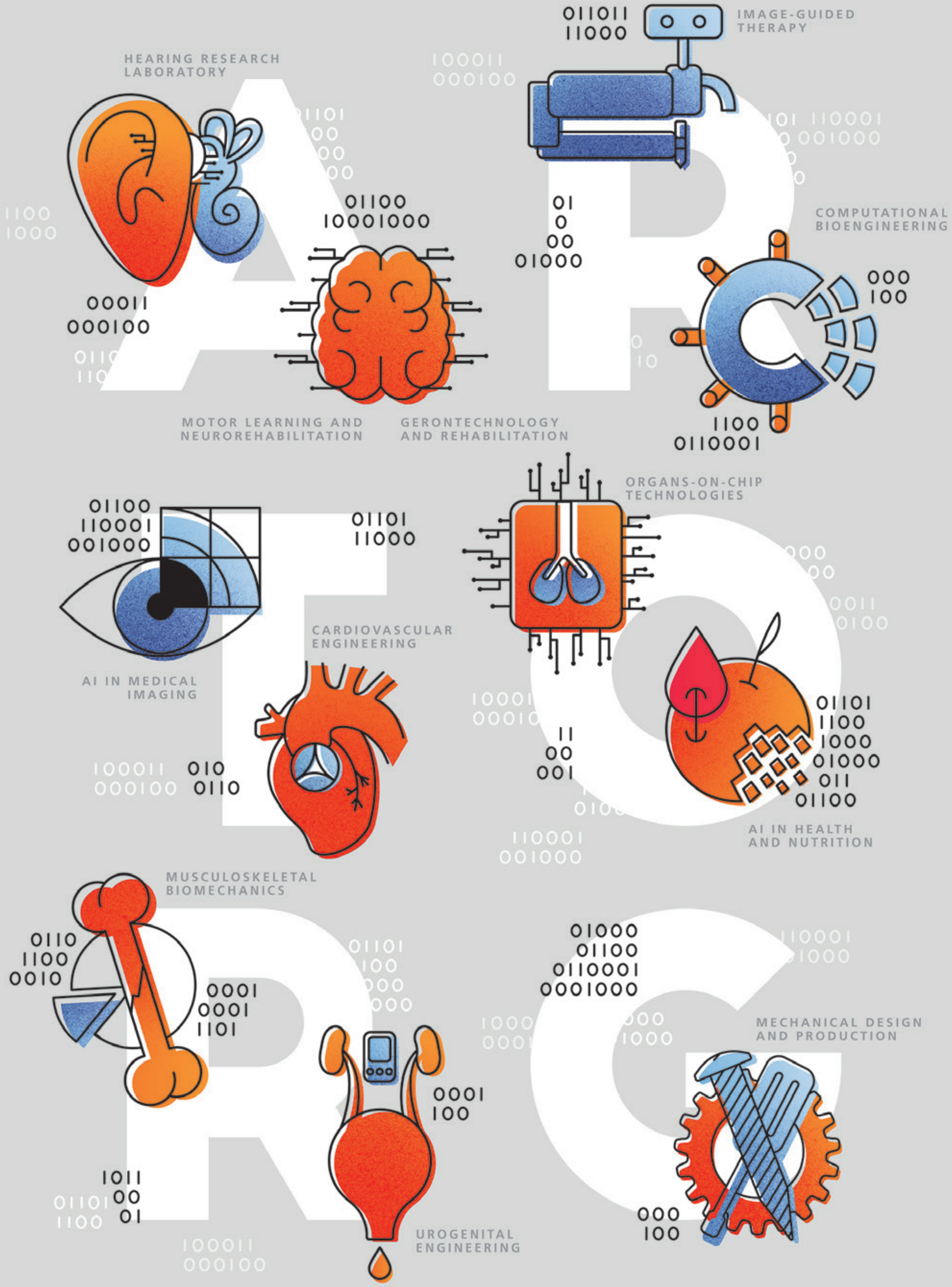
# Annual Report **2019**

UNIVERSITÄT
BERN

ARTORG CENTER
BIOMEDICAL ENGINEERING RESEARCH



# Groups

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**AIHN**
Artificial Intelligence in Health Nutrition

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**AIMI**
Artificial Intelligence in Medical Imaging

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**CB**
Computational Bioengineering

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**CVE**
Cardiovascular Engineering

↓
**GER**
Gerontechnology and Rehabilitation

↓
**HRL**
Hearing Research Laboratory

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**IGT**
Image-Guided Therapy

↓
**MLN**
Motor Learning and Neurorehabilitation

↓
**MSB**
Musculoskeletal Biomechanics

↓
**OOC**
Organs-on-Chip Technologies

↓
**UGE**
Urogenital Engineering

↓
**MDP**
Mechanical Design and Production

# Research Partners

- University of Bern
- Inselspital – Universitätsspital Bern – Hôpital Universitaire de Berne
- sitem-insel
- AlveoliX – In-vitro models inspired by nature
- HFR – hôpital fribourgeois – freiburger spital
- TU Wien – Technische Universität Wien – Vienna University of Technology
- AO Foundation
- HUG – Hôpitaux Universitaires Genève
- USI – Università della Svizzera italiana
- City of Hope
- Inria – Inventeurs du monde numérique
- university of groningen
- DLR
- Imperial College London
- University of Bristol
- Karolinska Institutet – Anno 1810
- University of Oxford
- FH – Bern University of Applied Sciences
- luzerner kantonsspital
- University of Southampton
- ulm university – universität uulm
- CASCINATION
- MDC – Max Delbrück Center for Molecular Medicine in the Helmholtz Association
- UKBB – University Children's Hospital Basel
- csem
- McGill University
- UCL
- CHUV
- MED-EL
- UZA
- Danderyds Sjukhus
- Newcastle University
- UniversitätsSpital Zürich
- DOMO CARE
- Oslo University Hospital
- Universitat d'Alacant – Universidad de Alicante
- ENIUS – European Network of Multidisciplinary Research to Improve the Urinary Stents
- Paul Scherrer Institut – PSI
- University of Maryland
- ETH zürich
- retinai
- The University of Nottingham – United Kingdom · China · Malaysia
- EPFL
- RMS – Testing · Research · Consulting – www.rms-foundation.ch
- Universitäre Psychiatrische Dienste Bern
- EMPA – Materials Science & Technology
- Rutgers – The State University of New Jersey
- HIPS – Helmholtz Institute for Pharmaceutical Research Saarland
- Spital Tiefenau – Inselgruppe
- Vascular Institute Switzerland

# Dissertations

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**Stefanos Apostolopoulos**
*Artificial Intelligence in Medical Imaging*
Reliable Registration and Tracking Framework for Disease Progression Monitoring using Optical Coherence Tomography

**Stergios Christodoulidis**
*Artificial Intelligence in Health and Nutrition*
Lung Pattern Analysis using Artificial Intelligence for the Diagnosis Support of Interstitial Lung Diseases

**Stephan Gerber**
*Gerontechnology and Rehabilitation*
Development and Evaluation of a Virtual Reality Setup for Cognitive Stimulation in Critically Ill Patients

**Alvin Chesahm**
*Gerontechnology and Rehabilitation*
Puzzling the Mind: Development and Evaluation of Puzzle Games to Assess Cognitive and Motor Function in Neurocognitive Aging

**Barna Becsek**
*Cardiovascular Engineering*
High-Performance Computing Numerical Fluid-Structure Interaction Framework for the Simulation of Aortic Valve Hemodynamics

**Farouk Chrif**
*Gerontechnology and Rehabilitation*
Technological Development and Usability Evaluation of a Novel Interactive Training Robot for Children with Neuromuscular Impairments

**Serife Kucur**
*Artificial Intelligence in Medical Imaging*
Exploration and Exploitation of Visual Fields: from Acquisition to Prediction of Glaucoma

Photography: Adrian Moser

# Master of Science
# Biomedical Engineering

Photography: Adrian Moser

## Key Features

- Cooperation between University of Bern and Bern University of Applied Sciences
- Two-year full-time program, part-time work possible
- International program in English
- Affiliated to a leading medical faculty in Switzerland: Inselspital, University Hospital Bern
- Oriented towards clinical applications
- Attractive location

## Admission Requirements

*BSc (FH/HES/SUP/Uni) in*

- Electrical Engineering
- Mechanical Engineering
- Microtechnology
- Systems Engineering
- Physics
- Computer Science
- Related fields

## Major Modules

- Biomechanical Systems
- Electronic Implants
- Image-Guided Therapy

## Perspectives

- Excellent job opportunities in industry, research institutions and hospitals
- Doctoral studies accessible
- BME alumni network

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Matthias Andreas Fontanellaz
Eleni Kapousidou

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Prof. Aristomenis Exadaktylos, Emergency Medicine, University Hospital Bern – Inselspital
Prof. Zeno Stanga, Diabetes, Endocrinology, Nutritional Medicine & Metabolism, University Hospital Bern – Inselspital
Prof. Thomas Geiser, Pneumology, University Hospital Bern – Inselspital
Prof. Manfred Essig, Internal Medicine and Gastroenterology, University Hospital Bern –Tiefenauspital

## Research Profile

The AI in Health and Nutrition Laboratory focuses primarily on the interface between machine learning, artificial intelligence and their applications to improving health. The laboratory creates innovation to translate "data into knowledge" and "research into clinical practice". Our research activities:

- AI-based innovative systems for dietary monitoring and assessment
- Reinforcement learning for optimization of insulin treatment
- AI-based computer-aided diagnosis for lung diseases

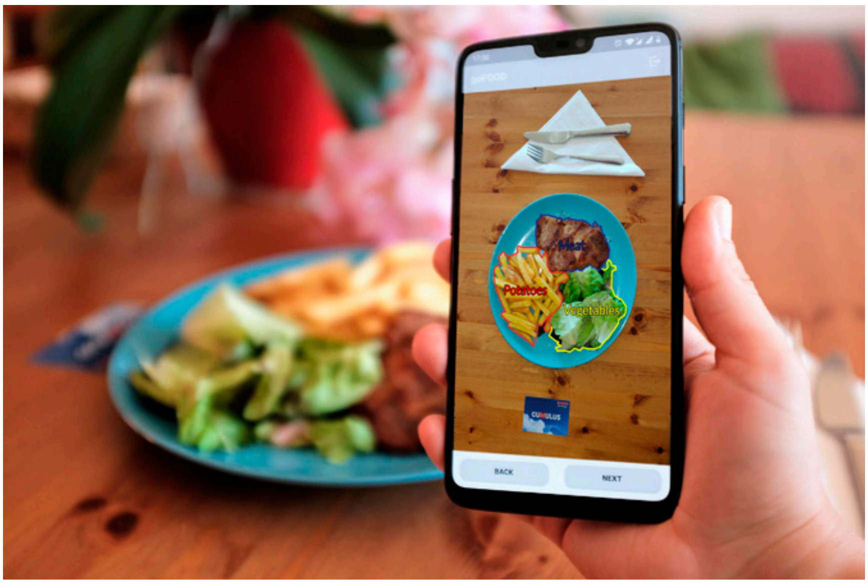


**Fig. 1:** AI-based algorithms automatically detect food types, estimate portion sizes and calculate the calories, carbohydrates, protein and fat from smartphone photo or video.

**Promoting the Mediterranean Diet by Using Meal Image Analysis**
*(Innosuisse #33780.1 IP-LS with Oviva S.A. & UZH)*

Non-communicable diseases (NCDs) are the leading cause of mortality and-disability worldwide. A balanced diet is a cornerstone in the prevention of both the onset and the progression of NCDs. The Mediterranean diet (MD), characterized by its balance not only in the consumed food, but also in the frequency of the meals, has demonstrated efficacy to decrease NCD risk among high risk and general populations.
The aim of the project is the development and validation of an automatic system for the assessment of a meal's adherence to the MD by using a meal image and computer vision. The assessment is performed on three levels: per meal, per day and per week. The system will be integrated into a smartphone application to increase users' engagement and promote healthy eating habits.

**Tackling Hospitalized Malnutrition**
*(SV Stiftung with Inselspital and Tiefenauspital)*

Disease related malnutrition in hospitalized patients is a serious condition with both clinical and economic implications. In Swiss hospitals, 20-30% of the admitted patients, is undernourished


**Fig. 2:** Example of food and volume detection of the patient's meal before (left) and after (right) consumption. The bottom table indicates the micro- and macronutrient consuption.

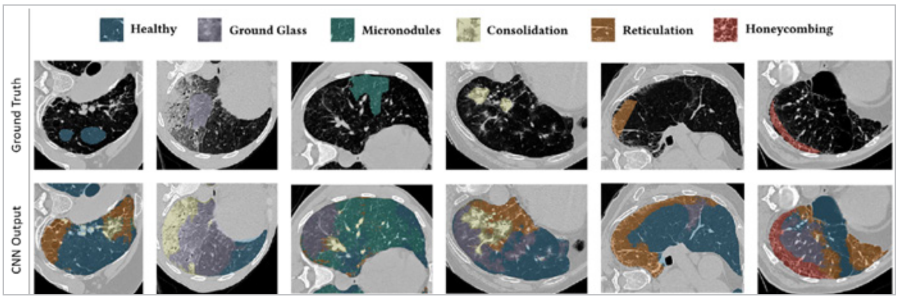


**Fig. 3:** Output examples of the INTACT's segmentation model for tissue characterization. Top row, ground truth; bottom row, model output. Each example has a different pattern annotated. From left to right: healthy (blue), Ground Glass - GGO (purple), micronodules (green), consolidation (yellow), reticulation (orange) and honeycombing (red).

or "at high risk" for malnutrition.
The main objective of the project is the development of an AI-based system that takes advantage of the availability of depth sensors and conceptual information to estimate the consumed energy, macro- and micronutrient content of hospitalized patients, as based on the automatic analysis of a patient's tray, before and after the meal (Fig. 2).

**Computer-aided Diagnosis Support** *(with Inselspital)*

Interstitial Lung Diseases (ILD) are a heterogeneous group of more than 200 chronic, overlapping lung disorders, characterised by fibrosis and/or inflammation of lung tissue. The diagnosis of a suspected ILD is based on high resolution computed tomography (HRCT) images and often presents a diagnostic dilemma. By achieving a reliable diagnosis on HRCT images, patients could avoid potential complications, as well as the high costs associated with a surgical biopsy.

The aim of this project is to develop a computational system (INTACT) that will assist radiologists with the diagnosis of ILDs, while minimizing the dangerous, expensive and time-consuming invasive biopsies. To this end, the system provides a computerized differential diagnosis, based on radiological data and clinical/biochemical markers and is focused on the discrimination between idiopathic interstitial pneumonias (Fig. 3). The newly introduced system consists of a sequential pipeline in which the anatomical structures of the lung are first segmented. Then the pathological lung tissue is identified, and this information is combined to give a final radiological diagnosis. The overall pipeline is based on novel machine-learning algorithms that have been designed for the task of diffusing pathological tissue segmentation. In all the implemented algorithms, experimental configurations and evaluation schemes, the main focus is the bridging between machine learning and medical diagnosis.

This research is carried out within the framework of the INTACT research project and is supported by Bern University Hospital, "Inselspital", the Swiss National Science Foundation (SNSF), Stiftung Lindenhof Bern, Roche and Hasler Stiftung

**Glucose Control Based on Deep and Reinforcement Learning Technologies** *(JDRF grant)*
Diabetes mellitus is characterised by elevated glucose levels with severe short-term and long-term complications. For individuals with type 1 diabetes, controlled insulin treatment and lifestyle adjustments (physical activity, eating habits) are needed, together with regular glucose monitoring. Correct prediction of future blood glucose levels can be used to provide early warnings of upcoming hypo-/hyperglycaemic events and thus to improve the patient's safety.

The project aims to enhance the accuracy of glucose prediction, particularly with the aims of predicting hypo- and hyper-glycaemic conditions. It is our highest priority to provide a solution that can predict the onset of hypo- and hyper-glycaemia at least 30 min in advance, so that the patient can take actions and prevent the onset of the condition. We aim to provide a solution based on powerful AI approaches that most effectively exploit the minimum amount of information and minimum amount of sensing devices, in order to provide patients with technologies and algorithms in the form of an easily accessible application that is able to meet their expectations for glucose control. To this end, AI algorithms are used to i) identify the effect of age, time of diagnosis, actual time, glucose concentrations, insulin intakes and different lifestyle events on the glucose control, and ii) to predict the onset of hypo- and hyper-glycaemic events.

**Selected Publications**


1. Ebner L., Christodoulidis S., Stathopoulou Th., Geiser Th., Stalder O., Limacher A., Heverhagen J., Mougiakakou S., Christe A., "Meta-analysis of the radiological and clinical features of usual interstitial pneumonia and nonspecific interstitial pneumonia", PLoS ONE, 15(1), e0226084, 2020.
2. Lu Y., Stathopoulou Th., Vasiloglou M., Christodoulidis S., Blum B., Walser Th., Meier V., Stanga Z., Mougiakakou S., "An artificial intelligence-based system for nutrient intake assessment of hospitalised patients," Conf Proc IEEE Eng Med Biol Soc. 2019 Jul;2019:5696-5699.
3. Christe A., Peters A.A., Drakopoulos D., Heverhagen J.T., Geiser T., Stathopoulou T., Christodoulidis S., Anthimopoulos M., Mougiakakou S.G., Ebner L., "Computer-aided diagnosis of pulmonary fibrosis using deep learning and CT images," Invest Radiol. 2019 Oct;54(10):627-632.
4. Sun Q., Jankovic M., Mougiakakou S., "RL-based adaptive insulin advisor for individuals with T1D under multiple daily injections therapy," Conf Proc IEEE Eng Med Biol Soc. 2019 Jul;2019:3609-3612.

# Artificial Intelligence in Medical Imaging

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Matthia Gallardo
Serife Kucur
Laurent Lejeune
Tatiana Fountoukidou
Thomas Kurmann
Vasily Tolkachev
Daniel Erpenbeck
Jan Stapelfeldt
Olen Andoni
Michel Hayoz
Britt Marlatt
Jana Starkova
Till Meyer vu Westram
Nina Huber

## Research Profile

The Artifical Intelligence in Medical Imaging (AIMI) lab is focused on designing novel machine learning and computer vision methods to solve unmet clinical needs. With a strong focus on methodology that spans basic-to-translational research, the emphasis is on engineering solutions in a holistic fashion, whereby taking into account how new approaches can be integrated in routine clinical care. As an interdisciplinary research team, the AIMI lab is involved with several research projects that involve research challenges in both diagnostic and interventional contexts.

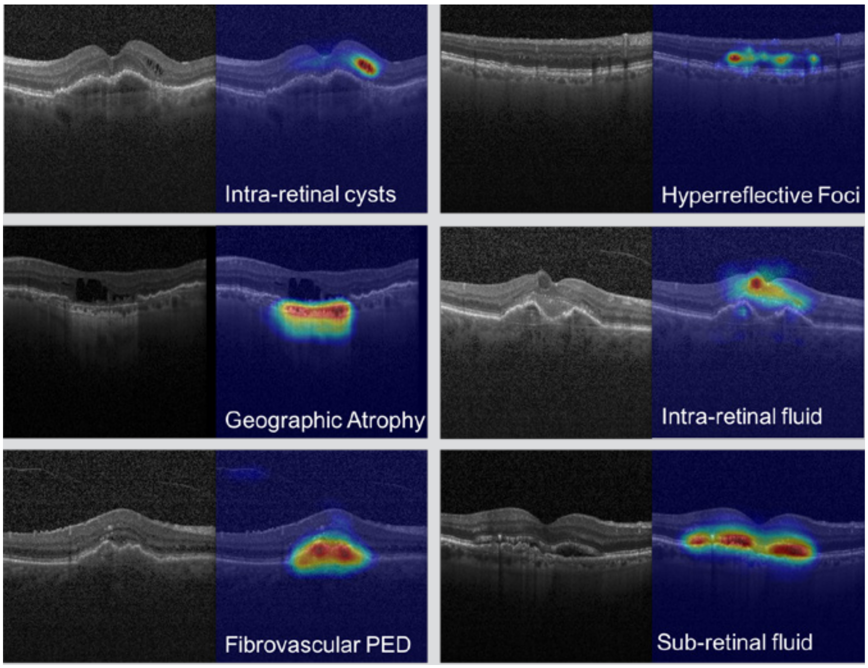


**Fig. 1:** Classifier activation maps for different biomarkers on selected examples. Red regions illustrates regions of the image that are automatically found by our method to correctly predict the corresponding biomarker.

### Expert-level Automated Biomarker Identification in Optical Coherence Tomography Scans

*(Innosuisse grant with Insel & RetinAi Medical AG)*

Retinal biological markers, or biomarkers, play a critical role in the management of chronic eye conditions and in the development of new therapeutics. While many imaging technologies used today can visualize these, Optical Coherence Tomography (OCT) is often the tool of choice due to its ability to image retinal structures in three dimensions at micrometer resolution. But with widespread use in clinical routine, and growing prevalence in chronic retinal conditions, the quantity of scans acquired worldwide is surpassing the capacity of retinal specialists to inspect these in meaningful ways. Instead, automated analysis of scans using machine learning algorithms provide a cost effective and reliable alternative to assist ophthalmologists in clinical routine and research. In this context, we have designed a machine learning method capable of consistently identifying a wide range of common retinal biomarkers from OCT scans. Our approach avoids the need for costly segmentation annotations and allows scans to be characterized by biomarker distributions. These can then be used to classify scans based on their underlying pathology in a device-independent way.

### Image Data Validation for Medical Systems

*(Innosuisse grant with Insel & RetinAi Medical AG)*

Data validation is the process of ensuring that the input to a data processing

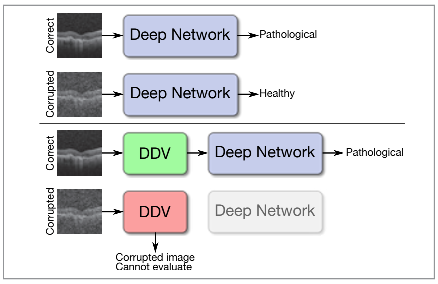


**Fig. 2:** Top: An automatic diagnosis method with no validation. However, the presence of corruption —noise in this case— leads to an erroneous healthy prediction. Bottom: Our DDV model learns the data distribution the network was trained on, and prevents any diagnosis when it detects an image outside the distribution.

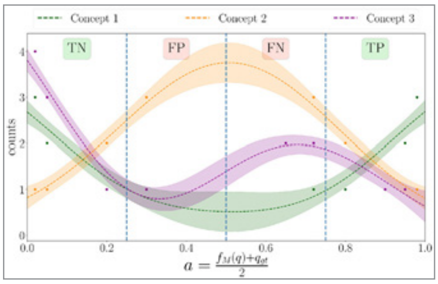


**Fig. 3:** Examples of our Gaussian Process for 3 different concepts (points are the observed counts, dotted line is the mean of a GP and the shaded area corresponds to the 95% confidence region).

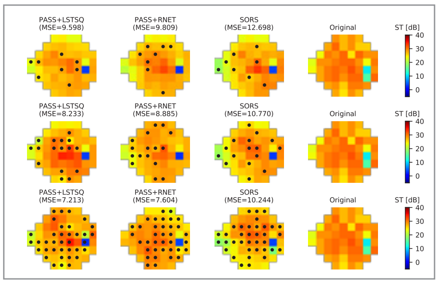


**Fig. 4:** Comparison of VFs reconstructed with PASS (first and second columns) and with SORS (third column) for a healthy patient. The last column shows the ground-truth. Black dots indicate the queried locations for each method. PASS adapts queries to the underlying VF.

pipeline is correct and useful. It is a critical part of software systems running in production. Image processing systems are no different, whereby problems with data acquisition, file corruption or data transmission, may lead to a wide range of unexpected issues in the acquired images. Until now, most image processing systems of this type involved a human in the loop that could detect these errors before further processing. But with the advent of powerful deep learning methods, tools for medical image processing are becoming increasingly autonomous and can go from data acquisition to final medical diagnosis without any human interactions. However, deep networks are known for their inability to detect corruption or errors in the input data. To overcome this, we have designed a deep validation method that learns to measure how correct a given image looks, and is able to raise human attention when the input image contains high levels of noise, unexpected occlusions, or corruption of any other kind. We have showed that the validity of our method and compare it with different baselines, reaching an improvement of more than 10% on a wide range of datasets.

### Concept-Centric Visual Turing Tests for Method Validation

Recent advances in machine learning for medical imaging has led to impressive increases in model complexity and their overall capabilities. With these advances however, the ability to discern the precise information a method is using to make decisions has lagged behind and it is often unclear how these performances are in fact achieved. In particular, conventional evaluation metrics that reduce method performance to a single number or a curve, only provide limited insights. Yet, systems used in clinical practice demand thorough validation that such crude characterizations miss. To this end, we present in this work a framework to evaluate classification methods based on a number of interpretable concepts that are crucial for a clinical task. Our approach is inspired by the Turing Test concept and how to automatically devise a test that adaptively questions a method for its ability to interpret medical images. To do this, we make use of a Twenty Questions paradigm whereby using a probabilistic model to characterize the method's capacity to grasp task-specific concepts and introduce a novel strategy to sequentially query the method according to its previous answers.

### Patient Attentive Sequential Strategy for Perimetry-based Visual Field Acquisition

*(Innosuisse grant with Insel & Haag-Streit AG)*

Perimetry is a non-invasive clinical psychometric examination used for diagnosing ophthalmic and neurological conditions. At its core, perimetry relies on a subject pressing a button whenever they see a visual stimulus within their field of view. This sequential process then yields a 2D visual field image that is critical for clinical use. Perimetry is painfully slow however, with examinations lasting 7–8 minutes per eye. Maintaining high levels of concentration during that time is exhausting for the patient and negatively affects the acquired visual field. We have designed a novel perimetry testing strategy, based on reinforcement learning, that requires fewer locations in order to effectively estimate 2D visual fields. PASS uses a selection policy that determines what locations should be tested in order to reconstruct the complete visual field as accurately as possible, and then separately reconstructs the visual field from sparse observations. Furthermore, PASS is patient-specific and non-greedy. It adaptively selects what locations to query based on the patient's answers to previous queries, and the locations are jointly selected to maximize the quality of the final reconstruction. In our experiments, we show that this new method outperforms state-of-the-art methods, leading to more accurate reconstructions in 70% of the time.

**Selected Publications**

1. Kurmann, T., Yu, S., Marquez Neila, P., Ebneter, A., Zinkernagel, M., Munk, M. R., Wolf, S. and Sznitman, R., "Expert-level Automated Biomarker Identification in Optical Coherence Tomography Scans", Nature Scientific Reports, 2019
2. Marquez Neila, P. and Sznitman, R., "Image data validation for medical systems". In Proceedings of the 20th International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI), 2019.
3. Fountoukidou, T. and Sznitman, R., "Concept-Centric Visual Turing Tests for Method Vali- dation". In Proceedings of the 20th International Conference on Medical Image Computing and Computer Assisted Intervention (MICCAI), 2019.
4. Kucur, S., Marqez-Neila, P., Abegg, M. and Sznitman, R., "Patient Attentive Sequential Strategy for Perimetry-based Visual Field Acquisition", Medical Image Analysis, 2019

# Computational Bioengineering

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## Research Profile

The Computational Bioengineering Group tackles challenges in medical research with modern computational simulation tools. Rather than focusing on the computational methods themselves, we are concerned with their appropriate application for the resolution of practical and fundamental clinical questions. Numerical methods are combined with experimental and clinical research in order to provide personalized biomechanical models.

Together with our collaborators, we constitute a strong team covering a wide spectrum of research topics. Besides our core expertise in applying finite element analysis to study skeletal biomechanics, we are seeking to improve surgical planning by developing numerical models of soft tissues such as cornea or arteries.

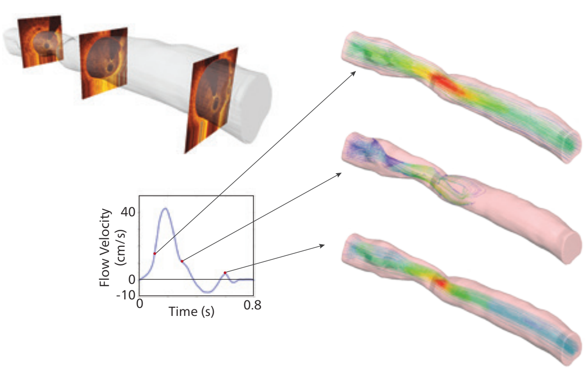


**Fig. 1:** Reconstruction of an artery of a patient suffering from peripheral arterial disease from OCT images obtained prior to balloon angioplasty. The hemodynamical condition computed at different time points of the cardiac cycle can be used as biomarkers indicating risks of restenosis.

### Understanding the Risk of Restenosis in Femoro-Popliteal Arteries

The femoro-popliteal (FP) segment is the most commonly diseased artery of the peripheral arterial circulation. While the Peripheral Arterial Disease is routinely treated with endovascular treatment approaches, the reoccurrence of the disease (restenosis) following the initial intervention continues to be an underlying problem in the FP arterial tract, leading to high rates of target lesion revascularization.

To understand the causes of restenosis and improve clinical outcomes, we developed numerical models based on patient-specific clinical data. A combination of imaging techniques, such as optical coherence tomography and X-ray angiography, was used to build a numerical frameworks able to model both the biomechanical response of the artery and the intra-arterial blood flow (Fig. 1).

Recently, we showed that adverse hemodynamical conditions immediately after treatment can be used as a marker of restenosis. This would allow clinicians to identify high-risk patients and chart their post-treatment strategies accordingly.

### Brain Under Pressure: Biomarkers for the Mechanical Impact of Brain Tumors

The compression of brain tissue by a tumor mass, the so-called 'mass-effect', is a major cause of the clinical symptoms in

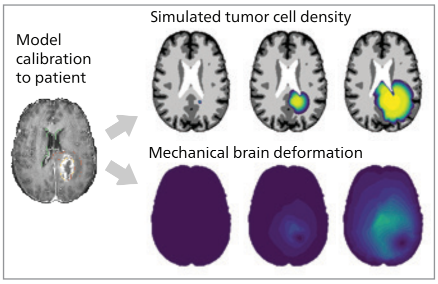


**Fig. 2:** Virtual tumors are seeded and grown in computational models of the patient's brain. Parameters that best describe the shape of the tumor provide insights on its mechanical impact on the patient's brain.

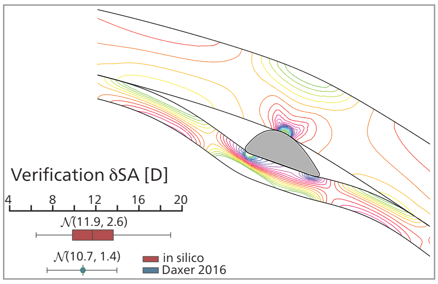


**Fig. 3:** Population-based modeling allowed us to better understand the biomechanical response of the human cornea to intra-corneal ring implantation, and to derive guidelines for their selection and positioning.

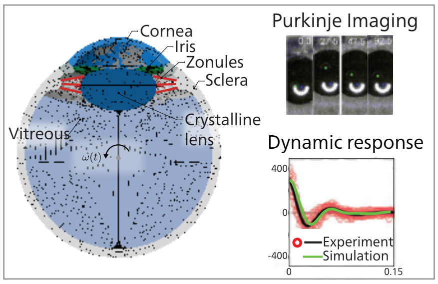


**Fig. 4:** Crystalline lens oscillations due to eyeball's saccadic rotation is recorded using Purkinje Imaging. Dynamic finite element simulations of the full eyeball are able to reproduce the in-vivo measurements.

patients with brain cancer. Indeed, solid stress, as generated by brain tumors, has been shown to impair neurological function. Biomechanical forces, such as those resulting from displacive tumor growth, also shape the tumor environment and affect tumor growth and evolution. In patients with glioblastoma, the most frequent malignant primary brain tumor in human adults, increased tumor mass-effect is associated to poor prognosis.

We develop patient-specific mathematical models to study the biomechanical impact of tumor growth and possible treatment implications (Fig. 2). We use these models to investigate determinants of tumor shape, such as the influence of tissue structure and growth location, and to evaluate quantitative image-based measures of tumor mass effect . Along with these models, we develop approaches for identifying patient-specific growth characteristics from clinical imaging data.

## Assessment of Intracorneal Ring Segments

Myopia is a visual impairement that will affect half of the population by 2050, with an estimated economic burden estimated at $202 billion / year. Low and mid myopia can be corrected using laser refractive surgeries. Unfortunately, the required amount of correction for high myopia is far too large for safe laser procedures. Clinically, plastic rings inserted inside the cornea represent an alternative for highly myopic patients. The rings are implanted in the middle of the cornea, and mechanically correct corneal curvature. However, it is challenging for the clinicians to select the appropriate implant for each patient, and to determine the implantation parameters to achieve the desired optical correction.

We proposed a virtual test bench to evaluate the impact of a continuous plastic ring; the Myoring (Fig. 3). Using a cohort of 2,000 virtual eyes based on population data, we were able to evaluate about 25,000 Myoring surgeries. Simulations showed a great agreement with clinical data (±1 D error in refractive error).

The study showed that the diameter of the ring is the predominant factor, while its thickness plays a fine-tuning secondary role. Numerical tools proved useful and have the potential to complement current planning tools.

## Orthokeratology

Orthokeratology is a refractive treatment aiming at correcting the refractive errors by a short-term modification of the corneal curvature. A rigid contact lens is worn overnight, which introduces a temporary deformation of the corneal epithelium. When the patient removes the lens in the morning, the epithelium slowly recovers its original shape, which provides a good vision during most of the day. The mechanisms responsible for the biomechanical behavior of the cornea remain insufficiently understood, especially concerning its short-term response.

We evaluate the hypothesis that the deformation of the cornea can be explained by the redistribution of the fluid within the corneal epithelium and stroma. Poroelastic models of the cornea are developed to study the evolution of the refractive outcome during the first day of orthokeratology treatment. Comparison with data collected on patients enable us to evaluate the validity of the material parameters.

## Cristaline Lens Wobbling

Post saccadic lens oscillations can be measured with Purkinje images and recorded with a high-speed camera. At the end of saccadic eye movement, the lens will immediately begin to oscillate due to the inertial forces and viscoelastic behavior of intra-occular structures. We aim at replicating the experimentally observed lens wobbling using a dynamic finite element model of the complete eyeball (Fig. 4).

We hypothesize that personalized simulations of this dynamic response have the potential to provide mechanical markers able to describe the condition of the patient, based on a simple and non-invasive clinical evaluation.

**Selected Publications**

1. Truffer O., Abler D., Pajic B., Grabner G., Kraker H., and Büchler P., "Optimization of surgical parameters based on patient-specific models: Application to arcuate keratotomy.," J. Cataract Refract. Surg., 45:1084–1091, Aug. 2019.
2. Gökgöl C., Diehm N., Räber L., and Büchler P., "Prediction of restenosis based on hemodynamical markers in revascularized femoro-popliteal arteries during leg flexion.," Biomech. Model. Mechanobiol., 18:1883–1893, 2019.
3. Studer D., Büchler P., and Hasler C. C., "Radiographic Outcome and Complication Rate of 34 Graduates After Treatment With Vertical Expandable Prosthetic Titanium Rib (VEPTR): A Single Center Report.," J. Pediatr. Orthop., 39:e731–e736, 2019.
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# Cardiovascular Engineering

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## Research Profile

The Cardiovascular Engineering (CVE) group focusses on the study of biomedical flow systems and works on the development of cardiovascular devices and diagnostic tools for cardiovascular diseases such as valvular heart disease and myocardial infarction. Translational research projects address unmet clinical needs that are identified together with clinical partners.

CVE operates a modern cardiovascular flow lab with state-of-the-art technology to simulate flow in the cardiovascular system and to measure hemodynamic parameters. High-speed cameras and laser-based methods are used to quantify flow at microscale (e.g. capillary flow) and at high Reynolds numbers (e.g. turbulent blood flow). Next to the experimental facilities, CVE develops and uses high-order flow solvers which are optimized for supercomputing platforms with GPUs to enable very large flow simulations. These solvers are used to model complex biomedical flows with fluid-structure interaction, and they are combined with medical imaging data to enhance the diagnosis of cardiovascular diseases.

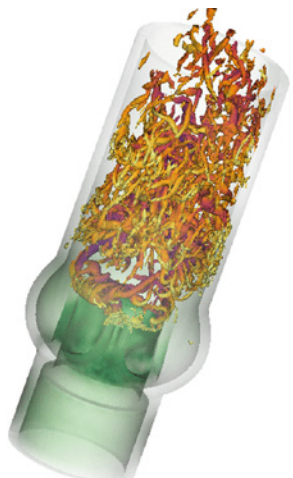

**Fig.1:** Laminar-turbulent transition in the turbulent systolic wake of a bioprosthetic valve.

### Laminar-turbulent Transition behind Aortic Valve Prostheses

Artificial heart valves are known to cause unphysiological turbulent blood flow in their wake. This turbulent flow is the result of hydrodynamic instabilities and laminar-turbulent transition mechanisms. For the design of better heart valve prostheses, it is indispensable to better understand these mechanisms. CVE invests in this basic research effort by studying hydrodynamic instabilities and laminar-turbulent transition in heart valves with theoretical methods of hydrodynamic stability theory, by high-order computer models (direct numerical simulations with fluid-structure interaction, fig. 1) and by experiments with valves mounted in silicone phantoms using laser-based measurement technology.

### Computer-augmented 4D Flow MRI for Quantitative Assessment of Turbulent Blood Flow

*(PASC grant with Profs. Kozerke & Konukoglu, ETH Zurich, Prof. Krause, USI Lugano, Profs. Carrel & von Tengg, Inselspital Bern)*
After aortic valve replacement, severely turbulent blood flow in the aortic root may lead to blood trauma and clotting, excessive wear of aortic valve prostheses, increased transvalvular pressure gradients and endothelial lesions in the ascending aorta possibly causing adverse events such as dissection or aneurysma. Quantitative assessment of turbulence intensity by 4D-Flow-MRI is limited →

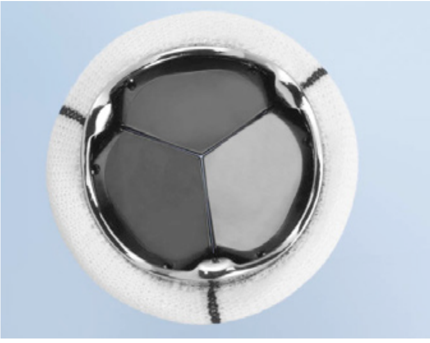

**Fig. 2:** Tri-leaflet mechanical heart valve Triflo by Novostia SA (Neuchâtel) with a novel hinge design to create more physiological blood flow.

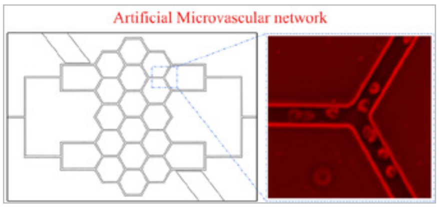


**Fig. 3:** (left) Network of micro-channels (width <10µm) mimicking a cerebral capillary network. (right) Porcine red blood cells at a diverging bifurcation of micro-channels where they show a tendency to enter the daughter vessel with higher velocity (Zweifach-Fung effect).

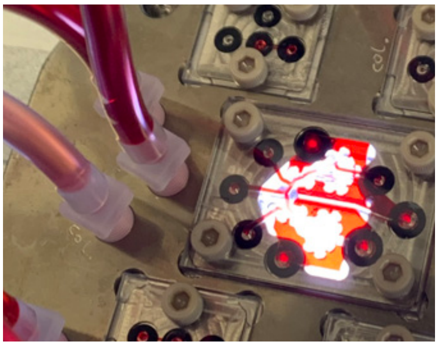

**Fig. 4:** Microfludic chip by NTB Buchs to study drug infusion in the coronary microcirculation with MVO.

by long MRI acquisition times, large voxel size and measurement artifacts. CVE develops a numerical tool for data assimilation based on Kalman filtering which combines 4D-Flow-MRI with a high-order Navier-Stokes solver. It yields computer-augmented 4D-Flow-MRI data which allow for a clinical quantitative assessment of turbulent blood flow.

**Non-thrombogenic Design of a Tri-leaflet Mechanical Heart Valve**
*(with Novostia SA, Neuchâtel)*
Mechanical heart valve (MHV) prostheses are notorious for creating unphysiological blood flow which may lead to blood clots. Therefore, patients with MHV are bound to life-long medication with anti-coagulants. The start-up company Novostia SA is developing a tri-leaflet mechanical heart valve (fig. 2) with a novel hinge design to enable more physiological blood flow that prevents clot formation. CVE supports this development with experimental studies of the three-dimensional flow field around this valve using a tomographic particle image velocimetry system (Tomo-PIV).

**Red Blood Cell Transport in the Cerebral Microcirculation**
*(SNF grant with Prof. Jenny, ETHZ, Prof. Weber, University of Zurich)*
Local concentrations of red blood cells in capillaries (tube hematocrit) are a factor in the oxygen supply to the surrounding tissue. CVE investigates mechanisms of red blood cell transport in capillary networks to better understand the local regulation of tube hematocrit in the brain which is known to be spatially and temporally heterogeneous. Solutions of porcine red blood cells are infused in microfluidic networks of micro-channels (width <10µm) mimicking capillary networks of the brain (fig. 3). Nonlinear behavior at diverging bifurcations leads to complex flow patterns which can be controlled by active dilation/contraction of the micro-channels.

**Aortic Blood Pump Based on Dielectric Elastomer Actuators**
*(supported by Werner-Siemens-Stiftung; with Prof. Perriard, EPFL and Prof. Carrel, Inselspital, Bern)*
CVE collaborates with the Center for Artificial Muscles CAM (Prof. Yves Perriard, EPFL) and Prof. Carrel (Inselspital Bern) in the development of a novel assist device for heart failure patients. The device comprises a dielectric elastomer actuator wrapped around the ascending aorta which pumps blood by controlled, repeated contraction of the aorta. Unlike classical ventricular assist devices, this pumping mechanism is less invasive and does not cause blood trauma.

**Catheter-based Diagnosis and Therapy of Microvascular Obstruction after Heart Attack**
*(Innosuisse R&D grant with CorFlow Therapeutics AG, Baar)*
Many heart attack patients suffer from microvascular obstruction (MVO) after successful primary treatment. MVO impairs their recovery and may contribute to the onset of heart failure. Reliable diagnosis and treatment of MVO in the catheter lab is not available today. Together with the start-up company CorFlow Therapeutics AG, CVE is working on the development of a catheter-based technology for quantitative diagnosis of MVO severity. It uses a multi-lumen catheter with a balloon to measure the hydraulic resistance of the vascular bed which increases with MVO. In a second step, the same system is used to infuse drugs to treat the MVO. CVE developed a multi-scale bench test for the coronary circulation which includes a microfluidic chip (fig. 4) to study the diagnostic method and to optimize the drug infusion into the microvascular bed.

**Selected Publications**

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# Gerontechnology and Rehabilitation

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René Vielgut
Julia Truttmann
Katja Erne

## Research Profile

The interdisciplinary Gerontechnology and Rehabilitation Research Group is a collaborative research effort with the goal to develop and evaluate novel, flexible and cost-efficient technologies to improve diagnostics, monitoring and therapies of neurological disorders both in the hospital and at home. Core methodologies include telemonitoring, telerehabilitation and virtual reality (VR) technology. The research group has partnered with the department of neurology (Claudio Bassetti) to establish the NeuroTec Loft which is an instrumented apartment within the sitem-insel to monitor human behavior and how neurological disorders influence daily life.

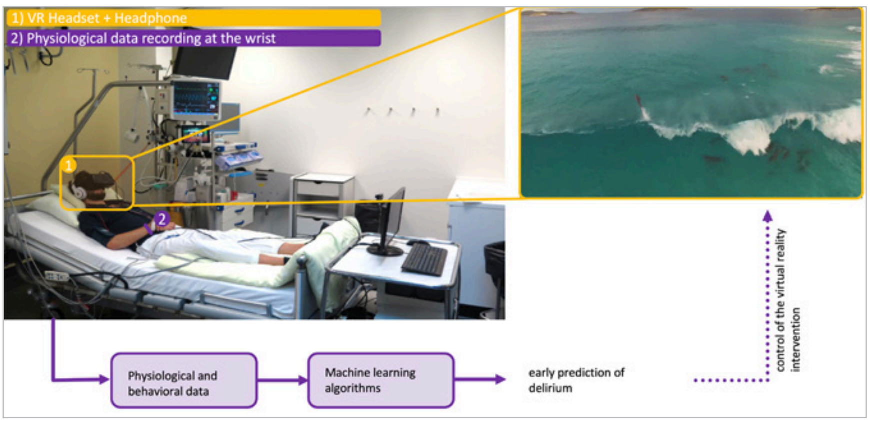


**Fig. 1:** Setup in an intensive care unit with physiological data recording and behavioural data recording (e.g. movement) for the early prediction of delirium. Once detected, a VR based cognitive stimulation will be used to comfort the patient and to reduce delirium.

### Virtual Reality Stimulation for Critically Ill Patients to Reduce Delirium

The aim of intensive care medicine is to treat the life-threatening conditions of critically ill patients, giving them the opportunity to continue their lives post-discharge. Unfortunately, the literature suggests that up to 50-75% of all critically ill patients experience short- and long- term cognitive impairment after a prolonged stay in the intensive care unit (ICU). It has been suggested that the cognitive impairment is a result of the noisy and stressful environment of the ICU. Therefore, one method of addressing this problem is coming up with solutions to help these critical care patients get some sensory reprieve. A promising new approach developed in our group is the use of virtual reality technology within the ICU. Virtual reality (VR) nature stimulation via a Head-Mounted-Display (HMD) moves the patient away from the ICU into a calming and pleasant environment (Fig. 1). Therefore, VR is a promising unexplored avenue to improve attentional-cognitive functions and to reduce chronic stress during an ICU stay.

Following a series of studies conducted by our group we can conclude that firstly, VR stimulation by using a HDM is safe to use within the intensive care unit, did not evoke any negative side effects, and was highly accepted by clinicians and patients. Moreover, the findings provided evidence that VR nature stimulation comforts critically ill patients. Secondly,

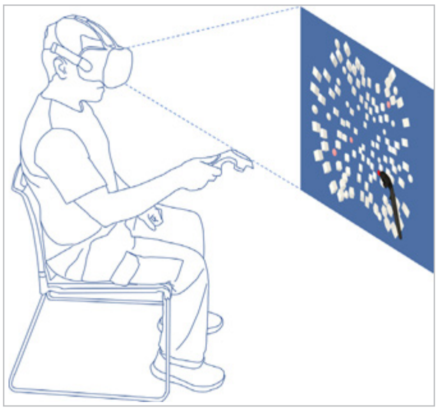

**Fig. 2:** Stroke patient using a head mounted virtual reality display for rehabilitation of visual neglect.

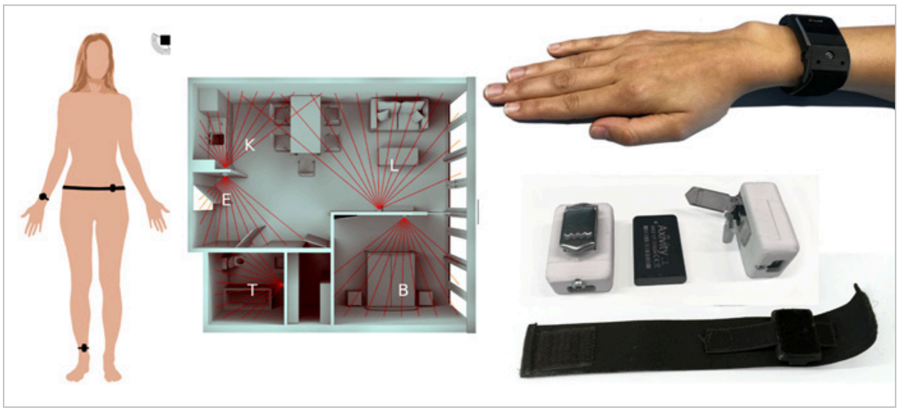


**Fig. 3:** Sensors placed in the home of parkinson's patients to regognize motor and non-motorw symptoms.

it was found that the VR stimulation had a relaxing effect in the participants, as shown in vital markers of physical stress. Therefore, this work highlighted the great potential to prevent and reduce cognitive impairment in critically ill patients. Future studies will continue to build on this work with a focus targeted towards delirium within the intensive care unit.

## Virtual Reality Training for Brain Injured Patients

Cognitive impairments are a frequent problem after right-hemispheric stroke. One kind of cognitive impairment is an attention disorder called spatial neglect, where subjects cannot detect or respond properly to visual stimuli coming from the contralesional side. Neglect results in a reduction in quality of life and performance in activities of daily living. In our work, we aim to develop a tool to assess and rehabilitate this neglect using virtual reality. The main idea for the rehabilitation is to guide the patients' attention back to the contralesional side using different kinds of stimuli. In a first pilot study, with a simple visual search task, a high usability and acceptance of the virtual reality system could been shown in stroke patients, as well as in young and elderly healthy participants (Fig 2). A second study in healthy subjects revealed that the combination of auditory and tactile cues is the best combination (compared to audio or tactile only) to guide the attention towards a certain target.

Another ongoing study regarding assessment is investigating the behavior of neglect patients in a dynamic search task compared to healthy participants, and its correlation with the impairments in daily living due to their neglect.

## Tele-monitoring for Neurodegenerative Disease – The Advancement of Pervasive Computing

Due to the advancements in technology in the past few years, pervasive technology has become more widely available. Small wearable sensors, such as smart watches, are able to track movement reliably through accelerometers and gyroscopes over extended periods of time, without disturbing the wearer. With the addition of photophletysmogram (PPG) sensors, heartbeat and all derivative values can be monitored without the need for a full ECG. Sensors placed on or around objects, such as ferro-electret mats for under the mattress, are able to monitor heart rate and breathing patterns during the night without the need for any contact sensors. And finally, ambient sensors placed permanently, yet unobtrusively in participants homes, can track location and behavioural patterns throughout the home. Technology used for this include passive infrared (PIR) sensors, magnetic door sensors, and radar-technology based sensors.

Unobtrusive, but continuous monitoring of health-related indicators has been shown to be both feasible as well as accepted by the target groups. Those groups include both the oldest old as well as patients with neurodegenerative diseases, such as Parkinson's disease. In a study with people with Parkinson's disease (PD), the acceptance and adherence to a set of ambient and wearable sensors was tested with very good feedback (Fig 3). The usage of wearable sensors is especially crucial for the monitoring of PD patients, as both the symptoms and the disease progression are highly individual in their manifestations. It's imperative for the treating doctors and therapists to adjust medication and therapy to the needs of the patients.

Current state of the art are self-reporting methods. Their accuracy is often limited by the patients recall bias, when filling in. Wearable sensors, worn on the movement-dominant body parts are able to track typical PD related motor symptoms, such as slowness of movement, tremors, rigidity or the typical medication side effect – dyskinesias. Through a series of signal processing based feature extractions and machine learning based symptom classification, we are working towards a more reliable symptom tracking system.

This not only helps the doctors and therapists, but also increases quality of life for the patients, by removing the burden of keeping a symptom diary.

### Selected Publications

1. Gerber SM, Jeitziner MM, Knobel SEJ, Mosimann UP, Müri RM, Jakob SM, Nef T. "Perception and Performance on a Virtual Reality Cognitive Stimulation for Use in the Intensive Care Unit: A Non-randomized Trial in Critically Ill Patients." Front Med (Lausanne). 2019 Dec 10;6:287.
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# Hearing Research Laboratory

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## Research Profile

The Hearing Research Laboratory is a clinically-oriented research team that integrates the expertise of engineers, otologists, audiologists and physicists. Our goal is to develop novel medical devices and technology to help hearing-impaired people and to support clinicians in the diagnosis and treatment of inner ear disorders.

The spectrum of research activities of our group includes psychoacoustic experiments, anatomical and electrophysiological studies, the design and implementation of medical software and devices, and the performance of observational and clinical studies. To promote sustainable research progress, our team members actively collaborate with leading medical, academic and industrial partners in hearing research.

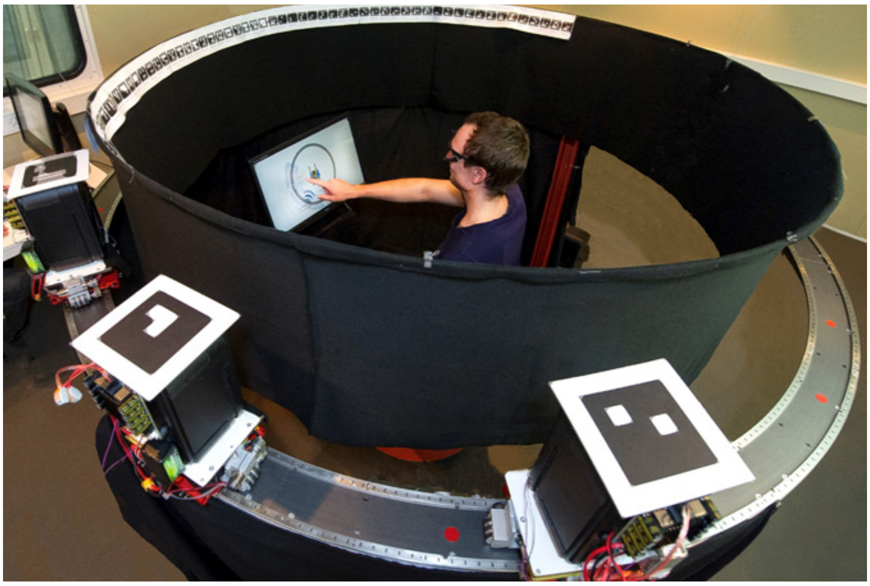

**Fig. 1.** Although sound localization is of great importance in everyday life, today's routine audiological tests provide only a limited interpretation of treatment outcomes regarding spatial hearing performance. Our robotic sound field audiometry setup enables realistic dynamic sound localization, discrimination and tracking experiments to evaluate and improve the outcome of patients treated with hearing aids and implants.

### Experimental Audiology

Sound field audiometry, in which acoustic test stimuli are delivered through loudspeakers instead of earphones, is an integral component in the evaluation of the clinical hearing rehabilitation progress. The assessment of hearing thresholds, speech understanding in quiet and noise, and sound localization abilities provides essential outcome measures that can be directly linked to the quality of life of patients that were treated with hearing implants.

In the area of experimental audiology, we are focussing on clinical studies aiming to contribute to the scientific communty and clinical practitioners alike. To enable a more lifelike but reproducible hearing assessment, our group develops methods to reproduce realistic sound environments and dynamic test situations that are required to capture the benefit of modern hearing implant technology (Fig. 1).

### Tinnitus Modelling and Diagnostics

Tinnitus is a phantom sound that affects the quality of life of millions of people around the world. Most tinnitus cases are associated with abnormal brain activity, however, it remains unclear how these activities relate to the perceived phantom sound.

In this project, we aim to develop an algorithm to identify tinnitus-associated

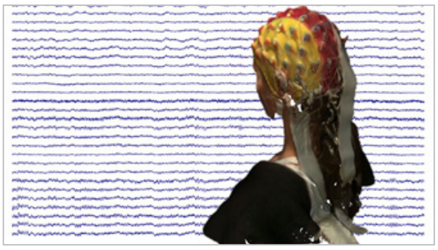

**Fig. 2.** Residual inhibition (RI) is a temporary quieting of tinnitus that can be caused by acoustic stimulation. In our current study, tinnitus suppression could be observed in about 75% of our study participants. We aim to use this phenomenon to detect tinnitus markers in brain activity.

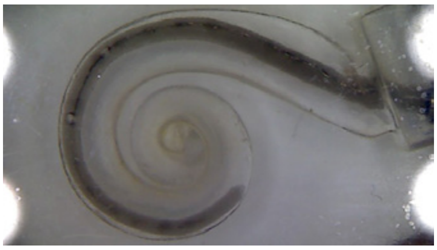

**Fig. 3.** In cochlear implantation, the optimal alignment of the electrode array insertion trajectory with respect to the cochlea is crucial for a minimally invasive outcome. This figure shows the robot-assisted insertion of an electrode array in a high-resolution model of a human cochlea.

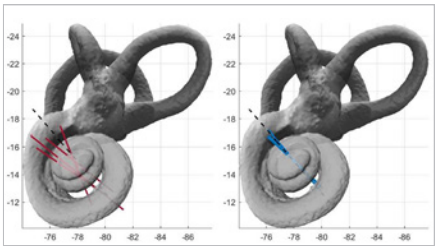

**Fig. 4.** The identification of the cochlear modiolar axis in clinical CT images is challenging, even for experts. The axes manually found by experts show large discrepancies (left), while our automatic detection algorithm yields reproducible results (right).

neural oscillations in electroencephalographic data. The objective assessment can be used for more specific diagnostics and can enable patient-tailored stimulation by hearing devices for alleviating tinnitus symptoms.

In addition, we develop a generative framework to predict changes in tinnitus intensity after acoustic stimulation (residual inhibition, RI and residual excitation, RE) using behavioral data of tinnitus subjects (Fig. 2). We model tinnitus perception based on the Bayesian brain approach, which characterizes tinnitus perception as a precision-weighted integration of sensory information and predictions (priors).

### Cochlear Implants

Cochlear implantation is a microsurgical procedure that demands a high level of surgical skills and experience due to the complex and variable anatomy of the human temporal bone.

To enable improved surgical aproaches, we are developing and evaluating software tools that empower surgeons to treat patients under consideration of their individual anatomy. As an example, preoperatively taken computed tomography images can be utilized to extract and reconstruct anatomical structures as three-dimensional models. The surgeon can use the virtual models to plan the surgical access and to optimize the electrode array insertion vector. Suitable lengths for the implanted electrode array can be selected depending on the cochlear size and the patient's residual hearing.

After implantation, our software tools can be applied to reproducibly assess the surgical outcome in postoperative image data sets. Moreover, suggestions for stimulus parameters for the first fitting of the implant can be derived.

To improve the surgical procedure and to assess the health status of the cochlea during and after implantation, we are developing new measurement algorithms based on non-invasive and readily available intraoperative telemetry recordings. These can be used in advanced insertion devices that derive the position of the implant from the electrical impedances of the intracochlear electrodes and the reactions of the auditory nerve, helping the surgeon to continously monitor the process (Fig. 3).

### Cochlear Morphology Analysis

We develop methods to objectively characterize the shape of the cochlea based on the natural growth in the embryo. Our approach models the morphogenetic process by a kinematic spiral motion, comparable to the formation of sea shells. The cochlea can then be viewed as a kinematic surface, i.e., a surface that was formed by tracing a generator curve along a kinematic center line. This relation can be used to extract the growth parameters that form a given three-dimensional surface model of the cochlea. Our method can be used to improve surgical planning approaches and to refine the postoperative fitting for cochlear implant patients (Fig. 4).

### Temporal Bone Laboratory

The activities of the Hearing Research Laboratory include projects that require research on human specimens, such as experimental tests with new implant prototypes, evaluation of implantation technology and surgical training.

For these purposes, a fully equipped facility with several work spaces for anatomical dissections and microsurgical procedures is operated in collaboration with the Institute of Anatomy of the University of Bern. Our laboratory is a key facility for experimental and translational research and plays an important role in the transfer of novel technology into clinical applications. The proximity to the Bern University Hospital (Inselspital) and the Translational Imaging Center at the SITEM enables for accompanying radiological examinations with state of the art imaging devices.

Current research topics focus on the improvement of cochlear implantat electrode array insertion procedures, surgical endoscopic accesses to the middle ear and lateral skull base, and anatomical studies of the middle and inner ear. In addition, the laboratory is used for surgical training and anatomical teaching, with one-to-one instructions by our experienced faculty members.

#### Selected Publications

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# Chair for Image-Guided Therapy

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Raffael Gfeller
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Milica Bulatovic
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Raluca Sandu
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Teo Eterovic
Oana Kofmehl
Thomas Winklehner

## Research Profile

Simulation and modelling, imaging and sensing, visualisation and robotics have reached sufficient quality and resilience for use in medical technologies that can be introduced into clinical care. Research in the Image Guided Therapy (IGT) investigates these technologies for applications that could replace the human operator in medical procedures. By considering the optimal, clinical outcome, it is conceivable for example that a partially autonomous technology could take over tasks better performed by "machines". Translational aims for projects mean close relationships with clinical co-investigators at the Inselspital and other National and International partners through clinical and academic collaborations.

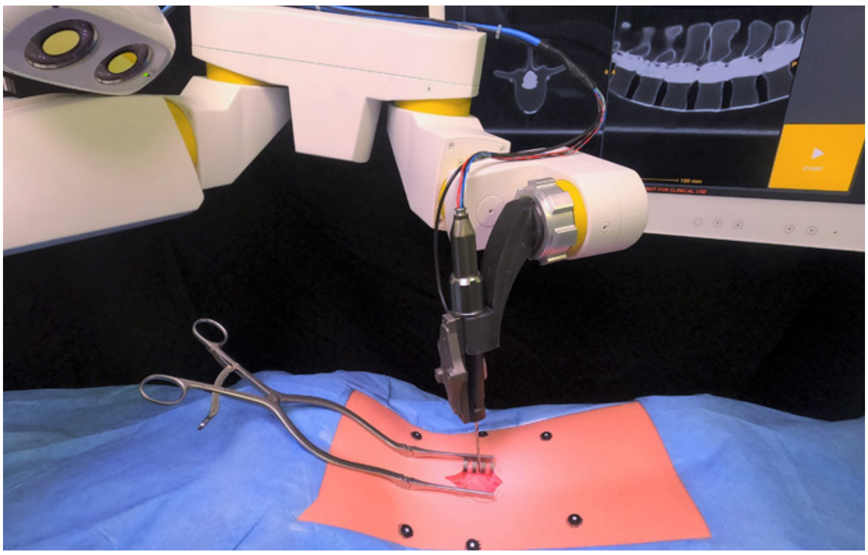

**Fig. 1:** Prototype of robotic system for pedicle screw placement.

**Robotic Spine Surgery**
*(Bridge Discovery 176498, Innosuisse 29936.1 IP-ENG)*

Spinal instabilities from degenerative spine diseases are increasing in an aging society. To treat it, surgeons implant pedicle screws to fuse adjacent vertebra. Placement of pedicle screws is challenging due to demanding needs in accuracy and high anatomical variability, resulting in up to 15% mal-positioned screws. The aim is to develop a robot based technology that will allow surgeons to place every single pedicle screw accurately.

In collaboration with the Department of Neurosurgery of the Inselspital, a workflow has been developed. A software allowing for intuitive intra-operative planning of pedicle screw positions in computed tomography images and robotic drilling of the planned borehole was developed.

Image-guidance alone does not provide the required security, hence additional sensor modalities need to be integrated. Drill bits with integrated electrodes have been produced together with different collaborators. Pose estimation based on tissue impedance and correlating force and torque measurements with bone density is hypothesized to assure the robot is correctly aligned with the planned trajectory.

→

**Fig. 2:** Image-guidance during surgical removal of a tumor from the lateral skull base. Additional to the endoscope image (right screen), the location of the instrument is displayed in CT images (left screen).

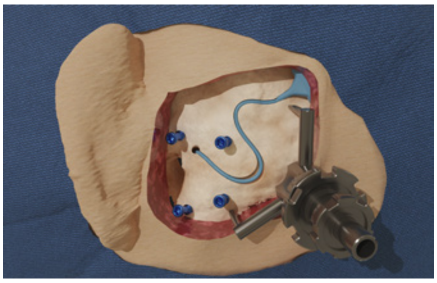

**Fig. 3:** A model of a patient-specific plannin for robotic lead channel milling. The channel stores the excessive lead under the surface of the mastoid bone. The fiducial screws and the tripod are used for the image-guidance.

**Fig. 4:** The surgeon is using the navigated instruments to locate and remove tumors in the liver. With the 3D glasses the surgeon gets a depth perception from the virtual anatomical structures and the real-time endoscopic image.

All components were assembled into a functional prototype enabling spinal robotic surgery. After validation of the concepts and workflow and verification of the accuracy, the technology will be validated in a clinical trial.

### Microsurgery in the Lateral Skull Base

*(SNSF 176007)*

The stapes is the smallest bone of the human body with geometric extensions of its structures in the micrometer range. It is located in the lateral skull base. Due to the geometric scale of anatomical structures in the lateral skull base, surgery there requires working at the limits of human faculties and dexterity. Image guidance and surgical robot systems can perform tasks beyond the limits of human perception, dexterity and scale making them inherently suitable for use in microsurgical procedure. Our group is interested in the advancement and clinical introduction of suitable guidance and robotic technology. More specifically, during the last several years, the group developed image-guidance technology in collaboration with CAScination allowing surgical instrument localization relative to anatomy with micrometer accuracy. To date clinical trial in collaboration with the ENT surgery team of the Inselspital is ongoing to validate the accuracy of the developed platform (Fig. 2).

*Robotic cochlear implantation*

In recent years, the procedure of robot-assisted cochlear implantation developed by our group has been further developed and translated into a medical device through CAScination with the HEARO system. Our group is now continuing research on other aspects of robot-assisted cochlear implantation, such as the embedding of the implant in the temporal bone and access to the inner ear. In order to reduce the risk of electrical failure of the implant device and electrode while improving reproducibility, we propose a new clinical workflow for implant embedding. This workflow comprises intraoperative planning of a safe electrode channel and the implementation of this planning by robotic milling. Research on inner ear access focuses on optimizing cochlear access either by cochleostomy, extended round window or round window approach to achieve atraumatic electrode insertion, better hearing retention and CI results.

### Fighting Liver Cancer

*(H2020 MSCA-ITN 722068 & Innosuisse 37855.1 IP-LS)*

*Quantitative methods for assessment of ablation*

In image-guided percutaneous ablation treatments of liver tumors, a successful treatment is defined as destroying the tumor and 5-10 mm tissue margin around it through coagulation necrosis. Currently, the treated tumor site is visually evaluated by a radiologist, making the treatment potentially subjective and qualitative. As part of the Horizon 2020 Innovative Training Network "HiPerNav", a study is being carried out to evaluate quantitative techniques for improving image-guided ablation treatments through automatic image segmentation.

*Thermal ablation with configurable shapes*

Thermal ablation typically delivers ellipsoidal or spherical shaped ablation volumes varying according to the device time and power. Consequently, irregularly shaped tumors can only be ablated by delivering volumes significantly larger than the target itself or by using of several needle applicators. In this Innosuisse funded project, the possibility of creating ablation volumes with configurable shapes through synchronous modulation of ablation power and applicator position using a surgical robot is currently investigated.

*Ultrasound-guided liver resections*

In non-anatomical liver resections only the tumor and a safety margin of 10 mm are resected. Compared to anatomical resections, they tend to spare more healthy liver tissue, which increases the possibility of retreating. However, it is more challenging to keep a negative resection margin since anatomical landmarks cannot be used for intra-operative guidance. As part of the Horizon 2020 Innovative Training Network "HiPerNav", a new navigation system based on ultrasound was developed and is currently evaluated in a clinical trial at Inselspital Bern.

**Selected Publications**


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3. Paolucci, I.; Sandu, R.; Sahli, L.; Prevost, G.; Storni, F.; Candinas, D.; Weber, S.; Lachenmayer, A.(2020). Ultrasound Based Planning and Navigation for Non-Anatomical Liver Resections – An Ex-Vivo Study. IEEE Open Journal of Engineering in Medicine and Biology
4. Hermann, J; Ledergerber, J; Wigger, M; Schneider, D; Müller, F; Weber, S; O'Toole Bom Braga, G (2019). Towards robotic embedding of cochlear implants in the temporal bone. CURAC 2019, Reutlingen **CURAC 2nd best paper award**
5. Anso J.; Dür C.; Apelt M.; Venail F.; ScheideggerO.; Seidel K.; Rohrbach H.; Forterre F.; Dettmer S.; Zlobec, I; Weber, K; Matulic, M; Zoka-Assadi, M; Huth, M; Caversaccio, M; Weber, S (2019). Prospective Validation of Facial Nerve Monitoring to Prevent Nerve Damage During Robotic Drilling. Frontiers in Surgery

# Motor Learning and Neurorehabilitation

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## Research Profile

At the interdisciplinary Motor Learning and Neurorehabilitation Laboratory, we aim to gain a better understanding of the underlying mechanisms associated with the acquisition of novel motor skills in order to develop innovative technology to improve the rehabilitation of neurological patients. Our research focuses on human-machine interfaces and biological learning, and, specifically, on the use of robotic assistance to aid people in learning motor tasks and rehabilitate after neurologic injuries. We complement the research on robotics with the use of immersive virtual reality (VR) and augmented reality (AR) to enhance patients' motivation and reduce their cognitive load during training.

**Fig. 1:** Neural correlates of motor learning. Participants sat on a height-regulated chair wearing the EEG cap while controlling a virtual boat, using a joystick, to sail on virtual waves displayed on the monitor. Photo: Adrian Moser for ARTORG Center

### Neural Correlates of Motor Learning
*(SNF grant PP00P2_163800)*

Understanding the underlying mechanisms of motor learning is crucial to improve neurorehabilitation. In an experiment with 36 healthy participants, we investigated the influence of explicitness of task instructions on participants' cognitive engagement during motor learning of a virtual sailing task (Fig. 1) using Electroencephalography (EEG). Different task instructions were provided (from implicit –i.e., letting participants sail freely – to explicit –i.e., instructing how to correctly align the boat – and explicit-implicit instructions –i.e., implicitly instructing to move using visual cues).

Training with explicit knowledge about the task rules and with visual cues implicitly enforcing these rules supports motor learning. Furthermore, training parameters such as the explicitness of task instructions modulate the cognitive engagement of participants and may be an important factor to consider in motor neurorehabilitation.

### Novel Robotic Training Strategies for Neurorehabilitation
*(SNF grant PP00P2_163800)*

A main challenge in robotic neurorehabilitation is to understand how robots should interact with patients to optimize motor learning. The active exploration of new motor tasks is crucial to boost motor learning. We propose that Model Predictive Controllers (MPC) can assist patients during training without enforcing a fixed trajectory.

We designed novel MPCs to support training of a rich dynamic task (a

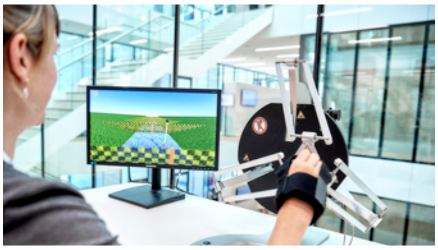

**Fig. 2:** Novel robotic training strategies. The task to be learned consists of swinging a virtual pendulum to hit incoming targets with a delta robot (Force Dimension, Switzerland). Photo: Adrian Moser for ARTORG Center.

**Fig. 3:** Exoskeletons for sensorimotor training. The experimental task consisted of inverting a pendulum and keeping it inverted, using ARMin exoskeleton as a visuo-haptic interface.

**Fig. 4:** Immersive VR to enhance neurorehabilitation. Virtual environment showing the avatar and three fruit types. The rehabilitation device is employed in a study with brain-injured patients.

pendulum task) using a delta robot (Fig. 2). We compared the effects of training with MPCs and a conventional haptic guidance controller (HG) on motor learning in a study with 40 healthy participants. Training with MPCs did not reduce movement variability during training, as opposed to HG. However, differences across controllers did not result in differences in motor learning.

**Exoskeletons for Sensorimotor Training**
*(Promobilia Stiftelsen 18155)*

Research on neurorehabilitation has emphasized that patient's effort and somatosensory information during physical training are crucial to provoke brain plasticity. To provide realistic sensory information while supporting patients, we employed novel controllers to achieve high transparency and fine haptic capabilities on the exoskeleton ARMin (Fig. 3), together with arm weight support.

The effect of haptic rendering and its interaction with arm weight support were evaluated with six healthy participants. The task consisted of inverting a virtual pendulum (Fig. 3). We found that haptic rendering of the pendulum dynamics affects how participants move. The weight support enhanced task performance and reduced participants' effort, while it did not affect their movements. Haptic rendering, together with weight support, are potential interventions to enhance neurorehabilitation due to the added somatosensory information.

**Immersive Virtual Reality to Enhance Neurorehabilitation**
*(SNF grant PP00P2_163800 and B.Braun)*

There is an increasing interest in using virtual reality (VR) in robotic neurorehabilitation. However, the use of conventional VR displays (i.e., computer screens), implies several transformations between the real movements in 3D and their 2D virtual representations that might negatively impact the rehabilitation interventions.

In a study with 20 healthy participants, we compared the impact on movement quality and cognitive load of novel vs. standard visualization technologies (Fig. 4): i) Immersive VR (IVR) head-mounted display (HMD), ii) Augmented reality (AR) HMD, and iii) Computer screen. The movement quality improved in IVR, compared to the computer screen. A trend to higher movement quality in AR than Screen but worse than IVR, was observed. No difference in the cognitive load was found between modalities. Our results provide evidence that VR interventions using HMDs are more suited for robotic neurorehabilitation than a computer screen.

**Body Ownership over an Avatar Enhances Motor Performance**
*(NCCR Robotics)*

In immersive virtual environments, the own body can be represented by an avatar. This may induce the sense of body ownership over the virtual limbs. Importantly, body ownership and the motor system share neural correlates. Yet, evidence on the functionality of this coupling is still missing.

We run an experiment to investigate the effect of body ownership on motor performance. Fifty healthy participants performed a decision-making (pressing a button as fast as possible) and a motor task (following a path). To modulate the level of body ownership, we provided congruent vs incongruent visuo-tactile stimulation. Unimodal conditions (i.e., only visual or tactile) controlled for congruency effects. We found that an increase in body ownership is associated with faster responses and better task accuracy. Enforcing body ownership may be beneficial for (re)learning motor tasks, especially if the received information during training is congruent.

**Novel Clinical-Driven Robotic Device for Sensorimotor Training**
*(Innosuisse 32213.1 IP-ICT)*

An Innosuisse project started this year that aims to design a novel clinical-driven robotic device based on the advanced technology of Force Dimension haptic devices (Fig. 2), to be employed in arm neurorehabilitation of brain-injured patients. The new design will target the specific needs of patients and clinicians undergoing sensorimotor training.

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# Musculoskeletal Biomechanics

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## Research Profile

Motivated by prevention, diagnosis and treatment of degenerative diseases the research of the musculoskeletal biomechanics group focuses on multi-scale structure-function relationships of bone from the extracellular matrix to the organ level. Combined theoretical, experimental, and numerical approaches are applied to model, validate and simulate the mechanical behaviour of bone tissue and bone-implant systems in the course of growth, aging, disease and treatment.

The group provides also biomechanical testing services and cooperates with local, national as well as international partners from academia, hospitals and industry to help reduce the burden of bone diseases and failure of the bone-implant interface.

**Fig. 1:** The new biomechanics laboratory on a sunny day. The infrastructure includes mainly a climatized tissue preparation room, microcomputed tomography, biaxial servo-hydraulic testing, nanoindentation and spinal segment testing.

### Compressive Properties of OI Bone ECM

*(SNF grant #165510 with EMPA & MGU)*

Osteogenesis imperfecta (OI) is a genetic bone disorder leading to an increase in bone fragility, but the origin of the decreased bone toughness remains unknown. Using focused ion beam (FIB), micro-pillars (d=5µm, h=10µm) were milled in healthy controls and three different types of OI bone biopsies. Each micro-pillar was tested quasi-statically in compression with a flat punch indenter, revealing its stress-strain behavior (Fig. 2). Composition of the bone extracellular matrix (ECM) was then measured at each micro-pillar site with Raman spectroscopy.

Surprisingly, we found that the strength of OI bone is not inferior compared to healthy bone at the ECM level and is mainly determined by the degree of mineralization.

### Micro-meso Scale Transition of Bone Strength

*(SNF grant #165510 with EMPA)*

Compression and tension experiments were realized on micropillars, respectively micro-tensile ovine bone samples along both axial and transverse collagen fibril orientation with a quasi-static strain rate. A size effect with an increase in strength by a factor of 2.5 compared to macroscopic data was observed. In contrast to compression that exhibited plasticity

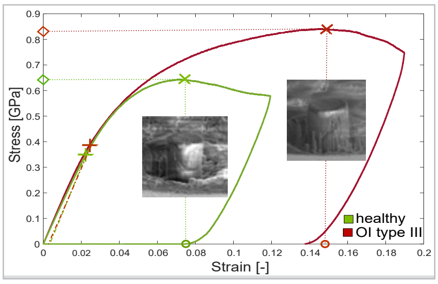


**Fig. 2:** Stress-strain behavior from micro-pillar compression test of representative healthy/control (green) and OI type III (red) samples with SEM images of the failed state.

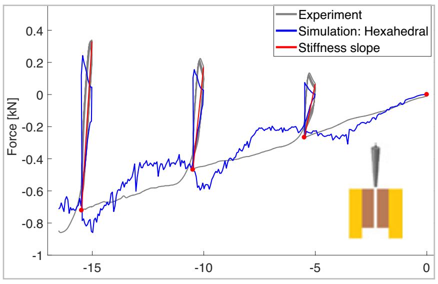


**Fig. 3:** Press-fit experiment inserting a conical implant in trabecular bone. Experimental and computational force-displacement curves with measurement of stiffness.

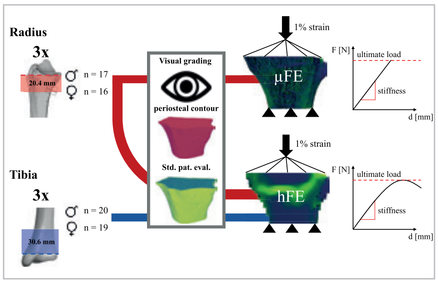


**Fig. 4:** Design of the reproducibility study of two kinds of finite element (FE) analyses estimating radius or tibia strength from multiple stack HR-pQCT scanning protocols.

followed by shear failure at higher strains, tension produced brittle failure associated with rough fracture surfaces. A composite failure model was proposed to explain the dependence with collagen fibril orientation. These experiments combined with SEM and TEM imaging deliver unique insight in the failure mechanisms of the bone extracellular matrix along the critical loading modes.

### Assessment of Bone-implant Stability Using Explicit Finite Element Analysis
*(with RMS)*

Non-linear finite element analysis (FEA) of the bone-implant interface is attractive to assess primary stability of a dental or orthopaedic implant. In the frame of a master thesis, titanium cones were press-fit into trabecular bovine bone cylinders using a quasi-static, displacement-driven cyclic loading protocol. An explicit, homogenized FEA of this experiment was conducted using an adapted elasto-plastic constitutive model with damage for bone and a unilateral contact law with friction for the bone-implant interface.

The FE model was able to predict the force and bone damage produced by the press-fit of the cone and the resulting stiffness of the bone-implant system (Fig. 3). The developed explicit FE methodology appears to be very promising for optimisation of dental and orthopaedic implants in terms of stiffness, strength, micromotions and potential loosening.

### HR-pQCT-Based Bone Strength Assessment by Homogenized FEA
*(with IS)*

In vivo assessment of bone strength estimated by finite element analysis (FEA) based on high-resolution peripheral quantitative computed tomography (HR-pQCT) becomes more important for identifying people at high risk of fractures. A recently established alternative finite element approach using homogenized constitutive models for trabecular bone, is computationally more efficient than traditional approaches and attractive for clinical use.

Current projects involve more than one-hundred patients, defines clinical in vivo precision of the methodology and provides a normative database for radius and tibia strength in the young healthy Swiss population (Fig. 4).

### AFFIRM-CT
*(SNF grant #183584 with HUG & IS)*

A Sinergia project started this year with the aim to develop an integrative risk calculator for hip fractures based on recycled CT images, DXA scans and further clinical variables. The MSB group will handle all biomedical engineering aspects of the project and contribute to the clinical study in Bern. The engineering tasks include CT calibration, 2D-3D reconstruction of DXA images, image processing, modelling of a fall on the hip, and implementation of an improved personalised FE model to compute femoral strength. However, the initial phase of the project focusses on preparation of the clinical study involving data management, calibration of the CT scanners, selection of activity sensors and testing of a stiffness measurement device for the soft tissues recovering the hip. The data collected during the clinical study will be used for validation of the fracture risk calculator.

### Biomechanical Testing

The move of the biomechanics laboratory in the sitem-insel building next to the university hospital was the major achievement of the year. With the financial support of the university, the servo-hydraulic testing system, microCT, nanoindenter and spine tester were successfully moved and reinstalled after months of planning. The laboratory is well-designed, climatized, bright (Fig. 1), and well-situated next to our clinical partners. Several experiments were conducted before or after the move including microCT scanning, press-fit of conical implants, calibration of a 6 DOF robot, nanoindentation of rabbit bone, mechanical testing of bioresorbable mandibular, development of a new stabilisation method of the atlantoaxial joint of canine spines, and evaluation of the primary stability of dental implant *(s)*.

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# Organs-on-Chip Technologies

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## Research Profile

The Organs-on-Chip Technologies Group focuses on the development of advanced in vitro models, in particular of the lung. We work at the interface of cell biology, microtechnology, microfluidics and lung micromechanics. Microstructured channels and wells are used to control the bio-physical cellular microenvironment of healthy and diseased tissues created in those systems. These so-called lung-on-chips are aimed at better understanding the pathophysiology of different lung diseases (lung fibrosis, lung cancer, emphysema, COVID-19, ...), at developing new drugs and at being implemented for precision medicine applications, using the patient's own cells in order to individualize and optimize their therapy.

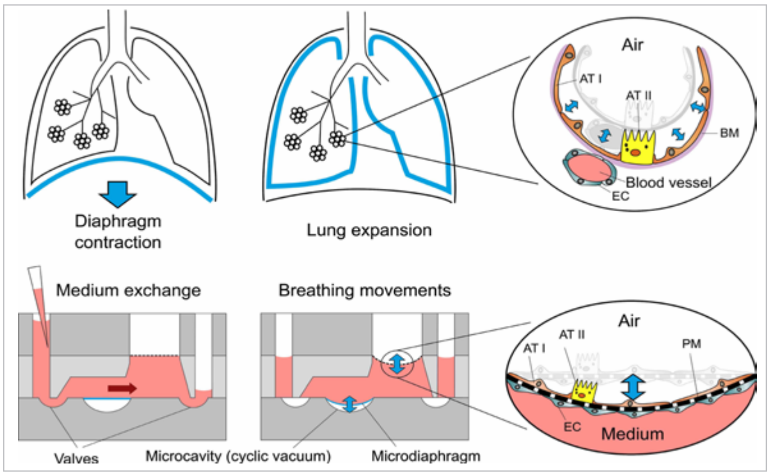


**Fig. 1:** Concept of the lung-on-chip: Top: in vivo, the lung expands following the contraction of the diaphragm, a movement that stretches the alveoli (right). The alveolar barrier consists among others of alveolar epithelial cells (AT I and AT II) and of endothelial cells (EC) that are supported by the basal membrane (BM). Bottom: schematic cross-sections of the lung-on-chip in two operation modes: the breathing and the medium exchange modes.

**Breathing Lung-on-chip**
*(Innosuisse grant # 27813.1; EU Eurostars Aim4Doc, both with AlveoliX)*

The complexity of the lung can be illustrated by its delicate tree-like architecture that ends with the alveolar sacs, where the gas exchange takes place. Oxygen and carbon dioxide diffuse through an extremely thin alveolar barrier. This barrier is mainly constituted by alveolar epithelial cells, capillary endothelial cells and of the basement membrane. This whole environment is subjected to the cyclic, breathing movements induced by the diaphragm, the main respiratory muscle. We developed an advanced in vitro model of the lung alveoli, called "lung-on-chip", which mimics the human lung alveolar barrier. In that system, the barrier is made of an ultra-thin, flexible polymeric membrane, on which lung cells are cultured on opposite sides. The polydimethylsiloxane (PDMS) membrane is porous (3µm pores), which enables the lung epithelial cells – top side of the membrane – and lung endothelial cells – bottom side, in contact with blood analogue – to communicate. This alveolar barrier is cyclically stretched in three dimensions as in the lung. The actuation of the barrier is created by a microdiaphragm (Fig. 1) that resembles the in vivo diaphragm. In addition to mimicking the in vivo situation, the lung-on-chip was designed to be robust and easy to use. A multi-well plate format was chosen, the standard format used in the biotechnology industry (Fig. 2). This lung-on-chip is one of the two systems worldwide able to reproduce the breathing motions of the alveolar barrier. The toxicity of aerosolised nanoparticles is currently assessed with this system.

### Second-generation Lung-on-chip

*(SNF grant # 205320_185365; EU Marie Skłodowska-Curie No. 812954)*

Although very innovative, the ultra-thin PDMS membrane used in the first-generation lung-on-chip is an artificial material, whose intrinsic nature, properties and size differ from the extracellular matrix (ECM) of the distal airways. To circumvent these drawbacks, we developed a second-generation lung-on-chip with an array of in vivo-like sized alveoli and a stretchable biological membrane. The membrane is made of two proteins found in the lung ECM: collagen and elastin. Its fabrication process is very simple. A drop of collagen-elastin solution is pipetted on an hexagonal gold mesh on which it spreads by surface contact forces. The solution slowly evaporates and creates a membrane of only a few micrometers thickness (Fig. 3). In addition, the hexagon size (about 260µm) is similar to that of in vivo alveoli. The gold mesh enables thus to mimic an array of tiny stretchable alveoli with physiological dimensions. The air-blood barrier is then reconstituted by culturing human primary lung alveolar epithelial cells from patients co-cultured with primary lung endothelial cells. Typical markers of lung alveolar epithelial cells are expressed in the model (Fig. 4). This advanced lung alveolar model reproduces some key features of the lung alveolar environment in terms of composition, alveolar size, mechanical forces and biological functions. Based on this system, an acute lung injury model integrating immune cells is currently developed.

### Microvasculature-on-chip

*(SNF grant # 205320_185365)*

Endothelial cells, in particular endothelial microvascular cells, present in the lung parenchyma, play an important role in inflammation and the initiation of fibrogenic events in lung pathologies, such as in idiopathic pulmonary fibrosis. Nevertheless, the clear mechanism on how and if these mechanisms are related is still unknown and requires novel in vitro models allowing reproduction of the microvasculature of the lung. In order to model the microvasculature of the lung, new in vitro models aiming at the creation of a perfusable microvasculature (Fig. 5) that mimics the lung capillary microenvironment were developed. Endothelial cells and pericytes or fibroblasts in fibrin gel are seeded in a microfluidic compartment, where they self-assemble and create stable and perfusable microvessels with diameter typically ranging from 20 to 200µm and length between 100µm to 2mm. The signaling of pericytes or fibroblasts located outside of this compartment enables to open the vascular lumens that can then be perfused. In addition, upon exposure to phenylephrine, a known vasoconstrictor, the vessels contract significantly as would have been expected in vivo. The models were further developed to investigate the effects of nintedanib, a drug used to treat idiopathic pulmonary fibrosis.

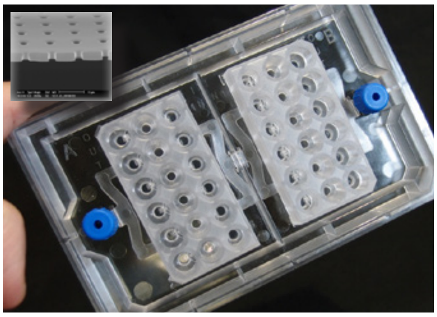

**Fig. 2:** Picture of a multi-well plate with 12 lung-on-chips separated in 2 inserts. Lung-on-chips are equipped with a 3µm-thin, porous and stretchable membrane (inset), on which cells are cultured. The system is actuated by an electro-pneumatic breather (not shown) via holes located at the bottom of the plate (developed in collaboration with AlveoliX AG).

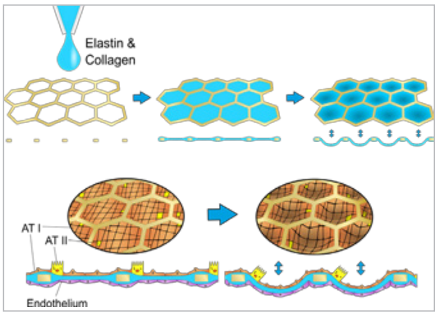


**Fig. 3:** Concept of the second-generation lung-on-chip: a drop of collagen and elastin is pipetted on a thin hexagonal gold grid. The stretchable membrane is formed by surface tension forces and evaporation. Zamprogno et al. BioRxiv, 2019.

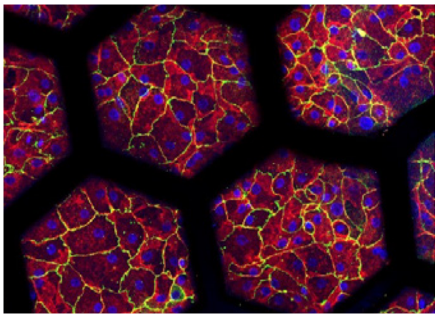

**Fig. 4:** Lung alveolar epithelial cells from patients cultured on the collagen-elastin membrane supported by an ultra-thin hexagonal gold grid (each hexagon is ca. 260µm wide). Zamprogno et al. BioRxiv, 2019.

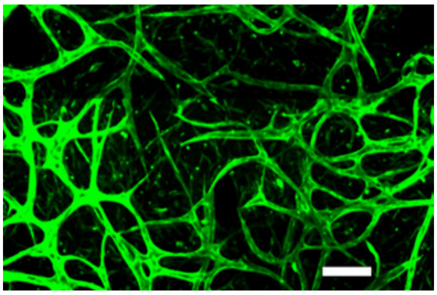

**Fig. 5:** Image of a functional microvasculature network made of self-assembled endothelial cells and lung fibroblasts on a chip. In green, the endothelial cell marker PECAM-1 (after 7 days in culture). Scale bar: 200µm. Zeinali et al. Angiogenesis, 2018.

**Selected Publications**


1. Guenat O.T., Geiser T., Berthiaume F., Clinically Relevant Tissue Scale Responses as New Readouts from Organs-on-a-Chip for Precision Medicine, Annu Rev Anal Chem (2020)
2. Zamprogno, P., Wüthrich S., Achenbach S., Stucki J., Hobi N., Schneider-Daum N., Lehr CM, Huwer H., Geiser T., Schmid R, Guenat OT., Second-generation lung-on-chip array with a stretchable biological membrane, BioRxiv (2019)
3. Felder M.*, Trueeb B.*, Stucki A.*, Borcard S., Stucki J., Schnyder B., Geiser T., Guenat O.T., Impaired Wound Healing of Alveolar Lung Epithelial Cells in a Breathing Lung-on-chip, Front. Bioeng. Biotechnol. (2019). (* shared first authorship)
4. Stucki J., Hobi N., Galimov A., Stucki A., Schneider-Daum N., Lehr C.L, Huwer H., Frick M., Funke, Chambour M., Geiser T., Guenat O.T., Medium throughput breathing human primary cell alveolus-on-chip model, Scientific Reports, 8, 14359, (2018)
5. Zeinali S., Bichsel C., Hobi N., Funke M., Marti T., Schmid R., Guenat O.T.*, Geiser T.*, Human Lung Microvasculature-on-chip: Efficacy of Nintedanib on in vitro Pulmonary Microvasculature Architecture, Angiogenesis, Jul. 2, (2018) (* shared senior authorship)

# Urogenital Engineering

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## Research Profile

The Urogenital Engineering (UGE) group focusses on the understanding and treatment of diseases of the urinary tract (UT), many of which have a significant impact on quality of life. The elderly, who signify an increasing percentage of the total population, are most commonly affected by bladder dysfunction and the treatment and management of chronic UT diseases have considerable impact on healthcare costs.

Using innovative engineering approaches, the UGE group is developing new methods to diagnose and treat diseases of the urinary tract with special focus on the underactive bladder, overactive bladder, incontinence and kidney/ureteral stones.

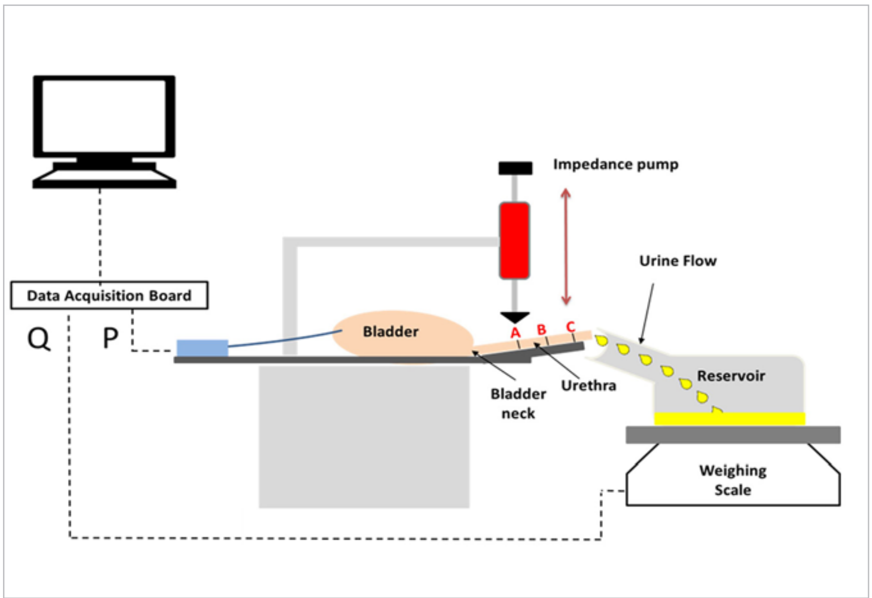


**Fig. 1:** Experimental setup for ex-vivo proof-of-concept-studies using porcine bladders and urethras. A linear motor was used as impedance pump to compress the urethra at three different sites: A, B, C and different frequencies.

### Our World's First Non-invasive Solution for Urinary Retention

*(Innosuisse grant 41236-1 with Bern University Hospital & EPFL)*

The UGE group is developing the world's first non-invasive solution for urinary retention. Patients suffering from urinary retention are unable to empty their bladder because of either a weak bladder muscle or/and a bladder outlet obstruction (e.g. enlarged prostate in men). The main complaints from these patients are: pain, urinary tract infections, continuous sleep disruption, the necessity to plan ahead for awareness of the location of toilets, impairment of social life, embarrassment and reduced self-esteem. To date, catheters are the most commonly used therapy for bladder emptying.

However, catheters are invasive and they cause very often urinary tract infections. Hence, a non-invasive solution for bladder emptying that does not lead to urinary tract infections is highly desirable. Our patent-pending technology is based on an innovative pumping principle (impedance pump), which generates urine flow by applying an external intermittent compression on the urethra (the outlet tube of the bladder) such that direct contact with urine is avoided. This solution can drastically reduce urinay tract infections. Proof-of-concept studies with porcine bladders have confirmed that this principle leads to complete bladder emptying (Figure 1). URODEA is a spin-off of the ARTORG Center and is focusing on bringing this technology to the patients.

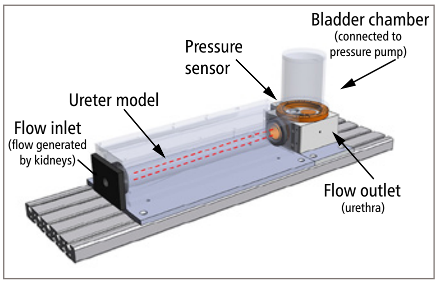


**Fig. 2:** CAD drawing of the in-vitro platform of the upper urinary tract. It allows fluid mechanical characterisation inside the ureter with/without ureteral stents by means of Particle Image Velocimetry.

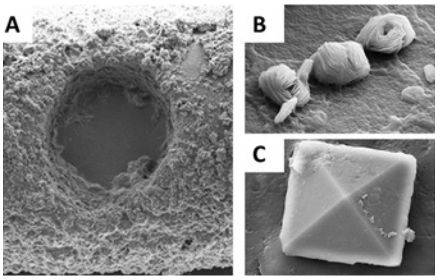


**Fig. 3:** Scanning Electron Microscopy (SEM) images of ureteral stents retrieved from patients: A) encrustation in the proximity of a side hole and associated B) calcium carbonate and C) calcium oxalate crystals.

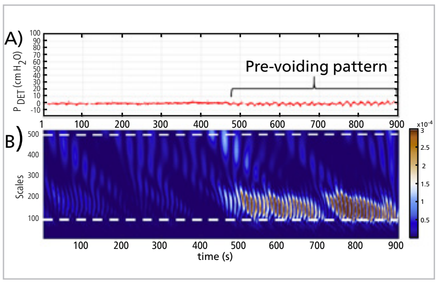


**Fig. 4:** Time frequency analysis is applied to identify pre-voiding patterns in patients suffering from overactive bladder: A) example of bladder pressure recording and B) corresponding scalogram.

### Interplay Between Fluid Mechanics and Encrustation/Biofilm Development in Stented Ureters

*(SNF grant ## IZCOZ0_182966 with Bern University Hospital, University of Oxford and University of Southampton)*

Ureters are conduicts conveying urine from kidneys into the bladder. Under obstructed conditions of the ureter (e.g. kidney/ureteral stones or tumours), ureteral stents are frequently used in clinical setting to maintain the drainage of urine. Once in place, ureteral stents extend along the whole ureter length, with side holes positioned at regular intervals. Encrustation and biofilm are considered the main causes of stent failure, and it has been shown that their development in stented ureters are strongly influenced by local fluid mechanics (e.g. shear stress).

UGE developed an in-vitro platform of the upper urinary tract which aims at improving the insight on the interplay between local fluid mechanics and encrustation in stented ureters. The platform has unique features as it mimics the physiological fluid-dynamic (pressure and flow) and geometrical environment inside the ureter allowing a full fluid mechanical characterisation. It consists of (Figure 2): i) a roller pump (to simulate the production of urine from kidneys) ii) a transparent ureter model and iii) a bladder compartment whose internal pressure can be controlled to simulate the physiological bladder pressures (during the filling and emptying cycles). The platform is combined with an index matched fluid to allow Particle Image Velocimetry (PIV) measurements within the lumen of the ureter with and without stents. In this research context, UGE is part of the ENIUS COST Action 'European network of multidisciplinary research to improve the urinary stents' and has well-established collaborations with the major research groups in the field.

### Assessment of Encrustation on Ureteral Stents Retrieved from Patients

*(with Bern University Hospital)*

Ureteral stents, once implanted in patients, are exposed to complex fluid dynamic and chemical (bacteria, crystals) enviroments. Current projects at UGE involve volumetric and chemical characterisations of encrustation (on ureteral stents retrieved from patients) by means of micro-computed tomography (µCT) and scanning electron microscopy (SEM), respectively (Figure 3). These investigations aim at identifying the regions of the stents that are more prone to develop encrustation and the associated crystals.

### Innovative Tools for Diagnosis and Treatment of Overactive Bladder and Incontinence

*(with Bern University Hospital & Bern University of Applied Sciences)*

Patients suffering from overactive bladder (OAB) live with a continous urge to urinate even at low bladder filling volumes, often leading to incontinence. OAB has an enormous impact on the quality of life of affected patients. Despite the high prevalence, the understanding of the mechanism underlying OAB remains limited and, as consequence, treatment options are scarce. UGE has developed several tools aiming at identifying specific patterns in bladder pressure and bladder nerve signals associated to overactive bladder. We developed an algorithm which is able to generate alarms before the start of an unwanted bladder contractions (Figure 4). The algorithm was succesfully tested first in rats and then in patients. It could be used to warn the patient about an impending bladder contraction ( to take action against incontinence) or/and to trigger conditional sacral nerve stimulation (i.e. stimulation of bladder nerves to inhibit the bladder contraction before incontinence).

Moreover our group has pioneered the use of cardiac catheters for minimally-invasive electrophysiological investigations in the urinary tract. In a proof-of-concept study, we have shown that cardiac catheters can detect and track the propagation of electrical signals in the lumen of the ureter. Further investigations will apply this technology to bladder smooth muscle.

**Selected Publications**

1. Clavica F. , Roth J., Schneider M.P., Civet Y., Burkhard F., Perriard Y., Obrist D. 'Urine-Contactless Device to Empty Bladders: Ex-Vivo Proof-of-Concept Study', Intern. Continence Society (ICS) conference, 2019
2. Clavica F., Zhao X., ElMahdy M., Drake M.J., Zhang X., Carugo D., 'Investigating the flow dynamics in the obstructed and stented ureter by means of a bio-mimetic artificial model.' PLOS ONE; 9(2):e87433, 2014.
3. Niederhauser T., Gafner E, Cantieni T., Grämiger M., Haeberlin A., Obrist D., Burkhard F., Clavica F. 'Detection and quantification of overactive bladder activ-ity in patients: Can we make it better and automatic?' Neurourology and Urody-namics, 1-9, 2018
4. Haeberlin A., Schurch K.,Niederhauser T.,Sweda R. Schneider M. P. Obrist D., Burkhard F., Clavica F. 'Cardiac electrophysiology catheters for electrophysio-logical assessments of the lower urinary tract Neurourology and Urodynamics 87-96, 2019.

# Mechanical Design and Production

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Simon Lüthi

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Christopher Balli

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## Research Profile

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


**Fig. 1:** Open Days 2019 at SITEM: the new machine room is a highlight. Photo: Adrian Moser

## Training & Education

The MDP group has a secondary role in training. This training encompasses the skills required to safely and proficiently operate machine shop tooling and equipment, the knowledge required to achieve the best results with a variety of materials and the skills needed to efficiently manage the design and production workflow.

In 2018, we selected Janosch Schär as our new apprentice and he began his training on 1 August 2019 as a polymechanic apprentice.

After four years of service as a mechanic Danaël Gasser decided to seek a new professional challenge and left he ARTORG Center at the end of December. We appreciate him as an independent and responsible worker, and wish him all the best in his future endeavors.

Our apprentice Simon Lüthi completed his basic training exam at the end of the second year with a grade of 5,5 and we congratulate him. On 15 June 2019, Simon also reached 1st place for Bern-Biel-Mittelland as part of a milling competition organized by FRAISA. In the coming two years his training will focus more on CAD-CAM technologies and manufacturing more ambitious parts.

Fabio Spena completed his four-year apprenticeship with a grade of 5.3 and thus the second-best result in Bern-Mittelland. On 25 June 2019, he was honored for this top result by the GIBB vocational school in Bern on the Muristalden


**Fig. 2:** Turning center ROMI.

**Fig. 3:** Dental implant insertion device.

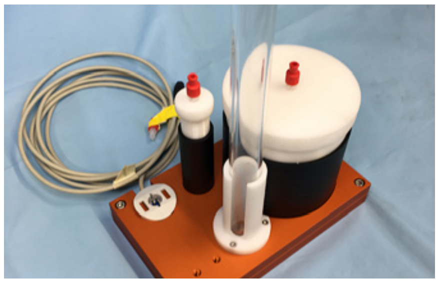

**Fig. 4:** Device for pressure sensor calibration.

campus. We employed him in our machine shop as a part-time polymechanic.

Due to a high demand of workload, we recruited a polymechanic, Christopher Balli, as alternative civilian-service employee. He performs administrative tasks and increases the productivity of our team. We thank him for the work he has accomplished in our workshop.

All students from the Department of Mechanical and Process Engineering at the ETH Zurich have to undergo an industrial practical training for at least five weeks.

This year, our machine shop provided six weeks of practical training for Ina Brodbeck. The training was very instructive and successful. We wish her much success in continuing her studies.

Moving the whole ISTB from Stauffacherstrasse to SITEM-insel was definitely this year's biggest challenge. In the course of the move from Wankdorf to Insel campus, our little workshop at the ARTORG Center on Murtenstrasse was shut down and all the equipment was integrated into the large workshop in the new building.

Since September, the Mechanical Design and Production group has been able to produce more complex turned parts for research assemblies on a fully automatic CNC (Computer Numerical Control) lathe ROMI (Fig. 2). The machine automatically switches between 12 built-in, partly driven tools. These driven tools make it possible to machine the workpieces on the front side outside the center, as well as on the circumference with drilling, milling, and threading tools. The new machine can be used for high-precision turning of metals and plastics and can produce smaller series of absolutely identical commissioned workpieces in a short time. As a fully automatic lathe, the new acquisition perfectly complements the existing portfolio of milling and turning machines in the workshop.

**Research Equipment Design & Manufacturing**

As expected, the requirements of a machine shop supporting research in the biomedical engineering field are as diverse as the research field itself. The variety of subjects researched in the ARTORG yield a number of diverse design and production requests from prototype clinical and surgical tooling to fixtures for mechanical, biological and kinematic testing, as well as imaging system accessories and calibration equipment. The following illustrations highlight two a few of this year's projects. Fabio Spena produced two devices as practical parts of his exam: the dental implant insertion device (Fig. 3) for the Musculoskeletal Biomechanics group (MSB) and the device for pressure sensor calibration (Fig. 4) for the Cardiovascular Engineering group (CVE).

*Dental Implant Insertion Device (MSB)*

The insertion device aims at visualizing compaction of the bone around the implant during the insertion process. It can be placed in a micro-CT scanner (MicroCT 100, SCANCO Medical, Switzerland). The dental implant is inserted in stepwise manner into the bone samples and micro-CT images are captured at each step. Digital volume correlation may be used to quantify the displacement field of the bone surrounding the implant. The overall structural response of the bone-implant system may finally be measured on a servo-hydraulic testing system.

*Device for Pressure Sensor Calibration (CVE)*

The device is designed to generate specific static fluid pressures in the range of physiological blood pressures. It is used to calibrate pressure sensors for cardiovascular research. Previously, pressure sensors were calibrated with ad hoc rigs made from flexible tubes. With the new device the calibration became more standardized and reproducible. The cylindrical calibration tube (2m high) can be filled with a water colum such that the desired pressure conditions can be set precisely and rapidly with the integrated ruler.

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