UNIVERSITÄT BERN

ARTORG CENTER
BIOMEDICAL ENGINEERING RESEARCH

ARTORG CENTER
ANNUAL REPORT 2020

Foreword

Dear friends, colleagues, collaborators, and partners

We present the annual report in our usual and well-established format, although this year has been nothing but unusual and a complete departure from what is considered established.

We continued to add to the scientific knowledge base with experiments carried out under tough circumstances and taking care of our co-workers by attending the Center in shifts and small groups. Students were given lectures, sat exams, defended their theses, and held journal club in online rooms. We made our clinical research continue, despite the huge pressure on our colleagues at the Inselspital and many other clinical centers of excellence that we have the privilege to collaborate with.

The excellent leadership team of the Center for AI in Medicine (CAIM) put together an outstanding opening as an entirely digital event. We welcomed well-wishers from politics, business, scientific expertise and over 300+ attendees who gave their thumbs up to the amazing organising committee led by Julia Spyra and Monika Kugemann. Our unique panel discussion and keynote talk were picked up by national and international outlets, raising the profile of CAIM and the ARTORG. CAIM started as it means to go on and launched with a big and positive virtual bang.

In this second year of operating the ARTORG in "COVID-19 safe mode", we have all demonstrated great resilience and found ways of motivating ourselves not to forget our mission of making the lives of patients better through our research.

It remains my sincere hope that the experience of the last 24 months will leave all the new and positive things of the digital world we discovered in place, only to add back what we cherish greatly from working together the analogue way.

I wish you all good health and an enjoyable read.

Sincerely,

Raphael Sznitman
ARTORG Director

Groups

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AIHN
Artificial Intelligence in Health Nutrition

↓
AIMI
Artificial Intelligence in Medical Imaging

↓
CB
Computational Bioengineering

↓
CVE
Cardiovascular Engineering

↓
GER
Gerontechnology and Rehabilitation

↓
HRL
Hearing Research Laboratory

↓
IGT
Image-Guided Therapy

↓
MIA
Medical Image Analysis

↓
MLN
Motor Learning and Neurorehabilitation

↓
MSB
Musculoskeletal Biomechanics

↓
OOC
Organs-on-Chip Technologies

↓
UGE
Urogenital Engineering

↓
MDP
Mechanical Design and Production

↓
CAIM
Center for Artificial Intelligence in Medicine

Research Partners

University of Bern
Inselspital – Universitätsspital Bern, Hôpital Universitaire de Berne, Bern University Hospital
sitem insel
AlveoliX – In-vitro models inspired by nature
force dimension
Novostia
UKBB – University Children's Hospital Basel
AO Foundation
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Optimeyes
UCL
Bern University of Applied Sciences
HFR – hôpital fribourgeois freiburger spital
Oslo University Hospital
The University of Electro-Communications
CASCINATION
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OVIVA – Freude am Leben
Universitat d'Alacant / Universidad de Alicante
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Paul Scherrer Institut PSI
University of Bristol
City of Hope
Hocoma
PDAG – Für Ihre psychische Gesundheit
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CorFlow Therapeutics
HUG – Hôpitaux Universitaires Genève
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university of groningen
csem
Inria – Inventeurs du monde numérique
RMS – Testing · Research · Consulting
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UniversitätsSpital Zürich
EPFL
MED-EL
URODEA
Vascular Institute Switzerland
ETH zürich
Newcastle University
Università della Svizzera italiana

Dissertations

↓

Fabian Balsiger
Medical Imaging Analysis
Quantitative Magnetic Resonance Imaging to Monitor and Diagnose Neuromuscular Diseases

Benjamin Eigl
Image Guided Therapy
On the role of image guidance technologies in the treatment of pancreatic cancer

Tom Gawliczek
Hearing Research Laboratory
Influence of coupling and fitting parameters on the benefit with bone conduction hearing systems

Alain Jungo
Medical Imaging Analysis
Applications and Insights of Uncertainty Estimates in Automated Brain Tumor Segmentation

Ya Lu
AI in Health and Nutrition
Dietary assessment based on computer vision and machine learning

Alberto Mantegazza
Cardiovascular Engineering
Experimental investigations of red blood cell partitioning in artificial microvascular networks

Marzieh Oviesy
Musculoskeletal Biomechanics
Primary stability evaluation of uncemented bone-implant interface using finite element modeling during implantation and subsequent loading

Iwan Paolucci
Image Guided Therapy
3D Ultrasound-based stereotactic image-guidance in hepatobiliary surgery

Daniel Schneider
Image Guided Therapy
Freehand stereotactic image-guidance tailored to lateral skull base surgery

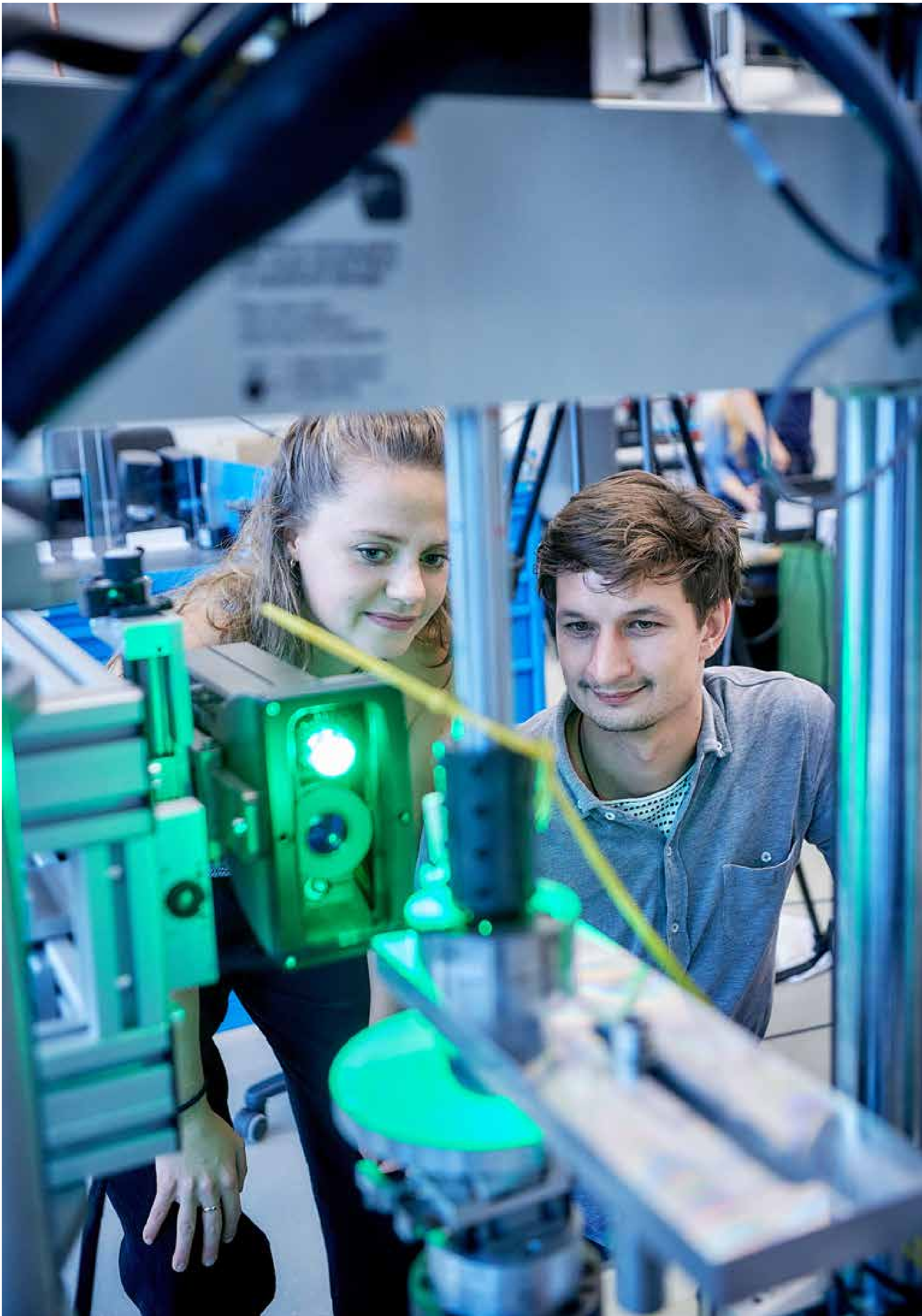
Qingnan Sun
AI in Health and Nutrition
AI-based Personalised Blood Glucose Regulation

Pauline Zamprogno
Organs-on-Chip Technologies
Development of second generation of air-blood barrier on chip

Soheila Zeinali
Organs-on-Chip Technologies
Functional in vitro Human Microvasculature

Guodong Zeng
Musculoskeletal Biomechanics
Effective and Efficient Deep Learning for 3D Image Segmentation of Musculoskeletal Structures

Hadi Zolfaghari
Cardiovascular Engineering
Impinging leading edge vortex instability in the bileaflet mechanical heart valves: direct numerical simulation, stability analysis, and adjoint-based control



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Master of Science
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Prof. A. Exadaktylos, Emergency Medicine, Inselspital
Prof. Z. Stanga, Diabetes, Endocrinology, Nutritional Medicine & Metabolism, Inselspital
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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 and management of lung diseases

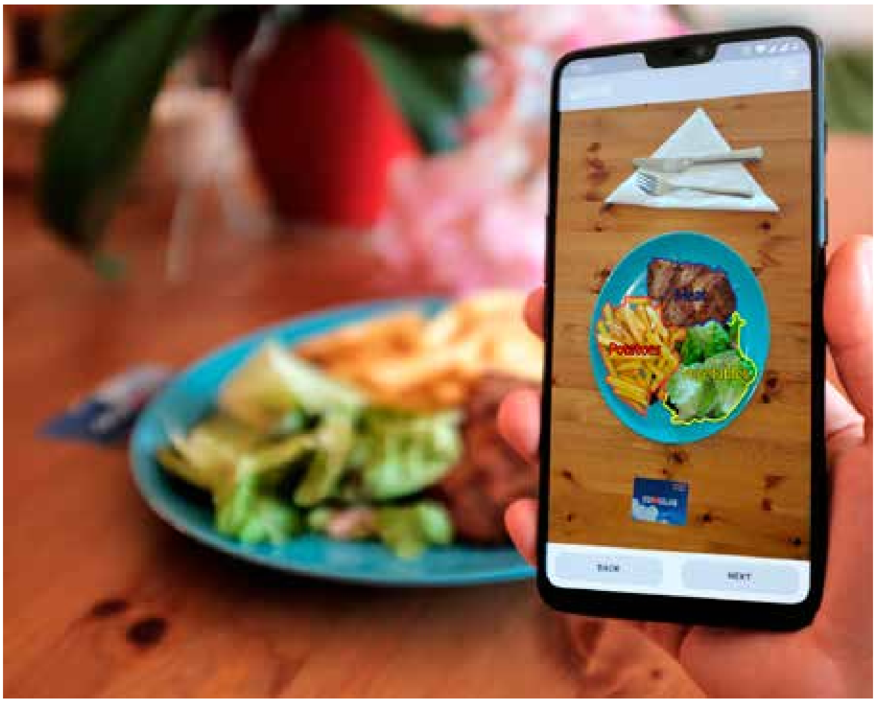

Fig. 1: AI-based algorithms automatically detect food types, estimate portion sizes and calculate the calories, carbohydrates, protein and fat from smartphone photo or video.

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 is integrated into a smartphone application to increase users' engagement and promote healthy eating habits.

Tackling hospitalized malnutrition

(SV Stiftung with Inselspital and Geriatrische Klinik St.Gallen AG)

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, are undernourished or "at high risk" for malnutrition. The main objective of the project is the validation of an in-house developed AI-based system that takes advantage of the availability of depth sensors and conceptual information to estimate

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.

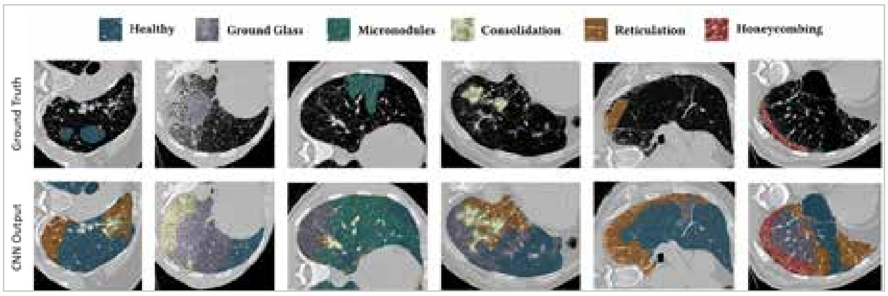

Fig. 3: Output examples of the INTACT's segmentation model for tissue characterization. Top row, ground truth; bottom row, model output. Each example has a different pattern annotated. From left to right: healthy (blue), Ground Glass – GGO (purple), micronodules (green), consolidation (yellow), reticulation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

the consumed energy, macro- and micronutrient content of hospitalized patients. The system is based on the automatic analysis of a patient's tray, before and after the meal (Fig. 2).

AI and lung diseases

(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, we investigate AI- and computer vision-based algorithms for the analysis of imaging, clinical /biochemical and other disease-related data for diagnosis and management of ILDs (Fig. 3). More specifically, algorithmic approaches for the fully automatic segmentation of lung and anatomical structures of the lung cavity, the segmentation and characterization of lung pathological tissue, and the calculation of disease distributions are introduced and continuously validated within the framework of research trials. The image analysis results along with the additional disease-related information are further analysed not only in order to support the faster diagnosis, but also for the more efficient disease management in the sense of treatment selections and disease progression.

In the last year, we attempted to translate the acquired knowledge to improve COVID-19 patient care by using imaging and medical disease-related data from Swiss medical centers along with AI algorithms, and particularly deep learning methodologies. Scope is to develop a decision support system to allow the early detection of the disease, to improve the distinction of COVID-19 from other types of pneumonias and proceed to assessment of the disease's severity.

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 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. Fontanellaz M, Ebner L, Huber A, Peters A, Löbelenz L, Hourscht C, Klaus J, Munz J, Ruder T, Drakopoulos D, Sieron D, Primetis E, Heverhagen JT, Mougiakakou S, Christe A. "A Deep-Learning Diagnostic Support System for the Detection of COVID-19 Using Chest Radiographs: A Multireader Validation Study." Invest Radiol. 2020 Nov 30.
2. Vasiloglou MF, Lu Y, Stathopoulou T, Papathanail I, Fäh D, Ghosh A, Baumann M, Mougiakakou S. "Assessing Mediterranean Diet Adherence with the Smartphone: The Medipiatto Project," Nutrients. 2020 Dec 7;12(12):3763.
3. Lu Y, Stathopoulou T, Vasiloglou MF, Pinault LF, Kiley C, Spanakis EK, Mougiakakou S. goFOODTM: An Artificial Intelligence System for Dietary Assessment. Sensors (Basel). 2020 Jul 31;20(15):4283.

Artificial Intelligence in Medical Imaging

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Alain Jungo
Lukas Zbinden
Vasily Tolkachev
Daniel Erpenbeck
Lars Doorenbors
Michel Hayoz
Sergio Tascon-Morales
Jana Starkova
Till Meyer vu Westram
Nina Huber
Javier Gamazo-Tejero
Maria Lopez-Antuna

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.

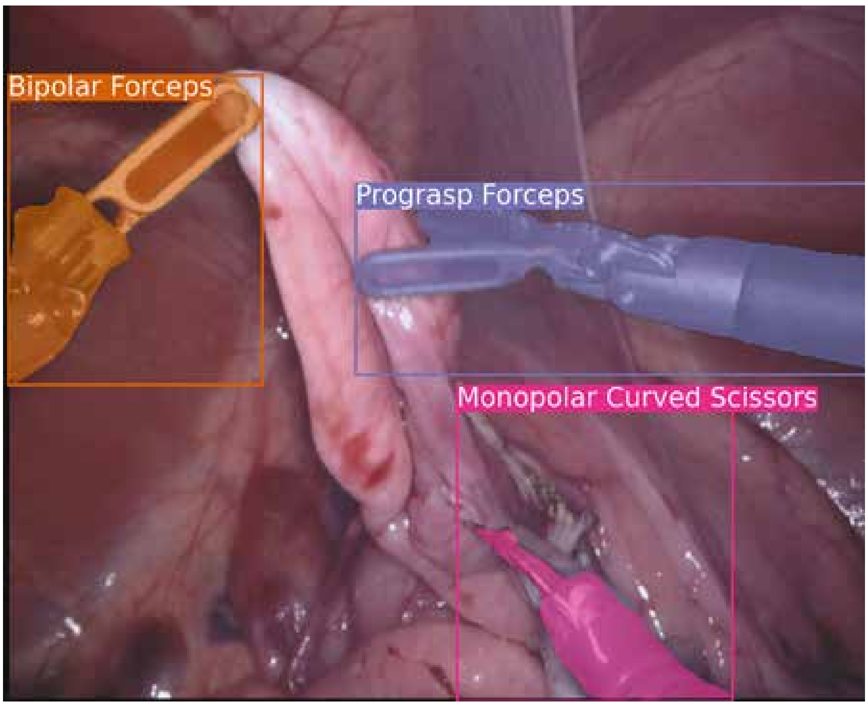

Fig. 1. Automatic detection and segmentation of surgical instrument during endoscopy.

Mask then Classify: Multi-Instance Segmentation for Surgical Instruments

The correct detection and segmentation of surgical instruments has been a vital step for many applications in minimally invasive surgical robotics including pose estimation, tracking and augmented reality. Historically, the problem was tackled from a semantic segmentation perspective, which has resulted in impressive performance in the case of binary instrument segmentation. Yet, these methods fail to provide good segmentation maps of instrument types and do not contain any information on the instance affiliation of each pixel. In order to improve the type segmentation and provide instance level information, we propose to tackle the problem using instance segmentation. We introduce a novel method for instance segmentation where a pixel-wise mask of each instance is found prior to classification. A encoder-decoder network is used to extract instrument instances, which are then separately classified using the features of the previous stages. Experiments are performed on the robotic instrument segmentation dataset of the 2017 endoscopic vision challenge. We perform a 4-fold cross validation and show an improvement of over 18% to the previous state-of-the-art. Furthermore, we perform an ablation study which highlights the importance of certain design choices and observe an increase of 10% over semantic segmentation methods →

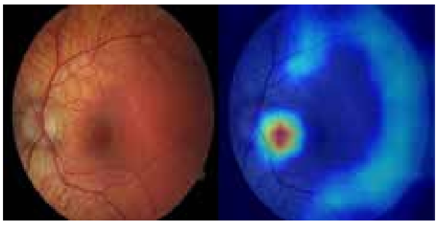

Fig. 2: Top: An automatic diagnosis method with no validation. However, the presence of corruption —noise in this case— leads to an erroneous healthy prediction. Bottom: Our DDV model learns the data distribution the network was trained on, and prevents any diagnosis when it detects an image outside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

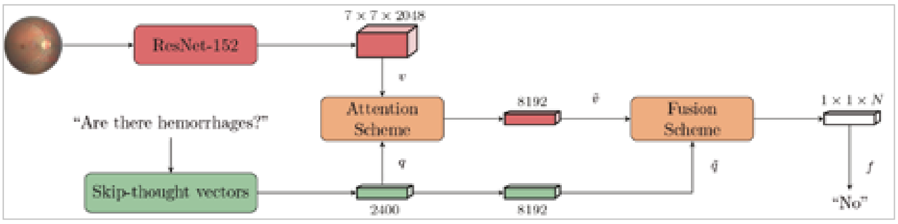

Fig. 3. The proposed Visual Question and Answering (VQA) model together with the attention mechanism. A ResNet-152 and Skip-thought vectors were used to extract image, and question features, respectively. These are combined using an attention mechanism in order to produce global image features, that are then fused with global question features, to output answer likelihoods.

Assessment of Patient Specific Information in the Wild on Fundus Photography and Optical Coherence Tomography

In this paper we analyse the performance of machine learning methods in predicting patient information such as age or sex solely from retinal imaging modalities in a heterogeneous clinical population. Our dataset consists of N = 135’667 fundus images and N = 85’536 volumetric OCT scans. Deep learning models were trained to predict the patient’s age and sex from fundus images, OCT cross sections and OCT volumes. For sex prediction, a ROC AUC of 0.80 was achieved for fundus images, 0.84 for OCT cross sections and 0.90 for OCT volumes. Age prediction mean absolute errors of 6.328 years for fundus, 5.625 years for OCT cross sections and 4.541 for OCT volumes were observed. We assessed the performance of OCT scans containing different biomarkers and note a peak performance of AUC = 0.88 for OCT cross sections and 0.95 for volumes when there is no pathology on scans. Performance drops in case of drusen, fibrovascular pigment epitheliuum detachment and geographic atrophy present. We conclude that deep learning based methods are capable of classifying the patient’s sex and age from color fundus photography and OCT for a broad spectrum of patients irrespective of underlying disease or image quality. Non-random sex prediction using fundus images seems only possible if the eye fovea and optic disc are visible. This puts in question how anomized images of these types really are and if measures should be taken to make them safer in the eyes of the public.

A Question-Centric Model for Visual Question Answering in Medical Imaging

Deep learning methods have proven extremely effective at performing a variety of medical image analysis tasks. With their potential use in clinical routine, their lack of transparency has however been one of their few weak points, raising concerns regarding their behavior and failure modes. While most research to infer model behavior has focused on indirect strategies that estimate prediction uncertainties and visualize model support in the input image space, the ability to explicitly query a prediction model regarding its image content offers a more direct way to determine the behavior of trained models. To this end, we present a novel Visual Question Answering approach that allows an image to be queried by means of a written question. Experiments on a variety of medical and natural image datasets show that by fusing image and question features in a novel way, the proposed approach achieves an equal or higher accuracy compared to current methods.

Comparative study between the SORS and Dynamic Strategy visual field testing methods on glaucomatous and healthy subject

To clinically validate the non inferiority of the Sequentially Optimized Reconstruction Strategy (SORS) when compared to the Dynamic Strategy (DS). SORS is a novel perimetry test strategy that evaluates a subset of test locations of a visual field (VF) test pattern and estimates the untested locations by linear approximation. Testing fewer locations, SORS has shown in computer simula-tions, to bring speed improvement to the conventional perimetry tests, while maintaining high quality acquisition. To validate SORS, a prospective clinical study was conducted at the Department of Ophthalmology of the University Hospital Bern, during 12 months. 83 subjects out of 114 participants were included in the study. The subjects underwent perimetry tests on an Octopus 900 using the G pattern with both DS and SORS. The acquired sensitivity thresholds (ST) by both tests were analyzed and compared. DS-acquired VFs were used as a reference. High correlations between individual STs as well as between mean defect values given by DS and SORS were obtained. The mean absolute error of SORS was under 3dB with a 70% reduction in acquisition time. SORS overestimate healthy VFs while slightly underestimating glaucomatous VFs. This clinical study showed that for healthy and glaucomatous patients, SORS-acquired VFs sufficiently correlated with the DS-acquired VFs with up to 70% reduction in acquisition time.

Selected Publications

1. Kurmann, T., Marquez Neila , P., Allan, M., Wolf, S. and Sznitman, R., “Mask then Classify: Multi-Instance Segmentation for Surgical Instruments”. International Journal of Computer Assisted Radiology and Surgery - Special Issue: IPCAI, 2021
2. Munk, M., Kurmann, T., Marquez Neila , P., Zinkernagel, M., Wolf, S. and Sznitman, R., “Assessment of Patient Specific Information in the Wild on Fundus Photography and Optical Coherence Tomography”. Nature Scientific Reports, 2021
3. Vu, M., Nyholm, T. Lofstedt, T and Sznitman, R.. “A Question-Centric Model for Visual Question Answering in Medical Imaging”. IEEE Transactions on Medical Imaging, 2020
4. Kucur, .S, Hackel, S., Stapelfeldt, J., Odermatt, J., Iliev, M., Abegg, M., Sznitman, R., Hohn, R., ”Comparative study between the SORS and Dynamic Strategy visual field testing meth- ods on glaucomatous and healthy subjects”, Translational Vision Science & Technology, 2020

Computational Bioengineering

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Malavika Nambiar
Simone Poncioni
Alexander Marc Probst
Osman Berk Şatir

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.

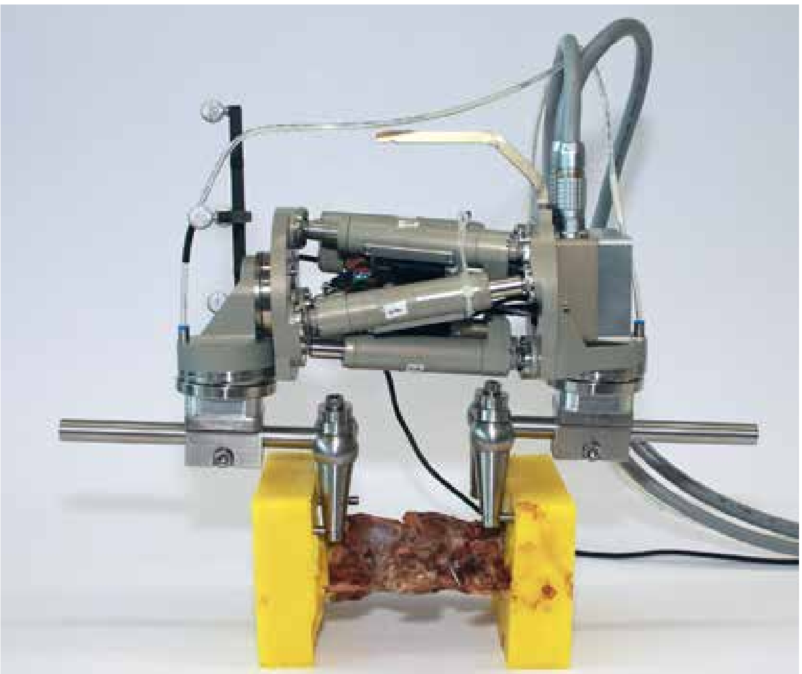

Fig. 1: The Spinebot is a robotic device developed to measure the biomechanical properties of the spine intraoperatively.

The Spinebot – A robotic device to intra-operatively quantify spinal stiffness

Degenerative spine problems and spinal deformities have high socio-economic impacts. Current surgical treatment is based on bony fusion that can reduce mobility and function. Precise descriptions of the biomechanics of normal, deformed, and degenerated spinal segments under in vivo conditions are needed to develop new approaches that preserve spine function. Therefore, we developed a system that intraoperatively measures the three-dimensional segmental stiffness of patient's spine.

SpineBot (Fig. 1), a parallel kinematic robot, was developed to transmit loads to adjacent vertebrae. A force/torque load cell mounted on the SpineBot measures the moment applied to the spinal segment and calculates segmental stiffnesses. SpineBot's accuracy is comparable to that of current reference systems but can take intraoperative measurements.

Intraoperative measurements can improve our understanding of spinal biomechanics in patients who have the pathology of interest, and take these measurements in the natural physiological environment, giving us information essential to developing new products.

OCT-based hemodynamics in femoro-popliteal arteries

Selecting the correct endovascular treatment approach for patients with

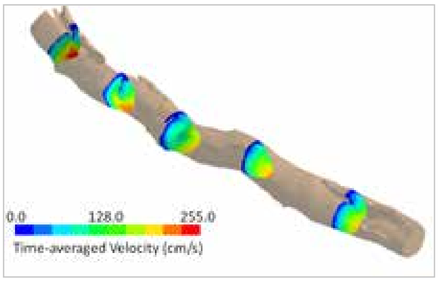

Fig. 2: Simulated hemodynamics condition in the femoro-popliteal artery of a patient following revascularization by percutaneous transluminal angioplasty.

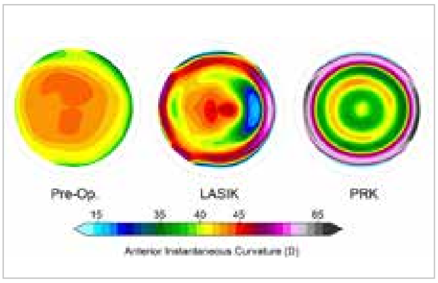

Fig. 3: Curvature maps of the cornea of a patient before, and after two types of refractive interventions - LASIK and PRK - showing the optical impact of the mechanical deformation of the cornea.

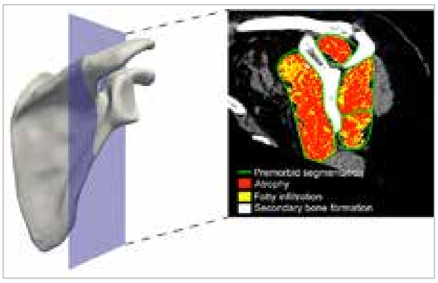

Fig. 4: Deep learning assessment of the degeneration of the shoulder rotator cuff muscles can automatically quantify muscle degeneration, fatty infiltration, and atrophy from CT datasets.

peripheral arterial disease is crucial to avoid the occurrence of restenosis in femoro-popliteal (FP) arteries. To reduce potential problems associated with stent implantation, clinicians are frequently performing percutaneous transluminal angioplasty (PTA) in biomechanically challenging anatomical regions affected by leg flexion. However, the impact of different treatment methods on the hemodynamic behaviors of FP arteries are poorly understood, as the imaging methodologies used in existing works are unable to accurately represent the post-treatment arterial geometry.

We proposed a unique algorithm that combines intra-arterial lumen geometry obtained from Optical Coherence Tomography (OCT) with centerlines generated from X-ray images to reconstruct the FP artery with an unprecedented accuracy. Computational fluid dynamics simulations were performed to investigate hemodynamic conditions before and after treatment (Fig. 2).

Our results showed that OCT-based numerical models have great potential to guide clinicians regarding the optimal treatment approach.

Biomechanical simulation platform for personalized refractive interventions

Myopia is a visual impairment that will affect half of the population by 2050, with an economic burden estimated at $202 billion per year. Corrective surgeries such as LASIK, SMILE and PRK are becoming increasingly popular but 15 % of cases fail to provide the desired correction rates. The lack of patient-specific information leads to a "one size fits all" approach. A possible solution to this problem is the incorporation of "patient-specific" parameters like corneal topography and patient-specific tissue properties into the surgical planning for patient specific diagnosis and treatment.

To this effect, we developed a framework to reconstruct patient-specific biomechanical models of different refractive interventions – LASIK, PRK, and SMILE – based on Pentacam elevation maps obtained from the patients as well as the desired optical correction. The mechanical impact of the intervention on the optical outcome for the patient can be calculated and assessed for each type of refractive interventions (Fig. 3).

Our models are in good agreement with the presurgical patient's corneal geometry and topography. More patient specific details like biomechanical properties of the corneal tissue will be incorporated in future models. We aim to collect this data using Brillouin imaging. We will further work towards improving the mechanical model and to validate the predictions.

Deep learning to quantify rotator cuff muscle degeneration from CT datasets

Knowledge of the status of rotator cuff (RC) muscles is key in various shoulder disorders, not only RC tendon tears but also glenohumeral osteoarthritis. In particular, muscle degeneration parameters, such as fatty infiltration and atrophy, influence surgical decision-making and overall patient management. Although magnetic resonance imaging offers higher contrast resolution for the evaluation of soft tissues, computed tomography (CT) is widely available, fast and well accepted by patients, and this examination is increasingly being used in the imaging evaluation of glenohumeral osteoarthritis and preoperative planning of shoulder arthroplasty.

Therefore, we developed a neural network able to automatically assess RC muscles from shoulder CT images. Unlike traditional segmentation tasks, this neural network must not only segment the structures currently available in the images, but also learn the pre-existing locations, shapes, and boundaries of RC muscles from invariant anatomical structures visible on CT sections (Fig. 4).

We showed that deep learning can provide a rapid and reliable automatic quantification of RC muscle atrophy, fatty infiltration, and overall muscle degeneration directly from preoperative shoulder CT scans of osteoarthritic patients.

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5. M. A. Ariza-Gracia, J. Flecha-Lescún, P. Büchler, B. Calvo, "Corneal Biomechanics After Intrastromal Ring Surgery: Optomechanical In Silico Assessment", Translational vision science & technology, 9(11):26, 2020

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.

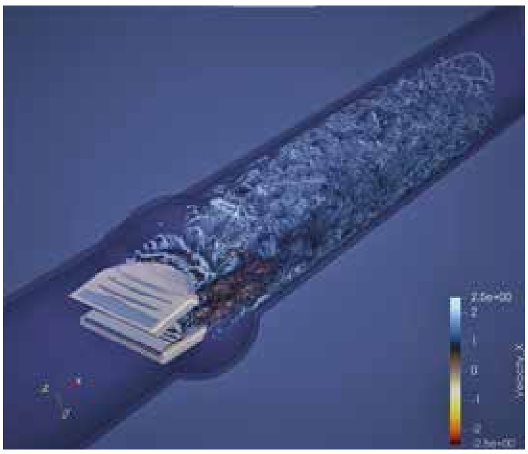

Fig. 1: Direct numerical simulation of the laminar-turbulent transition behind a bi-leaflet mechanical heart valve. (GPU-accelerated numerical solution of the Navier-Stokes equations on 335 million grid points performed on the Cray XC40/50 supercomputer at the Swiss Supercomputing Centre CSCS.)

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, figure 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. →

Fig. 2: Tri-leaflet mechanical heart valve Triflo by Novostia SA (Epalinges) with a novel hinge design to create non-thrombogenic, physiological blood flow.

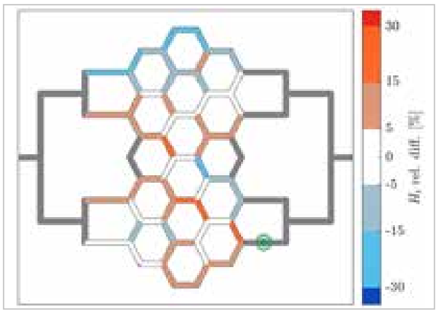

Fig. 3: Relative hematocrit increase in a model of a cerebral capillary network by activating the pericyte model (green symbol). (Mantegazza et al., Frontiers Physiology, 2020)

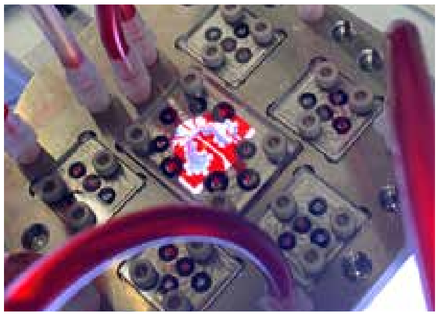

Fig. 4: Microfludic chip developed together with OST – Fachhochschule Ostschweiz, Buchs SG, to study drug infusion in the coronary microcirculation with MVO.

➔ Quantitative assessment of turbulence intensity by 4D-Flow-MRI is limited 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 (figure 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).

Blood flow regulation in models of cerebral capillary networks with pericytes

Local concentrations of red blood cells in capillaries (tube hematocrit) are a factor in the oxygen supply to the surrounding tissue. CVE investigates 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. Experiments with pericyte models indicate that local hematocrit can be increased by more than 25 % by actively dilating and contracting micro-channels (figure 3).

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 (figure 4) to study the diagnostic method and to optimize the drug infusion into the microvascular bed.

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Gerontechnology and Rehabilitation

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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 partners with the department of neurology (Claudio Bassetti) to establish the NeuroTec Loft wich is an instrumented apartment within the Sitem NeuroTec 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 is 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 →

Fig. 2: Living room in the instrumented apartment (SITEM Neurotec Loft).

Fig. 3: Kitchen with a number of contact-free sensors (SITEM Neurotec Loft).

Fig. 4: Bedroom with in the integrated sensors (SITEM Neurotec Loft).

evidence that VR nature stimulation comforts critically ill patients. Secondly, 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 subject cannot detect or respond properly to visual stimuli coming from the left 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 left side using different kind 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. A second study in healthy 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 about to show 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 wider 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. The usage of wearable sensors is especially crucial for the monitoring of PD patients, as both the symptoms and the disease progress 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.

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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: The inner ear houses the senses of hearing and balance. Multi-symptom diseases associated with the inner ear (sudden deafness, Ménière's disease, tinnitus, sound-induced vertigo, migraine, etc.) are generally poorly understood, although very common. Our system introduces new diagnostic technology to investigate these diseases and enable a better treatment (patent *WO2020254462A1* pending).

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. Moreover, we are developing novel mechatronic devices for hearing and balance assessment (Fig. 1).

Tinnitus Research

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.

Our group aims to develop algorithms to identify tinnitus-associated neural oscillations in electroencephalographic →

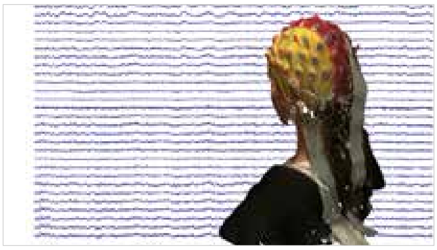

Fig. 2: Residual inhibition (RI) is a temporary quieting of tinnitus that can be caused by acoustic stimulation. In our current study, tinnitus suppression could be observed in about 75% of our study participants. We aim to use this phenomenon to detect tinnitus markers in brain activity.

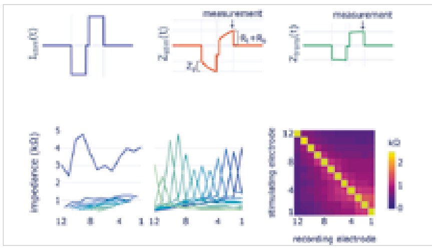

Fig. 3: In cochlear implantation, the optimal alignment of the electrode array insertion trajectory with respect to the cochlea is crucial for a minimally invasive outcome. This figure shows the robot-assisted insertion of an electrode array in a high-resolution model of a human cochlea.

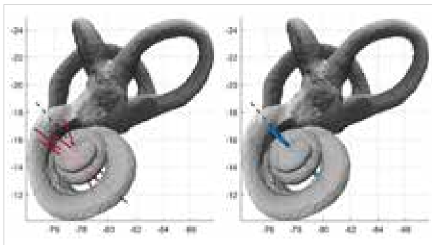

Fig. 4: The identification of the cochlear modiolar axis in clinical CT images is challenging, even for experts. The axes manually found by experts show large discrepancies (left), while our automatic detection algorithm yields reproducible results (right).

data. The objective assessment can be applied 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 concept, which characterizes tinnitus perception as a precision-weighted integration of sensory information and predictions (priors). We actively collaborate with the industry to implement our research findings in future hearing aid solutions (Innosuisse 44423.1 IP-LS with Bernafon AG).

Cochlear Implants

Cochlear implantation is a microsurgical procedure that demands a high level of surgical skills and experience due to the complex 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 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 characterize the shape of the cochlea based on the natural growth in the embryo. Our approach models the morphogenetic process by a kine-matic spiral motion, comparable to the formation of sea shells. The cochlea can then be modeled as a kinematic surface, i.e., a surface that was formed by tracing a generator curve along a kine-matic center line. 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.

Foquipped 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. 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.

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Chair for Image Guided Therapy

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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.

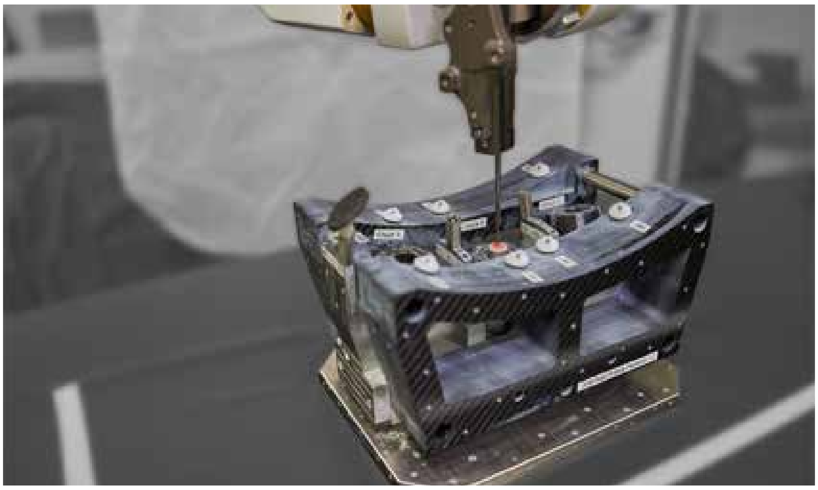

Fig. 1: Verification of drilling accuracy of a robotic spine surgery system using a custom-built phantom. It's imitating a patient's lumbar region of the back. Performing such measurements allows engineers to determine important performance parameters of the prototype platform.

Robotic spine surgery
(Bridge Discovery 176498, Innosuisse 29936.1 IP-ENG)

One approach to treat spinal instabilities is to implant pedicle screws and fuse adjacent vertebra. Placement of pedicle screws is challenging. In recent years, a robotic spinal surgery application prototype was developed to assist with this task. To verify its accuracy, multiple phantoms were created, each focusing on different aspects of the workflow (Fig. 1). This allows to quantify the sources of error and helps to identify rooms for improvement.

Robotic cochlear implantation
(SNF Project Number 176007)

The recently proposed procedure by our group for robot-assisted cochlear implantation has been further investigated. To reduce the risk of device failure while improving outcome reproducibility, we propose a new clinical workflow that consists of intraoperative planning of the electrode lead channel, and its robotic execution. Research on inner ear access focuses on optimizing planning to achieve atraumatic electrode insertion, better hearing retention and outcomes.

➔

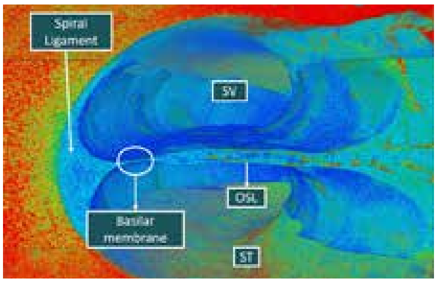

Fig. 2: Nano-CT imaging at 2.4 µm of a non-decalcified human cochlea. SV – scala vestibuli; ST – scala tympani; OSL – osseous spiral lamina.

Fig. 3: Realistic micro-neurosurgical simulator for medical resident training developed by SurgeonsLab AG.

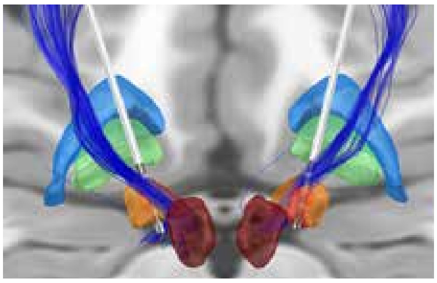

Fig. 4: Reconstruction of Deep Brain Stimulation leads and subcortical structures. Subthalamic nucleus in orange, volume of tissue activated in red, and tractography streamlines in blue.

➔ *Virtual Histopathology of the Inner Ear by Nano-CT*

Anatomical investigations of the human cochlear cells are challenging due to the organ's helical shape and encasement in the petrous bone. The limitation of histopathological studies is that is does not allow for realistic isotropic perception or reconstructions. Novel 3D imaging techniques can improve the evaluation of cochlear structures after therapeutic procedures. With the aid of geometric enlargements, angular scanning, and noise reduction, nano-CT systems can provide focal spot sizes down to 200-500 nm. Association with tissue staining and decalcifying techniques will potentially improve the 3D reconstruction (Fig. 2).

Fighting liver cancer

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

Current clinical practice for thermal ablation treatment is more favorable towards small spherical tumors. Subsequently, the treatment of large and/or irregularly shaped tumors remains challenging, since it requires overlapping of several ablation volumes. If overlapped improperly, it may result in residual tumor tissue which has high risk of recurrence. Therefore, our group further focuses on the clinical implementation of an automated ablation system that aims to produce tumor-specific ablation volumes, which can be customized through robotic control of needle position and energy delivery.

CT-guided irreversible electroporation treatment of locally-advanced pancreatic cancer

(H2020 MSCA-ITN 722068)

Irreversible electroporation (IRE) is an attractive adjunctive treatment for patients with locally advanced pancreatic cancer. Due to the complexity of needle placement and heterogeneity of placement techniques, adoption of this treatment is slow and results in high variation of oncologic outcomes. The use of a CT-guided navigation system can standardize the treatment. To demonstrate safety and feasibility, we are conducting a clinical study on CT-guided stereotactic percutaneous IRE treatment, with to date two successful patient treatments.

Micro Neurosurgical Realistic Simulator

(Innosuisse 51144.1 IP-LS, Herzstiftung FF20061)

Microsurgical skills are generally acquired in a self-directed way through hours of hands-on experience. Conventionally, standard modalities like surgical assistance, supervised operating, and video practice are used. However, this training does not allow trainees to develop sufficient hands-on experience. Because brain surgeries are complex and high-risk, access to the learning process is limited. For this reason, the collaborative project of SurgeonsLab AG and the Department of Neurosurgery and Neuroradiology aims to bring to the market physical simulators for realistic micro-neuro-interventions. These simulators enable resident training, can be used for preoperative surgery practice, and allow experienced surgeons to keep their skills and competencies (Fig. 3).

Mapping and modelling of Deep Brain Stimulation

(SNSF Ambizione 186142)

The Brain Neuromodulation sub-group has continued its research on mapping and modelling of deep brain stimulation. Regarding mapping, we have published stimulation maps for essential tremor and for chronic cluster headache, as well as results of electrophysiological recordings with directional electrodes. Regarding modelling, we have set up an improved pipeline starting from the neuroimaging sequence via image preprocessing to finally computing brain connectomes and extracting pathways. We plan to use this for patient-specific surgical planning and stimulation programming, e.g. for movement disorders and chronic poststroke pain (Fig. 4).

Selected Publications

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2. I. Paolucci et al., "Stereotactic Image-Guidance for Ablation of Malignant Liver Tumors," in Liver Cancer, IntechOpen, 2019.
3. P. Tinguely et al., "Stereotactic Image-Guided Microwave Ablation for Malignant Liver Tumors-A Multivariable Accuracy and Efficacy Analysis.," Front. Oncol., vol. 10, p. 842, 2020.
4. B. Eigl, A. Andreou, M. Peterhans, S. Weber, and B. Gloor, "Computer Assistance in the Minimally Invasive Ablation Treatment of Pancreatic Cancer," in Pancreatic Cancer [Working Title], IntechOpen, 2020.
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Medical Image Analysis

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PhD
Alain Jungo (2020) "Applications and Insights of Uncertainty Estimates in Automated Brain Tumor Segmentation".
Fabian Balsiger (2020) "Quantitative Magnetic Resonance Imaging to Monitor and Diagnose Neuromuscular Diseases". Best PhD thesis 2020 – Graduate School for Cellular and Biomedical Sciences, University of Bern.

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Research Profile

The Medical Image Analysis group develops advanced medical image analysis technologies, and related translational biomedical engineering technologies, to quantify, diagnose, and follow-up diseases and disorders. A strong focus is given to disorders related to the central nervous system.

The group develops novel techniques for multimodal image segmentation and analysis of brain lesions, presently including glioblastoma multiforme, and ischemic stroke. The results of these developments are aimed at advancing the fields of radiomics for the discovery of innovative non-invasive imaging biomarkers used to characterize disease and guide the decision-making process, as well as in radiotherapy, neuro-surgery, drug-development, etc.

The developments revolve around the vision of scalable, adaptable and time-effective machine learning algorithms developed with a strong focus on clinical applicability.

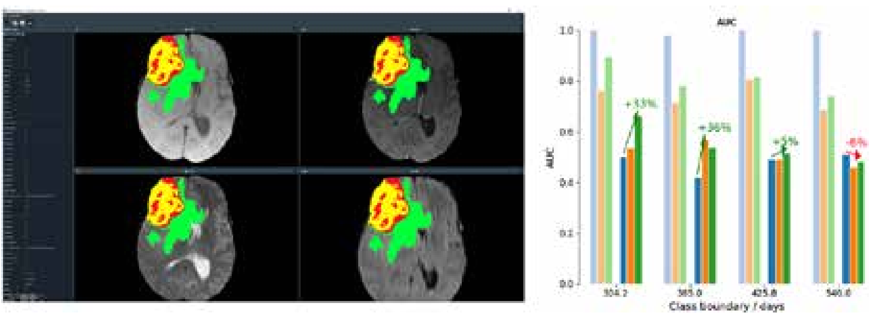

Fig. 1: Figure 1. Left: Deep Learning based automated quantification and analysis of brain tumor lesions – DeepBraTumIA software. Right: Favoring robustness in radiomics analysis can further improve overall accuracy of prediction models, demonstrated in overall survival prediction tasks.

Accurate Quantification and Radiomics Analysis in Medical Image Computing

Magnetic Resonance Imaging (MRI) and its variants are a powerful imaging modality that encompasses rich anatomical and physiological information at a high resolution. In neurosciences, these modalities have become a standard in clinical practice. However, the interpretation of the images requires the combined use of different modalities, which leads to the need of computer-assisted technologies.

Based on A.I technologies our group has developed methods and produced related translational technologies to automate the delineation of brain tumors. We have made these technologies available for the research community but also further developed them for future clinical use. In this regard, a unique feature of our translational developments has been in incorporating the capability of the technology to progressively adapt to changes in imaging modalities. In addition, the developed technologies feature an inclusive model, where state-of-the-art approaches worldwide can be fused to enhance performance and robustness. Beyond lesion contouring our current research activities lie on rethinking and challenging current A.I technologies such that they are optimized to the clinical end-goal. In these →

regards, in radiation oncology, we are investigating A.I learnability approaches targeted directly towards metrics derived from the clinical-end goals.

Radiomics is an emerging research area where image analysis methods are employed to mine imaging information to answer clinical questions. Our research in radiomics is focused in investigating patters of robustness of radiomics-based imaging biomarkers in multi-center studies where imaging variability is inherent. We have highlighted current challenges to setup robust radiomics analysis in brain tumor imaging, and proposed methodologies to compensate these issues when models trained in single-center datasets are employed for multi-center radiomics analysis. Due to the pandemic, our group joined efforts to investigate deep learning-based quantification and radiomics strategies for the prognosis and severity prediction of COVID-19 patients, employing a multi-omics approach relying on imaging and non-imaging information. During 2020 our group also contributed with novel deep learning-based methodologies to enhance the accuracy and clinical adoption of magnetic resonance fingerprinting.

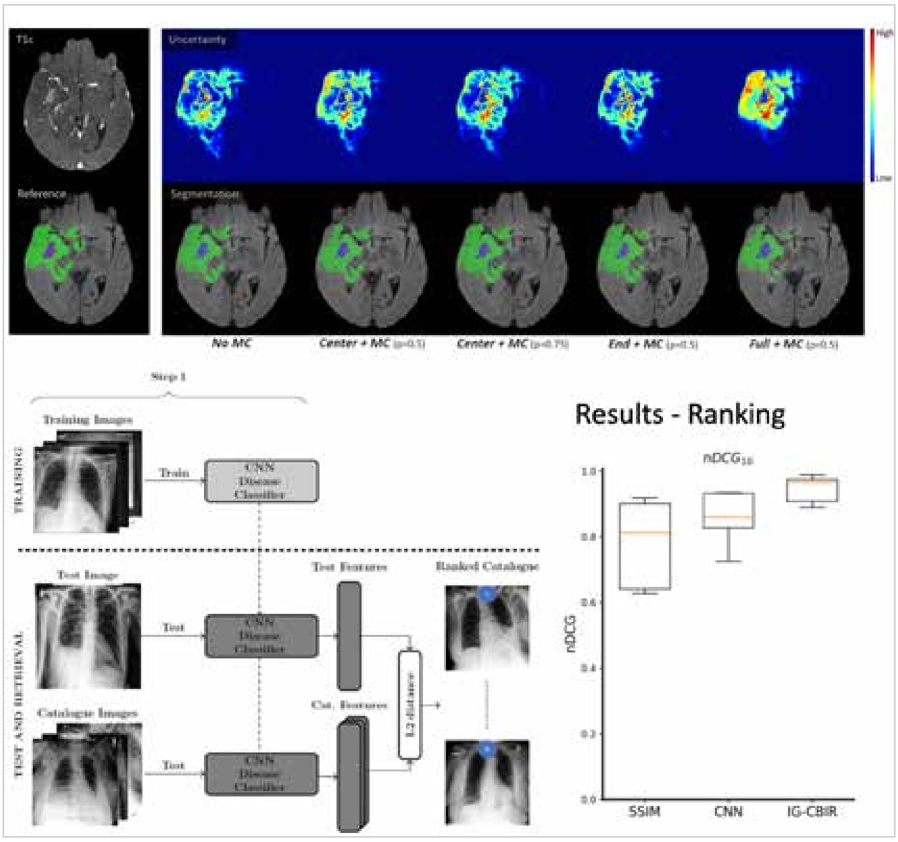

Fig. 2: Top: Investigating uncertainty estimation in medical image segmentation for the task of brain tumor segmentation. Bottom: Interpretability-guided medical image retrieval.

Uncertainty and Interpretability of Deep Learning based Medical Image Analysis

Next to accuracy, the robustness of computer-assisted technologies is fundamental for their effective deployment and integration in medicine. Particularly, it is crucial to develop technologies that can cope with computer errors stemming from the large heterogeneity of medical images, the complex pathophysiology of disease, among other factors. Towards a better understanding and clinical adoption of medical imaging A.I technologies, our group is researching on interpretability approaches to leverage our understanding on the underlying learning mechanisms of AI systems, as well as to identify areas where their robustness is affected in clinical imaging scenarios. Our group has also investigated on the reliability of uncertainty estimates of AI-based automated delineation systems, where we have reported the current challenges and potential avenues towards safe and reliable utilization of these technologies. Beyond interpretability approaches, our group is investigating other innovative methodologies to employ interpretability results of AI systems in order to improve sample selection and trainability of these systems.

Selected Publications

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6. Reyes M., Meier R., Pereira S., Silva C., Dahlweid FM., von Teng-Kobligk H., Summers R., and Wiest R. On the interpretability of Artificial Intelligence in Radiology: Challenges and opportunities. Radiology: Artificial Intelligence, 2(3): e190043, 2020.

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: Novel robotic training strategies. We combine new robotic control strategies and EEG measurements to enhance sensorimotor training of patients with neurologic injuries.
Photo: Adrian Moser for ARTORG Center

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 pendulum task) using a delta robot (Fig. 1). 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. The results showed that training with MPCs promoted movement variability and enhanced learning of task dynamics.

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

In an Innosuisse project, a novel robotic device for sensory-motor hand rehabilitation of brain-injured patients is being developed. To assess the clinical needs, a survey with 33 participants (health professionals) was conducted. The results showed that grasping, eating and personal hygiene were amongst the most important activities of daily living to be exercised. Finger and wrist extensions were reported as crucial movements to ➔

Fig. 2: The prototype of novel clinical driven hand rehabilitation device for sensorimotor training.

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 virtual reality to enhance neurorehabilitation. Experimental setup showing the rehabilitation device and virtual environment for a future study in stroke population.

be trained. Moreover, participants would like to spend less than ten minutes for the setup of a patient. The prototype of the novel design (Fig. 2) focuses on an easy setup, offers a large range of motion while guaranteeing physiological finger movements and provides haptic rendering to enhance somatosensory feedback during training. The design is currently being refined and the development of a serious game with dynamic and interactive training tasks has been initiated.

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 surfing task using Electroencephalography (EEG). Different task instructions (implicit to explicit knowledge about the task rules) were provided during training.

Training with explicit knowledge about the task rules and with visual cues implicitly enforcing these rules enhanced motor performance. 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.

Exoskeletons for Sensorimotor Training
(Promobilia Stiftelsen 18155)

During physical training, patient's effort and the provision of realistic sensory input are crucial to provoke brain plasticity. We employed novel controllers to achieve high transparency and fine haptic capabilities on the exoskeleton ARMin (Fig. 3), together with arm weight support. This approach was evaluated with six healthy participants during a virtual pendulum task. The weight support enhanced task performance and reduced participants' effort, while haptic rendering of the pendulum dynamics affected how participants move (e.g., increased speed and higher workspace exploration). These novel controllers 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 young and 20 elderly participants, we compared the impact on movement quality, cognitive load, motivation, and usability of novel visualization technologies (Fig. 4): Immersive VR (IVR), augmented reality (AR) and computer screens. The movement quality improved in IVR, but also -to a smaller extent- in AR, compared to the computer screen. No difference in the cognitive load was found between modalities. Young participants rated the IVR display as most motivating and usable. A follow-up study with stroke participants is in preparation.

Enhancing Touch Sensibility with a Novel Robotic System
(UniBE Initiator Grant, IFARHU-SENACYT)
Up to date, robotic neurorehabilitation has mainly focused on promoting motor recovery, neglecting sensory training. In this project, we assess and simultaneously train patients' tactile capabilities with a novel robotic system. We deployed a robotic virtual task that consists of discriminating the "odd texture" among three visually identical haptically rendered textures. The tactile capabilities during active or passive texture exploration will be compared in an on-going study with healthy participants.

Body Ownership over an Avatar Enhances Motor Performance
(NCCR Robotics, UniBE ID Grant)

We recently found behavioral evidence for a functional coupling between embodiment and motor performance with 50 healthy young participants. In a follow up clinical experiment, stroke patients will perform an activity of daily living with robotic support in immersive VR. To modulate the level of body ownership, an avatar will be shown from the first- versus third-person perspective. We will record behavioural and neurophysiological (EEG) signatures of motor learning during motor task performance in virtual reality. We expect that embodiment modulates attentional-motor brain networks engaged during motor learning and that motor learning is significantly increased in high versus low embodied avatars.

Selected Publications

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2. Wenk N., Penalver-Andres J., Buetler K. A., Müri R.M., Marchal-Crespo L., "Effect of Immersive Visualization Technologies on Cognitive Load, Motivation, Usability, and Embodiment." Virtual Reality, 2021. [In Press].
3. Özen Ö., Penalver-Andres J., Ortega E. V., Buetler K. A. and Marchal-Crespo L. , "Haptic Rendering Modu-lates Task Performance, Physical Effort and Movement Strategy during Robot-Assisted Training," 2020 8th IEEE RAS/EMBS International Conference for Biomedical Robotics and Biomechatronics (BioRob).
4. Rätz R., Müri R.M., Marchal-Crespo L., "Assessment of Clinical Requirements for a Novel Robotic Device for Upper-Limb Sensorimotor Rehabilitation after Stroke", International Conference on Neurorehabilitation, 2020.

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 bon-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: Fig. 1 Selected members of the musculoskeletal biomechanics group at sitem-insel (from right to left): Michael Indermaur, Patrik Wili, Christina Wapp, Alice Dudle, Benjamin Voumard, Daniela Frauchiger, Denis Schenk and Philippe Zysset.

Current Research Projects

Multiscale mechanical properties of bone in osteogenesis imperfecta
(SNF grant # 165510 with EMPA, MGU and MEREO Pharma)

Osteogenesis imperfecta (OI) is a genetic bone disorder affecting collagen quality and leading to an increase in bone fragility. Micropillar compression tests were performed to quantify the mechanical properties at the bone matrix level on 6 OI and 6 control human trans-iliac crest biopsies. Unexpectedly, OI bone matrix tends to show higher mechanical properties compared to healthy matrix and the variation is driven by the degree of mineralisation. At the apparent trabecular level, fabric-elasticity relationships were assessed in silico for OI versus healthy tibias. Finally, a homogenized finite element (hFEA) method accounting for the degree of mineralisation of the matrix was developed to investigate the influence of a new medication on bone strength at the organ level.

Polarized Raman spectroscopy and micropillar compression
(PHRT grant #2017-304 with EMPA)

At the microscale, the anisotropic elastic properties of bone are known to depend on the orientation of the mineralised

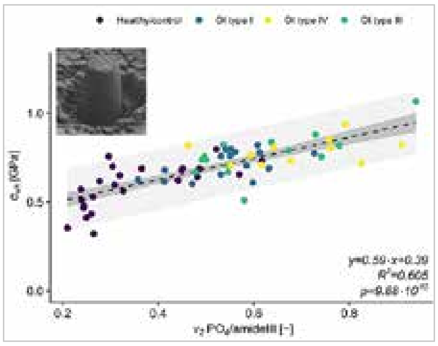

Fig. 2: Compressive bone strength of OI bone ECM is dominated by the extent of mineralisation.

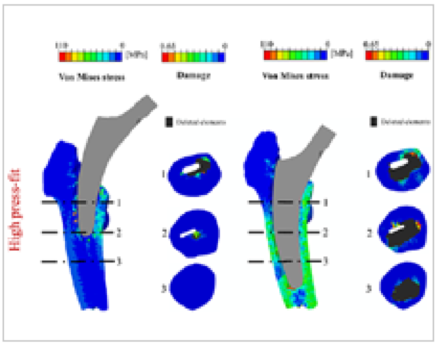

Fig. 3: Levels of stress and damage during high press-fit insertion of a femoral stem.

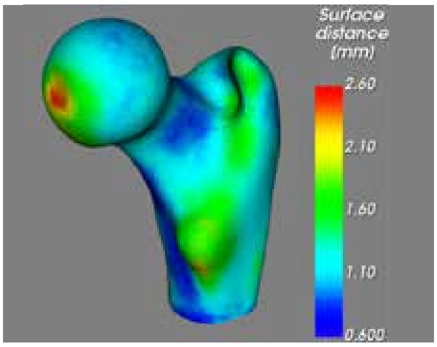

Fig. 4: Evaluation results of the 2D-3D reconstruction. Average distance between bone surfaces [mm].

→ collagen fibrils (MCF), but little is known about this influence on post-yield properties. In this work, a polarized Raman spectroscopy method was calibrated for determination of MCF orientation and validated with micro-computed tomography as well as small angle X-ray scattering. Compression tests on bovine cortical bone micropillars with known MCF orientation were then performed. The degree of anisotropy of yield stress (2.54) was found to be lower than the one of elastic modulus (3.80).

Explicit finite element analysis of femoral stem insertion and loading
(with RMS)

Primary stability in uncemented total hip arthroplasty (THA) is often assessed by insertion force, relative micromotions at the interface or subsidence of the femoral stem. We employed an explicit finite element model to assess primary stability in these terms. The bone was modelled as an elasto-plastic material with element deletion based on damage. The implantation phase was simulated using a displacement constraint that led the implant to self-position by frictional contact. Implantation force and work, implant subsidence and relative micromotions during a gait cycle were quantified for low and high press-fit conditions. Not surprisingly, all outcome variables were significantly affected by press-fit.

HR-pQCT-Based Homogenized FEA of multiple sections of the distal radius and tibia
(with EUT, IS and VUT)

Personalised in vivo assessment of bone strength estimated by finite element analysis (FEA) based on high-resolution peripheral quantitative computed tomography (HR-pQCT) becomes successful in identifying people at high risk of fractures. This year we examined clinical repeatability and reference values of our refined FE estimation of bone strength at the distal radius and tibia using more than one-hundred patients.

AFFIRM-CT
(SNF grant 183584 with HUG and IS)

The preparation of the clinical study continued during the past year, despite the pandemic. It included the harmonisation of the study protocol between Bern and Geneva and the finalization of the RedCap database. In parallel, different aspects of the risk model for hip fractures are in development, such as a finite element analysis software for the assessment of hip strength. A second part consists in developing estimation models for the fall risk and the impact force, based on the medical assessments included in the study. A third component of the project is the 2D-3D reconstruction of DXA scans of the femur, starting with the evaluation of an existing method.

Biomechanical Testing and Simulation
(ZMK)

Despite the restrictions associated with the pandemic crisis, two projects could be conducted in the biomechanics laboratory with appropriate safety measures. On the one hand, artificial intervertebral discs with biomimetic microstructures were successfully tested on the spinal loading simulator for characterisation of their multi-axial stiffnesses. On the other hand, primary stability of a specific dental implantation system and protocol was investigated in human jawbone samples. Finally, an explicit micro-FE model was exploited to compare two distinct drilling protocols in bovine trabecular bone for the same dental implant system.

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Organs-on-Chip Technologies

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Tobias Weber
Pauline Zamprogno
Soheila Zeinali
Sandra Zwyssig

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.

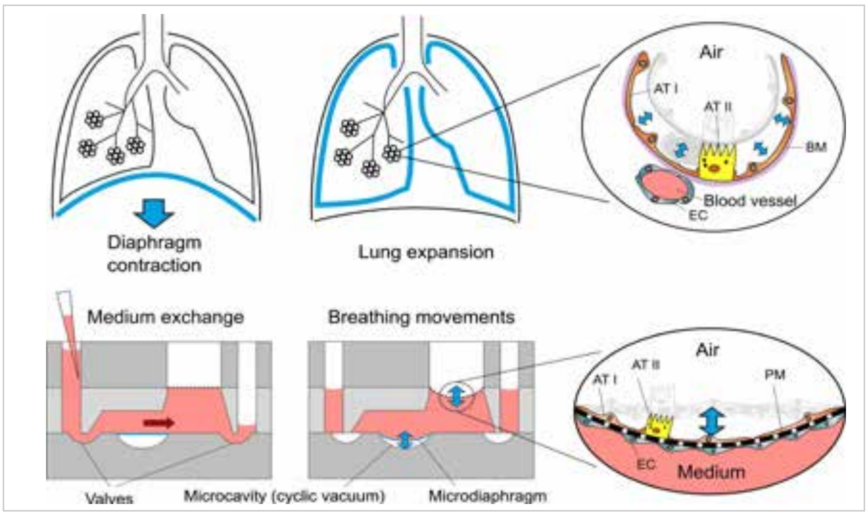

Fig. 1: Concept of the lung-on-chip: Top: in-vivo, the lung expands following the contraction of the diaphragm, a movement that stretches the alveoli (right). The alveolar barrier consists among others of alveolar epithelial cells (AT I and AT II) and of endothelial cells (EC) that are supported by the 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

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

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 with endothelial cells from the central chamber 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.

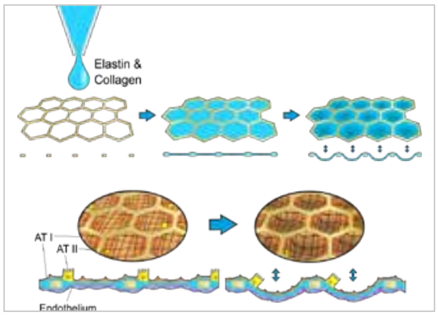

Fig. 3: Concept of the second-generation lung-on-chip: a drop of collagen and elastin is pipetted on a thin hexagonal gold grid. The stretchable membrane is formed by surface tension forces and evaporation. Zamprogno et al. BioRxiv, 2019.

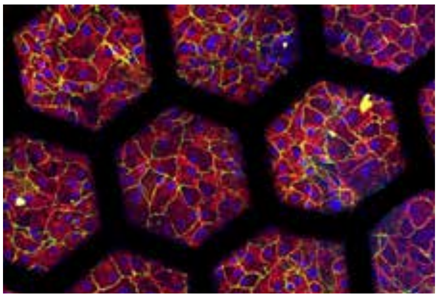

Fig. 4: Lung alveolar epithelial cells from patients cultured on the collagen-elastin membrane supported by an ultra-thin hexagonal gold grid (each hexagon is ca. 260µm wide). Zamprogno et al. BioRxiv, 2019.

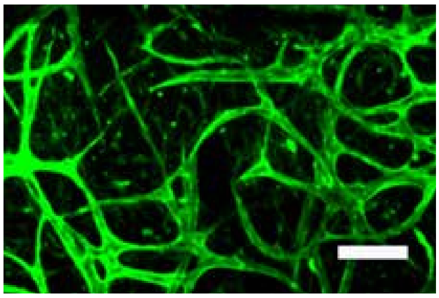

Fig. 5: Image of a functional microvasculature network made of self-assembled endothelial cells and lung fibroblasts on a chip. In green, the endothelial cell marker PECAM-1 (after 7 days in culture). Scale bar: 200µm. Zeinali et al. Angiogenesis 2018.

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., Thoma G., Cencen V., Ferrari D., Putz B., Michler J., Fantner G., Guenat O.T., Mechanical Properties of Soft Biological Membranes for Organ-on-a-Chip Assessed by Bulge Test and AFM, ACS Biomaterials Science & Engineering (2021).
3. 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-a-chip array with a stretchable biological membrane, Nat. Commun. Biol. 4, 168 (2021).
4. Zeinali S., Thompson E., Gerhardt H., Geiser T. Guenat O.T., Remodeling of an in vitro microvessel exposed to cyclic mechanical stretch, APL Bioengineering, 2021.

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.

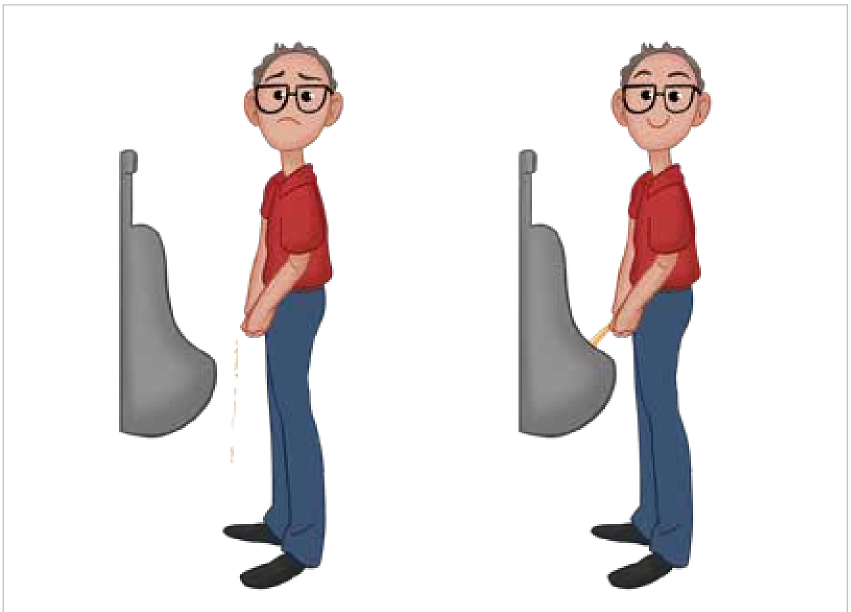

Fig. 1: Our solution for patients suffering from urinary retention consists of an external and non-invasive device. The device is handheld and discreet as it can be used only when needed.

Our world's first 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. This research has led to an external and discreet device (Figure 1). URODEA is a spin-off of the ARTORG Center and is focusing on bringing this technology to the patients.

➔

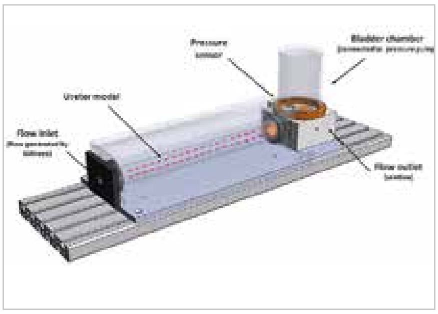

Fig. 2: CAD drawing of the in-vitro platform of the upper urinary tract. It allows fluid mechanical characterisation inside the ureter with/without ureteral stents by means of Particle Image Velocimetry.

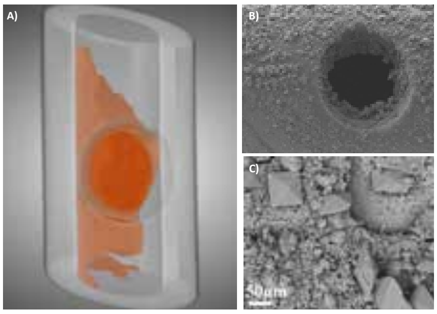

Fig. 3: A) Example of micro-computed tomography image of a stent side hole with encrustation (orange). Examples of scanning electron microscopy images of B) the stent side hole with the typical c) calcium-based encrustations

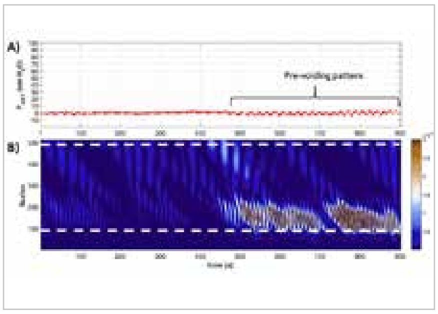

Fig. 4: Time frequency analysis is applied to identify pre-voiding patterns in patients suffering from overactive bladder: A) example of bladder pressure recording and B) corresponding scalogram.

➔ 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: 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 unwanted bladder contractions. 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. Zheng S., Carugo D., Mosayyebi A., Turney B., Burkhard F., Lange D., Obrist D., Waters S., Clavica F. 'Fluid mechanical modelling of the upper urinary system: a review' WIREs Mechanisms of Disease, 2021
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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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 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: CNC street

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 2020 we performed two trial apprenticeships and elected Piravin Jeyendran as our new apprentice and he will begin his 4-year training next year on 1st of August as a Polymechanic EFZ apprentice.

Due to a high demand of workload, we recruited two polytechnician, Christopher Balli and our former apprenzice Lukas Rufener as alternative civilian-service employees. They performed administrative tasks and increased the productivity of our team. We thank both of them for the work they have accomplished in our workshop.

Owing to the outbreak of the COVID-19 pandemic, the workshop had to stop production on 17 March. During home office, all employees were able to design some parts for new projects and create drawings. From April 27, production was recommenced, but with reduced staff attendance.

New 4-Axis Milling Center

Since February, i.e. shortly before the Covid lockdown was pronounced, the Mechanical Design and Production group has been able to produce more complex milling and drilling parts for research assemblies on a fully automatic CNC (Computer Numerical Control) 4-Axis Milling Center.

The machine is equipped with a tool turret system. This means that 30 defined tools are available. The tool change is automatic, which is why the operator does not have to remain at the machine and can carry out other work. This circumstance also leads to the fact that the productivity can be increased. The built-in and CNC-controlled fourth axis makes it possible to machine four sides and one surface on a workpiece in a single operation. This fourth axis also contributes to the increase in production.

Together with the CNC lathe purchased last year, the workshop has modern equipment and has become much more attractive for apprentice training.

Fig. 2: New machine. 4-axis Milling center FEHLMANN P56TOP

Platform sitem-insel Support Funds

Since August the workshop is accredited as official research platform of the sitem-insel Support Funds (SISF). This could trigger a further push to find new research partners and future customers.

In September we took the accreditations as an opportunity to hold a public event “Open Workshop”. This event was mainly held for all platforms in the sitem-insel building, but potential partners from the University of Bern and the Inselspital were also invited. During this afternoon we were able to present our services, which we also offer to external research partners. Despite the high demands on the security concept because of COVID-19, many visitors were able to get a first impression and get to know our workshop as well as the MDP team.

Fig. 3: Open door

Research Equipment Design & Manufacturinjg

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 Center yield a number of diverse design and production requests from prototype clinical and surgical tooling to fixtures for mechanical, biological and kinematic testing, as well as imaging system accessories and calibration equipment. The following illustrations highlight a few of this year’s projects.

Move and rebuild TOMO-PIV System

As the last relocation activity of the Cardiovascular Engineering group (CVE), the Tomographic Particle Image Velocimetry (TOMO PIV) system was moved to the sitem-insel building. In contrast to the previous suspension on the wall (Fig4), a new fixture had to be designed and built so that the system could be mounted on an air-bearing table.

Fig. 4: TOMO PIV before

Fig. 5: TOMO PIV after

Dental bridges

We received an order from an external research partner to manufacture titanium dental bridges. The challenge for us was to machine high-precision cones and outer contours with 1.5 mm diameter milling tools. With this order we could test our manufacturing possibilities on the new CNC milling machine.

Fig. 6: Dental bridges

Center for Artificial Intelligence in Medicine (CAIM)

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Technology for better patient care

Digital technologies like Artificial Intelligence (AI) and robotics are steadily becoming everyday tools in clinical reality. To take leadership in the direction of research and development of AI in Medicine, the University of Bern and the Inselspital, Bern University Hospital, together with partners from sitem-insel, the Swiss Institute for Translational and Entrepreneurial Medicine, and the University Psychiatry Services (UPD) have founded the Center for AI in Medicine "CAIM".

Bringing together world-class scientists and clinicians to join with collaborators in industry, in patient advocacy and in medical ethics, researchers will enable the investigation and translation of advanced digital and robotic technologies to deliver a new generation of diagnostics, treatments and interventions. CAIM started operations in January 2021 driven by the existing expertise in AI in medical research, engineering and healthcare digitalization education within the Bern network to bring forward AI in Medicine solutions with positive impact for patients everywhere.

Profile

The Center for Artificial Intelligence in Medicine is a research, teaching and translation platform that investigates AI medical technologies that can facilitate the work of doctors and nurses and bring better care to patients. CAIM capitalizes on the significant presence of scientific, healthcare and medical technology industry players in the capital of Switzerland. It is a virtual Center of the University of Bern's medical faculty and the Inselspital, Bern University Hospital in partnership with the University Psychiatry Services (UPD) and the Swiss Institute for Translational and Entrepreneurial Medicine, sitem-insel. The University of Bern, the Inselspital, Bern University Hospital ("Digital Hospital") and the Canton of Bern ("Engagement 2030") have major, strategic digitalization in healthcare goals. CAIM plays a key part in these efforts and connects engineers, physicians and scientists in the area of AI in Medicine, providing them with resources and access to infrastructure so they can innovate AI and robotic technologies that are fit to make it into the clinic. As the newest member of the Bern Biomedical Engineering Network, CAIM will also gain access to industry and local resources and networks. CAIM will foster commercialization of AI technology innovation, support start-up incubation and create sustained value and economic growth through best in class research and translation.

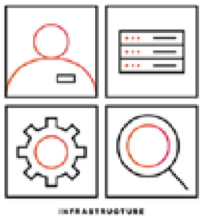
Organization

CAIM's activities are organized on four pillars:

Pillar I: Digitalization & AI Education

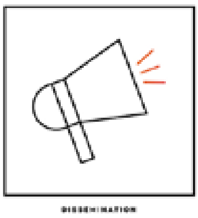
CAIM provides tailored AI in Medicine education for medical doctors and engineers through a portfolio of competitive and purposefully designed post-graduate programs to equip participants for Healthcare 4.0.

Pillar III: Computational Facilities



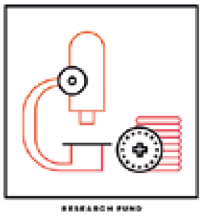
CAIM facilitates access and availability to computer infrastructure, computational and data resources to support advanced digitalization and AI research within the Bern Medical Hub.

Pillar II: Network & Dissemination



CAIM transmits trustworthy knowldege on AI in Medicine. This supports policy makers, educators and the general public by shaping the current debates on AI in Medicine with evidence-based information.

Pillar IV: Research Project Fund



CAIM promotes technological innovation by funding projects with strong potential to be groundbreaking clinical approaches and a realistic pathway towards patient benefit.

AI in Medicine – Fields of Research and Education

In the age of digitalization and data-based healthcare, Artificial Intelligence (AI) is an indispensable tool for analyzing large amounts of health data and rendering it into easy-to-use form to support diagnosis, treatment decision and disease management.

Various fields of AI in Medicine are currently being explored in Bern. Some examples include:

- Quantitative biosignal processing
- Biomarker identification in medical imaging
- Clinical data exploration with deep learning
- Monitoring of chronic disease progression
- Precision medicine (e.g. oncology)
- Real-time surgical navigation
- Surgical and rehabilitation robotics

CAIM provides important insights, evaluation and perspective for introducing novel AI technologies into clinicalcare by translating state-of-the-art research into tools for clinicians and healthcare professionals.

Targeted educational programs and courses of the University of Bern provide AI researchers and clinicians with cutting-edge know-how and qualifications in the field. This includes courses in "Digitilization and AI" for medical students, a dedicated Master's programme for AI in Medicine for engineers (starting fall 2021) and AI in healthcare-related postgraduate training and further education offers.

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