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ARTORG CENTER
BIOMEDICAL ENGINEERING RESEARCH

ARTORG CENTER
ANNUAL REPORT 2024

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STAGE UP Award 2024 Winners Silje Jahren, Emmanuel Zimmer, Pascal Buchs

Foreword

Dear friends, colleagues, collaborators, and partners

2024 has been an exceptional year of growth and consolidation for ARTORG, exemplifying our long-term strategy for translating medical technology research into tangible clinical applications. Rather than pursuing fleeting trends or short-term gains, continue to pursue foundational, patient-centric research that addresses the unmet needs of both patients and practitioners.

This year, ARTORG continued strides in publishing high-impact research, securing competitive research funding (over CHF 4.7 million in third-party funding, including from SNSF, Innosuisse, and EU sources), conducting evidence-based clinical studies, and creating defensible intellectual property. These achievements have paved the way for new ventures and investments while maintaining our dedication to training the next generation of biomedical engineers.

Our achievements in 2024 reflect our commitment to advancing healthcare innovation:

- Pioneering research and recognition: Amith Kamath from the Medical Image Analysis Lab won the Falling Walls Competition in Fribourg for his AI-enhanced radiotherapy project, which aims to reduce treatment times for glioblastoma patients from two weeks to near-instant.
- Translation of technology: ValTech Lifesciences secured CHF 150,000 through the Venture Kick program to advance next-generation heart valve prostheses.
- Fostering innovation: New cohort members TightValve™ received the SNSF BRIDGE Proof of Concept grant, marking our fourth BRIDGE grant, and IMPLANZ™ received full Innosuisse support, continuing our success with the national innovation funder.
- Inclusion and equity: The Diversity in AI for Medicine (DAIM) initiative won the prestigious Prix Lux 2024 for its work in addressing biases in AI systems, fostering inclusivity, and promoting diversity scholarships.
- Fellowships for excellence: ARTORG hosted UniBE Venture and CAIM fellows, supporting projects that span groundbreaking technologies in precision medicine, advanced biomedical devices, and digital health solutions, further strengthening our translational focus and gender parity.

These successes highlight our overarching vision to advance knowledge, empower clinicians, and enhance patient care. While the path forward is neither quick nor easy, it is deliberate and driven by thoughtful collaboration. We are deeply grateful for the collective efforts that have driven our progress and remain committed to the success of those we serve and collaborate with in advancing medical research.

I hope you will enjoy exploring a selection of our projects showcased on the following pages.

Sincerely,

Raphael Sznitman
ARTORG Director

Groups

AIHN
Artificial Intelligence in Health Nutrition

AIMI
Artificial Intelligence in Medical Imaging

CVE
Cardiovascular Engineering

CB
Computational Bioengineering

GER
Gerontechnology and Rehabilitation

HRL
Hearing Research Laboratory

MIA
Medical Image Analysis

MSB
Musculoskeletal Biomechanics

NRG
Neuro Robotics Group

OOC
Organs-on-Chip Technologies

UGE
Urogenital Engineering

MDP
Mechanical Design and Production

Master of Science
Artificial Intelligence in Medicine

Master of Science
Biomedical Engineering

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Research Profile

The Artificial Intelligence in Health and Nutrition (AIHN) laboratory focuses primarily on the interface between machine learning, artificial intelligence (AI), and their applications for improving health. The laboratory develops innovation to translate "data into knowledge" and "research into clinical practice." Our ongoing research activities include AI-powered innovative systems for:

- dietary monitoring, assessment and management
- diabetes self-management and treatment optimisation
- diagnosis, prognosis and management of acute and chronic lung diseases
- diagnosis for emergency medicine

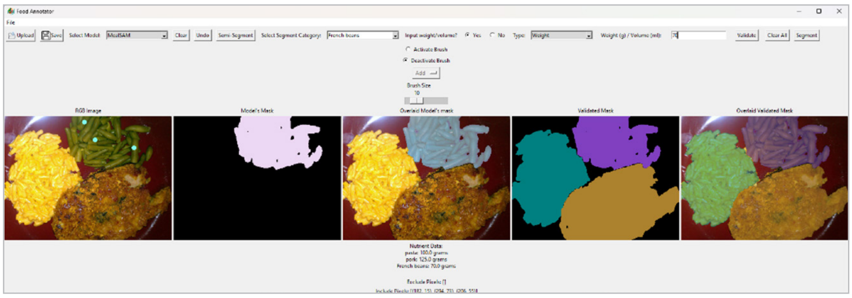

Fig. 1: Illustration of meal image segmentation with annotated labels and volume estimation via semi-automatic tool.

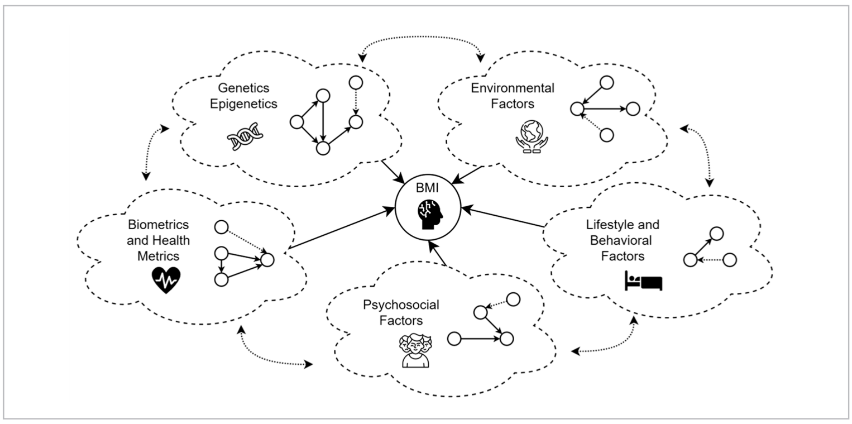

Fig. 2: Conceptual overview of a causal graph illustrating obesity factors across five key variable domains.

Nutrient Intake Monitoring and Diet Assessment

Maintaining a healthy diet is vital for preventing and managing conditions like malnutrition, cardiovascular diseases, diabetes, and obesity. Traditional dietary assessment methods, while common, are often time-consuming, costly, and prone to error due to reliance on self-reported memory. To overcome these challenges and streamline the process, image-based automatic dietary assessment systems have been developed, leveraging advancements in artificial intelligence (AI) and computer vision (CV). However, two main challenges persist: the scarcity of annotated food data for training and evaluating models and the vast diversity of food types and eating habits worldwide.

To address these gaps, we created an open-source food image annotation tool, that uses a prompt-based segmentation model (SAM) for efficient, user-friendly food segmentation and categorization, with optional weight and volume annotation. Additionally, we fine-tuned SAM (MealSAM), specifically tailored for food image segmentation, to encourage collaborative efforts and expand annotated datasets. Furthermore, we explored post-hoc out-of-distribution (OOD) detection methods within fine-grained food recognition, an area with limited research. Our findings show that Virtual-logit Matching excelled at distinguishing non-food items, as well as detecting food items from unknown distributions, enhancing the robustness of AI in dietary assessment across diverse real-world scenarios.

Causal AI for Personalized Obesity Intervention

Obesity is a complex, chronic condition linked to higher risks for various non- →

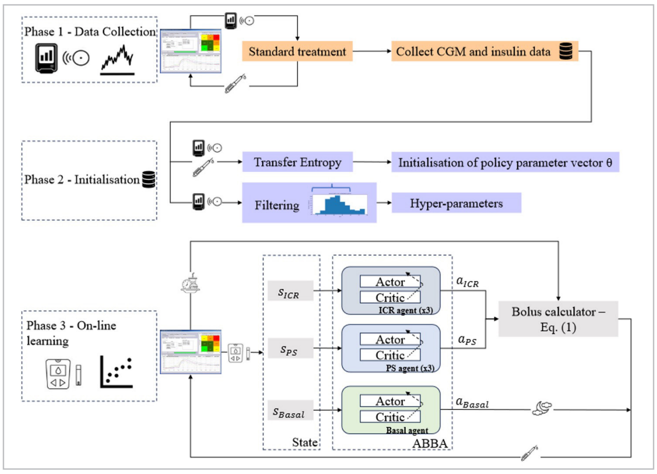

Fig. 3: Adaptive Basal-Bolus Advisor for personalise insulin adjustment to people with diabetes on intensive insulin treatment.

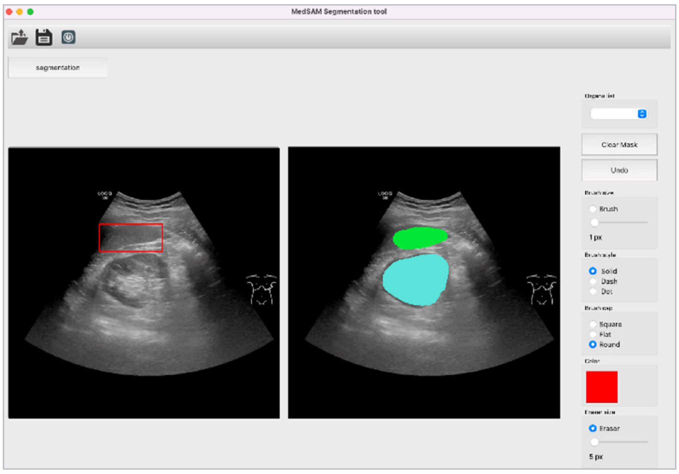

Fig. 4: Annotation tool for segmenting ultrasound images.

communicable diseases. According to WHO, as of 2022, nearly 60% of adults in Europe are overweight or obese, with global obesity prevalence having doubled since 1990. The BETTER4U project (Preventing obesity through Biologically and bEhaviorally Tailored inTERventions for you) is a 4-year Horizon Europe initiative launched in 2023 across 21 countries to explore the causal drivers of obesity. The AIHN Lab is leading efforts in designing an AI model to extract causal links from datasets contributed by partners across genetics, anthropometrics, environmental, lifestyle, and psychosocial factors. Leveraging federated learning, our model prioritizes privacy, processing distributed datasets securely while building a causal graph to understand individual and population-level influences on obesity. By applying causal inference AI, our model will personalize interventions, generating targeted and effective recommendations for sustainable weight management tailored to each individual's unique health profile. This approach supports healthcare professionals by offering precise, data-driven insights, advancing a scalable, evidence-based framework for obesity management in various healthcare settings.

Diabetes Management and Personalised Insulin Treatment

Treating type 1 diabetes and some cases of type 2 diabetes requires the infusion of exogenous insulin. An innovative algorithm has been developed by the AIHN laboratory and allows daily adjustment of the insulin treatment based on fluctuations in the person's glucose and lifestyle-related information. Specifically, data from glucose monitoring devices (self-monitoring of blood glucose or continuous glucose monitors) and lifestyle (food intake) trackers provide input to the algorithm, which outputs basal daily insulin and boluses for the case of pump or insulin pens users. The algorithm is based on reinforcement learning, and continuously learns from real-time data, avoiding biases associated with pre-training datasets. It implements a linear policy to enhance interpretability and predictability. The approach is data-driven, real-time, and of low computational cost. The algorithm is evaluated in-silico, using with the US FDA-approved diabetes simulator for three months period, under extreme scenarios of disturbances, uncertainties, and variabilities, showing significant improvement in the performance. A feasibility study and a multicenter clinical trial involving 450 people with diabetes under insulin treatment will start within the next year. This trial will also assess a newly developed AI-driven alarm system that proactively warns individuals of potential hypo- and hyperglycaemic episodes using retrospective study data. This alarm system empowers people with diabetes to better manage and prevent these episodes, potentially increasing their time-in-range and enhancing their overall quality of life.

Multimodal Data Analysis for Diagnosis and Disease Prediction

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. We investigate AI- and CV-based algorithms on high resolution computed tomography images (HRCT) specifically for the diagnosis and management of ILDs. 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 to support the faster diagnosis, but also for the more efficient disease management in the sense of treatment selections and disease progression. Recently, we started to explore multi modal methods for diagnosing pneumonia in elderly patients, assessing whether ultrasound (US) can provide a low-cost efficient solution. We have access to a specific dataset where patients have US, X-ray and HRCT images taken, along with clinical and demographic information. Lasty, we are collaborating with Inselspital in the development of fully automated AI tools with regards to abnormalities in abdomen US. As a first step, we have developed a semi-automatic segmentation tool based on MedSAM and plan to open source this next year.

Selected Publications
1. 10.1111/dom.15521
2. EP24206753.6 "Adaptive Drug Management System" (filed)
3. 10.3233/FAIA241033)
4. Abdur RL, et al. „Benchmarking Post-Hoc Unknown-Category Detection in Food Recognition, Accepted in Proceedings of the MADIMa2024/ICPR2024.
5. 10.1109/ACCESS.2024.3350430

Artificial Intelligence in Medical Imaging

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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.

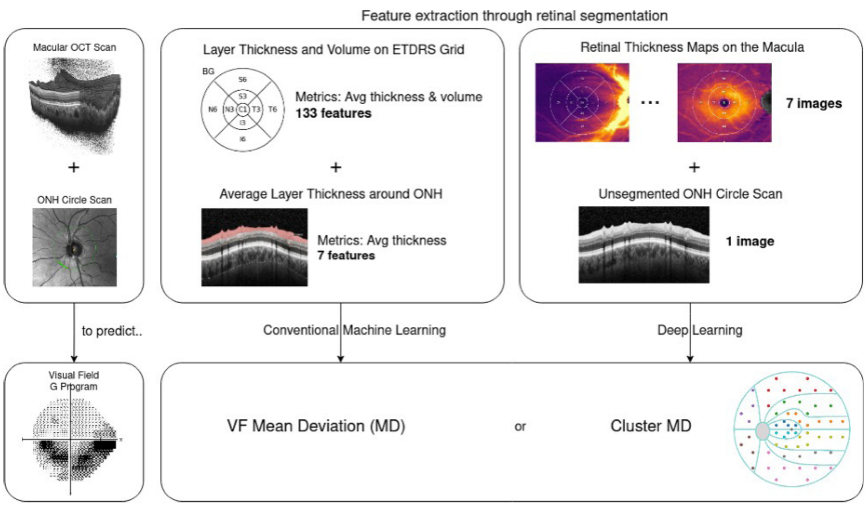

Fig. 1: We investigated two problems with significant clinical impacts: the estimation of the MD and the estimation of cluster MDs. Clusters are defined based on the RNFL bundles' entry into the optic disc. Clusters are numbered from 1 to 10 in a counterclockwise direction starting from the temporal location. We evaluated a deep-learning approach described below for both problems and compared it to a baseline model composed of a linear regression model fitted on the retinal layer thicknesses, averaged over the entire ETDRS grid in the case of macular scans.

Visual Field prognosis from OCT image in Glaucoma patients

We explore the structural-functional loss relationship from optic-nerve-head– and macula-centered spectral-domain Optical Coherence Tomography OCT images in the full spectrum of glaucoma patients using deep-learning methods. Using a cohort comprising 5238 unique eyes classified as suspects or diagnosed with glaucoma was considered. All patients underwent ophthalmologic examination consisting of standard automated perimetry (SAP), macular OCT, and peri-papillary OCT on the same day. Using retinal thickness maps, deep learning models were trained to estimate G-pattern visual field (VF) mean deviation (MD) and cluster MD. Combining multiple modalities, such as optic-nerve-head circular B-scans and retinal thickness maps from macular OCT images, improves the performance of MD and cluster MD prediction. Our proposed model demonstrates the highest level of accuracy in predicting MD in the early-to-mid stages of glaucoma. Objective measures recorded with SD-OCT can optimize the number of visual field tests and improve individualized glaucoma care by adjusting VF testing frequency based on deep-learning estimates of functional damage.

Online 3D reconstruction and dense tracking in endoscopic videos

3D scene reconstruction from stereo endoscopic video data is crucial for advancing surgical interventions. In this work, we present an online framework for online, →

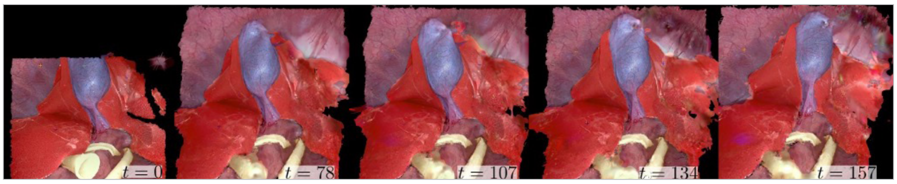

Fig. 2: 3D semantic segmentation as a downstream application. Semantic classes are overlayed: gall-bladder (purple), liver (red) and plastic tubes (yellow).

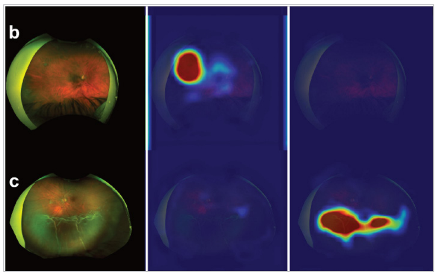

Fig. 3: Examples of UWF images with corresponding grad-CAM overlay. (b) Image with retinal break. (c) Image with retinal detachment.

dense 3D scene reconstruction and tracking, aimed at enhancing surgical scene understanding and assisting interventions.

Our method dynamically extends a canonical scene representation using Gaussian splatting, while modeling tissue deformations through a sparse set of control points. We introduce an efficient online fitting algorithm that optimizes the scene parameters, enabling consistent tracking and accurate reconstruction. Through experiments on the StereoMIS dataset, we demonstrate the effectiveness of our approach, outperforming state-of-the-art tracking methods and achieving comparable performance to offline reconstruction techniques. Our work enables various downstream applications, thus contributing to the advancement of the capabilities of surgical assistance systems.

Learning Non-Linear Invariants for Unsupervised Out-of-Distribution Detection

The inability of deep learning models to handle data drawn from unseen distributions has sparked much interest in unsupervised out-of-distribution (U-OOD) detection, as it is crucial for reliable deep learning models. Despite considerable attention, theoretically-motivated approaches are few and far between, with most methods building on top of some form of heuristic. Recently, U-OOD was formalized in the context of data invariants, allowing a clearer understanding of how to characterize U-OOD, and where methods leveraging affine invariants have attained state-of-the-art results on large-scale benchmarks. Nevertheless, the restriction to affine invariants hinders the expressiveness of the approach. In this work, we broaden the affine invariants formulation to a more general case and propose a framework consisting of a normalizing flow-like architecture capable of learning non-linear invariants. Our novel approach achieves state-of-the-art results on an extensive U-OOD benchmark, and we demonstrate its further applicability to tabular data. Finally, we show our method has the same desirable properties as those based on affine invariants.

Correlation-aware active learning for surgery video segmentation

Semantic segmentation is a complex task that relies heavily on large amounts of annotated image data. However, annotating such data can be time-consuming and resource-intensive, especially in the medical domain. Active Learning (AL) is a popular approach that can help to reduce this burden by iteratively selecting images for annotation to improve the model performance. In the case of video data, it is important to consider the model uncertainty and the temporal nature of the sequences when selecting images for annotation. This work proposes a novel AL strategy for surgery video segmentation, COWAL, COrrelation-aWare Active Learning. Our approach involves projecting images into a latent space that has been fine-tuned using contrastive learning and then selecting a fixed number of representative images from local clusters of video frames. We demonstrate the effectiveness of this approach on two video datasets of surgical instruments and three real-world video datasets.

Deep Learning-Based automated detection of retinal breaks and detachments on fundus photography

This study aimed to develop a deep learning algorithm to detect retinal breaks and retinal detachments on ultra-widefield fundus (UWF) optos images using artificial intelligence (AI). Optomap UWF images of the database were annotated to four groups. The fundus image data set was split into a training set and an independent test set following an 80% to 20% ratio. Image preprocessing methods were applied. An EfficientNet classification model was trained with the training set and evaluated with the test set. The classification models achieved an area under the receiver operating characteristic curve (AUC) on the testing set of 0.975 regarding lesion detection, an AUC of 0.972 for retinal detachment, and an AUC of 0.913 for retinal breaks. A deep learning system to detect retinal breaks and retinal detachment using UWF images is feasible and has good specificity. This is relevant for clinical routine as there can be a high rate of missed breaks in clinics. Future clinical studies will be necessary to evaluate the cost-effectiveness of applying such an algorithm as an automated auxiliary tool in large practices or tertiary referral centers. This study demonstrates the relevance of applying AI in diagnosing peripheral retinal breaks in clinical routine in UWF fundus images.

Selected Publications

1. Scandella, D., Gallardo, M., Seda Kucur Ergu nay, S., Sznitman, R., and Unterlauft, J., "Visual Field Prognosis from Macula and Circumpapillary Spectral Domain Optical Coherence Tomography", Translational Vision Science and Technology, 2024
2. Doorenbos, L., Sznitman, R., and Marquez Neila, P., "Learning Non-Linear Invariants for Unsupervised Out-of-Distribution Detection". European Conference on Computer Vision (ECCV), 2024.
3. Wu, F., Marquez Neila, P., Zheng, M., Rafii-Tari, H., and Sznitman, R., "Correlation-aware active learning for surgery video segmentation." IEEE/CVF Winter Conference on Applica- tions of Computer Vision (WACV), 2024.
4. Christ, M., Habra, O., Monnin, K., Vallotton, K., Sznitman, R., Wolf, S., Zinkernagel, M., and Marquez Neila, P. "Deep learning-based automated detection of retinal breaks and detachments on fundus photography", Translational Vision Science and Technology, 2024

Cardiovascular Engineering

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Research Profile

The Cardiovascular Engineering (CVE) group develops diagnostic and therapeutic technology for cardiovascular diseases. Our research aims to improve the durability and biocompatibility of cardiovascular devices and to establish novel diagnostic tools. These translational research projects address unmet clinical needs that were identified with our clinical partners who are closely integrated in our research teams from start to finish.

CVE operates a modern cardiovascular flow lab with state-of-the-art measurement technology to simulate physiological conditions in the cardiovascular system and to measure hemodynamic parameters. This includes highspeed cameras and laser-based methods for flow quantification. Next to the experimental facilities, CVE develops and uses custom-tailored computer models of cardiovascular flows, including fluid-structure interaction and turbulent blood flow. Large-scale flow simulations are enabled by using the high-performance computing infrastructure at the Swiss Supercomputing Center CSCS. For the development of patient-specific models, we work closely with radiologists to integrate clinical image data into experimental and computational models.

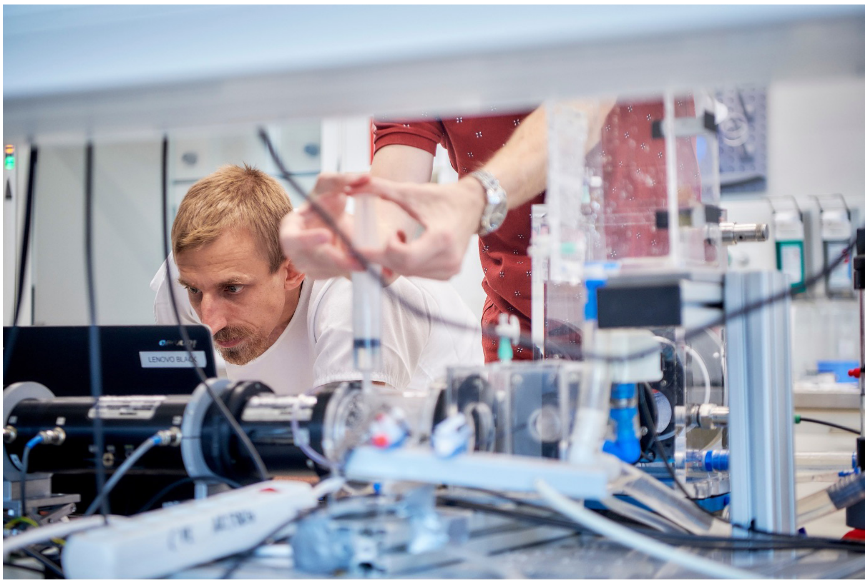


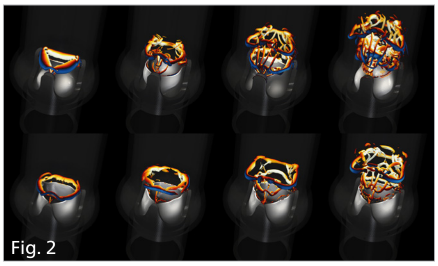
Fig. 1: Testing of heart valves in the Cardiovascular Flow Lab.

Heart Valve Replacement

Insufficient durability and biocompatibility of heart valve prostheses are limiting factors for the clinical use of these devices. In an ageing society where patients expect to be able to continue their active lifestyle after heart valve replacement, these limiting factors represent an unmet clinical need.

A detailed understanding of hemodynamic mechanisms governing valve tissue deterioration and blood trauma paves the way for the design of more durable and biocompatible devices. To this end, we have developed a sophisticated experimental and computational infrastructure for the study of heart valves. This includes mock loops replicating pulsating blood flow, silicone phantoms of large blood vessels, and modern measurement technology for quantifying complex three-dimensional turbulent blood flow fields (Fig. 1). This experimental expertise allowed us to support the development of a non-thrombogenic, durable heart valve prosthesis (TRIFLO by Novostia SA, Epalinges, Switzerland) which has been implanted for the first time in patients in December 2023.

Our experimental work is complemented by high-fidelity computer models for turbulent flow and fluid-structure interaction in cardiovascular systems. In collaboration with the Swiss Supercomputing Center CSCS, we have optimized these models for high-performance GPU-accelerated supercomputing platforms. This allows us to study complex turbulent flow phenomena in the human body at unparalleled speed which allows us to gain new insight into disease mechanisms (Fig. 2). In recent studies, we established a direct connection between turbulent blood flow and aortic valve calcification, →



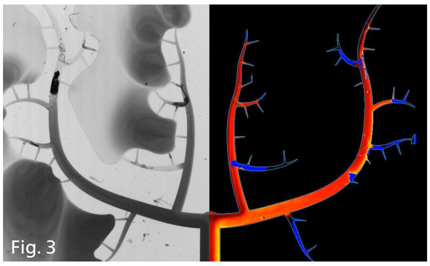


Fig. 2: Onset of turbulent flow in a fluttering (top row) and non-fluttering (bottom row) bioprosthetic valve.

Fig. 3: Drug transport in a microfluidic model of the cardiac microcirculation with microthrombi.

and we investigated which valve designs are more prone to lead to blood clots. This information is used to design better heart valve prostheses with higher durability and lower thrombogenicity. These efforts resulted in the spin-off company ValTech which promotes a novel idea to improve prosthetic valve design.

Aortic assist device

Together with the Center for Artificial Muscles from EPFL, we are working on a novel cardiac assist device in a project supported by the Werner-Siemens Stiftung. In contrast to classical ventricular assist devices (VADs) that use rotary blood pumps, the Dielectric Elastomer Actuator (DEA) device directly compresses and dilates a section of the aorta to support the function of the heart by reducing the afterload. We have developed an in vitro benchtop model with a circulatory mock loop to optimize the design and actuation pattern of the DEA device, and we are conducting in vivo trials at the experimental surgery laboratory to test and enhance its efficiency.

Computer-augmented 4D-Flow-MRI for plaque rupture

4D-Flow-MRI is a method for non-invasive and non-ionizing measurement of blood flow patterns in large blood vessels. It has great potential to be used for the diagnosis of cardiovascular diseases such as carotid stenosis. However, the lack of sufficient spatial resolution limits the applicability of this imaging modality in the clinic, and it is known that luminal wall-shear stress (an important factor in atherosclerotic plaque progression) is underpredicted by 4D-Flow-MRI. We combine data from 4D-Flow-MRI with advanced computational models to enhance the predictive quality of these measurements. This includes classical CFD models which are used to regularize the measured flow fields and statistical machine learning models which are trained with CFD data to yield very fast and accurate predictions of luminal wall-shear stress patterns that can be used in clinical practice.

Myocardial Infarction

In myocardial infarction (heart attack), the supply of the heart muscle with oxygen and nutrients is blocked by an obstruction of a coronary artery. Even after recanalization of this artery, secondary obstructions in the cardiac microcirculation (Microvascular Obstruction, MVO) may lead to local underperfusion of the heat muscle negatively affecting the long-term patient outcome. MVO is an underdiagnosed condition because it cannot be detected during acute treatment in the catheter lab. Moreover, there exists no established treatment for MVO.

We are addressing this unmet clinical in collaboration with the Swiss med-tech start-up CorFlow Therapeutics. We have developed a multi-scale benchtop model of the coronary circulation which allows us to study the pathophysiology of MVO and to develop novel diagnostic and therapeutic methods for MVO. This model comprises a microfluidic chip mimicking the cardiac microcirculation (Fig. 3). We are using this model to enhance the efficiency of drug-based treatment of MVO and we were able to show that microvascular thrombi may be resolved by micro-doses of thrombolytic drugs. This clinically important result opens a new field of therapeutic options because the use of high-dose thrombolytic drugs is very limited by adverse side effects such as bleeding.

Microvascular Blood Flow Regulation

Oxygen and nutrient exchange between blood and surrounding tissue takes place in the capillary networks of the microcirculation. They comprise capillaries as small as 5 micrometers, such that red blood cells must squeeze through these vessels. In contrast to blood flow in larger blood vessels, capillary blood flow follows different physical laws and the mechanics of red blood cells plays a dominant role. We study blood flow in complex capillary networks as they may be found, for instance, in the brain, and investigate how the network topology affects the distribution of red blood cells in the network and how the system reacts to local vasodilation and obstructions. We use computational as well as experimental models to better understand to complex interactions of blood flow, red blood cell mechanics and metabolic exchanges with the parenchymal tissue.

Selected Publications

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8. Tsolaki E., Corso P., Zboray R., Avaro J., Appel Ch., Liebi M., Bertazzo S., Heinisch P. P., Carrel T. C., Obrist D., Herrmann I. Multiscale multimodal characterization and simulation of structural alterations in failed bioprosthetic heart valves, Acta Biomaterialia 169:138-154, doi:10.1016/j.actbio.2023.07.044, 2023.

Computational Bioengineering

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Research Profile

The Computational Bioengineering Group tackles challenges in medical research with modern computer simulation tools. We focus not on the computational methods themselves, but on their appropriate application to address practical and fundamental clinical questions. Numerical methods are combined with experimental and clinical research to create personalized biomechanical models. Together with our collaborators, we form a strong team covering a wide range of research topics. In addition to our core expertise in applying finite element analysis to study skeletal biomechanics, we seek to improve surgical planning by developing numerical models of soft tissues, such as the cornea or intervertebral disc.

Fig. 1: A spinal suspension system was developed to measure spinal stiffness in adolescent idiopathic scoliosis patients.

A preoperative spinal stiffness test for adolescent idiopathic scoliosis

A precise understanding of the biomechanics of the spine is essential for planning the surgical correction of scoliosis and for understanding degenerative spine disorders. Current clinical tests of preoperative spinal biomechanics do not measure true mechanical stiffness because they assess spinal displacement without considering the force required to deform the spine. To address this limitation, we introduce a noninvasive, preoperative method for quantifying three-dimensional, patient-specific stiffness of the spines in adolescent idiopathic scoliosis patients. Our approach utilizes a spinal suspension test designed to simultaneously track both the force applied on the spine and the resulting vertebral displacements (Fig.1). This system exerts a force equivalent to 30% of the patient's body weight, while orthogonal X-rays capture the positions of the vertebrae under load. The suspension test is designed for use in a low dose biplanar X-Ray imaging system and can be combined with numerical modeling techniques to provide a comprehensive biomechanical assessment of patients with adolescent idiopathic scoliosis.

Depth-dependent biaxial characterizationof corneal stroma

More than 185,000 corneal transplants are performed each year, but more than half of the world's population does not have →

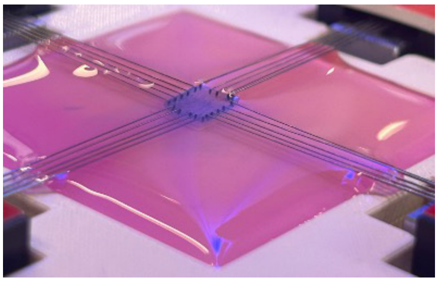

Fig. 2: Biaxial tests are used to characterize the depth-dependent biomechanics of the corneal stroma.

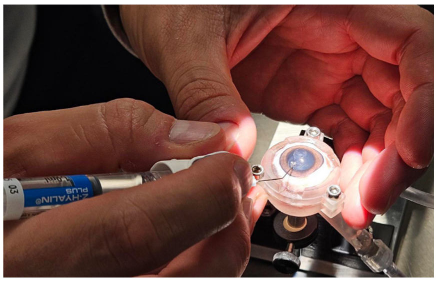

Fig. 3: Hydrogel injection into a pocket cut inside the cornea is used to reshape the cornea and correct hyperopia.

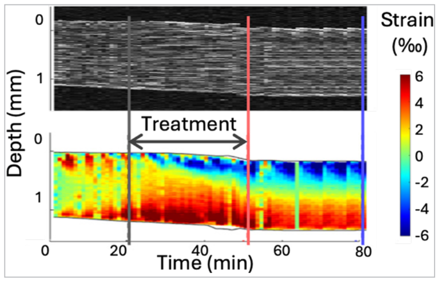

Fig. 4: Optical coherence tomography can quantify the strain within the corneal depth during the crosslinking treatment.

access to donor corneas, compromising patient care and research opportunities. Comprehensive knowledge of corneal bio-mechanics is critical to improving the treatment of diseases such as keratoconus, corneal ectasia and ulcers to reduce the need for corneal transplants. We investigate the biomechanical properties of the corneal stroma by biaxial tensile testing at different corneal depths: anterior, central and posterior (Fig. 2). Our results provide a detailed characterization of the mechanical behavior of the corneal stroma under a load that resembles the physiological situation and show a significant decrease in stiffness from the anterior to the posterior corneal layers, probably due to differences in the alignment of collagen fibers. This research provides valuable data for the development of numerical models of corneal biomechanics that can contribute to a better understanding of current treatments and pathologies. These models can also drive innovation in corneal repair and reconstruction techniques and support the development of new solutions for corneal surgery and biomaterials.

Hydrogel microinjections for vision correction

By 2050, it is estimated that more than 5 billion people will be affected by refractive vision disorders, including presbyopia, myopia and astigmatism. Although laser eye surgery offers correction by reshaping the cornea through tissue removal, this method weakens the corneal structure and can lead to complications. In addition, patients with thin corneas or high refractive errors are often unsuitable for laser-based procedures. To address this, we introduce an innovative treatment that uses hydrogel injections into the cornea to correct hyperopia without compromising the integrity of the cornea. Our method is a viable alternative for patients who are not candidates for conventional laser treatment, including patients with conditions such as keratoconus. Unlike laser correction, this technique restores vision through precise hydrogel microinjections that create customized implants directly in the cornea, reshaping and strengthening it at the same time. This approach eliminates the need for external implants as the cornea is dynamically adjusted during the controlled injection process. Our ex-vivo studies in animal models have shown consistent vision correction, with refractive adjustments of over 15 diopters (Fig. 3).

Quantifying Corneal Cross-Linking with Optical Coherence Elastography

In vivo quantification of corneal biomechanics is crucial for understanding treatment outcomes but remains a major challenge. To solve this problem, we have used Optical Coherence Elastography (OCE), a technique that can capture dynamic mechanical changes in the cornea at high resolution. OCE has a high spatial resolution, and we were able to investigate the strain induced in the cornea by the osmotic effects of different preservative media and by corneal cross-linking (CXL). Experiments in porcine eyes showed that different preservation media led to distinct strain patterns, with deswelling or swelling occurring depending on the tonicity of the medium. Additionally, in eyes treated with CXL, OCE detected a marked deswelling in the anterior stroma after UV irradiation (Fig. 4), indicating increased tissue rigidity.

These biomechanical changes could explain the refractive changes observed clinically in the patients. To further investigate and predict these effects, a finite element model (FEM) was validated to simulate the refractive outcomes of CXL in the clinical setting. Data from two cohorts of patients undergoing standard or customized CXL were compared with the FEM predictions. Customized CXL resulted in greater corneal flattening, which was accurately predicted by the FEM simulations. Together, OCE and FEM provide powerful tools for optimizing CXL treatment planning and understanding corneal biomechanics.

Selected Publications

1. Frigelli M., Büchler P., Kling S. "Dynamic Evaluation of Corneal Cross-Linking and Osmotic Diffusion Effects Using Optical Coherence Elastography." Scientific Reports, 2024.
2. Osman Berk S., Eghbali P., Becce F., Goetti P., Meylan A., Rothenbühler K., Diot R., Terrier A., Büchler P. "Automatic Quantification of Scapular and Glenoid Morphology from CT Scans Using Deep Learning." European Journal of Radiology, 2024.
3. Eghbali P., Becce F., Goetti P., Büchler P., Pioletti D.P., Terrier A. "Glenohumeral Joint Force Prediction with Deep Learning." Journal of Biomechanics 163, 2024.
4. Cedric R., Lüscher D., Poux L., Schori M., Deml M.C., Hasler C.C., Bassani T., Galbusera F., Büchler P., and Schmid S.. "Predicted vs. Measured Paraspinal Muscle Activity in Adolescent Idiopathic Scoliosis Patients: EMG Validation of Optimization-Based Musculoskeletal Simulations." Journal of Biomechanics, 2024.

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Research Profile

The interdisciplinary Gerontechnology and Rehabilitation Research group is a collaborative research effort with the goal of developing and evaluating novel, flexible, and cost-efficient technologies to improve diagnostics, monitoring, and therapies of neurological and psychiatric disorders in the hospital, in the instrumented apartment and at home. Core methodologies include digital biomarkers, telemonitoring and telerehabilitation technology. The research group partnered with the department of neurology (Prof. U. Fischer) to establish the NeuroTec Loft, which is an instrumented apartment within the sitem NeuroTec to monitor human behaviour and to investigate how neurological and psychiatric disorders influence daily life.

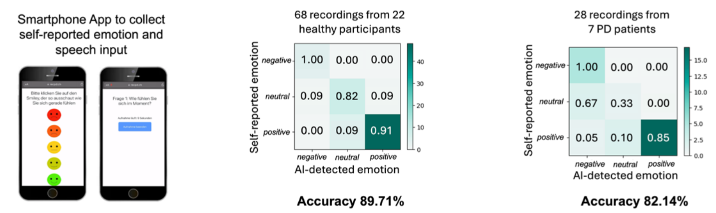

Fig. 1: Smartphone-based emotion recognition in everyday life situations: This pilot study examined whether speech capture via a smartphone app (iOS and Android) works in everyday life. Mobile measurements present challenges, including significant interference with audio quality due to factors like microphone placement, background noise, and audio compression. However, they enable highly relevant, repeated measurements (e.g. multiple recordings per day) over extended periods (e.g. several weeks). In this study, healthy volunteers (N=22) and PD patients (N=7) installed a prototype of the smartphone app on their devices to record their mood via a questionnaire and capture speech samples. Randomized prompts were sent via mobile text message between 8:00 and 20:00 o'clock, instructing participants to open the app and rate their current mood on a smiley scale. Subsequently, the same question was asked again, allowing participants to respond verbally while their speech was recorded. The collected speech samples were analyzed for their semantic content using a large language model, and the current emotion was estimated. Gross errors, such as swapping positive with negative (and vice-versa), occurred in 0.05 % of cases for patients. Acceptance of the app and adherence were positive among healthy subjects and very positive among patients.

Speech-based digital biomarkers for emotion recognition

With increasing life expectancy, the number of people affected by neurodegenerative disease (e.g., Parkinson's disease) will continue to grow, as aging is one of the primary risk factors. The presence of motor (e.g., bradykinesia, tremors) and non-motor symptoms (e.g., neuropsychiatric symptoms) can severely affect the patient's quality of life. Even though neuropsychiatric fluctuations can be more disabling than motor symptoms, they are poorly recognized and, thus, inadequately treated. There is, indeed, a need for methods and tools to assess non-motor symptoms over time that do not rely only on the subjective reports of patients or caregivers. Treatments like Deep Brain Stimulation (DBS) have been studied as a solution to lessen symptoms, even neuropsychiatric symptoms. However, to work optimally, they must dynamically adapt their parameters (e.g., type and amount of stimulation) according to the patient's current health status (e.g. closed-loop DBS). In this context, we aim to develop a multimodal (audio and context) AI-based pipeline that continuously detects the emotion state and mood from Swiss German spontaneous speech collected several times daily at home using patients' smartphones. This method will allow clinicians to develop a patient-tailored. treatment by gathering information on both motor and non-motor symptoms remotely and continuously over the day. →

Fig. 2 and 3: The NeuroTec Loft is a state-of-the-art, sensor-equipped three-room apartment featuring a kitchen, living room, bathroom, and bedroom. Designed to study behavioral aspects of neurological and neuropsychiatric disorders, this unique facility provides a setting that closely replicates natural living conditions. Equipped with 300 sensors, it enables precise quantification of motor function, cognition, and mood. Additionally, the Loft serves as a testing environment for innovative technological developments. The NeuroTec Center is an integral part of the department of neurology, and it is operated by Profs. Schindler (Neurology) and Nef (ARTORG Center).

→ Sensor-based digital biomarkers in the hospital: Digital care assistant

Currently, there is a significant shortage of skilled workers and pressure to reduce costs in the health care system, which is particularly evident in the personnel-intensive and time-consuming care characteristic for acute geriatric psychiatric hospitals but also nursing, and care homes. Furthermore, as the number of patients, especially the number of dementia patients is steadily growing in the context of increasing life expectancy and the baby boomer cohort retiring, the shortage of nurses will further escalate. Sensor-based digital biomarkers have the potential to be used in a clinical setting to provide objective and reproducible data about the patient's status and to support healthcare professionals at the ward. Especially remote continuous monitoring of patients allows to immediately detect slight changes in health status. We developed an unobtrusive sensor system, a so-called digital care assistant, that monitors behavioral and physiological parameters to support and ease the workload of medical professionals of an old age psychiatric ward.

We have equipped twenty patient rooms with sensors (e.g., bed sensor, lidar sensor, and radar sensors). A smartphone-based app displays information about the patient's status and helps healthcare professionals (e.g. nurses) to keep an overview of all patients of their ward. We are currently testing acceptance and effectivity of the sensor-based digital care assistant.

The instrumented apartment NeuroTec loft (Fig. 2+3) is used as a test environment for the sensor technology.

Pocket-size device to measure and train fine-motor function and cognition

The Smart Sensor Egg (Fig. 4) is a newly developed device to assess and train fine finger movement and cognitive abilities for patients with neurodegenerative diseases and brain injury. It is a pocket-sized, sensor-based tool designed to enhance dexterity (coordinated finger movements) and hand function (grip and grasp), which are often impaired in this patient population. In an initial study, the first prototype of the Smart Sensor Egg, equipped with a gyroscope, an accelerometer, and four pressure sensors, was evaluated. Participants, supervised by a clinician, successfully used the device, which was connected to a laptop running a single game. The device was well-received, and the gamified environment proved motivating for training hand function. To enable the use of this innovative device in a home-based setting, further development is ongoing, both in the technical design of the device and the accompanying game-based software.

Alongside the technical developments and clinical evaluation, the transition to market implementation is underway with the establishment of a new ARTORG spin-off company.

Fig. 4: A healthy participant plays a motor-cognitive game. Sensors in the silicone egg measure the pressure applied by each finger as well as the movement of the wrist, which control the computer game. This is used both as a digital biomarker for fine motor function and cognition and for training purposes. The graph on the right shows the measured user satisfaction with the device on a scale from 1 to 7 (1 = maximum satisfaction).

Selected Publications

1. Saner H, Möri K, Schütz N, Buluschek P, Nef T. Sleep characteristics and self-reported sleep qual-ity in the oldest-old: Results from a prospective longitudinal cohort study. J Sleep Res. 2024 Sep 19:e14348. doi: 10.1111/jsr.14348. Epub ahead of print. PMID: 39300712.
2. Rusz J, Dusek P, Tykalova T, Novotny M, Illner V, Simek M, Kouba T, Kryze P, Zogala D, Ruzicka E, Sousa M, Jorge A, Nef T, Krack P. Is speech function lateralised in the basal ganglia? Evidence from de novo Parkinson's disease. J Neurol Neurosurg Psychiatry. 2024 Sep 23:jnnp-2024-334297. doi: 10.1136/jnnp-2024-334297. Epub ahead of print. PMID: 39288960.
3. Single M, Bruhin LC, Naef AC, Krack P, Nef T, Gerber SM. Unobtrusive measurement of gait parameters using seismographs: An observational study. Sci Rep. 2024 Jun 24;14(1):14487. doi: 10.1038/s41598-024-64508-4. PMID: 38914628; PMCID: PMC11196696.

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Research Profile

The Hearing Research Lab focuses on advancing precision tools and data-driven approaches to address complex challenges in cochlear implantation and otologic surgery. With a translational approach that bridges foundational research and clinical application, we engineer solutions designed for seamless integration into surgical workflows. Our interdisciplinary team develops and refines artificial anatomical models, sensory-driven monitoring systems, and machine learning algorithms that offer insights into surgical dynamics and patient-specific anatomy. By working closely with clinicians at the Inselspital, we aim to improve surgical precision, minimize trauma, and enhance hearing outcomes, contributing to the next generation of personalized auditory rehabilitation.

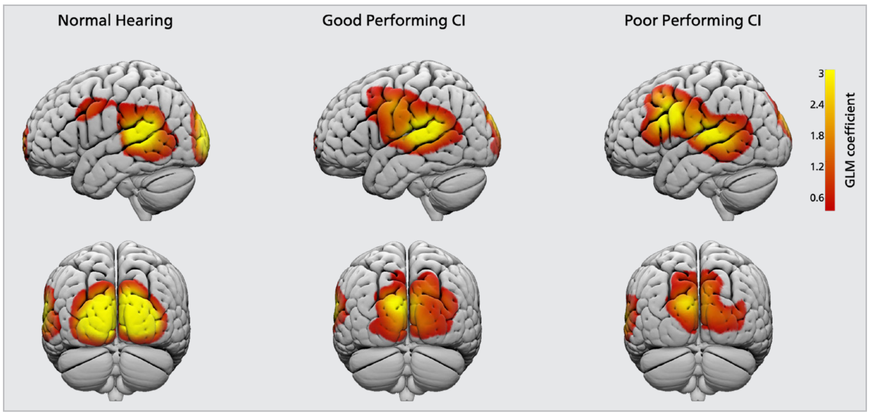


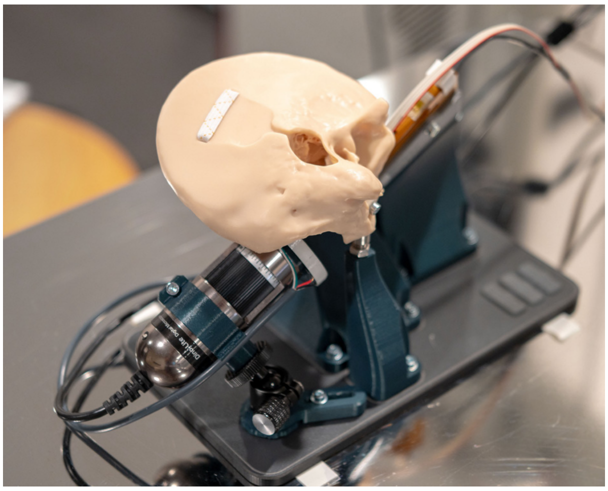
Fig. 1: Brain activity during audiovisual listening condition. Good-performing cochlear implant patients had reduced occipital activity with more involvement in language-related precentral regions, while poor-performing patients displayed increased activation in this region, indicating greater reliance on visual speech cues.

Advancing Surgical Solutions for Cochlear Implantation

One of the primary challenges in cochlear implant (CI) surgery is the potential loss of a patient's residual hearing due to the procedure. This issue is compounded as hearing disorders often progress over time, meaning patients must endure a period of severe hearing loss before qualifying for treatment. Given that inner ear structures are micrometer-sized and sensitive to nanometer-level deflections, implant placement demands extraordinary precision and control. To address these challenges, we employ a multi-faceted strategy, developing advanced artificial models for surgical training, creating surgical tools that minimize stress on cochlear structures, and refining methods to extract detailed structural and positional data through electrophysiological measurements.

Quantitative Insights for Surgical Training

The cochlea's intricate anatomy demands precise, low-risk surgical practice. Our lab addresses this need with high-fidelity artificial temporal bone models, replicating the human ear's anatomical and mechanical properties. These models incorporate sensors to monitor insertion force and →



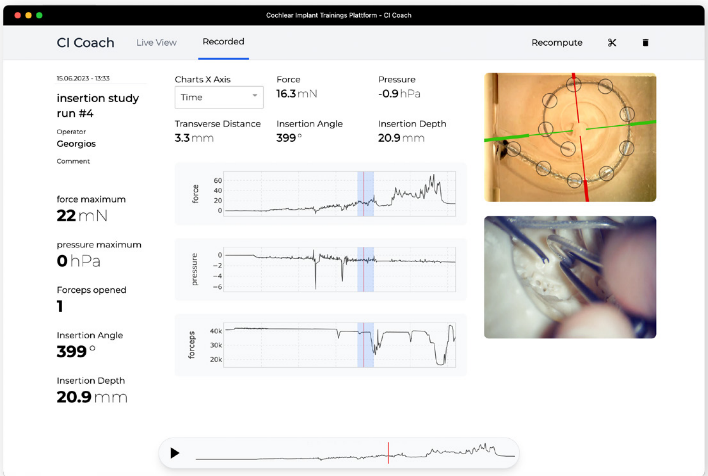


Fig. 2: High-fidelity temporal bone model for cochlear implant surgical training. This model provides a realistic anatomical environment paired with detailed, evidence-based feedback on the microstructural effects of surgeons' actions, allowing them to refine their techniques in a controlled environment.

intracochlear pressure, providing real-time feedback on surgical technique. The feedback allows surgeons to assess the microstructural impact of their actions and refine their techniques accordingly. Additionally, modular components support training in a variety of clinical scenarios, such as malformations and age-related anatomical differences. Compared to traditional cadaver models, these models offer a controlled, repeatable, and ethically sustainable training environment, equipping surgeons with the confidence and precision required for improved patient outcomes.

Intraoperative Cochlear Health Monitoring

Electrocochleography (ECochG) is a method to measure auditory responses of the inner ear, increasingly used to monitor residual hearing in cochlear implant patients during surgery. Current ECochG methods are based on models of the healthy cochlea, which limits their use in CI patients. In a prospective study, we recorded intraoperative ECochG from 30 CI patients, analyzing relevant signal features using our previously published objective algorithms. By integrating ECochG features with pre- and post-operative computed tomography scans, we achieve a combined analysis of residual hearing. Our findings reveal a direct relationship between changes in ECochG patterns and residual hearing performance, supporting ECochG as an objective biomarker for cochlear health and enhancing residual hearing monitoring for CI patients.

Radiation-Free Localization of Implanted Electrodes

Impedance telemetry is a standard in cochlear implants traditionally employed to ensure electrode integrity and customize audio processor settings. We previously showed that it can also be used as a radiation-free method to localize electrode contacts within the cochlea. By combining impedance telemetry with computed tomography data from over 130 patients, we identified key predictors of the electrode positioning. Our machine learning model achieves an average localization accuracy of under one millimeter compared to radiological ground truth measures. It surpasses previous methods, especially in partially inserted electrodes. As follow-up validation in pediatric patients demonstrates its clinical utility, highlighting impedance-based localization as a viable, radiation-free alternative to computed tomography for routine practice.

Imaging Brain Plasticity in Response to Cochlear Implantation

Alongside these surgical aspects, rehabilitation is an essential component for successful outcome of cochlear implantation. The adaptation to cochlear implant stimulation is critical to hearing rehabilitation, with cortical plasticity playing a central role. Our neuroimaging studies identify neural markers that explain variations in speech understanding among CI recipients. Results demonstrate examples of successful cortical-level adaptation, as well as irregular brain activity associated with poorer speech outcomes. These findings underscore neuroplasticity's role in adaptation, guiding improved approaches to cochlear implant therapy and patient care.

Selected Publications

1. Aebischer, P., Sarbach, B., Weder, S., Mantokoudis, G., Caversaccio, M., and Anschuetz, L. „Development and Evaluation of a Reusable, Force Measuring Tool for the Robot-Assisted Insertion of Cochlear Implant Electrode Arrays," IEEE Transactions on Biomedical Engineering, 2024
2. Bálint, A., Rummel, C., Caversaccio, M., & Weder, S. „Three-dimensional Infrared Scanning: An Enhanced Approach for Spatial Registration of Probes for Neuroimaging," Neurophotonics, 2024
3. Aebischer, P., Anschuetz, L., Caversaccio, M., Mantokoudis, G., & Weder, S. „Quantitative In-vitro Assessment of a Novel Robot-assisted System for Cochlear Implant Electrode Insertion," International Journal of Computer Assisted Radiology and Surgery, 2024
4. Andonie, R. R., Wimmer, W., Schraivogel, S., Mantokoudis, G., Caversaccio, M., & Weder, S. „Electrocochleography in Cochlear Implant Recipients: Correlating Maximum Response With Residual Hearing," Ear and Hearing, 2024
5. Schmeltz, M., Ivanovic, A., Schlepütz, C. M., Wimmer, W., Remenschneider, A. K., Caversaccio, M., Stampanoni, M., Anschuetz, L., & Bonnin, A, „The Human Middle Ear in Motion: 3D Visualization and Quantification Using Dynamic synchrotron-based X-ray Imaging," Communications Biology, Springer Nature, 2024

Medical Image Analysis

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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. The group develops novel techniques for multimodal image segmentation and analysis of brain lesions, presently including glioblastoma multiforme, brain metastases, and related conditions. The results of these developments are aimed at advancing the discovery of innovative non-invasive imaging biomarkers used to characterize disease and guide the decision-making process, as well as in radio-therapy, neuro-surgery, drug-development, etc. A special focus is to develop algorithms and methodologies to improve the robustness and interpretability of AI-based solutions for medical image analysis. The developments revolve around the vision of scalable, adaptable and time-effective algorithms developed with a strong focus on clinical applicability.

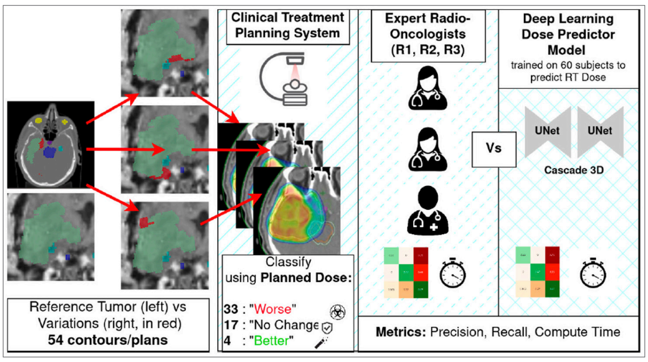

Fig. 1: Is a deep learning dose prediction model able to ascertain dosimetric impact of tumor target volume contour changes when compared to radiation oncologists? An experimental study is run with 54 contour variations which are individually re-planned to generate three categories of results: "Worse", "No Change" and "Better". Adapted from Kamath et al. MIDL 2024.

Accurate, Robust and Clinically Translated AI-based Quantification in Medical Image Computing

Magnetic Resonance Imaging (MRI) and its variants continue to serve as essential imaging modalities, offering high-resolution anatomical and physiological insights. In neurosciences, MRI is a cornerstone of clinical practice. However, effective interpretation of these images often requires combining multiple imaging modalities, which underscores the need for advanced computer-assisted technologies.

Our team has developed and refined AI-based methods for the automated delineation of brain tumors. These technologies have been shared with the research community and are advancing toward broader clinical use. After securing FDA approval (510k) in collaboration with the U.S.-based start-up Neosoma in 2022, our efforts have expanded in 2023. In 2024 Neosoma established a dedicated Swiss branch to drive the development of AI technologies specifically aimed at improving the care of brain cancer patients. Our work in 2024 continues to focus on enhancing the system for brain metastasis detection, with a multicenter clinical evaluation of its performance and robustness in a variety of clinical settings.

In 2024, we have further advanced AI learning paradigms in radiation therapy, focusing on end-goal clinical metrics. We have explored how deep learning models can predict radiation therapy dose →

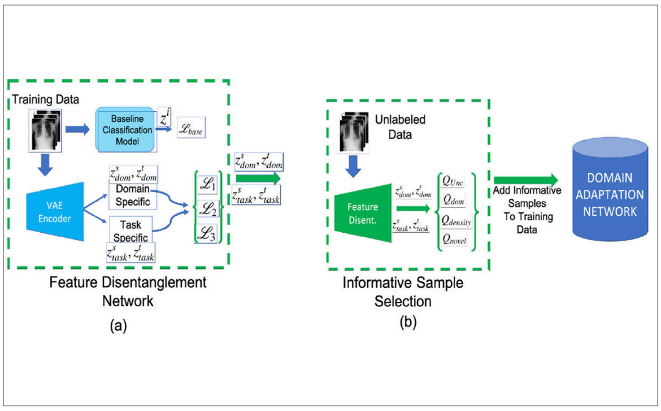

Fig. 2: ALFREDO: Active Learning with FeatuRe disEntangelement and DOmain adaptation for medical image classification. (a) Feature Disentanglement: Training data goes through an autoencoder to obtain different components. After training is complete we get domain and task specific features. (b) For informative sample selection we obtain disentangled feature representations of the unlabeled data and calculate the informativeness score of each sample in the batch. Adapted from Mahapatra et al. MedIA 2024.

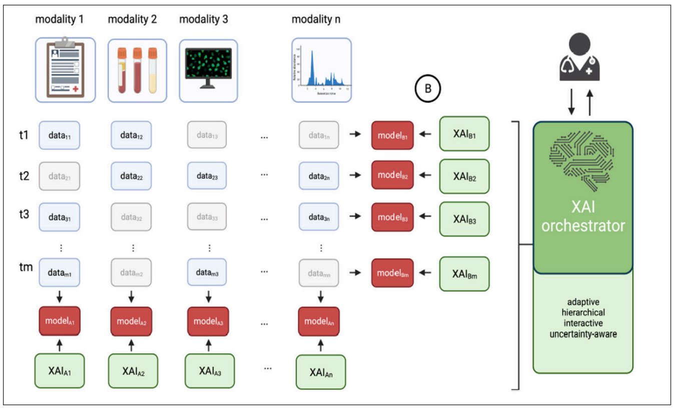

Fig. 3: The XAI orchestrator concept acting as information bridge between the expert and the specialized AI systems working with multimodal and longitudinal patient information. Adapted from Pahud et al. NPJ Digital Medicine 2024.

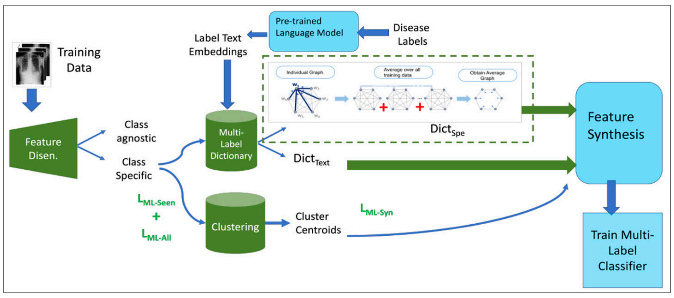

Fig. 4: Multi-Label Generalized Zero Shot Chest Xray Classification By Combining Image-Text Information With Feature Disentanglement. T raining data goes through a feature disentanglement stage, followed by multimodal and multi-label dictionary learning and clustering, feature synthesis and training of a multi-label classifier. Adapted from Mahapatra IEEE Trans. Med. Imag. 2024.

sensitivity, while in other studies we presented novel active learning techniques to improve medical image classification. In parallel, we have developed AI-based quality assurance technology, which supports dosimetric compliance in near real-time, enabling physicians to assess how segmentation variations may impact dosimetry and overall treatment outcomes.

Interpretability of Deep Learning-based Medical Image Analysis

Beyond accuracy, it is essential that computer-assisted technologies are both robust and interpretable, ensuring safe and effective clinical integration. The heterogeneity of medical images and the complexity of disease pathophysiology require AI systems that can adapt to such variability. In 2024, our team has made significant strides in interpretability research, building on our expertise to improve AI transparency and reliability in medical imaging.

In 2024 we contributed to understanding how explainable AI can be orchestrated for multimodal and longitudinal data in medical imaging. Furthermore, our group is integrating these interpretability strategies into AI systems to guide learning and improve system robustness. This year we also demonstrated how interpretable monitoring of deep learning models can enhance safety and reliability in clinical use, as presented in key workshops like iMIMIC.

We have also developed frameworks, that utilize disease-weighted attention refinement to improve the accuracy and clinical relevance of AI outputs. These advancements ensure that our AI technologies are not only state-of-the-art but also aligned with clinical needs, providing transparent, robust, and reliable tools for medical professionals.

Selected Publications

1. Aurélie Pahud de Mortanges, Haozhe Luo, Shelley Zixin Shu, Amith Kamath, Yannick Suter, Mohamed Shelan, Alexander Pöllinger, and Mauricio Reyes. Orchestrating explainable artificial intelligence for multimodal and longitudinal data in medical imaging. NPJ digital medicine, 7(1):195, 2024.
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3. Dwarikanath Mahapatra, Antonio Jimeno Yepes, Behzad Bozorgtabar, Sudipta Roy, Zongyuan Ge, and Mauricio Reyes. Multi-label generalized zero shot chest x-ray classification by combining image-text information with feature disentanglement. IEEE Transactions on Medical Imaging, 2024.
4. Lena Maier-Hein, Annika Reinke, Patrick Godau, Minu D Tizabi, Florian Buettner, Evangelia Christodoulou, Ben Glocker, Fabian Isensee, Jens Kleesiek, Michal Kozubek, et al. Metrics reloaded: recommendations for image analysis validation. Nature methods, 21(2):195{212, 2024.
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7. Suhang You, Roland Wiest, and Mauricio Reyes. Sarf: Saliency regularized feature learning improves MRI sequence classification. Computer methods and programs in biomedicine, 243:107867, 2024.
8. Amith Kamath, Zahira Mercado Auf der Maur, Robert Poel, Jonas Willmann, Ekin Ermis, Elena Riggenbach, Nicolaus Andratschke, and Mauricio Reyes. Comparing the performance of radiation oncologists versus a deep learning dose predictor to estimate dosimetric impact of segmentation variations for radiotherapy. In Medical Imaging with Deep Learning, 2024.
9. Zahira Mercado, Amith Kamath, Robert Poel, Jonas Willmann, Ekin Ermis, Elena Riggenbach, Lucas Mose, Nicolaus Andratschke, and Mauricio Reyes. Autodoserank: Automated dosimetry-informed segmentation ranking for radiotherapy. In MICCAI Workshop on Cancer Prevention through Early Detection, pages 221-230. Springer, 2024.
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11. Haozhe Luo, Aurelie Pahud de Mortanges, Oana Inel, and Mauricio Reyes. Dwarf: Disease-weighted network for attention map refinement. In iMIMIC, page 311. Springer, 2024.

Musculoskeletal Biomechanics

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Research Profile

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

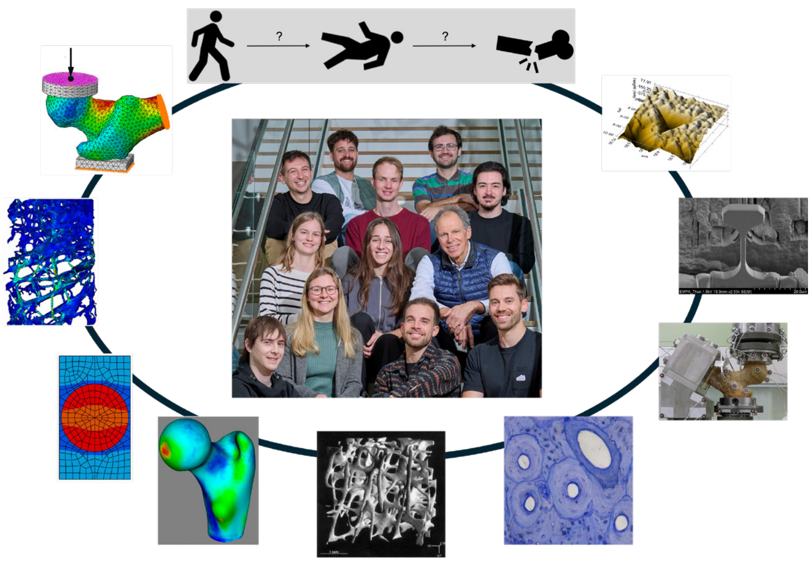

Fig. 1: Musculoskeletal biomechanics (MSB) research team combining experimental, imaging, computational and clinical studies.

Imaging of single mineralised collagen fibrils *(postdoc grant UniBE with LBNL)*

Bone is a complex material that offers a unique blend of strength, toughness, and lightness. The key feature contributing to this outstanding combination of material properties is the hierarchical arrangement spanning across the length scales.

At the lowest level, bone is built up of mineralized collagen fibrils (MCFs). In this highly collaborative project, we used advanced transmission electron micro-scopy (TEM) techniques to assess the structural organization of the MCFs. We used TEM to visualize the arrangement of collagen molecules and minerals within the MCFs at the nanoscale (Fig. 2). We also measured the orientation of individual mineral crystals within the MCFs. The capabilities of the TEM allow us to resolve MCF organization and composition down to the nanoscale and even Angstrom level, opening-up new venues for research into how bone diseases and treatments affect the ultrastructure of bone.

Contribution of Bone Tissue Properties to Strength of the Ageing Human Hip *(SNF grant # 200365 with EMPA, PSI, VUT & MUG)*

This project investigates structure-property relations in the femoral neck cortex and their change with age. Ninety-four →

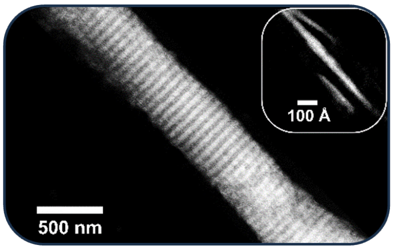

Fig. 2: TEM image of a mineralised collagen fibre, with a zoom-in view of the mineral crystal.

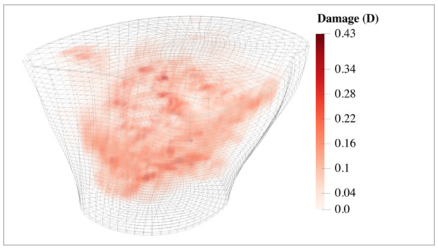

Fig. 3: Distribution of damage on an HR-pQCT-based hFE mesh of the distal tibia following uniaxial compression.

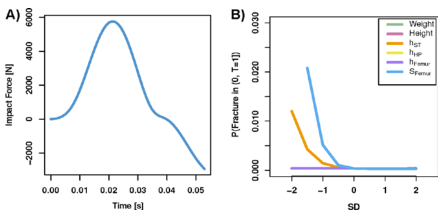

Fig. 4: A) Impact force resulting from sideways fall. B) Sensitivity of fracture risk to variations in femoral strength and other anatomical quantities.

femurs were analyzed through histology and small-angle x-ray scattering (SAXS) for micro- and nano-structural analysis, respectively. Selected samples underwent in-depth investigation through micropillar compression and 3D structural analysis by small- and wide-angle x-ray scattering tensor tomography (SASTT and WASTT). Histological analysis suggested a steady microstructure with age.

Besides experiments, an elasto-plastic constitutive model of bone tissue was extended to account for its viscoelastic behaviour at multiple time scales. This model was validated with experiments at different strain rates, including quasi-static and drop-tower tests.

HR-pQCT-Based Diagnosis of Osteoporosis *(with IS & MG)*

The motivation driving this project is the prevention of osteoporosis. The objective is to develop a diagnostic method that makes use of high-resolution peripheral quantitative computed tomography (HR-pQCT). In vivo imaging of the distal radius and tibia allows the generation of non-linear homogenised finite element (hFE) models that are capable of accurately predicting stiffness and strength.

The introduction of a novel meshing technique using a smooth, structured, hexahedral mesh improves both mapping of material properties and computational efficiency. By creating smooth meshes, the complex geometry of the thin cortical bone is preserved, resulting in better predictions of strain fields. By creating structured meshes with consistent element to element correspondence, a comparison between patient models or in longitudinal settings, becomes accessible and provides a supplementary clinical information (Fig. 3).

A Fragility Fracture Integrative Risk Model for CT Recycling *(SNF grant # 183584 with HUG, IS, & MUG)*

Experimental results characterising the properties of soft tissues covering the hip were exploited to develop a 1D impact model for the sideways impact of the human hip resulting from a fall from standing height. The developed impact model was combined with a previous fall risk model and a computer tomography (CT)-based FE method for bone strength estimation, constituting an integrative approach to hip fracture risk.

Data collected in the parallel clinical study over the past years was used to perform a sensitivity analysis of the mechanistic-stochastic fracture risk model (Fig. 4). In addition, the relations between trochanteric soft tissue thickness and clinical variables, such as BMI, were explored. CT-like images constructed using statistical shape models from standard DXA were analysed to examine alternative inputs for the fracture risk model where CT images are not available.

Biomechanical Stability of Dental and Orthopaedic Implants *(Innosuisse grant # 115.975 with ZMK, AO & industry partners)*

Primary stability (PS) is a key factor for promoting osseointegration and long-term success of dental implants, particularly for immediate loading scenarios. Implant size and design, insertion protocol and especially bone quality are major factors influencing PS. Current methods for assessing PS are either per- or postoperative and an objective measure of PS is therefore missing in surgical planning today.

The development of a potential solution to bridge this gap was undertaken that consists in combining a calibrated cone beam computer tomography (CBCT) reconstruction with a non-linear finite element analysis to predict PS for different protocols before surgery (Fig. 5).

Similarly, primary implant stability is crucial for successful total hip arthroplasty. Thus, geometric characteristics of the human proximal femoral medullary canal were investigated in relation to sex and age and were captured in a statistical shape model.

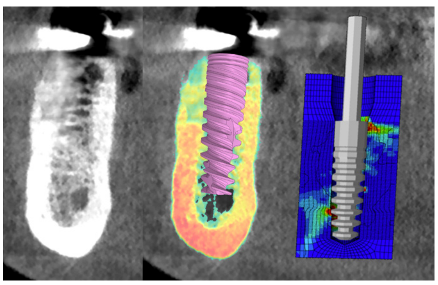

Fig. 5: Process illustration starting from the CBCT image to bone density assessment, virtual implant placement and finite element simulation.

Selected Publications

1. Dudle A., Ith M., Egli R., Heverhagen J., Gugler Y., Wapp C., Frauchiger D., Lippuner K., Jackowski C., Zysset Ph., „Asynchronous calibration of a CT scanner for bone mineral density estimation: sources of error and correction" JBMR Plus 8:ziae096, 2024.
2. Vautrin A., Thierrin R., Wili P., Voumard B., Rauber C., Klingler S., Chappuis V., Varga P. and Zysset Ph., „Homogenized finite element simulations can estimate the primary stability of dental implants in human jawbones", J Mech Behav Biomed Mater 158:1066887, 2024.
3. Dudle A., Gugler Y., Berk Satir O., Gewiess J., Klein S. and Zysset Ph., „QCT-based spatio-temporal aging atlas of the proximal femur BMD and cortical geometry", Bone Reports 22:101786, 2024.
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5. Simon M., Indermaur M., Schenk D., Voumard B., Zderic Y., Mischler D., Pretterklieber M. and Zysset Ph., „Homogenised finite element analysis of distal tibia sections: achievements and limitations", Bone Reports 21:101752, 2024.
6. Wapp Ch., Mittaz A.-G., Rikkonen T., Hilfiker R., Biver E., Kröger H., Ferrari S., Zwahlen M. and Zysset Ph., „Validation of a fall rate prediction model for community-dwelling older adults: a combined analysis of three cohorts with 1850 participants", BMC Geriatrics 24:287, 2024.
7. Indermaur M., Casari D., Kochetkova T., Willie B., Michler J., Schwiedrzik J. and Zysset Ph., „Does tissue fixation change mechanical properties of dry ovine bone extracellular matrix", J Mech Behav Biomed Mater 150:106294, 2024.

Neuro Robotics Group

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Research Profile

The Neuro Robotics Group (NRG) focuses on the development of surgical instruments for neurosurgery based on robotics and micromechatronics technology. Our goal is to develop innovative robotic systems and mechatronic devices to improve the precision, efficiency, and safety of neurosurgical procedures. At the core of our work is the close collaboration with medical professionals, emphasizing the crucial synergy between technological innovation and clinical expertise. This partnership ensures that our developments are seamlessly aligned with the clinical needs of neurosurgery.

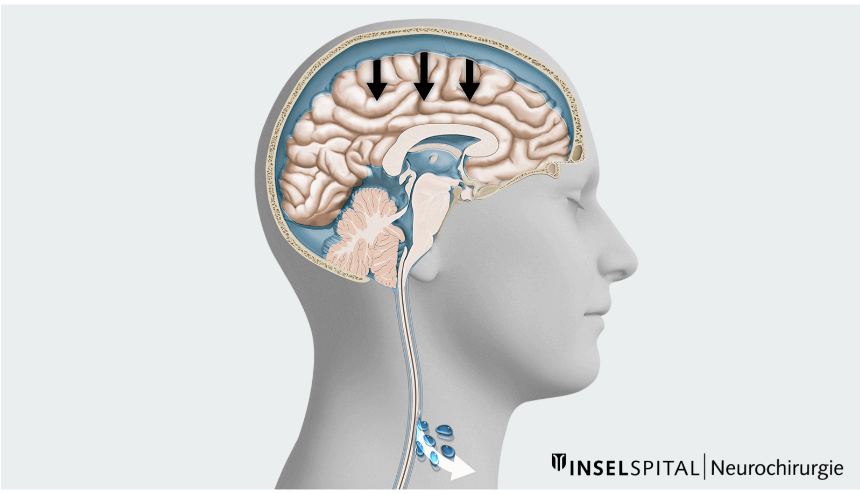

Fig. 1: A Cerebrospinal fluid (CSF) leak can occur in the spinal column. As a result, the brain sags downwards in an upright position as it is no longer sufficiently surrounded by protective cerebrospinal fluid. Image: Universitätsklinik für Neurochirurgie, Inselspital Bern © CC BY-NC 4.0

Improving the outcomes of Spontaneous Intracranial Hypotension (SIH) interventions

The brain and the spinal cord are embedded in around 140 ml of cerebrospinal fluid (CSF). The presence of this fluid is relevant for the metabolism of the nerve cells as well as for the protection against external mechanical influences and acceleration forces, such as vibrations. Around 500 ml of this fluid is produced and reabsorbed every day. In case of a CSF loss syndrome also known as spontaneous intracranial hypotension (SIH) cerebrospinal fluid is lost through a lesion. A standing position of the affected person results in a sagging of the brain, which causes various symptoms from mild headaches to impairment of consciousness. The lesion must be located and closed to prevent severe sequelae like chronic pain and potential paralysis.

The treatment of spontaneous intracranial hypotension (SIH) is a poorly addressed clinical challenge. Funded through the Innovation Booster Robotics (powered by Innosuisse) we are developing technological solutions to improve the outcomes of SIH interventions together with our implementation partner Brütsch Elektronik AG.

Tackling the challenge of suturing in deep-seated locations

In neurosurgery, accessing the brain or spinal cord requires opening the dura mater, the outermost layer of the meninges. →

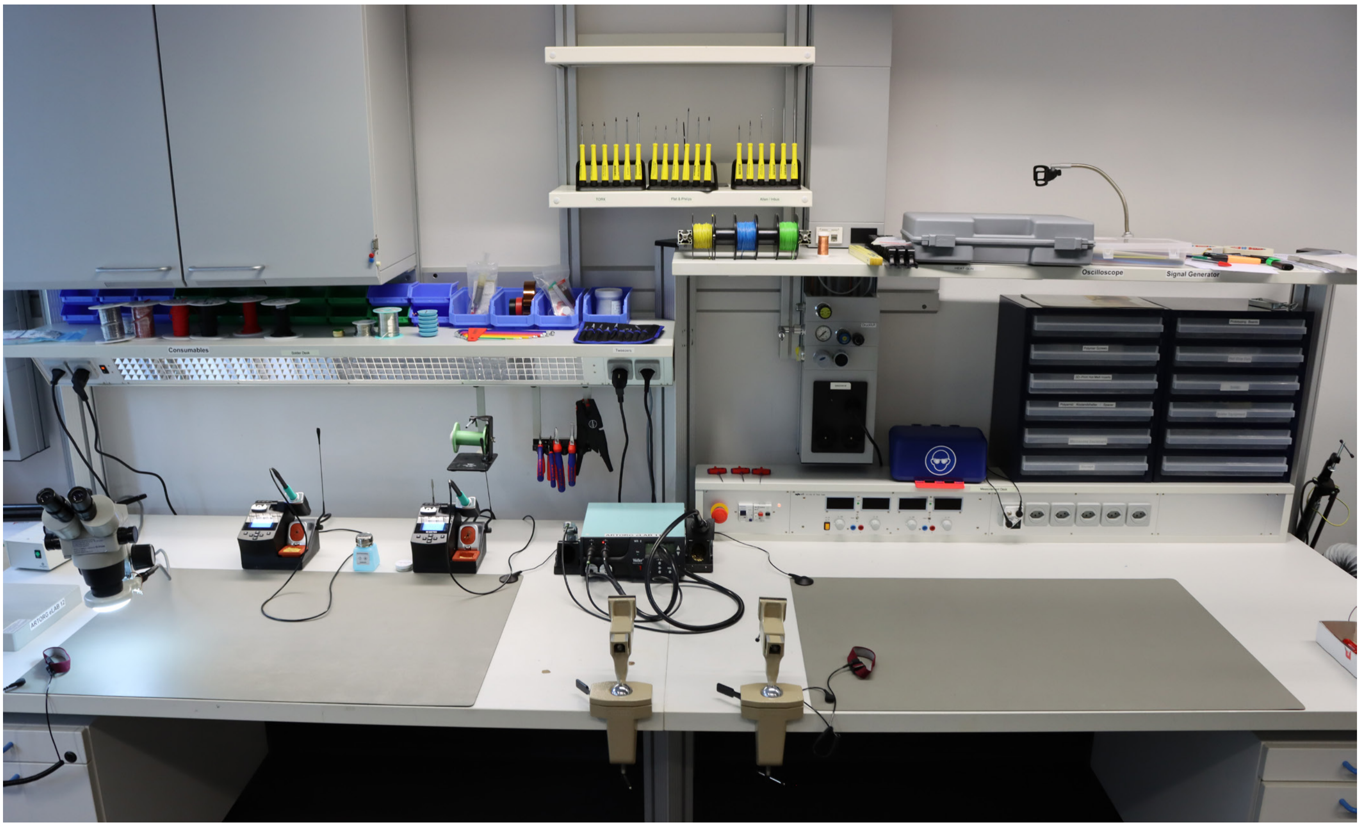

Fig. 2: ARTORG core facility for electronics.

The dura mater surrounds the central nervous system and plays a vital role in protecting the brain and spinal cord. Suturing of the dura mater may be necessary as part of wound closure after surgical access to the spinal cord or brain. Additionally, dural closure can be the primary goal of a surgical intervention, such as in cases of spontaneous intracranial hypotension (SIH), where a dura leak forms spontaneously. We focus on CSF leaks in spinal surgery, where a minimally invasive surgical access is generated through a tubular retractor and under visualization through a surgical microscope. The limited manipulation space within the tubular retractor is a test on fine motor skills and sensory feedback for surgeons. We are studying the surgical difficulties of suturing the dura mater through a tubular retractor and develop technological solutions to address these challenges.

ARTORG Services

The ARTORG Center offers a range of services to the research community of the Bern Biomedical Engineering Network. The Neuro Robotics Group manages two of these facilities.

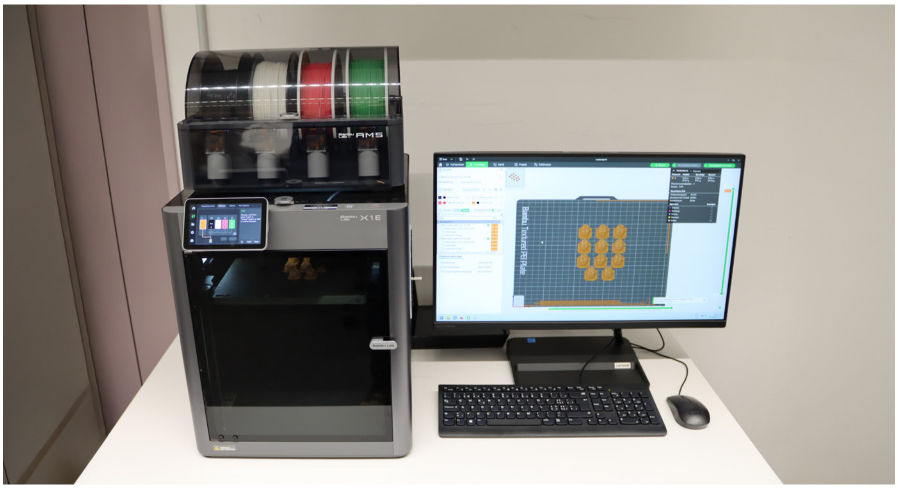

Fig. 3: ARTORG core facility for 3D-printing.

Electronics laboratory

Electronics are an integral part of many devices in medical technology. These devices include, for example, a large number of sensors for evaluating patients' health parameters. In order to create a workplace where electrical and electronic prototypes can be produced to high-quality standards, the electronics laboratory has been refurbished.

3D printing laboratory

The 3D printing facility has already facilitated many groundbreaking projects, including customized patient-specific skull implant molds, models for perioperative planning of complex aortic arch surgery, liver resection planning models, and aneurysm models for surgical coiling and surgical clipping. The facility has been expanded with further state-of-the-art additive manufacturing and 3D printing systems to continue to offer these possibilities.

Organs-on-Chip Technologies

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Research Profile

The Organs-on-Chip Technologies Group focuses on the development of advanced in-vitro models. Such devices aim at reproducing the smallest functional unit of a tissue, by mimicking the cellular composition and microenvironment. The group particularly focuses on modelling the human lung and microvasculature, in healthy and disease states. To achieve this, multidisciplinary research is performed at the interface of cell biology, biomechanics, microtechnology, and microfluidics. These systems are deemed to be implemented for precision medicine, in which the treatment efficiency can be tested with the patient's cells to individualize and optimize the therapy.

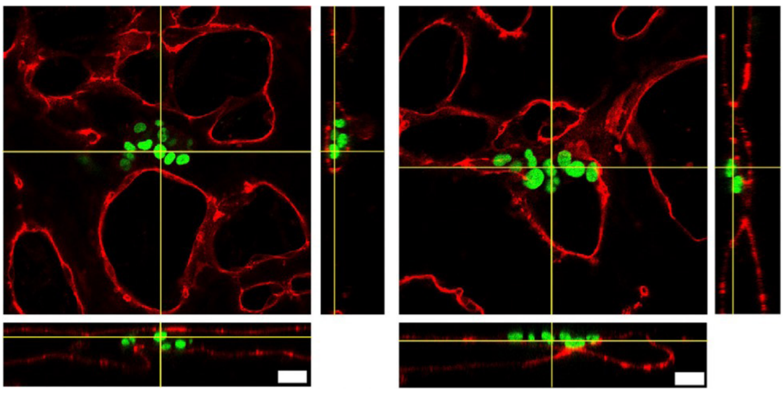

Fig. 1: Circulating lung cancer cells are shown within a bioengineered microvasculature network, created with endothelial cells (stained red with PECAM1) and fibroblasts. Cancer cells, depicted in green, are transported by blood flow and extravasate at distant sites to form secondary colonies. The extravasation process is selective based on cellular phenotype. Assessment of the A549 lung cancer cell line reveals distinct extravasation properties. Cells with an epithelial phenotype (left), holoclones, remain within the microvasculature, while cells with a mesenchymal phenotype (right), paraclones, successfully extravasate into the surrounding matrix. Scale bar: 20um. Ref: 4.

Assessing the metastatic potential of circulating tumor cells (CTCs)

Metastatic lung cancer continues to be a leading cause of death globally, with its complex metastatic cascade presenting significant challenges for researchers and clinicians alike. Despite considerable advancements in our understanding of the metastatic cascade, many details remain unclear. During metastasis, only a small number of CTCs evade the immune system and survive the stresses of the bloodstream, including cell detachment-induced death. This resilience allows a select few CTCs to travel to distant sites in the body and form secondary colonies.

Microfluidic vasculature-on-chip models have emerged as valuable tools in cancer research, allowing for the simulation of specific stages of tumor progression. In this study, we examine the extravasation behaviours of A549 lung cancer cell subpopulations, uncovering distinct differences related to their phenotypes. Our findings indicate that holoclones, which possess an epithelial phenotype, do not extravasate, whereas paraclones, defined by a mesenchymal phenotype, exhibit a significant capacity for extravasation (Fig. 1). Additionally, we found that paraclones migrate considerably faster than holoclones within the microvasculature model. Importantly, depleting vascular endothelial growth factor (VEGF) effectively hinders →

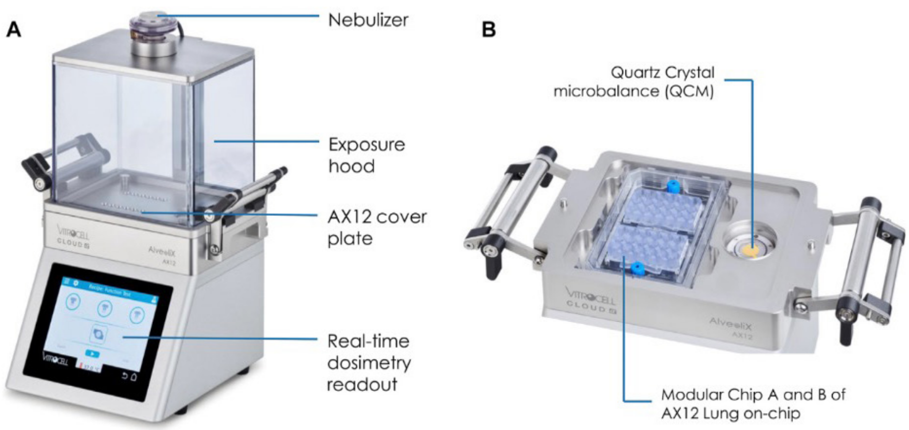

Fig. 2: Inhalation study utilizing two technologies: an aerosol nebulizer from Vitrocell and the Lung-on-Chip (AX12 plate) developed by our start-up AlveoliX as part of a Eurostar project. A) The Cloud α AX12 features a stainless-steel base module maintained at 37 °C, with the AX12 plate positioned on top and covered by a steel plate. The holes in the steel base align with the wells of the AX12 plate. The nebulizer employs a piezoelectric vibrating mesh to generate a consistent aerosol cloud from the nebulized solubilized substance. B) A detailed view of the platform shows the integration of the AX12 with a quartz crystal microbalance (QCM), which quantifies the delivered dose to the cells in real time. Ref:3.

the extravasation of paraclones. These results emphasize the value of microfluidic models in mimicking critical aspects of the metastatic cascade. The insights from this study highlight the potential of these models to enhance precision medicine by enabling the evaluation of patient-specific cancer cell dynamics and drug responses. This approach could lead to better strategies for predicting metastatic risk and tailoring personalized cancer therapies, potentially involving the collection of cancer cells from patients during tumor resection or biopsies.

Inhalation Platform for Aerosol Delivery in Breathing Lung-on-Chip

Prolonged exposure to environmental respirable toxicants can contribute to the development and exacerbation of serious respiratory diseases, such as asthma, chronic obstructive pulmonary disease (COPD), and fibrosis. The limited number of FDA-approved inhaled medications for these conditions has prompted a shift from in vivo studies to alternative in vitro human-relevant models that better predict the toxicity of inhaled particles in preclinical research. Although various inhalation exposure models exist for the upper airways, the delicate and dynamic nature of the alveolar microenvironment has hindered the creation of reproducible exposure models for the distal lung.

In this project, we report about a mechanistic approach utilizing a new generation of exposure systems, the Cloud α AX12 (Fig. 2). This innovative in vitro inhalation tool comprises a cloud-based exposure chamber (VITROCELL) integrated with the breathing AX Lung-on-Chip system (AlveoliX). The ultrathin, porous membrane of the AX12 plate allows for the development of a complex multicellular model that simulates key physiological conditions: the air-liquid interface (ALI) and three-dimensional cyclic stretch (CS).

Human-relevant cellular models were developed for the distal alveolar-capillary interface using primary cell-derived immortalized alveolar epithelial cells (AXiAECs), macrophages (THP-1), and endothelial cells (HLMVEC). Primary human alveolar epithelial cells were employed to validate the toxicity findings from the immortalized cell lines. To simulate in vivo-relevant aerosol exposures with the Cloud α AX12, we created three different models using: a) titanium dioxide (TiO_2) and zinc oxide (ZnO) nanoparticles, b) polyhexamethylene guanidine (PHMG) a toxic chemical, and c) the anti-inflammatory inhaled corticosteroid fluticasone propionate (FL).

PHMG is a disinfectant that was implicated in a severe lung disease epidemic in South Korea in 2011, where it was used in humidifiers to prevent algae growth. While it initially appeared to be completely safe, PHMG proved hazardous when inhaled as an aerosol. Our study revealed its toxicity, showing that the combination of air-liquid interface and cyclic mechanical stress led to a complete breakdown of alveolar epithelial barrier integrity after just four hours of exposure. A similar effect was noted when the alveolar barrier was exposed to an aerosol containing titanium dioxide, which is commonly found in paints, cosmetics, and food additives (Fig. 3). These exposures trigger an inflammation insult leading to epithelial barrier disruption and cytotoxicity. Our study reveals a clear effect of physiological levels of CS associated with ALI cell culture. In addition, the anti-inflammatory potential of inhaled FL treatment with the Cloud α AX12 platform, was demonstrated showing its applicability for aerosolized drug screening studies. To our knowledge, this is the first in vitro inhalation exposure system for the distal lung that incorporates breathing lung-on-chip technology. The Cloud α AX12 model thus represents a cutting-edge preclinical tool for studying inhalation toxicity risks, drug safety, and efficacy.

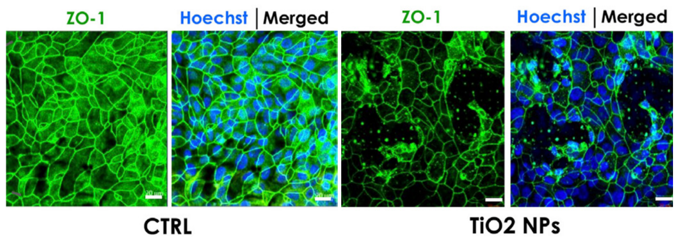

Fig. 3: Staining of confluent alveolar epithelial cells in the lung-on-chip revealed significant damage to the alveolar epithelial barrier in the TiO_2-exposed samples (bottom) compared to the control group (top). Scale bars: 20um. Ref: 3.

Selected Publications:
1. van Os L, Yeoh J, Witz G, Ferrari D, Krebs P, Chandorkar Y, Zeinali S, Sengupta A, Guenat OT. Immune cell extravasation in an organ-on-chip to model lung inflammation. Eur J Pharm Sci. 2023 Aug 1;187:106485.
2. Van Os L, Engelhardt B, Guenat OT. Integration of immune cells in organs-on-chips: a tutorial. Front Bioeng Biotechnol. 2023 Jun 1;11:1191104.
3. Sengupta A, Dorn A, Jamshidi M, Schwob M, Hassan W, De Maddalena LL, Hugi A, Stucki AO, Dorn P, Marti TM, Wisser O, Stucki JD, Krebs T, Hobi N, Guenat OT. A multiplex inhalation platform to model in situ like aerosol delivery in a breathing lung-on-chip. Front Pharmacol. 2023 Mar 6;14:1114739.
4. Schmid KF, Zeinali S, Moser SK, Dubey C, Schneider S, Deng H, Haefliger S, Marti TM, Guenat OT. Assessing the metastatic potential of circulating tumor cells using an organ-on-chip model. Front Bioeng Biotechnol. 2024 Oct 8;12:1457884.

Urogenital Engineering

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Francesco Clavica
Pedro Amado
Amandine Delaunay
Cornel Dillinger
James Fox
Sofia Melone

Research Profile

The urinary tract (UT) consists of two kidneys, two ureters, a bladder and one urethra. For normal urination to occur, all components must function together in a coordinated and efficient manner. The Urogenital Engineering (UGE) group focuses on developing innovative, engineering-based solutions to enhance the understanding, diagnosis, and treatment of UT diseases, many of which significantly impact health and quality of life. Our primary research areas include urinary obstructions (e.g., stones), underactive bladder, overactive bladder and urinary incontinence. Our translational projects address unmet clinical needs, identified and discussed in close collaboration with our clinical partners.

In parallel with computational fluid dynamics studies, we conduct biomedical flow experiments using advanced technologies, such as computer-controlled setups, a variety of sensors (for pressure, flow, volume and impedance), high-speed cameras and laser-based flow measurement systems.

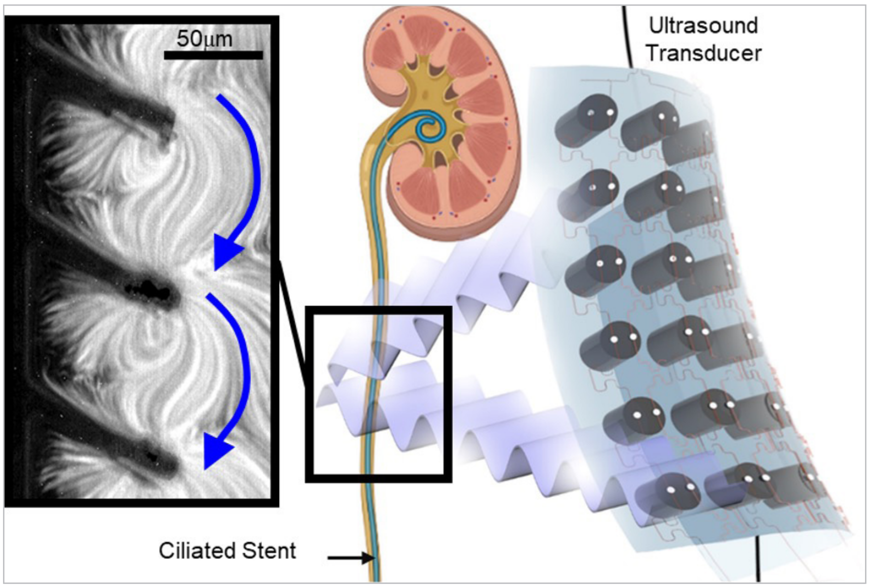

Fig. 1: Our envisioned solution for transcutaneous cleaning of urinary stents and catheters using surfaces equipped with ultrasound-activated cilia.

Encrustation and biofilm

One of our primary research foci is to improve the urine drainage performances of both urinary stents and catheters. Ureteral stents are inserted in the ureter to maintain urine drainage from the kidneys to the bladder, especially when ureteral obstructions (such as stones or tumors) are present. Urinary catheters are typically inserted either through the urethra (transurethral catheterization) or via a puncture in the abdominal wall (suprapubic catheterization) to empty the urinary bladder. Once implanted, both stents and catheters are often blocked by encrustation and biofilm formation, which also increase the risk of urinary infections. Understanding the location and extent of encrustation and biofilm on ureteral stents across various diseases can provide valuable insights for patient management and guide the development of improved designs. In this context, our current projects involve: (i) utilizing micro-computed tomography (µ-CT), combined with semantic segmentation, to quantify encrustation and biofilm volume on ureteral stents retrieved from patients, and (ii) employing scanning electron microscopy (SEM) with energy-dispersive X-ray analysis (EDX) for detailed morphological and chemical characterization of the crystals. These investigations aim to identify regions on stents that are most susceptible to encrustation and correlate these regions with local fluid dynamics. We are also developing our own solutions to prevent/reduce encrustation and biofilm formation in both stents and catheters. In this direction, we are developing the first non-invasively →

cleanable stent that combines ultrasound technology with artificial micro-cilia, positioned both inside and outside a ureteral stent. These cilia are hair-like structures inspired by those found in the respiratory system and inner ear. When exposed to ultrasound, the micro-cilia vibrate at high frequencies, each generating a pair of vortices. Collectively, the vibrating cilia produce a directed fluid jet known as acoustic streaming. Our goal is to utilize this acoustic streaming to effectively clean encrusted stents. (Figure 1).

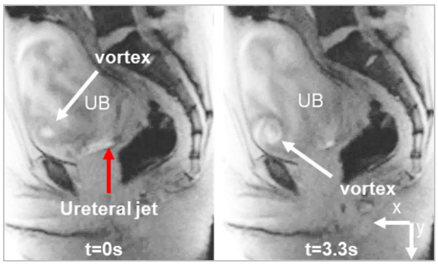

Fig. 2: Examples of MRI magnitude images of the lower urinary tract (sagittal plane) illustrating vortex formation in the urinary bladder (UB) at rest in a healthy volunteer.

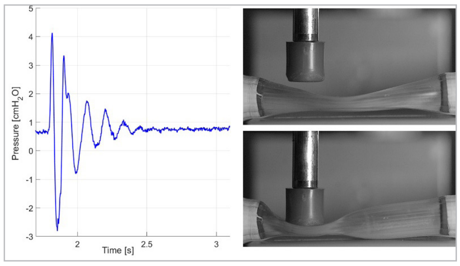

Fig. 3: Impedance pumping: in-vitro investigations on wave propagation/reflections in urethral models combining measurements from pressure sensors and high-speed cameras.

Urinary Tract Modelling

A thorough understanding of normal urinary tract (UT) function and its alterations due to pathologies is essential for developing innovative medical devices to aid patients. To this end, we have created advanced platforms that integrate in-silico, in-vitro, and ex-vivo models for biofluid mechanical investigations within the UT. These platforms enable comprehensive fluid mechanical characterization and allow testing of a range of medical devices, including those for urinary incontinence and retention, as well as urinary stents and catheters.

Quantitative measurements in physiological/ pathological conditions are crucial for validating our models/platforms. In this regard, we are exploring the use of Magnetic Resonance Imaging (MRI) and Phase-Contrast MRI to accurately measure tissue/organ deformation and urine velocity within the UT. For instance, we have demonstrated the presence of vortices within the bladder, even at rest, which may originate from the ureteral jets and can significantly impact overall bladder flow and shear stress patterns (Figure 2).

Overactive Bladder and Incontinence

Patients suffering from overactive bladder (OAB) live with a continuous urge to urinate even at low bladder filling volumes, often leading to urinary incontinence.

OAB has an enormous impact on the quality of life of affected patients. Despite its high prevalence, the understanding of the mechanism underlying OAB remains limited and, as a consequence, treatment options are scarce. UGE has developed several tools that aim to identify specific patterns in bladder pressure and bladder nerve signals associated with overactive bladder. For example, we have developed an algorithm that generates alarms before the start of an unwanted bladder contraction. The algorithm was successfully tested first in rats and then in patients using classical urodynamic signals. It could be used to warn the patients about an impending bladder contraction (to act against incontinence) or/and to trigger conditional sacral nerve stimulation. Moreover, our group has recently shown that pressure-volume catheters, designed to measure cardiac pressure and volume, could be used in urology to better diagnose and treat lower urinary tract dysfunctions. These catheters could enable the evaluation of the bladder contractile function and the identification of local changes of bladder volume (e.g., associated with non-voiding bladder contraction which are typical in OAB patients) for more tailored treatment options.

Our 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. To date, catheters are the most common therapy for bladder emptying. However, catheters are invasive and very often cause urinary tract infections. Hence, a non-invasive solution for bladder emptying that does not lead to urinary tract infections is highly desirable. Our solution for urinary retention is based on the impedance pump principle. An impedance pump is a valveless pump which drives a directed flow by means of an impedance mismatch: traveling waves are generated by externally compressing (and releasing) an elastic tube at a specific frequency and location (Figure 3). Reflections of these waves at the points of impedance mismatch create a complex pattern of nonlinear wave interference. The result of these wave-interactions can be a directed net flow. Hence, by applying this principle to the urethra, urine flow can be generated, and bladder emptying can be supported. By avoiding direct contact with urine, this solution has the potential to significantly reduce urinary tract infections. A first prototype has been produced and tested in 10 male patients (i.e., first-in-man study). URODEA AG (www.urodea.com) is a spinoff of the ARTORG Center and is focusing on bringing this technology to the patients.

Selected Publications

1. Drake M., Clavica F., Murphy C., Fader MJ 'Innovating Indwelling Catheter Design to Counteract Urinary Tract Infection' European Urology Focus 2024 DOI: 10.1016/j.euf.2024.09.015
2. Dillinger D., Amado P., Obrist D, Bukhard F., Ahmed D., Clavica F. 'On-demand Encrustation-repellent Ureteral Stents and Catheter surface: a Novel Bioinspired ultrasonic Approach. Annual Meeting of the International Continence Society (ICS), Madrid, 2024 DOI:10.1016/j.cont.2024.101594.
3. Amado P., Zheng S., Lange D., Carugo D., Waters S., Obrist D., Burkhard F., Clavica F. 'The interplay between bacterial biofilms, encrustation, and wall shear stress in ureteral stents: a review across scales.' Frontiers in Urology 2024 DOI:, 10.3389/fruro.2023.1335414
4. Jahren S.E., Obrist D., Haenggi M., Burkhard F., Clavica F. 'Can Cardiac Pressure-Volume Catheters Improve Urodynamic Assessment? An Ex-Vivo Proof-of-Concept.' Frontiers in Urology 2023, 3, DOI:10.3389/fruro.2023.1258649
5. Zheng S, Amado P, Obrist D, Burkhard F, Clavica F., 'An in vitro bladder model with physiological dynamics: Vesicoureteral reflux alters stent encrustation pattern' Frontiers in Bioengineering and Biotechnology, 2023. DOI:10.3389/fbioe. 2022.1028325
6. Zheng S., Obrist D., Burkhard F., Clavica F. , 'Fluid mechanical performance of ureteral stents: The role of side hole and lumen size' Bioengineering & translational medicine Wiley, 2022. DOI: 10.1002/btm2.10407

Mechanical Design and Production

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Piravin Jeyendran
Killian Brenan
Steve Bäriswil

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.

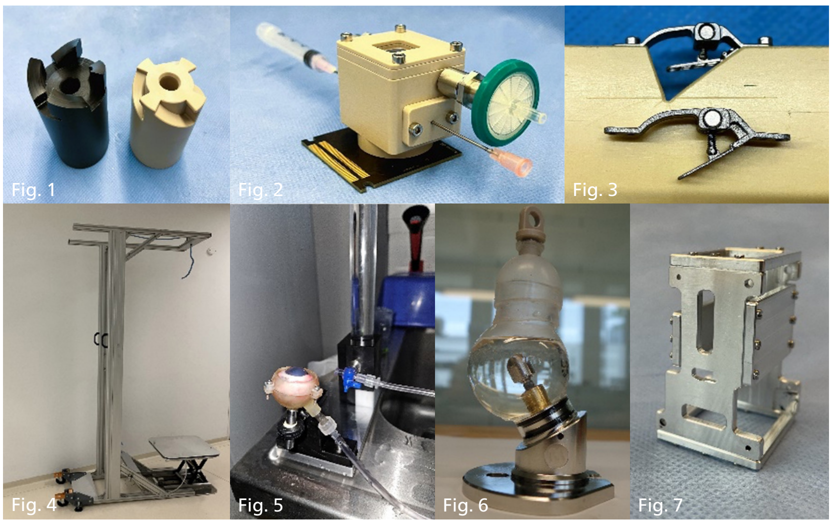

Fig. 1: Device with bayonet lock for mounting aid, **Fig. 2:** Tissue culture chamber, **Fig. 3:** on top: Device for bone augmentation conventionel produced last year, on bottom: same device in 3D metal printing, **Fig. 4:** Frame for scoliosis analysis, **Fig. 5:** Eye pressure device with water column, **Fig. 6:** Chamber for dental implant loading and collection of any nanoparticles, **Fig. 7:** Microrobot housing

Training and Education

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

In 2024 our apprentice Lio Ritschard finished his basic education in the workshop of the physics institute of the University of Bern and since June 1, he has been working with us to expand his knowledge and skills.

Our apprentice Piravin Jeyendran left us at the end of March and has found a new polymechanic apprenticeship that meets his expectations. We wish him continued success and will remain in contact with him.

We were able to employ our former apprentice Janosch Schär as a polymechanic and he left us at the end of June to take on a new challenge. We would like to take this opportunity to thank him for his commitment to our workshop and wish him a successful future.

Due to two large projects, we were looking for a new polymechanic and were able to welcome Simon Balz as a new employee in our workshop on September 1st. He is doing a training as a production specialist and works 80 % of the time. →

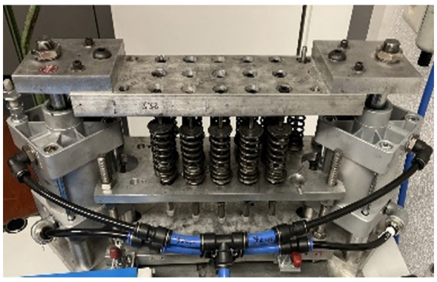
Fig. 8: Test machine before overhaul

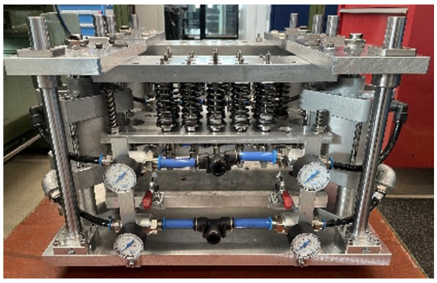
Fig. 9: Test machine before overhaul


Fig. 10: Ultrasonic saw blade

After 34 years in the role of workshop manager (MDP), I am due to retire at the end of June next year and we have found a new workshop manager in the person of Ralf Kreienbühl. He has been working with us since May 1 and during this long transition period I can pass on my knowledge and experience to him. This will also ensure that the high quality of the MDP is maintained. I would like to take this opportunity to wish him every success in his new position as head of the MDP.

In Due to a high demand of workload, we recruited this year two polytechnician, Killian Brennan and Steve Bäriswil as alternative civilianservice employees. They performed administrative tasks and increased the productivity of our team. We would like to thank them both for their commitment and support for our team and thank them for the work that Killian and Steve have done in our workshop.

Research Equipment Design and Manufacturing

This year we were only able to work on a few small projects for ARTORG and hope that in future we will again be able to work on more internal projects. As might be expected, the requirements for a workshop supporting research in biomedical engineering are as diverse as the research field itself. The diversity of topics researched at ARTORG and by external research partners results in a range of different design and production requirements, from prototypes for clinical and surgical tools to fixtures for mechanical, biological, and kinematic testing to accessories for imaging systems and calibration equipment. The following illustration shows some of this year's projects.

Overhaul of two tooth testing machines ZMK

The Clinic for Tooth Preservation, Preventive and Pediatric Dentistry has two pneumatically driven testing machines. Fig 8 These had to be overhauled after many years of use. During this overhaul, we redesigned and adapted the upper pressure plate so that it was additionally reinforced with four new vertical guides. This adjustment was necessary because the plate could tilt with the previous design and the printing force could not be evenly distributed over the 15 test stamps. The tilting of the upper plate also impaired the function of the pneumatic cylinders, causing them to wear excessively. Fig. 9 shows the overhauled unit and the tests were successfully started.

Sitem-Insel Support Found (SISF) Projects

This year, the SISF supported two projects relating to our workshop. We would like to take this opportunity to thank the SISF and all those who contributed to the funding of these projects and placed their trust in our workshop.

The first project

"Interdisciplinary translation of an innovative instrument for selective bone processing in the spine" from the University Clinic for Orthopaedic Surgery and Traumatology Inselspital. This project aims to create a fundamental understanding of the cutting behaviour of blades on bone as a function of design and thus form a scientific basis for effective optimization and future developments. To achieve this, innovative cutting blades with different geometries and properties will be produced and tested in close cooperation with all project partners. Our mission is to produce many different types of saw blades and to help develop a simple way of attaching the saw blades to an ultrasonic source. Fig. 10

The second Project

"Development of a Medical Cart for polarimetry-based AI-Assisted Cancer Diagnosis in Open Surgery" from the Artificial Intelligence in Medical Imaging (AIMI) ARTORG Groupe. This project plan outlines the roadmap for developing a medical cart integrating a polarimetry-based optical system for enhanced cancer diagnosis during open surgeries. The detailed phases and substeps emphasise thorough design, iterative development, rigorous testing, user feedback incorporation, regulatory compliance, and documentation, ensuring a functional and impactful medical solution for the surgical environment.

Dissertations

Alba Segura Amil
Image-Guided Therapy
Improving DBS therapy with patient-specific tractography

Jan Schulte
Organs-on-Chip Technologies
Development of a novel alveoli-on-chip model for mechanical investigations on primary human alveolar epithelial cells

Yvan Gugler
Musculoskeletal Biomechanics
Evaluation of 3D DXA Reconstructions of the Proximal Femur for FE-Based Strength and Fracture Risk Predictions

Sergio Tascon-Morales
Artificial Intelligence in Medical Imaging
Spatial Awareness and Logic for Robust Visual Question Answering

Aleksandra Ivanovic
Hearing Resaerch Laboratory
Hearing under the Lens: Exploring the Human Middle Ear with Synchrotron-based Phase-contrast Microtomography

Ioannis Papathanail
Artificial Intelligence in Health and Nutrition
Machine Learning-based System for Dietary Assessment

Raphael Rätz
Motor Learning and Neurorehabilitation
Novel Clinical-Driven Robotic Devices for Sensorimotor Training

Prisca Dotti
Artificial Intelligence in Medical Imaging
Detection, Localization, and Classification of Subcellular Ca^2+ Release Events: Using a Deep Learning Approach

Karoline-Marie Bornemann
Cardiovascular Engineering
Instability mechanisms leading to laminar-turbulent transition past bioprosthetic aortic valves

Stephan Schraivogel
Hearing Resaerch Laboratory
Impedance Telemetry-Based Insertion Depth Estimation for Cochlear Implants - From Research to Clinical Application

Lukas Zbinden
Artificial Intelligence in Medical Imaging
Advances in Automated Non-Invasive Liver MRI Phenotyping and Stochastic Segmentation

András Balint
Hearing Resaerch Laboratory
How patterns of Brain Activation Predict Speech Understanding

Javier Gamazo Tejero
Artificial Intelligence in Medical Imaging
Overcoming Data Limitations through Optimization: From Annotation Strategies to Real-World Application

Lars Doorenbos
Artificial Intelligence in Medical Imaging
Reliably Processing Unexpected and Ambiguous Images in Computer Vision

Research Partners

- Universität Bern
- Inselspital – Universitätsspital Bern / Hôpital Universitaire de Berne / Bern University Hospital
- sitem insel
- Universitäre Psychiatrische Dienste Bern
- 3RCC Swiss 3R Competence Centre
- COST – European Cooperation in Science and Technology
- Hasler Stiftung
- Johnson & Johnson
- ALEXIS
- CSEM
- haute école arc – neuchâtel berne jura
- Karolinska Institutet – Anno 1810
- AlveoliX – In-vitro models inspired by nature
- Debiotech
- Helmholtz Centre for Infection Research
- krebsliga schweiz
- AO Research Institute Davos
- domo.health
- HSLU Hochschule Luzern
- LEM Surgical – Spine Robotics Reinvented
- BFH – Bern University of Applied Sciences
- Empa – Materials Science and Technology
- Horizon 2020
- luzerner kantonsspital
- Bristol Urological Institute – Improving care by advancing knowledge
- EPFL
- HUG – Hôpitaux Universitaires Genève
- Maastricht University
- CASCINATION
- ETH zürich
- Imperial College London
- McGill
- Charité – Universitätsmedizin Berlin
- EURICE – European Research and Project Office GmbH
- Innosuisse
- MED-EL
- CHUV
- European Commission
- Intuitive Surgical
- Medizinische Universität Graz
- Cochlear
- eurostars
- IROC
- Mount Sinai
- CorFlow Therapeutics
- Fond'Action contre le cancer
- JDRF – Improving lives. Curing type 1 diabetes.
- National and Kapodistrian University of Athens

Research Partners (continued)

neosoma
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UNIVERSITY OF OXFORD

Novostia
sanitas
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University of Southampton

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