positive and negative pressure levels, are determined by pressure regulators and solenoid valves that are controlled via software, based on the Pulse Width Modulation (PWM) theory. In addition, analog pressure sensors accurately monitor the pressure for feedback and parameter calculation. This information is transferred by an electronic signal conditioning board to a data acquisition device controlled by LabVIEW software, running on a touch panel PC. The software allows for two different control methods: ECG synchronous and asynchronous rhythms. This dual pneumatic driver does not only function as planned and offers a broad range of controls, but it is also compact, affordable and has an intuitive user interface. It is very well suited for laboratory research and in vivo experiments and also allows us to use VADs as simulations of the heart function for other research projects.
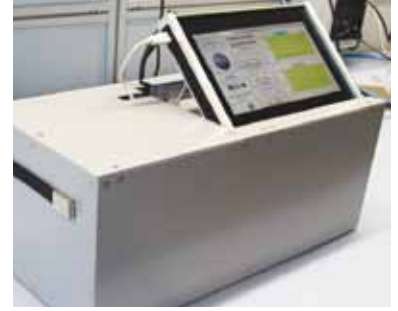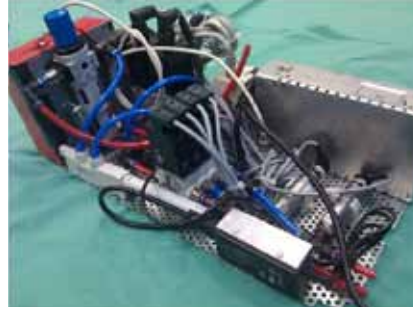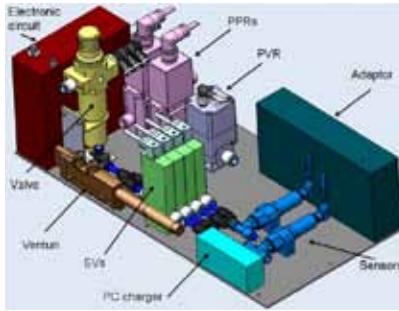
Inside and outside views of the pneumatic VAD driver. SV: solenoid valve; PPR: proportional pressure regulator; PVR: proportional vacuum regulator.

Hydraulic Resistor for Baroreflex Simulation

Evaluation of therapeutic devices such as blood pumps, catheters, or artificial valves is often performed in cardiovascular simulators. These are often simple displacement pumps connected to a tube circuit with occluders to set an 'arterial' pressure level.

As part of our goal to develop a more realistic simulator that takes into account the real hemodynamic function of the heart and reflex mechanisms that are intrinsic to the human body, we developed a resistor that can be programmed to simulate the baroreflex mechanism. This mechanism controls a person's blood pressure and is important when changes to posture, activity level, or disease come in to play. The baroreflex exercises its body pressure regulating capacity by contraction of small arteries and capillaries, thereby controlling peripheral resistance. Our linear hydraulic resistor should therefore be able to regulate the pressure within a range observable in the human body (0.53 – 1.2 [mmHg·s/ml]). In order to improve the controllability of the hydraulic resistor, its pressure-flow characteristic should be linear. Since most commercially available resistors show highly nonlinear characteristics, we developed our own laminar flow element (LFE) which guarantees a high linearity. The simple principle follows the division of the flow into many small parallel streams (1500 canals). To adjust the resistance, and thus the blood pressure in the simulator, canals can be selectively closed off by a slider. In order to allow precise and fast positioning, the slider is controlled by a stepper motor. The canals are arranged according to a specific geometry that brings about linearity of the resistance adjustment as the slider moves up and down.
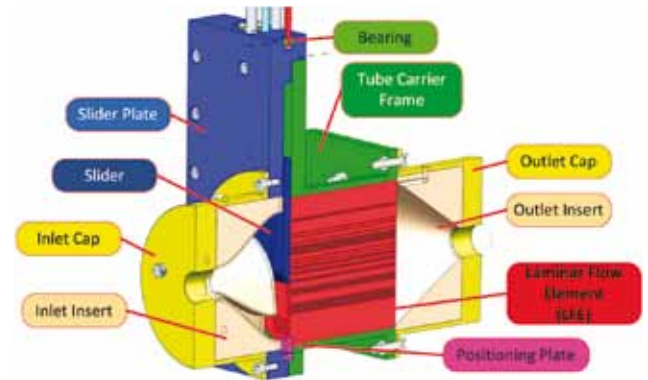
Section view of the hydraulic resistor with the Laminar Flow Element as central component.
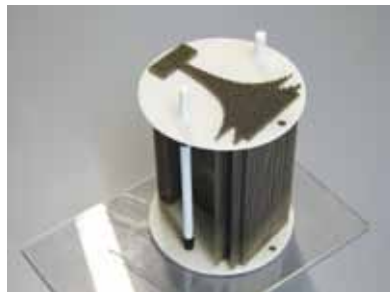
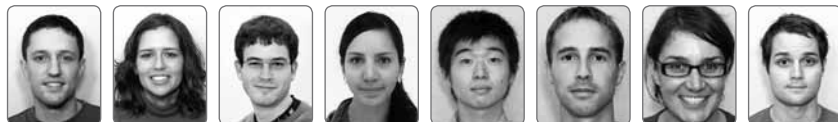*Pictures of the completed resistor with drive mechanism (left) and of the Laminar Flow Element that sits inside (right).*

Center for Computer Assisted Surgery (Part ARTORG)

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Research Profile

The Center for Computer Assisted Surgery (CCAS) is a collaborative effort between the ARTORG Center for Biomedical Engineering Research, the Institute of Surgical Technologies and Biomechanics (ISTB) and the University Hospital (Inselspital) Bern, Switzerland. It specifically focuses on clinically related research and development activities in the broad area of image guided surgery. It aims to provide novel technologies for diagnostics, therapy, and implantation to the interested clinical communities and enable their evaluation in clinical routine. Our activities are primarily centred on supporting medical image analysis and diagnosis as well as surgical and interventional treatments by improving accuracy and reproducibility. Modern clinical technologies such as image processing, stereotactic image-guidance, medical and surgical robotics, and rapid prototyping techniques are applied. Currently, our research focuses on applying classical methods and approaches of image guided interventions to novel clinical areas such as micro surgery on small anatomical structures (i.e. the ear), soft tissue surgery of the liver and the brain and by using advanced imaging technology.

Current Research Areas

Image Guided Micro Surgery on the Ear

During the last year, the focus of the robotics project has been the improvement of the overall system accuracy with maximum errors below the 0.5 mm mark. Focus has been placed on three areas which at present account for the largest portion of the final error: model based fiducial localization in 3D image data sets, patient-image registration using force based localization, and high accuracy optical tracking/ visual servoing. Surgical interventions involving the direct acoustical cochlear stimulator (DACS) place increased mental burden on the surgeon due to the positioning requirements, which constrain the location of the mounting hardware, and similarly limit the size and shape of the

The robot system compensates for kinematic errors and deflections of its robotic arm as well as for patient movement by means of an optical tracking system with an accuracy of less than 20 microns.

corresponding mastoidectomy. Our custom otological planning software OtoPlan has been enhanced to include functionality to allow the surgeon to plan the position of a DACS implant considering the final desired location of the actuator and the mounting hardware on the mastoid surface.

In an initial study in one clinical case a 3D model of the plan was produced to give the surgeon an additional intraoperative reference. A comprehensive study of this planning approach and its effects on operative outcome is planned for the near future.

Computer Assisted Liver Surgery

Image guided liver surgery, initially developed by CCAS together with the Department of Visceral Surgery and Medicine (Daniel Candinas) and now commercialized through its start-up CAScination AG, is an emerging and new approach to precise and reproducible liver surgery. Throughout 2011 several clinical trials with clinical partners in Germany and Switzerland have been initiated. On a research level, systematic approaches to improve the overall guiding accuracy are being investigated.


Image guided resection of tumors in the liver.

Image Guided Intraoperative Brachytherapy

Intra-operative interstitial high-dose-rate brachytherapy (HDR-IOBT) has the potential to gain importance as an integrated approach to the complex, multidisciplinary treatment of advanced cancer. This novel technique may eliminate the time interval between surgery and radiotherapy, thus the risk of possible tumor recurrence could be minimized. Accuracy of the radiation source placement has a great impact on the delivered radiation dose and is subject to experience of interventional radiation oncologist. However, in many cases a reiterate repositioning of catheters is required causing excess of a prescribed intervention time. Thus, the main challenge in HDR-IOBT is to precisely apply the treatment plan to the patient and facilitate image-guided implantation of the applicator according to it. In a common project CCAS, the Departments for Radiation Oncology (Daniel Aebersold) and Medical Radiation Physics (Peter Manser) jointly investigate the possibility for stereotactic instrument guidance system that allows accurate placement of the catheter according to the pre-interventional information.
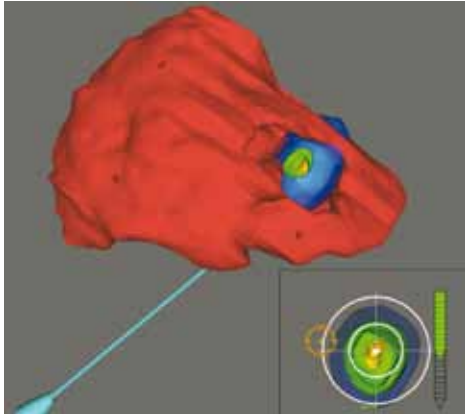
A plastic catheter for the later delivery of a radiation dose is guided by the navigation system and according to the treatment plan.

Rapid Prototyping in the OR

Cranioplasty is a commonly performed procedure in which parts of the skull are replaced by implants, made either from titanium or polymer materials. Aesthetic outcomes can be improved by use of implants specifically manufactured based on a reconstruction of the defect apparent in an individual patient. However, high costs of implant production limit their accessibility. Throughout the last years, CCAS together with the Department for Neurosurgery (Andreas Raabe) developed a technique that allows creating patient specific Polymethylmethacrylate (PMMA) implants using 3D printed (Rapid prototyping) negative mold templates. The molds are first virtually designed based on available CT scans of the skull and then produced in 3D. Once brought into the operating room, they can be used for fast and reproducible building of the actual PMMA implant. We applied our solution to more than 20 patients with positive outcomes and no complications related to implant and surgical technique.
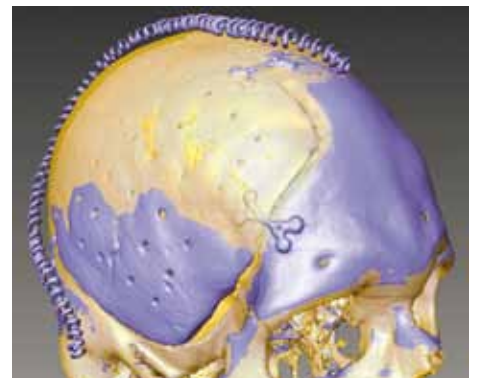
Postoperative situation of PMMA implant indicating an optimal fit with the skull and a good reconstruction of the skull geometry.

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 Division of Endocrinology, Diabetes and Clinical Nutrition at the University Hospital of Bern (Inselspital).

Maintaining glucose concentration levels within normoglycemic range is essential for individuals with diabetes mellitus and prevents them from life-threatening events, such as severe hypoglycemias, and long-term complications. New technologies on glucose sensing, insulin delivery, carbohydrate (CHO) estimation and monitoring of vital signals are needed towards enhanced glycemic control and improved quality of life for many individuals living with diabetes.

Using biomedical engineering approaches DTRG is performing complex, cutting edge research towards an artificial pancreas. Technologies on simulation and control of physiological systems, machine learning, computer vision, and e-/m-Health solutions are explored in projects related to control of glucose profile, estimation of CHO intake and quantification of glycemic variability. The ultimate goal is the development of an integrated patient-centric computational system which will function as an external artificial pancreas closing the loop between glucose sensors and insulin delivery devices. Furtermore, the usability of the proposed technologies is further investigated in other research areas related to management of chronic diseases.

Current Research Areas

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 an external automatic closed-loop control system. The components of the artificial pancreas are a Continuous Glucose Monitor (CGM), a continuous insulin infusion pump and a control algorithm to estimate the rate of insulin infusion.
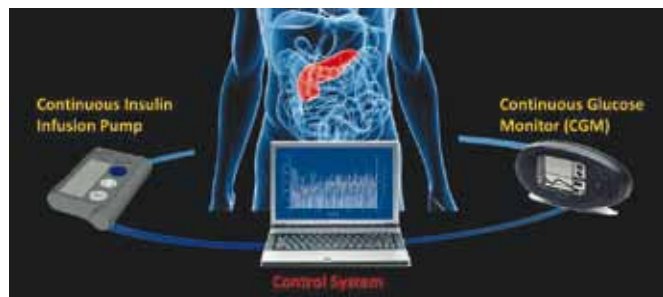

Scheme of the external artificial pancreas.

Development of Novel Algorithm for Closing the Loop

Aim of the on-going project is the design, development and evaluation, both *in silico* and in clinical environment, of a novel control algorithm for the optimal, personalized estimation of insulin infusion closing the loop between CGM and insulin pump. The first version of a novel control algorithm based on optimal control techniques is proposed by the DTRG. The algorithm, aiming to compensate on the diverse complexities derived from the function of the physiological system and the CGMs, is expected to provide efficient glycemic regulation in type 1 diabetic patients. The controller is online adaptive in order to handle the high inter- / intra- patient variability occurring from the diversions of insulin sensitivity, physical activity and other environmental factors. 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 basal-bolus treatment.

Example of estimated glucose concentration (blue line) and insulin infusion rate (green line) in a trial for 12 days using the educational version of the FDA accepted in silico diabetic patient.
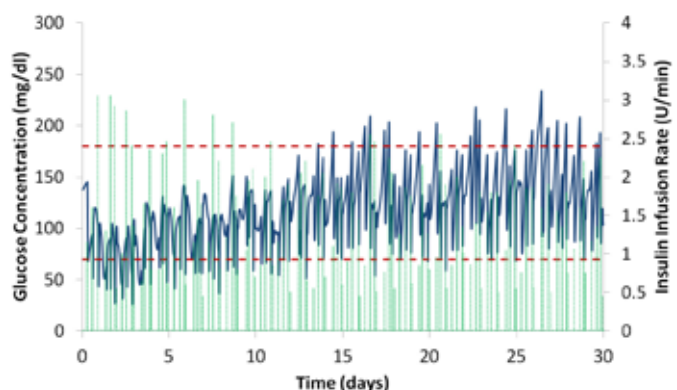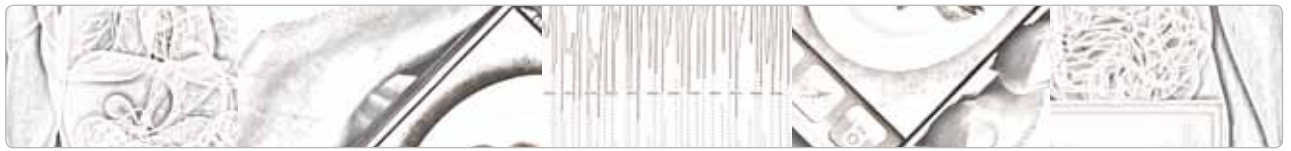
Hypoglycemia Prediction based on Data-Driven Models

Intensive insulin treatment has an inherent risk for hypoglycemic events. 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 hypoglycemic 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 results have shown that both types of models are able to be personalized in real time and to estimate accurately the glycemic profile in prediction horizons up to 45 minutes.

Measured (blue line) and predicted by one model (green line) glucose concentration. Red circle emphasizes the prediction of hypoglycemia.
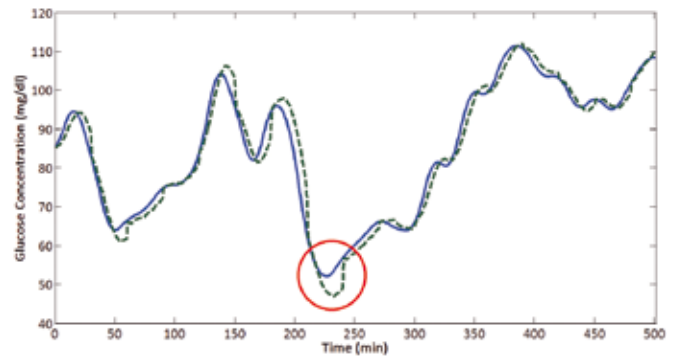
Carbohydrate Estimation based on Computer Vision

Balanced nutrition, in terms of CHO, fat and protein, is associated with improved glycemic outcomes. In addition, the determination of optimum prandial insulin needs, requires accurate estimation of the CHO content of meals. However, recent studies have shown that even well trained diabetic patients do not count CHO accurately and commonly either over or underestimate CHO in a given meal.

Scope of the project is the design, development and evaluation of a computational system which will support individuals with type 1 diabetes to estimate automatically and in near real-time the grams of CHO of their meal. In a typical usage scenario the individual with diabetes will acquire a picture of the incoming meal through a mobile phone camera. The acquired image will be processed in order to estimate a set of characteristic features describing the type of nutrition and the corresponding grams of CHO.

As a first step towards this direction a visual dataset and an advanced computational algorithm for the recognition of the food type on the plate have been developed. The visual dataset includes a broad spectrum of European food and meals of interest for diabetic patients. The dataset, which refers to non-labeled food as used at home or restaurants, consists of images and videos from 104 meals acquired under control conditions, and 12620 meal images downloaded from internet under different shooting conditions.

The foods represented in the images have been classified into five main categories and 17 sub-categories based on the Diabetes Food Pyramid. The food recognition algorithm is based on bag of features approach and currently is able to define the exact food type among 14 categories.

Through a Mobile Phone Application the picture of a meal can be analyzed and the corresponding grams of CHO estimated.
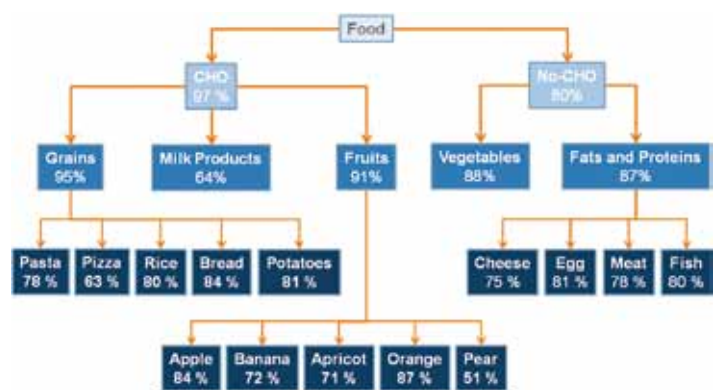
Performances for the 14th categories problem following a hierarchical classification, where the system first recognizes if the image belongs to CHO or no-CHO, and then it proceeds to the food recognition.

Gerontechnology and Rehabilitation

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Research Profile

The interdisciplinary Gerontechnology and Rehabilitation Research Group was established in May 2010 as a collaborative research group 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.

Current Research Areas

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 environments as long as possible. This often leads to trade-offs between the patient's desire to live at home and the risks that increase with the progression of the cognitive decline. The risks includes safety issues arising from discontinuous supervision, including a lack of medical compliance, acute medical events (e.g. stroke, heart attack), accidents and other events (e.g. falls), and disorientation (e.g. day/night disturbances, getting lost). We expect that, in combination with existing (i.e. Spitex) and new (i.e. ambulant old-age psychiatry) clinical and social caregiving approaches, assistive technology will play an important role in reducing risks associated with independent living. Numerous technical approaches (e.g. wearable fall sensors, watches with integrated emergency buttons) have been developed to assist independent living for elderly people. In this project, we use existing sensor technology to develop and evaluate an assistive technology system that meets the specific needs of elderly patients with cognitive impairment. One

key feature of the envisioned system is that it would not require any active interaction between the system and the supported patient. In collaboration with Damedics GmbH, we have developed a wireless sensor system that measures environmental data (e.g. light distribution, movement patterns). The scientific challenge lies in developing dedicated algorithms to detect unusual situations (e.g. falls, wandering), to estimate the patient's wellbeing, assess the patient's ability to cope with activities of daily living, and predict short- and long-term risks.

Five to ten sensor nodes are positioned throughout the patient's home to measure environmental data (temperature, light, IR-radiation, acceleration). The sensors are battery-powered and the data is transferred via radio-communication allowing quick and cable-free installation in the patient's home.

Cognitive Performance and Driving Behaviour in Older Adults

The objective of this study is to better understand how cognitive performance and aging influence individual driving behavior and traffic-related risks. We have developed a dynamic, computer-based test to measure driving-relevant cognitive and motivational competences such as processing speed, decision making, anticipation of speed, and motion perception. The test and the human-machine interface are specifically developed for elderly people and the system is intended to serve as a screening tool to assess driving-relevant cognitive performance. In a study of 120 participants, performance in the computer-based test is compared with simulated driving performance. For this purpose, a commercially available driving simulator has been modified to study simulated driving behavior of elderly drivers while measuring neurophysiological parameters (e.g. eye movements, skin conductance). Based on these findings, we intend to derive cognitive training schemes that help elderly to maintain driving relevant cognitive skills as long as possible.

A test subject during the computer-based dynamic cognitive testing. Visual stimuli are presented on the computer screen and the subject's reactions are recoded via a steering wheel and foot pedal.

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

Both younger and older drivers are challenged by reduced vision in low-light conditions during night driving. Contributing factors are age-related increased glare sensitivity and decreased mesopic visual acuity. We assume that the visual exploration behaviour 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 behaviour and on simulated driving performance. In collaboration with Haag-Streit AG (Köniz, Switzerland), we are developing a screening tool for the Octopus 900 perimeter that will support and enhance "fitness-to-drive" assessments and decisions.

New test to assess visual exploration behaviour in the Octopus 900 hemisphere.

Test driving in a visual exploration experiment. The test subject wears a helmet with an integrated eye tracking camera to measure gaze direction.

Street-Crossing Behaviour of Younger and Older Pedestrians and Car Drivers

Crossing a street as pedestrian or driver is a challenging task that requires gathering information over a large area. The challenge is to acquire the necessary information for a decision of when to cross within a limited window of time. To better understand how the acquired information leads to a crossing decision, we have modified the driving simulator to study street- and intersection-crossing behaviour.

The figure shows the visual fixations of a patient (green dots) and of a healthy test subject (red dots).
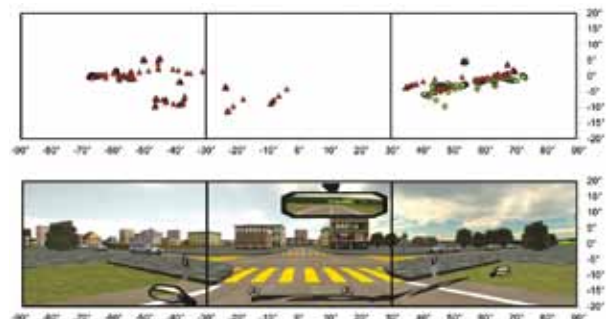
Outlook and Acknowledgments

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 plan to develop home-based cognitive and physical training based on innovative gaming platforms (e.g. Wii and Kinect). We will place a special focus on strategies to increase motivation, fun and self-confidence.

Lung Regeneration Technologies

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Research Profile

The Lung Regeneration Technologies (LRT) Group, which was established in November 2010, is a collaborative effort between the ARTORG Center, the Division of Pulmonary Medicine and the Clinic for Thoracic Surgery both from the University Hospital (Inselspital) of Bern and the Swiss Center for Electronics and Microtechnology (CSEM SA).

The objectives of the Lung Regeneration Technologies Laboratory are to develop advanced microfluidic devices able to recreate in-vivo-like conditions of the lung, including the complexity of the alveolar-capillary barrier, the gas exchanges and the mechanical stimulation of the respiratory movements of the lung. Microfluidic devices offer structures with length scales that are comparable to the intrinsic dimensions of mammalian cells. The diameters of these microchannels are typically the size of a human air (50 to 150µm), in which cells are cultured. Such microsystems have the capability to accurately control the cell microenvironment, for example by perfusing the cells to reproduce the shear stress created by the blood flow or by recreating the extracellular milieu by micropatterning surfaces for selective surface adhesion. They are becoming competitive tools for in-vitro cell culture, promising alternatives to animal studies and are also intended to be implemented for personalised medicine approach where the number of cells is limited.

Current Research Areas

Microfluidic Platform for Chemoresistive Testing of Lung Cancer

A novel in-vitro microfluidic platform able to reproduce the conditions of the cell microenvironment was developed to investigate the characteristics of cancer stem cells (CSC) in malignant pleural mesothelioma (MPM). Three-dimensional (3D) cell culture systems, such as cell spheroids, better reflect the in-vivo behavior of cells in tumour tissues and are excellent surrogate to predict tumourigenic potential in-vivo. The combination of 3D cell cultures and of microfluidics can lead to more accurate anti-tumour screening and also provide a rationale for personalized therapeutic test strategies. MPM is an aggressive tumour, which is increasing in incidence throughout the world. It is a therapy-resistant neoplasm associated with exposure to asbestos. MPM is typically diagnosed in the fifth to seventh decade of life, and is characterized by a locally aggressive growth pattern in the lower parietal pleura and subsequent metastasis as the disease progresses. The median survival time is less than 12 months after diagnosis. The current standard therapeutic approach consists of a combination of chemotherapy, surgery and radiation, however prognosis remains poor. A recent hypothesis states the involvement of cancer initiating cells in solid tumours. These cancer stem cells (CSCs) have been described in a number of different tumours including the lung. The aim of this project is to load and trap CSC spheroids and expose them to chemotherapeutic agents in a confined and controlled microenvironment. The CSC spheroids will be evaluated of drug response to cisplatin and pemetrexed, which are the standard chemotherapeutical treatment used today for MPM and compared with standard cell culture method.

Schematic of the microfluidic channel in which the spheroids are trapped. The spheroids follow the path with the smallest fluidic resistance. Once a spheroid is trapped, the resistance of the blocked channel becomes higher; the next spheroid follows the meander and stops in the next trap.
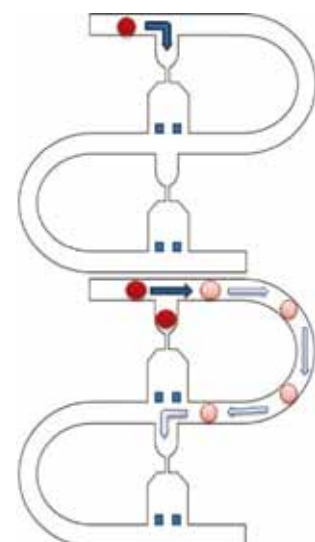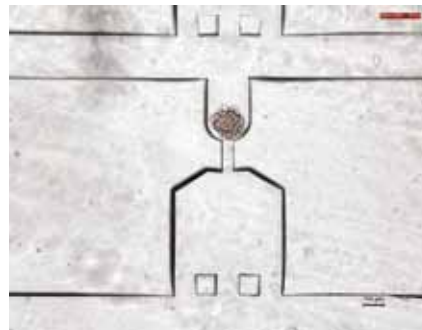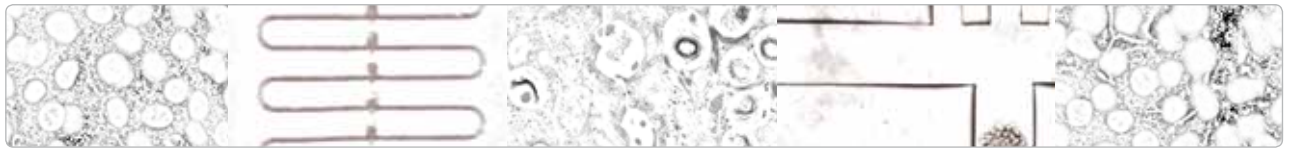
Picture of a microfluidic platform bonded on a glass slide. Each microfluidic channel can trap eight spheroids. The two channels (red and yellow) can be used to run at the same time control vs. treated samples (left).

Picture of a H2052 cell spheroid trapped in a microfluidic channel (right).

Lung Epithelial Wound-Healing on a Microfluidic Chip

A microfluidic chip aimed to investigate lung epithelial wounding and healing was developed. Lung epithelial microinjuries are one of the characteristics of idiopathic pulmonary fibrosis (IPF), a poorly understood chronic lung disease with poor prognosis. This disease is usually characterized by a progressive scarring of the lung alveolar epithelium with an irreversible loss of lung function, whose main symptom is breathing difficulty.

The capacity of cell-based microfluidic devices to accurately control the cell microenvironment is particularly important for this project that focuses on the regeneration of injured epithelial cells through the action of hepatocyte growth factor (HGF). A polymeric microfluidic device made of polydimethylsiloxane (PDMS) with a 900µm wide microchannel was fabricated by rapid prototyping technique. Human alveolar A549 epithelial cells were seeded in this microchannel and intermittently perfused until reaching confluence. Subsequently, the epithelial layer was wounded in the microchannel, based on a microfluidic flow focusing technique. The effect of HGF on the epithelial healing was investigated and found to be significantly larger than without HGF. Furthermore, the phenotype of the regenerated cells was preserved in particular the tight junction properties of the epithelial layer that defines its permeability.
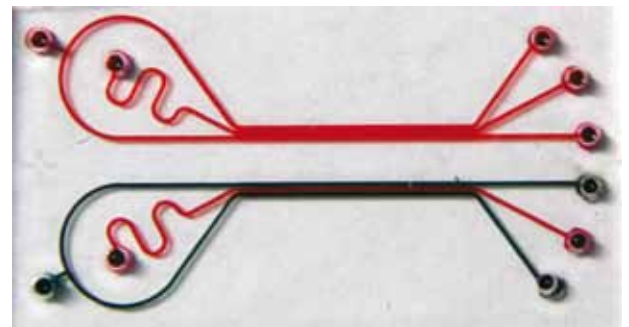
Picture of a 20 x 35mm microfluidic chip aimed for the studies of lung epithelial wound-healing.
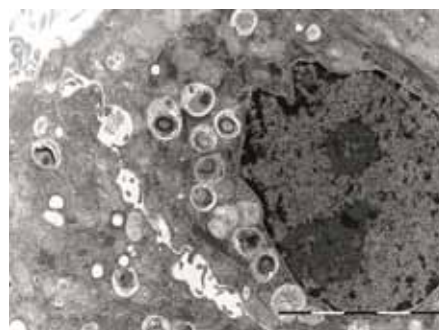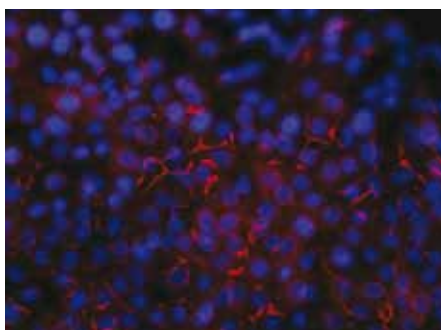
Fluorescent images showing phenotypical preservation using immunostainings for zona-occludens (ZO-3) expression with the cell nuclei counterstained with DAPI (left).

Transmission electron micrographs (TEM) of A549 cells grown to confluence in the microfluidic channel after being regenerated (right).

Bioartificial Membrane to Mimic the Respiratory Movements of the Lung

The objective of this project is to develop an advanced in-vitro model that reproduces the blood-gas barrier in the lung with special emphasis on dynamic processes present in a normal and injured lung (ventilation- and perfusion-based dynamics). Current in-vitro techniques used to investigate pulmonary diseases are mostly performed on rigid cell culture plates or porous membranes. Such in-vitro models do poorly reproduce the in-vivo conditions of the lung, in particular the mechanical stretching induced by the respiratory movements. A novel microfluidic system was developed that is equipped with a very thin PDMS membrane (about 9µm thin) on which epithelial cells were cultured and deflected to reproduce the respiratory movements of the lung.
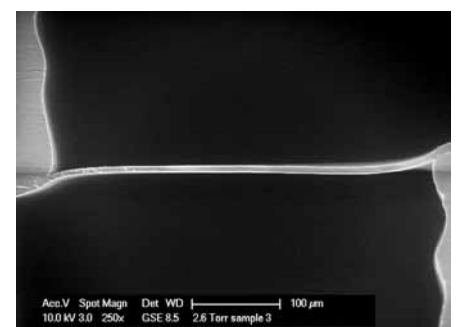
SEM picture of a 9µm thin PDMS membrane on which lung alveolar epithelial cells were cultured.

Ophthalmic Technologies

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Research Profile

The Ophthalmic Technology Group is dedicated to the development of innovative surgical and diagnostic instruments and techniques in the area of ophthalmology. The novel engineering solutions should allow for an increased surgical precision, while at the same time diminish the risks for patients and reduce the costs for the intervention. We are focused on projects that are clinically relevant and we are committed to advance the project development to a state were a 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 Op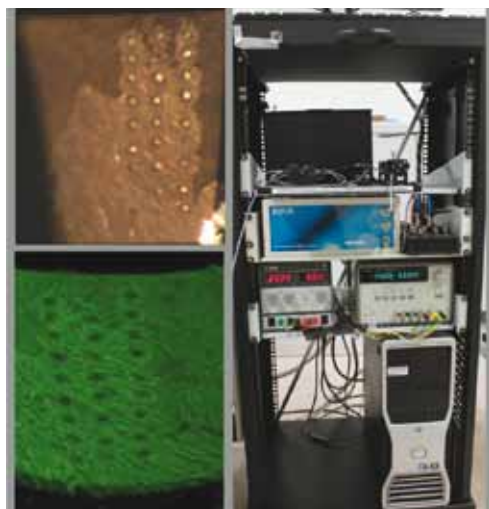hthalmic Technology Group consists of a multi-disciplinary team of engineers and clinicians. Our core competencies are in mechatronic systems design, signal processing, computer-vision and computer-graphics.

Current Research Areas

Computer Assisted Retinal Sub Threshold Laser Photocoagulation

Laser photocoagulation of the retina has become an established and important treatment modality for diabetic retinopathy, age-related maculopathy, neovascular complications after vascular occlusion, and a variety of other eye pathologies. Some of these diseases have an enormous social and economic impact. Current setups to deliver laser photocoagulation typically consist of a slit lamp equipped with a laser unit, where the ophthalmologist aims the laser beam manually. Sub-threshold laser therapy selectively destroys the cells in retinal pigment epithelium layer. The layer regenerates itself after a few days resulting in an improved metabolism of the eye. However the placed laser lesions are invisible, which is very challenging during the treatment procedure. Computer assistance offers the potential for improvements for such a setup with respect to accuracy, individualized spot patterns, execution time, safety, and therefore treatment efficiency. To compensate for the missing visual feedback we are working on an high resolution OCT Integration to provide dosimetry control during the treatment. The general goal of this project is to develop an integrated computer assisted retinal laser photocoagulation system for specific applications based on sub-threshold lasers.

Experimental high-resolution OCT to providing dosimetry control for sub-threshold laser photocoagulation. Reconstructions of RPE Layer OCT's with laser lesions are shown on the left.
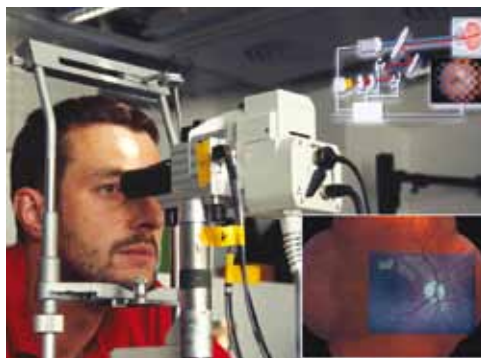
Automatic laser-photocoagulation setup with planned laser spots during treatment execution.

Computer Assisted Proton Beam Radiotherapy and Radioactive Plaque Therapy for Intraocular Tumors

A challenging topic in ophthalmology is the treatment of intraocular tumors by irradiation. Melanoma of the choroid and ciliary body, such as the posterior uveal melanoma, are the most common primary intraocular malignant tumors of the eye, and they are life threatening if left untreated. Proton beam irradiation is an established treatment modality for intraocular tumors. In order to deliver the necessary radiation dose to the tumor tissue but sparing the surrounding tissue, precise planning and delivery of the charged particle beam are mandatory. Different image modalities such as fundus photographs, ultrasound images, and computed tomography or magnetic resonance image data are combined to develop the treatment plan. To co-register the different image modalities and to position the patient's eye for irradiation, often tantalum marker elements are sutured to the globe in a preceding operation. The relative position of the tantalum markers and their distance to the limbus are important parameters for the therapeutic plan and are usually measured intra-operatively by a pair of compasses. This project is aiming at the development of an advanced planning/navigation system for proton beam radiotherapy and radioactive plaque therapy by employing state of the art image co-registration and tracking techniques.
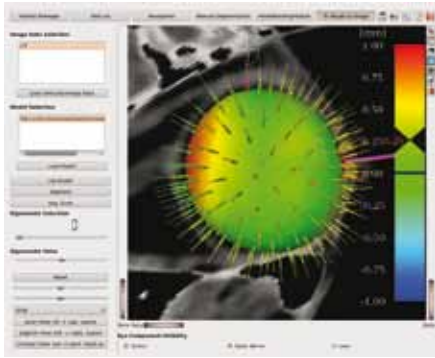

Statistical eye model used to automatically segment anatomical structures of the patient eye.

Automatic Layer Segmentation and Statistical Modeling of the Retina

Optical Coherence Tomography (OCT) is a non-invasive technology used for imaging the layers of the retina. This imaging technology has revolutionized the early detection and also follow-up examination of retinal pathologies such as macular holes, epiretinal gliosis, macular edema and also optic disc pathologies. The introduction of high speed and spectral domain OCT devices allows a faster image acquisition and offers a better image resolution in the daily clinical practice. However, the continuous growth of image data for diagnosis demands sophisticated data processing strategies to help the ophthalmologist focussing on potentially pathological structures while screening the huge amount of data. In addition, objective quantification of pathologies (thickness measurements, detection of changes in reflectivity of certain structures, loss of layers in degenerative pathologies) is an indispensable tool to diagnose disease progression and also regression as a basis for effective treatment strategies. The objectives of this project are twofold: first to analyze the potential of statistical shape and appearance models in the context of OCT segmentation and second to implement, test, and validate new segmentation strategies to reliably identify individual structures of the retina, and localize potentially pathological areas within the retina that will need the attention of the investigator.

Optical coherence tomography slice stacks with automatically segmented layers allowing to differentiate the individual layer of the human retina as well as pathological degeneration.
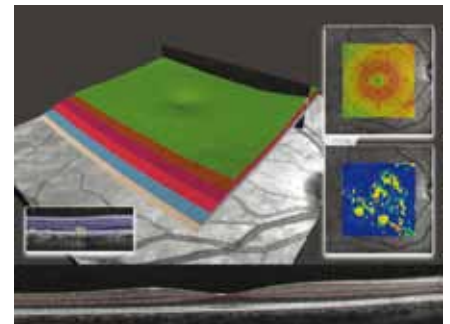
Advanced 3D Stereoscopic Navigation

The 3D shape of the human retina plays an important role in ophthalmic diagnostics (especially pathologic degeneration of the shape) as well as in surgical applications (e.g. membrane peeling). Some imaging devices provide the ophthalmologist with a stereoscopic view of the retina and offer some depth perception. However this perception is often quite poor. Computer assistance could increase objectivity in diagnosis and the safety during surgical interventions. For this a 3D reconstruction of the retina surface becomes necessary.

The goal of this project is to automatically extract the 3D shape from pairs of stereoscopic images of the retina. The 3D information should then be overlaid and will provide an augmented visualization of the anatomical structures of the posterior eye. 3D-augmented reality visualization can be used intra-operatively during vitreo-retinal surgery but also for diagnostic purposes to inject complementary imaging modalities such as OCT's.
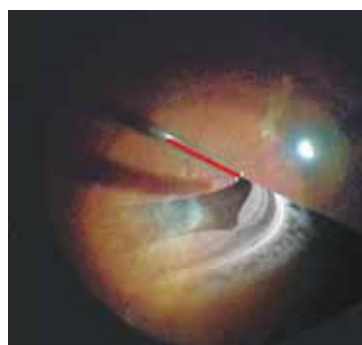
Stereoscopic image acquisition during vitreo-retinal surgery using a microscope (left).
Augmented reality system: Microscope view with OCT overlay during vitreo-retinal surgery (right).

Spine Research Center

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Group Members

Benjamin Gantenbein	Stephen Ferguson	Sara Barcos	Samantha Chan	Elena Calandriello	Stefan Guggisberg	Angelina Hofstetter	Cherry Malonzo	Patrick Käppeli

Clinical Partners of Inselspital

Klaus Siebenrock	Lorin Benneker

Research Profile

The focus of the Spine Research Center of the ARTORG platform is:

- to improve the basic understanding of biomechanical and physiological factors that lead to intervertebral disc (IVD) disease
- to explore intervertebral disc repair using cell-assisted therapy, in particular using autologous bone marrow derived mesenchymal stem cells, and to define strategies for in vitro pre-conditioning towards disc-like precursor cells
- to develop engineered therapies for the degenerative spine, together with industrial partners, covering the spectrum from inert to bioactive materials and implants

The mission of the Spine Research Center (SRC) is to identify clinical needs to improve the treatment of patients suffering from chronic low back pain due to age-related degeneration, trauma or bone fragility. The SRC aims to bridge basic research with clinical applied research to improve diagnostic and therapeutic tools for spine surgeons. The SRC is co-directed by Klaus Siebenrock, B. Gantenbein-Ritter and S.J. Ferguson. The SRC's activities build on the program of spinal biomechanics research that has been running at the Institute for Surgical Technology and Biomechanics (ISTB) for nearly two decades. Details of related spinal research at the ISTB can be found in the institute's annual report (http://www.istb.unibe.ch).

Current Research Areas

Understanding the Biological Response of Intervertebral Disc to Complex Loading

The ARTORG SRC defined a mechano-biological aim to better understand the mechanisms that drive intervertebral discs to failure under the complex loading of daily activities. For this reason, the ARTORG SRC collaborated closely with engineers from the Orthopaedic Biomechanics group of the Institute for Surgical Technology and Biomechanics (ISTB) to design and develop a novel loading device to enable two degrees of freedom loading (i.e. "twisting" and "compression") of motion spinal segments kept viable under organ culture conditions. These organ cultures contain living disc cells, which serve as a model for the human intervertebral disc cells. The concept and design of a multi-axial bioreactor is unique and the ARTORG SRC was the first to report about this technology and a culture technique using short-term, repetitive, biaxial loading, where we have shown both potentially beneficial and detrimental effects of complex loading, depending on magnitude. The ARTORG SRC is currently investigating complex loading patterns to highlight the mechanical causes of disc herniation and the challenging environment for treatment of this problem. This project is supported by the Swiss National Science Foundation for three years (2010-13). Conclusions from this project will have implications for physiological and hyper-physiological mechanical loading parameters for the IVD and for the future proof-testing of e.g. nucleus replacement or annulus repair implants. This project aims to target patients between 25-60 years, who are most likely to suffer from a disc herniation, and represent the highest potential cost for society.
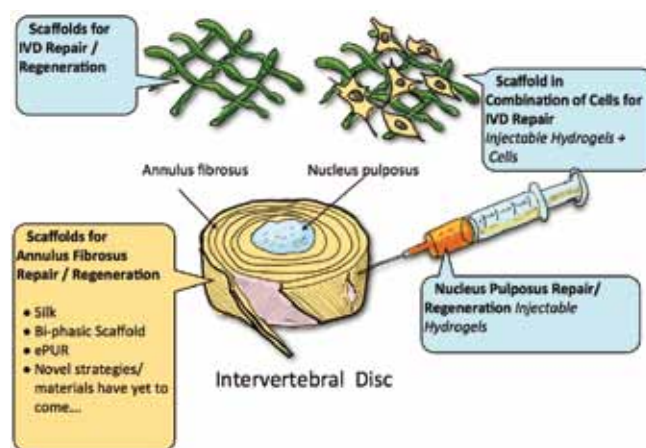
*Tissue-engineered solutions for the intervertebral disc.*

Two-degree of freedom loading device to culture bovine intervertebral discs under uni-axial compression and torsion. The device has been designed to be removed easily from the incubator unit and the entire set-up can be either force or way-controlled. A real-time processor unit is located outside of the incubator which is recording data and controlling the device.

Cytotherapy using Mesenchymal Stem Cells to Rescue the Degenerated Intervertebral Disc
Preconditioning of Cells towards Intervertebral-disc like cells

Two regenerative approaches, which might prove successful for the treatment of early degenerative lumbar intervertebral discs (IVDs) are being investigated i) injection of growth factors, and ii) application of autologous stem cells. On the side of cell therapy, autologous bone-marrow-derived mesenchymal stem cells are discussed as a suitable cell source to rescue "mildly" degenerated discs. A current research focus internationally is on the identification of the "best", or better said the "most adapted" cell phenotype to be transplanted into degenerated discs. The question of whether MSCs can be injected into the "harsh" environment of the intervertebral disc, and whether these cells subsequently would survive, has been previously addressed by our group and others. Recent studies on trancriptomics of primary chondrocytes of the articular cartilage versus disc cells isolated from the nucleus pulposus and the annulus fibrosus of the IVD identified potential marker genes to distinguish these tissues from each other. The ARTORG SRC currently conducts research to "pre-condition" hMSCs embed-ded into 3D hydrogels and to differentiate these stem cells towards "disc-like" phenotypes by the combined application of biomechanical stimuli and growth factors.

Uni-axial compression device is available to apply force-controlled strain onto hydrogel carriers.
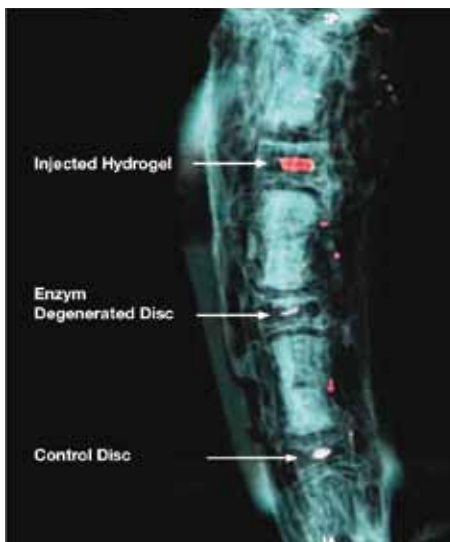
Regeneration of the Centre of the Intervertebral Disc (Nucleus pulposus) by Smart Hydrogels

The feasibility of nucleus pulposus repair with "smart" hydrogels is the focus of the third research area. Here, we test in the context of a Hansjörg Wyss Start-up grant granted by AOSpine International a polyN-isopropylacrylamide (pNIPAM) thermo-reversible hydrogel. The gel is formed at temperatures > 32°C and can be turned back into a fluid by cooling (< 32°C). The patented hydrogel is currently under investigation as a nucleus pulposus filler material in our enzyme-induced intervertebral disc degeneration organ culture model. This is a collaboration with the research group of David Eglin from the AO Research Institute, Davos, who invented this hyaluronic acid based hydrogel. We test the material in combination of mesenchymal stem cells and under weak mechanical loading conditions for seven and 14 days of loading.

Magnetic Resonance Image of p-NIPAM thermo-reversible hydrogel under investigation injected into an enzyme-induced intervertebral disc degeneration model in the bovine tail. A cavity is initially created by enzyme injection and 2 day incubation into which then the p-NIPAM hydrogel was injected.

Acknowledgments

MSc & PhD Degrees
at the ARTORG Center for Biomedical Engineering Research

MSc in Biomedical Engineering

In a continuing effort to support Swiss innovation and ensure a critical mass of skilled labor in the field of Bioengineering, the University of Bern's Medical Faculty in collaboration with the University of Applied Sciences Bern are offering a masters degree by coursework. The program is composed of advanced classes covering a wide variety of topics within our current focus areas, which are electronic implants, image-guided therapy, and musculoskeletal system. Students who hold at least a bachelor degree from a regular university or a university of applied sciences (Fachhochschule) in biomedical, mechanical, electrical, systems or civil engineering or in micro technology, mechatronics, computer science, physics, medicine or closely related fields are eligible for the master study course biomedical engineering. For further information visit the program's web site at www.bme.master.unibe.ch.

PhD in Biomedical Engineering

The doctorate degree in biomedical engineering at the ARTORG Center is undertaken within the Graduate School for Cellular and Biomedical Sciences at the University of Bern, which is jointly administered by the Faculties of Medicine, Science and Veterinary Medicine (Vetsuisse). The programme usually lasts three years and offers structured post-graduate training in experimental research. For further information please visit the graduate schools web site at www.gcb.unibe.ch.

Master Theses

Asgari S
MSc, University of Bern, Switzerland
An Automated Pneumatic Driver for Ventricular Assist Devices (VADs)

Ben Messaoud M
MSc, University of Bern, Switzerland
Intracorporeal Energy Harvesting from Arterial Deformation

Brun D
MSc, University of Bern, Switzerland
Low Volume Flow Probe Calibrator

Gerster S
MSc, University of Bern, Switzerland
Impedance Tomography

Griessen M
MSc, University of Bern, Switzerland
Autostereoskopische Visualisierung für die Medizin

Guggisberg S
MSc, University of Bern, Switzerland
Interaction of Synthetic PEG Scaffold, Growth Factors and Mechanical Loading on Mesenchymal Stem Cells

Güder C
MSc, University of Bern, Switzerland
Periodicity Analysis of the Electrocardiogram in Epilepsy Patients

Hofstetter A
MSc, University of Bern, Switzerland
Differentiation of Human Mesenchymal Stem Cells towards the "Intervertebral Disc-like" Phenotype in a Microfluidic Device

Hugi A
MSc, University of Applied Sciences Biel, Switzerland
Entwicklung einer neuen Zoomoptik für die Retinale Laser Photocoagulation

Imfeld T
MSc, University of Bern, Switzerland
Integration of a Microcontroller Based Beam Deflection Device into a Computer Assisted Retinal Laser Photocoagulation System

Jungo M
MSc, University of Bern, Switzerland
E2corder (Esophageal ECG recorder) – Anchoring System

Keller M
MSc, University of Bern, Switzerland
Steuerbare Kathetersysteme für perkutane Aortenklappenimplantation

Kohler L
MSc, University of Bern, Switzerland
E2corder (Esophageal ECG recorder) – Filter Design

Lauber S
MMed, University of Bern, Switzerland
Simulation of Volume Controlled Perfusion

Lovis Y
MSc, University of Bern, Switzerland
Trans-Catheter Mitral Valve Repair: Proximal Anchor

Sallin P
MSc, University of Bern, Switzerland
Lung on Chip: Effects of Hepatocyte Growth Factor on Injured Alveolar A549 Epithelial Cells in Vitro in Microfluidic Systems

Schneider A
MSc, University of Basel, Switzerland
Augmented Reality in CMF Surgery

Schoeni A
MSc, University of Bern, Switzerland
Interaction Between Alveolar Epithelial Cells and Mesenchymal Stem Cells in a Microsystem: Development of a Microfluidic Platform

Steiner T
MSc, University of Bern, Switzerland
Comparing a Stochastic Loading Pattern to Cyclic Loading in an in vitro Testing of Rabbit Flexor Digitorum Profundus Tendons

Toy F
MSc, University of Bern, Switzerland
Development and Characterization of a Linear Hydraulic Resistor for Baroreflex Simulation

Widmer D
MSc, University of Bern, Switzerland
FEM Analysis on the Temporal Bone

Williamson T
MSc, University of Bern, Switzerland
Visual Servoing of a Surgical Manipulator

Wimmer W
MSc, Erasmus Student, Graz University of Technology, Austria
Automated Gesture Recognition in Soundlokalisation

Wüthrich O
MSc, University of Bern, Switzerland
Trans-Catheter Mitral Valve Repair: Distal Anchor

Dissertations

Oliveira dos Santos T
PhD, University of Bern, Switzerland
Multimodality-based Navigation System for Biopsy Procedures and Intra-operative Tumour Localization

Editorial & Review Contributions

African Invertebrates
American Journal of Cardiology
Apoptosis
Archives of Mechanics
Artificial Intelligence in Medicine
Atherosclerosis
Automatisierungstechnik
BMC Geriatrics
Cardiac Catherization and Intervention
Computer Aided Surgery
Computer Methods and Programs in Biomedicine
eCells and Materials
EURASIP Journal on Advances in Signal Processing
European Heart Journal
European Journal of Cardiothoracic Surgery
European Spine Journal

Editorial & Review Contributions

HNO
IEEE Robotics and Automation Society Magazine
IEEE Transactions on Biomedical Engineering
IEEE Transactions on Information Technology in Biomedicine
IEEE Transactions on Instrumentation and Measurement
IEEE Transactions on Mechatronics
IEEE Transactions on Neural Systems and Rehabilitation Engineering
IEEE Transactions on Pattern Analysis and Machine Intelligence
IEEE Transactions on Robotics
IEEE Transactions on Systems, Man, and Cybernetics, Part B
International Journal of Cardiovascular Imaging
International Journal of Heat and Mass Transfer
International Journal of Medical Robotics and Computer Assisted Surgery
International Journal of Telemedicine and Applications
Investigative Ophthalmology and Visual Science Journal
Journal for Computer Methods and Programs in Biomedicine
Journal of Computer Aided Radiology and Surgery
Journal of Diabetes Science and Technology
Journal of Sensors and Actuators (A. Physical)
Journal of Interventional Cardiology
Journal of Nanoengineering and Nanosystems
Journal of Negative Results in Biomedicine
Journal of Orthopaedic Research
Journal of Rehabilitation Research and Development
Journal of the American College of Cardiology
Journal of Tissue Engineering and Regenerative Medicine
Medical and Biological Engineering and Computing
Medical Engineering and Physics
Medical Image Analysis
Medical Physics
Micro Nanofluidics
Minimally Invasive Therapy and Allied Technologies
Molecular Phylogenetics and Evolution
Ostheoarthritis and Cartilage
Physical Review Letters
Spine
Surgical Innovation
Tissue Engineering Part A
Tissue Engineering Part B
World Journal of Orthopaedics

Editorial Board Member

European Spine Journal
Journal on Medical Devices
World Journal of Orthopaedics

Review Activities for Funding Agencies

AO Spine International
Austrian Research Promotion Agency (FFG), Austria
Bundesministerium für Bildung und Forschung, Germany
Collaborative Health Research Projects Program (CHRP), Natural Sciences and Engineering Research
Council of Canada (NSERC)
Cyprian Research Promotion Foundation, Cyprus
Department of Health, Great Britain
Deutsche Forschungsgemeinschaft, Germany
ERC Starting Grant, European Research Council
Natural Sciences and Engineering Research Council, Canada
Royal National Institute of Deaf People, Great Britain

Review Activities for Academic Institutions

Bern University of Applied Sciences, Switzerland
Ecole Polytechnique Fédérale de Lausanne EPFL, Switzerland
Eidgenössische Technische Hochschule Zürich ETH, Switzerland
University of Bern, Switzerland

Review Activities for Conferences

American Society of Orthopaedic Research
Annual International Conference of the IEEE Engineering in Medicine and Biology Society
CARS, Computer Assisted Radiology and Surgery
CURAC, Annual conferences of the German society for computer and robot assisted surgery CURAC
IEEE EMBS, International Conference on Engineering in Medicine and Biology Society
IEEE International Conference on Imaging Systems and Techniques 2011
IEEE International Conference on Information Technology and Applications in Biomedicine
IEEE IROS, International Conference Intelligent Robots and Systems
IEEE ISBI, International Symposium on Biomedical Imaging
IPCAI, Information Processing and Computer Aided Interventions
MICCAI, Medical Image Computing and Computer Assisted Interventions
6th International Conference on Microtechnologies in Medicine and Biology
10th International Workshop on Biomedical Engineering

Awards

CSL Behring Price for outstanding MSc in Biomedical Sciences
Sallin P
Lung on chip: Effects of Hepatocyte Growth Factor on Injured Alveolar A549 Epithelial Cells in vitro in Microfluidic Systems
Medical Faculty, University of Bern, Bern, Switzerland

Nominated for CTI Medtech Award
Stieger C, Frey F, Guenat JM, Schütz D, Arnold A, Kruse A, Wiedmer S, Auderset A, Messerli H, Uehlinger D, Häusler R, Caversaccio M
Novel Body Access
CTI Medtech Event, Bern, Switzerland

CTI Medtech Poster Award, 1st rank
Caversaccio M, Stieger C, Bell B, Arnold A, Salzmann J, Gerber N, Roder S, Gavaghan K, Williamson T, Paci F, Nauer C, Hamacher V, Weber S
High-Precision Robot for Implantable Hearing Systems
CTI Medtech Event, Bern, Switzerland

Forschungspreis Alumni MedBern 2010
Pfenniger A, Koch V, Vogel R
Human Energy Harvesting by Intravascular Turbine Generator
Tag der Klinischen Froschung, University of Bern, Switzerland

Hanjörg Wyss Start-up Award from AO Spine International
Gantenbein-Ritter B, Eglin D, Benneker LM
Biological Response of Mesenchymal Stem Cells seeded in Thermo-Reversible HA-Hydrogel implanted in Intervertebral Disc Organ Culture under Twisting Motion
AO World Spine Conference, Barcelona, Spain

International Committee MMB Conference Chair Award
Guenat O
Conference Chair of the 6th International Conference on Microtechnologies in Medicine and Biology (MMB2011), Lucerne, Switzerland

Nominated for Swiss Technology Award
Peterhans M, Weber S
Spin-Off CAScination
Swiss Technology Award, Basel, Switzerland

Awards

Poster Award
M'Rabet Bensalah K, Czerwinska J, Kalicki RM, Uehlinger DE
Multiscale Hemodynamic Modeling the Intrarenal Circulation using the COMSOL Multiphysics Software
BME Day, Bern, Switzerland

Transferkolleg 2011
Meier C, Kowal J, Asshauer T
OCT Integrated Instruments for Vitreo-Retinal Surgery
Schweizerische Akademie der Technischen Wissenschaften, Zurich, Switzerland

Invited Lectures

Czerwinska J
Computational Methods for Multiphase Flows
International Workshop and Summer School, Poland, June

Gantenbein-Ritter B
Cell Therapy for Intervertebral Disc Repair - which Cells to Take and which Disc to Rescue?
Swiss Experimental Surgery Symposium, Fribourg, Switzerland, January 21-22

Gantenbein-Ritter B
Bioreactors in Mechano Biology - The Missing Link
Masters in Biomedical Engineering, ETH Zürich, Switzerland, May 12

Gantenbein-Ritter B
Regeneration of the Intervertebral Disc - Lessons from Mechano-Biology
Artificial Organs: Fact or Fiction? Swiss MD-PhD Association (SMPA), Inselspital, Bern, Switzerland, October 14

Gantenbein-Ritter B
The Intervertebral Disc - Can We Regenerate or Repair It?
Seminar Series at Institute of Pharmacology, University of Bern, Switzerland, November 2

Gantenbein-Ritter B
Mechano-Biologie der Bandscheibe
Orthopaedic Department, Inselspital, Bern, Switzerland, November 10

Gantenbein-Ritter B
Intervertebral Disc Regeneration – Fact or Fiction?
Center for Applied Biotechnology and Molecular Medicine (CABMM), Zurich, Switzerland, November 17

Guenat O, Felder M, Sallin P, Barbe L, Gazdhar A, Geiser T
Microfluidic Wound Healing Assay to Investigate the Regenerative Effect of HGF on Epithelial Regeneration
6th Swiss Aerosol Conference, Bern, Switzerland, November 2

Kowal J
Computer Assisted Sub-Threshold Laser Photocoagulation
Swiss Experimental Surgery Symposium, Fribourg, Switzerland, January 21-22

Nef T
Roboter und andere Helfer für die Rehabilitation und die Pflege
Bildungsprogramm Niederhelfenschwil, Switzerland, March 14

Nef T
Technik und Autofahren bei Senioren
Workshop der interdisziplinären Expertengruppe Fahreignung bei Demenz des Vereins Swiss Memory Clinics, Kursaal Bern, Bern, Switzerland, June 25

Nef T
Roboter für die Bewegungstherapie nach Schlaganfall
Symposium zum Forschungspreis 2011 der Fürst Donnersmarck-Stiftung, Berlin, Germany, September 16

Nef T
Assistive Technology for Elderly People with Cognitive Impairment
RITZ – Rehabilitation Initiative and Technology Platform Zürich, ETH and University of Zürich, Zurich, Switzerland, October 4

Nef T
Assistive Technology for Elderly People with Cognitive Impairment
Ospedale Regionale di Lugano, Lugano, Switzerland, October 10

Nef T
Roboter und andere Helfer für die Rehabilitation und die Pflege
Seniorenuniversität Bern, Bern, Switzerland, October 21

Nef T
Assistive Technology for Elderly People with Cognitive Impairment
Grand Rounds, Laboratory of Robotics, Faculty of Electrical Engineering, University of Ljubljana, Slovenia, December 15

Stieger C
Implantable Hearing System Research: Use of Human Anatomical Whole Head Specimens
Swiss Experimental Surgery Symposium, Fribourg, Switzerland, January 21-22

Stieger C
BAP: Fixierung, Anatomie und Schallemission
Workshop BBraun, Aeskulap Klinik, Tuttlingen, Germany, March 29

Stieger C
DACS Activities at University Bern
Research Meeting Cochlear, University Bern, Bern, Switzerland, May 2

Stieger C
Audiologische Technologien
8. Medizintechnik Tagung, Inselspital, Bern, Switzerland, June 16

Stieger C, Guenat JM
Novel Body Access
CTI Medtech Event, Bern, Switzerland, August 23

Stieger C
DACS and Vibrant Soundbridge
OMMIT Surgical Course, Bern, Switzerland, August 31

Stieger C
Implantable Hearing Devices
Vistit-Swiss Association of Science Journalism, September 16

Stieger C, Bernhard H, Kompis, M, Caversaccio M
Erste Erfahrungen mit dem C-DACS
ADANO Arbeitsgemeinschaft Deutschsprachiger Audiologen und Neurootologen und Otologen, Regensburg, Germany, September 29

Stieger C, Kompis M, Caversaccio M
C-DACS Patients Bern
Cochlear C-DACS Investigator Meeting, Hannover, Germany, November 1

Vandenberghe S
Cardiac Assist Devices: From Human to Animal
Swiss Experimental Surgery Symposium, Fribourg, Switzerland, January 21-22

Vandenberghe S
Large Animal Studies: a Slow Learning Curve
DKF progress Report, Bern, Switzerland, May 18

Invited Lectures

Vandenberghe S
How to Set up Large Animal Studies?
Cardiovascular Research Retreat Prof. Rieben, Faulensee, Switzerland, July 1

Vandenberghe S, Pirbodaghi T, Weber A, Axiak S, Traupe T, Gempp T, de Marchi S
Physiologic Effects of a Speed Modulated Levitronix CentriMagTM Blood pump
Physiological Fluid Mechanics Conference, Brunel University, Uxbridge, Great Britain, July 14-15

Vandenberghe S
Fitness Equipment for the Heart
Inselspital Cardiology, Bern, Switzerland, October 12

Vandenberghe S
The Evolution of Cardiac Assist: Past, Present, Future
9th General Assembly of the Swiss MD-PhD Association, Bern, Switzerland, October 14

Vogel R
Coronary Guide Wires: The View of a User
Intermediate Training Biotronik, Bülach, February 28 and October 10

Weber S
The Challenge of Instrument Navigation in Moving Organs
Swiss Experimental Surgery Symposium, Fribourg, Switzerland, January 21-22

Weber S
Image Guided Liver Surgery - Clinical Applications and Scientific Trends
University of Leeds, Leeds, Great Britain, June 1

Weber S
Computer Assisted Micro Surgery - Experiences from ORL Surgery
CAOS Conference, Workshop on Smart Instrumentation, London, Great Britain, June 15

Weber S
Image Guided Liver Surgery Clinical Applications and Technological Trends
Annual Meeting of the Swiss Society for Biomedical Engineering, Bern Switzerland, August 22-23

Weber S
Image Guided Micro Surgery on the Ear
OMMIT Workshop, Bern, Switzerland, August 30

Weber S
Robot and Image Guided Micro Surgery on the Ear
Swiss Society for Computer Aided Surgery, Delemont, Switzerland, October 20

Weber S
Robot and Image Guided Micro Surgery on the Ear
Vanderbilt University, Nashville, USA, December 1

Keynote Lectures

Kowal J
Sub-Threshold Laser Therapy for Ophthalmic Pathologies
Annual Meeting of the Swiss Society for Biomedical Engineering, Bern, Switzerland, August 22-23

Publications - Journal Papers

Amstutz CA, Bechrakis N, Nolte LP, Foerster MH, Kowal JH
Intra-operative Localization of Tantalum Markers for Proton Beam Irradiation of Choroidal Melanoma by an Opto-Electronic Navigation System
International Journal of Radiation Oncology Biology Physics. 2011 [Epub ahead of print]

Bachman T, Bahma J, Verkaik J, Vandenberghe S, Kormos R, Antaki J
In vitro Evaluation of Ventricular Cannulation for Rotodynamic Cardiac Assist Devices
Cardiovascular Engineering and Technology. 2011; 2(3):203-11

Bell B, Stieger C, Gerber N, Arnold A, Nauer C, Hamacher V, Kompis M, Nolte L, Caversaccio M, Weber S
A Self-Developed and Constructed Robot for Minimally Invasive Cochlear Implantation
Acta Oto-Laryngologica [In Press]

Bell B, Roder S, Gerber N, Gavaghan K, Stieger S, Caversaccio M, Weber S
Computerassistierte Präzisionschirurgie am Ohr
AT-Automatisierungstechnik. 2011; 59(10):638-48

Bernhard H, Stieger C, Perriard Y
Design of a Semi-implantable Hearing Device for Direct Acoustic Cochlear Stimulation
IEEE Transactions on Biomedical Engineering. 2011; 58(2):420-8

Broehan AM, Rudolph T, Amstutz CA, Kowal JH
Real-Time Multimodal Retinal Image Registration for a Computer Assisted Laser Photocoagulation System
IEEE Transactions on Biomedical Engineering. 2011 [Epub ahead of print]

Brokaw EB, Murray T, Nef T, Lum PS
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