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Annual Report 2020/21  Content
The years 2020/2021 were characterized by radical change both in the way we work together and in environmental circumstances guiding research and development of medical technology. The pandemic has challenged us to develop new ways to innovate, capitalizing on digitalization and flexibility and opening our horizons across national borders. Stronger regulation through the MDR and Switzerland’s non-associative status in Europe have further pushed us to orientate our energies to both local and international markets.

Even in these turbulent times and as we emerge into a new era of renewed personal encounters, the Bern Biomedical Engineering Network continues to leverage its assets with strong partners in research, industry, and clinic. Our network has prevailed in bringing a great number of successful start-ups forward and has made a difference to patient care and pushed the boundaries of what doctors and nurses are capable of doing.

It is through this spirit of collaboration, entrepreneurship, and the diversity of our expertise that we form an unparalleled biomedical engineering hub at the heart of Switzerland. Inspired by past pioneers and capitalizing on the unique Bernese constellation for disruptive medtech development and translation we never lose sight of patient benefit as our primary driver and goal.

The Bern Biomedical Engineering Network continues its important role in the medtech research and industry cluster of Switzerland’s capital region. We have come forward with new ideas and energies and educate the next generation of experts with unabated enthusiasm. Our network offers top-quality master courses with cutting-edge specialisation choices. With their academic excellence and practical expertise in the clinics, our graduates are prepared to shape the medtech landscape on an international scale, and to effectively transform medicine and healthcare through technology.

The BBEN partners remain committed to promoting shared interests, generating synergies in resources and infrastructure, and leveraging the location advantage of the medtech sector of the Canton of Bern to foster:

• Translation of medical technology for patient benefit.
• World-class research and discovery through multi-disciplinary collaboration.
• Globally leading biomedical engineering graduate and post-graduate education and training.

Prof. Dr. Raphael Sznitman
Director
ARTORG Center
University of Bern

Prof. Dr. med. Thomas Geiser
Director Teaching and Research Inosspital, Bern University Hospital

Prof. Dr. Sebastian Wörwag
President
Bern University of Applied Sciences BFH

Prof. Dr. Alex Dommann
Head of Department
Empa

Simon Rothen
CEO
sitem-insel AG
Institutional Overview

Swiss Institute for Translational and Entrepreneurial Medicine
Freiburgstrasse 3, 3010 Bern

Inselhospital, Bern University Hospital
Freiburgstrasse, 3010 Bern

Institute of Computer Science
Neubrückstrasse 10, 3012 Bern

Department for BioMedical Research (DBMR)
Murtenstrasse 35, 3008 Bern

Institute of Applied Physics
Sidlerstrasse 5, 3012 Bern

BFH Institute for Medical Informatics (HHIM)
Höheweg 80, 2503 Biel/Bienne

BFH Institut for Human Centered Engineering HUCE
Quellgasse 2, 2501 Biel/Bienne

Institute for Rehabilitation and Performance Technology
Postaltorstrasse 20, 3400 Burgdorf

Empa
Feuerwerkstrasse 39, 3002 Thun

ARTORG Center for Biomedical Engineering Research
Murtenstrasse 50, 3008 Bern

Department of Clinical Research (DCR)
Mitteleinstrasse 43, 3012 Bern

BFH Centre for Health Technologies
Aarbergstrasse 44, 2503 Biel/Bienne

BFH Bern Pavement Lab
Stadtbachstrasse 64, 3012 Bern
Bringing innovation to the patient – by connecting people

The medical technology and pharmaceutical industries are cornerstones of the Swiss economy. Their product development relies on collaborations with university hospitals. Translational medicine should therefore be understood as a process-oriented and actor-centered discipline that necessarily involves numerous stakeholders from industry, academia, clinics, and authorities.

Such close and diverse collaboration among authorities, research, the startup scene, and industry is thus only made possible by institutions such as the Swiss Institute for Translational and Entrepreneurial Medicine: sitem-insel.

sitem-insel has set itself the goal of establishing, operating, and continuously developing a national center of excellence for translational and entrepreneurial medicine, which professionalizes translational research for the benefit of patients, society, and science.

sitem-insel is located at the Insel Campus Bern and benefits from its proximity to the University Hospital (Inselspital) and the University of Bern. In sitem-insel, a wide variety of representatives from clinics, industry, research, and education are networked to innovate for the benefit of the patient. As a business, medical, and research campus, sitem-insel promotes innovation and collaboration among all partners and stakeholders.

sitem-insel opens its doors to all disciplines of translational medicine as a non-profit corporation and public-private partnership (PPP).

Three pillars

sitem-insel strongly believes in an entrepreneurial team approach as a solution to speed up the leap from innovation in industrial development and basic research into clinical applications.

sitem-insel’s operational strategy is based on three pillars: Connecting minds: sitem-insel School (with the University of Bern) promotes professionalization by educating researchers and training executives in the field of translational medicine and biomedical entrepreneurship from a holistic perspective. The school teaches students practice-oriented high-quality knowledge, provides a strong network between people involved in the translational process, and offers training recognized by the University of Bern.

Delivering impact: sitem-insel Enabling Facilities provide infrastructure for researching and developing medical device technologies, biomedical technologies, as well as combination products and diagnostics. Taking disruptive developments into account, the infrastructural design of sitem-insel’s new building guarantees flexibility.

Our new building was opened in 2019—a great success in terms of costs, time, and quality. Run by public partners from university and university hospital as well as private industry partners, the premises comprise, among others, the first biosafety laboratory (BSL 3) available to external renters on a project basis, 7 Tesla MR, a diabetes research center, a clinical anatomy training and research unit, and an open space for start-ups and spinoffs, with more planned for the future.

Delivering insight: sitem-insel Promoting Services respond to the major challenge of demanding and constantly changing regulatory requirements for translational projects. With the help of its partners, sitem-insel Promoting Services support companies in accelerating their process from invention to commercialization.

Our programs cover the most up-to-date thinking in translational science:

- Translational Medicine and Biomedical Entrepreneurship
- Artificial Intelligence in Medical Imaging
- Medical Device Regulatory Affairs and Quality Assurance (MDRQ)

Group Members

Dr. Simon Rothen, CBO
Dr. Julie Risse, CBO & HR
Dr. Stefanie Hofer, CCO & HR
Dr. Christian Rosser, CDO & director sitem-insel School
Dr. Christian Blankart, Director sitem-insel Promoting Services

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Sitem-insel Promoting Services operate a network of manufacturers, associations, scientists, and other healthcare institutions to support companies, clinics, and academia in regulatory and administrative matters.

Overall, sitem-insel Promoting Services reduce silo-building between industries, between disciplines, and, in terms of educational inputs, within individual people.

The three operational units, School, Enabling Facilities, and Promoting Services, together with the supporting units Centralized Services and Network & Communication, build sitem-insel’s core organization.

Clinical Anatomy Training and Research Unit (CATR): The development of innovative diagnostic-therapeutic medtech products and learning how to use them correctly requires access to a highly equipped operation room (OR)-environment. The training can involve the use of animal or human specimens, simulation, or robotics. High ethical standards and specific infrastructure are required to work with cadaveric components. This infrastructure has been set up in the sitem-insel building as a CATR and is supported in its development and operation by, among others, the anatomy of the University of Bern and Prof. Michael D. Mueller, Co-Director of the University Clinic for Gynecology. The CATR has received generous financial support from the companies Darz and Anklin. CATR received DFG-early-career-funding in 2021. The platform with its state-of-the-art infrastructure is extremely attractive for a variety of training courses, not only for physicians from the Inselspital but also from the canton, Switzerland, and abroad.

Biosafety Level 3 (BSL-3) Laboratory: The BSL3 laboratory, already mentioned in the last report, was successfully commissioned on schedule in 2020 despite the COVID-19 pandemic and the first lockdown phase. The Institute for Infectious Diseases of the University of Bern (Ifik) operates the Biosafety Lab and the Biosafety Center. Twenty percent of the laboratory space is financed by sitem-insel and made available for external projects. First tenants for the two BSL3 spaces of sitem-insel were found quickly. In both cases the tenants work on SARS-CoV-2 projects.

Next to its own units, the sitem-insel community includes a wide variety of about 30 units from clinics, industry, research, and education to service-providers. All are joined together under one roof and drive innovation for the benefit of the patient.

Shaping the future of translational medicine - some high-lights

NeuroTec Opening

NeuroTec, the newly opened research unit within sitem-insel, accelerates innovation and explores novel medical technology to improve diagnostics and the treatment of neurological diseases. The aim is to shift diagnosis and therapy from the hospital to the patient’s home.

At the core of NeuroTec is the “Living Suite” - a smart home where human behavior is monitored and researched to understand how neurological disorders affect daily life. Areas of interest include the analysis of physiological and pathological body movements, cognitive performance, and sleep-wake patterns in both health and disease. Overall, NeuroTec promises to address problems of our aging society and thereby improve the cost-effectiveness and quality of healthcare for patients with neurological disorders.

NeuroTec posts the clinical knowledge of Inselspital, University Hospital Bern, and the expertise in medical technology of the University of Bern and the medtech scene in Bern. The facilities at sitem-insel enable an active exchange with researchers in the field.

NeuroTec is run by the Department of Neurology of Inselspital, University Hospital Bern in close collaboration with the ATCOSIN Center for Biomedical Engineering Research of the University of Bern, with project-specific partners from academia, non-profit research institutions, and industrial partners in public-private partnerships.

Covasc Consortium within sitem-insel’s BSL-3 laboratory

Shortly after its opening, one of the rooms of the biosafety level-3 laboratory (BSL-3) within sitem-insel, was rented out to the Covasc consortium.

The Covasc consortium is a group of four research project leaders and 10 project partners that connects experts in heart research, vascular biology, and neuroimmunology as well as in vitro, together they investigate how and if heart and vascular cells are prone to be infected by the SARS-CoV-2 and potential consequences thereafter.

The National Research Program 70 initiated by the Swiss National Foundation finances this project.

Screen & Care: An international public-private consortium of 35 partners, including sitem-insel and the University of Bern. Launched ScreenCare - a research project that aims to significantly shorten the time required for rare disease diagnosis and efficient intervention by utilizing genetic newborn screening and advanced analysis methods such as machine learning.

The project will run for a period of five years with a total budget of EUR 25 million provided by the Innovative Medicines Initiative (IMI 2-JULI), a joint undertaking of the European Union and the European Federation of Pharmaceutical Industries and Associations (EFPIA).

Education at the CATR: Cutting-edge education is an important part of the translational process. The Clinical Anatomy Training and Research Unit (CATR) at sitem-insel has picked up speed and has been hosting international and national surgical training courses in 2021 in its state-of-the-art infrastructure.

• 20.02 - 21.02: First GESEA course and certification in Switzerland
• 03 - 25.05: European Endometriosis Laparoscopic Masterclass
• 02.08 - 03.09: 5th Swiss Endoscopic Ear Surgery Course SEES and the 17th Endoscopic Paranasal Sinus & Skull Base Hands-on Course PSSB

New Units

Towards the end of 2021, sitem-insel welcomed the Bern University of Applied Sciences (Berner Fachhochschule BFH) with a lease agreement for two offices into its building and is looking forward to fruitful collaborations.

Furthermore, a new collaborative project has been successfully launched by the Inselspital Bern and Empa Dübendorf. Across from the Translational Imaging Center on sitem-insel’s second ground floor, where we host one of the two nationwide 7 Tesla MRI machines, the installment of the new “Dynamic Imaging Center” is taking shape. What is it all about?

The aim of the new center is to establish a novel, state-of-the-art musculoskeletal biodynamics laboratory to conduct fundamental and translational research in the area of musculoskeletal movement biomechanics, with a high-speed Dynamic Biplane Radiographic Imaging (DBRI) system at the heart of the setup.

The modern, high-speed (up to 1500 fps) imaging system is capable of directly capturing/bounding motion of various musculoskeletal joints. This allows direct in vivo imaging of bones during functional activities with sub-millimeter accuracy. The system comprises high-speed video cameras, x-ray, and large-sized image intensifiers suitable for dynamic imaging of various musculoskeletal joints, including shoulder, knee, ankle, hip, and spine.

The technology has progressed to a point where it is now feasible to pose-and obtain answers to – specific questions regarding joint arthro-kinematics, particularly with respect to differences between healthy and diseased joints.

This endeavour, which includes management of the DBRI system as well as the area of musculoskeletal research in general, is necessarily interdisciplinary, requiring expertise from orthopaedics, radiology, surgery, physiotherapy, and engineering. The consortium comprising the Inselspital and Empa, along with the project partners and prospective principal investigators of planned research topics, brings together a broad network of Swiss scientists, clinicians, clinician-scientists, and engineers to conduct cutting-edge research and development work.

sitem-insel’s projects and collaborations, brand strategies, and its corporate governance guidelines are all characterized by a long-term perspective. The sitem-insel team is driven by innovation and strives to make sitem-insel a pioneer and operational center of excellence in translational research.
Research Profile
Our research laboratory develops X-ray methodologies for understanding materials structure in life and materials science. We combine the expertise of X-ray-based imaging technology (trans- and micro-X-CT, 2D, 3D to 4D), X-ray diffraction (XRD, HRXRD), and wide- and small-angle scattering methods (WAXS, SAXS, XPCI). The gap between X-ray methods is bridged by their combination and/or fusion. Studies of dynamical processes on surfaces, at interfaces, and in fluids have a central part. Models for the understanding of complex systems such as low-density and low-contrast materials like bio-systems and polymers are established, especially for the biomedical domain and in collaboration with partners from research institutions, Swiss hospitals, and industry.

The X-ray team concentrates on life-sciences research (Health and Performance), computational modeling, life science, and technology to generate innovative solutions. Empa as part of the ETH domain also supports teaching at universities and universities of applied sciences (UAS) and is active in organizing scientific conferences and advanced training courses through the Empa-Academy. Confereces, lecture series, seminars, and courses are aimed at scientists, professionals from industry and the private sector, and also the general public.

Alex Dommann
Head of Department

Characterizing the Intravascular Clot in Acute Stroke with Multi-parametric Imaging (SNF grant 32003B_183382)

Stroke is the first cause of acquired deficit and the second cause of death in the industrialized world. Due to the aging population, stroke incidence and the corresponding medical and economic burden imposed on society are expected to increase. Detailed volumetric information on the composition of the blood clot of the stroke patient is very valuable to understand the mechanical properties, like stiffness, of clots, which are crucial in selecting the most efficient mechanical thrombectomy (MTT) method for clot extraction. This research combines multi-modal and high-resolution imaging and analytical methods like phase-contrast microCT, electron microscopy, and X-ray diffraction. Different clot types retrieved by mechanical thrombectomy from patients of acute ischemic stroke were evaluated through propagation-based phase-contrast microCT. The results were correlated with high-resolution scanning electron microscopy (SEM) images, confirming detected cellular and fibrillary structures. X-ray diffraction was used to identify potential endogenous calcifications. Calcifications appeared as glassy opacity areas with a moderately intense signal on microCT images, also proved by energy-dispersive spectroscopy and X-ray diffraction. Further development of automated post-processing techniques, also based on machine learning algorithms, for X-ray PB/micro/ nanoCT will enable high-throughput analysis of blood clot composition and their 3D histological features on large sample cohorts. This can provide statistically significant information about the biological and mechanical properties of clot types, and then, implications on the relation between clot composition and MTB outcome. This is beyond reach for state-of-the-art
Structural in-situ investigations for Particle Systems and Their Early Event Dynamics in Bio-logical Environments
(SNF grant 205021_178202)

Today, nanoparticles (NPs) applications in biomedical fields and medicine are increasingly important. However, after transferring NPs to a biological environment, their interactions are complex and poorly understood. Different parameters such as ionic strength and pH conditions, and the presence of biomolecules such as proteins initiate alterations in NPs' structure and therefore influence their colloidal stability.

For applications in nanomedicine, the NPs' colloidal stability in a biological environment is a crucial property as it strongly influences the product safety and efficiency. Therefore, we are especially interested in a detailed investigation on NPs' interactions and their structural changes in early events in a biological environment. In our lab, we developed a characterization method based on small-angle X-ray scattering (SAXS) for in-situ label-free, and dynamic studies on the early and advanced stages of NPs interactions after exposure to a biological environment. A microscope system is designed and fabricated, which is combinable with SAXS instruments in the laboratory and at synchrotron facilities. Silica NPs are selected to individually investigate the effect of changes in pH, ionic strength, and the presence of proteins in the environment on NPs for their colloidal stability. It is concluded that the presence of the protein reduces silica NPs' colloidal stability drastically.

NPs' interactions in the presence of different protein concentrations are studied with respect to effects of NPs' size and surface modification. Gold NPs with 5 and 40 nm in diameter, and two surface modifications such as citrate and polyethylene glycol (PEG) are investigated. Each surface modification shows distinct stabilization mechanisms. Citrate NPs in appropriate protein concentrations stabilize by protein adsorption on their surfaces. In contrast, 5 nm PEGylated NPs show stabilization by generating self-assembled 3D-ordered domains in different protein concentrations, which can be followed in detail using the designed micromixer-SAXS setup.

A related topic in our lab is the study of drug delivery systems where the support structures, namely electroporous fibers, influence the drug release kinetics. Ongoing work involves the fabrication of fibrous membranes with tailored architectures for the design of advanced drug delivery systems.

Quantifying Phase Orientation and Morphology of Mineralized Turkey Leg Tendons: A Multiscale and Multimodal X-ray Analysis

Hierarchical arrangements observed in bone biocomposites like bone and tendons, range from the macroscale down to the molecular level. The multiscale complex morphology, based on a large extent on correlated orientation of their constituents, contributes significantly to the outstanding mechanical properties of these biomaterials. We established a road map to quantify the hierarchical structure of a mineralized turkey leg tendon (MTLT) in a holistic multiscale evaluation by combining micro-Computed Tomography (micro-CT), small-angle X-ray scattering (SAXS), and wide-angle X-ray diffraction (WAXD). The interplay of the main MTLT components is analyzed with respect to highly ordered organic parts such as collagen fibers and integrated inorganic components like hydroxyapatite (HAp). The microscale fibrous morphology revealing different types of porous features and their orientation was quantified using micro-CT. The quantitative analysis of the alignment of collagen fibrils and HAp crystals was established from SAXS using the Kikuchi approach and the broadening of azimuthal profiles of the small- and wide-angle diffraction peaks. We observe a relatively lower degree of orientation of HAp-crystals compared to the collagen fibrils.

Selected Publications
Acrylate-based bio-compatible nanocomposite ink that is reinforced by more problematic. In this study, we report the formulation of a novel meth-
ination of such enhanced materials at the micro- and nanoscale, remains
e or (left) were manufactured where three different CNC concentrations
were used for the 3D micro-fabrication (middle). Their structure-
mechanical properties were determined by means of micro-compres-
sion (right) and Raman measurements.

Overview of the 3D printing of microscale cellulose nanocrystal-
reinforced nanocomposites by two-photon polymerisation (2PP) and their microstructural characterisation. Inks of GBL, CNC, and IP-S
(left) were manufactured where three different CNC concentrations
are used for the 3D micro-fabrication (middle). Their structure-
mechanical properties were determined by means of micro-compression
(right) and Raman measurements.

Research Profile
Our mission is to enable materials innovation in major Swiss manufacturing
areas, such as medical technologies, miniature and precision mechanics,
and surface engineering. We synthesise novel materials via atomic layer
deposition, physical vapour deposition, or electrochemical methods ex-
ploiting both research and industrial scale deposition equipment. We de-
velop microfabrication methods such as 3D microprinting techniques and
cleanroom-based conventional lithography processes to engineer surfaces
and miniature devices. In particular, we investigate mechanical properties
of inorganic and biological materials at the nano- to the millimeter-scale
under extreme conditions of humidity, strain rate, and temperature and
develop novel nano-mechanical and microanalysis instrumentation.

Microscale 3D Printing and Characterization of Cellulose Nanocrystal Reinforced Composites
Pcmaterials have gained importance across nearly all fields of engineer-
ing. They are an interesting alternative to classical engineering materials
due to the possibility of tuning their behavior over a wide range in the
material property space by a careful design of their nanostructure. Such
materials are of special interest for biomedical implants and scalable
tools for tissue engineering where specific structure-mechanical charac-
teristics are desired. One main objective is to enhance the mechanical performance of these scaffolds that serve as a structural support for cell
attachments and the subsequent tissue development. However, the fabri-
cation of such enhanced materials at the micro- and nanoscale, remains
a challenge and using reinforcement phases makes their synthesis even
more problematic. In this study, we report the formulation of a novel meth-
acrylate-based bio-compatible nanocomposite ink that is reinforced by

Bone fractures pose a significant challenge for healthcare systems all over
the world. The number of fragility fractures is increasing yearly, so are the
associated healthcare costs. The most severe fractures (ex. hip, vertebra)
lead to a full or partial immobilization of the patients and consequently re-
duced life quality. The current clinical methods for fracture risk prediction
rely on bone mineral density, which only partially explains the variation
seen in patients. It is therefore of high importance to investigate addi-
tional bone parameters responsible for the bone quality and to develop
accessible and accurate methods of measurement of such parameters.

Within the Special Focus Area Personalized Health and Related Technol-
ologies of the ETH Board, this study aims to translate recent advances in
microscale mechanical and tissue characterization techniques into
clinical practice to improve current diagnostic tools by the knowledge
of extracellular matrix (ECM) composition, proteoty, and micromechan-
ical properties of individual patient biopsies. The femoral neck slices
are collected during total hip arthroplasty together with the anonymized
patient information from the Inselspital and Spital Thun in Bern. The
microscale morphology and mineral density of the biopsies are meas-
ured using micro-CT. Tissue quality is evaluated from the structure-me-
chanical property relationships on the microscale, which are assessed
via site-matched polarized Raman spectroscopy and micromechanical
compression experiments following previously developed methodology
(Kochetkova et al., Acta Biomater. 2020). Moreover, a novel laser ablation
protocol for the microparticle fabrication is developed in collaboration with
ALPS Institute at the Berner Fachhochschule, allowing us to perform high
throughput microscale compression analysis. The data on the microscale
morphology and tissue quality is then complemented by proteinomic anal-
ysis, which is carried out in the Metabolomics and Proteomics Platform
at the University of Fribourg. The proteomics is used for the detection
cellular bone ECM proteins and their comparison between the cohorts of
patients. It will be assessed by machine learning approaches if knowl-
dge of proteotype and microscale structure-property relationships may
help to estimate the femoral strength of individual patients at higher
accuracy.

Selected Publications
[2] T. Kochetkova, C. Peruzzi et al. (2021), Combining polarized Raman spectroscopy and microparticle compression to study

The schematic of the study on combining bone proteotype and multiscale extracellular matrix properties for improved clinical
fracture risk prediction.
Artificial Intelligence in Health and Nutrition

Editorial
ARTORG CENTER FOR BIOMEDICAL ENGINEERING RESEARCH

The ARTORG Center at the University of Bern is a multidisciplinary Med-Tech Center of Excellence joining engineers, computer, material- and life scientists, clinicians, and biologists in a mission to develop innovative and clinically-proven healthcare technology for diagnostic, monitoring, treatment, and rehabilitation for patient benefit.

Through technical expertise in data science, flow mechanics, computational biomechanics, medical image analysis, microfabrication, organ-on-chip and robotics in surgery and rehabilitation, ARTORG with its twelve independent research groups co-headed by technical and clinical group heads is a strong partner of the Bern Biomedical Engineering Network.

With the foundation of the Center for Artificial Intelligence in Medicine (CAIM) as our overarching sister organization for innovation in digitalized medicine in 2021, we are expanding our strong focus on AI technologies for data-driven medical approaches, imaging, precision medicine and autonomous surgical robotics. Together with clinical experts from the Inselspital and the University Psychiatry Services, CAIM sets out to deliberately shape the digitalized healthcare future, including ethical issues of medical AI implementation with the CAIM Embedded Ethics Lab.

ARTORG’s entrepreneurial spirit has enabled it to innovate biomedical technologies directly into clinical routines. The ARTORG stands for highly successful startup incubation with three MedTech Award wins within the last decade. With five of our research groups located at the Swiss Institute for Translational and Entrepreneurial Medicine, sitem-insel since mid-2019, we further strengthen our ability for a fast and successful translation of ARTORG innovations.

The ARTORG is committed to excellence in academic education and delivers globally leading masters and doctoral programs in biomedical engineering, specialist courses for clinicians and networking events with industry partners. Always starting from a clinical perspective, it has newly launched a master’s program ‘AI in Medicine’, introducing young data science engineers to AI fundamentals, and enabling them to translate skills and academic experiences at the forefront of healthcare.

Raphael Sznitman
Director ARTORG Center

Nutrient Intake Monitoring and Diet Assessment
Food is a key element of our life; it is socially and culturally important and plays a vital role in the definition of health. Preventing the onset and progression of diet-related acute and chronic diseases (e.g., diabetes, obesity, kidney disease) requires reliable and intuitive systems that can translate food intake into nutrient intake. To this end, systems based on innovative technologies are being introduced to exploit recent advances in computer vision, machine learning, wearable sensors, and smartphone technologies. Since 2008, AIHN has been developing technologies for monitoring nutrient intake and assessing diet by analyzing food multimedia data with AI. We have introduced the first fully operative system that estimates the

Tackling hospitalised malnutrition: The system for hospitalised patients receives as input the daily menu and the tray images and estimates the volume of each dish before and after consumption.

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 management and treatment optimisation
• diagnosis, prognosis, and management of acute and chronic lung diseases

Raphael Sznitman
Director ARTORG Center
An innovative algorithm has been developed by the engineers of the AIHN laboratory and allows daily adjustment of the insulin treatment based on fluctuations in the patient’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, physical activity) trackers provide input to the algorithm, which outputs basal daily insulin and boluses for the case of pump users or suggestions for the case of users under multiple daily injections (MDI). The algorithm learns while being used by the patient and is able to achieve glucose control over the course of four virtual trials that lasted three months, under extreme scenarios of disturbances, uncertainties, and variabilities. After the in silico clinical trials, the algorithm was implemented on a mobile application. A feasibility study will start within the next months.

**AI and Lung Diseases**

Interstitial Lung Diseases (ILD) are a heterogeneous group of more than 200 chronic, overlapping lung disorders, characterised by fibrosis and/or inflammation of lung tissue. The diagnosis of a suspected ILD is based on high-resolution computed tomography (HRCT) images and often presents a diagnostic dilemma. By achieving a reliable diagnosis on HRCT images, patients could avoid potential complications, as well as the high costs associated with a surgical biopsy. To this end, we investigate AI- and computer vision-based algorithms for the analysis of imaging, clinical/biochemical, and other disease-related data for diagnosis and management of ILDs. More specifically, algorithmic approaches for the fully automatic segmentation of lung and anatomical structures of the lung cavity, the segmentation and characterization of lung pathological tissue, and the calculation of disease distributions are introduced and continuously validated within the framework of research trials. The image analysis results along with the additional disease-related information are further analysed not only in order to support the faster diagnosis, but also for the more efficient disease management in the sense of treatment selections and disease progression.

During the last two years, we extended our research activities in the field of COVID-19 pneumonia detection, severity assessment (acute COVID-19), and prognosis (including long COVID-19) based on the AI-powered analysis of imaging, clinical/laboratory, and patient history data.
A Positive/Unlabeled Approach for the Segmentation of Medical Sequences using Point-Wise Supervision

The ability to quickly annotate medical imaging data plays a critical role in training deep learning frameworks for segmentation. Doing so for image volumes or video sequences is even more pressing as annotating these is particularly burdensome. To alleviate this problem, this work proposes a new method to efficiently segment medical imaging volumes or videos using pointwise annotations only. This allows annotations to be collected extremely quickly and remains applicable to numerous segmentation tasks. Our approach trains a deep learning model using an appropriate Positive/Unlabeled objective function using sparse point-wise annotations. While most methods of this kind assume that the proportion of positive samples in the data is known apriori, we introduce a novel self-supervised method to estimate this prior efficiently by combining a Bayesian estimation framework and new stopping criteria. Our method iteratively estimates appropriate class priors and yields high segmentation quality for a variety of object types and imaging modalities. In addition, by leveraging a spatio-temporal tracking framework, we regularize our predictions by leveraging the complete data volume. We show experimentally that our approach outperforms state-of-the-art methods tailored to the same problem.

Selected Publications


Cardiovascular Engineering

Research Profile

The Cardiovascular Engineering (CVE) group studies biomedical flow systems to develop diagnostic and therapeutic technology for cardiovascular diseases. Our research aims to improve the durability and biocompatibility of therapeutic devices and implants and to develop novel diagnostic tools. These translational research projects address unmet clinical needs that were identified with our clinical partners who are closely integrated in the 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 heart and to measure hemodynamic parameters. This includes high-speed 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 high-performance computing infrastructure at the Swiss Supercomputing Center CSCS.

Heart Valve Replacement

Numerous designs of heart valve prostheses have been in use for more than half a century. Insufficient durability and biocompatibility of heart valve prostheses are limiting factors for the clinical use of these 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, compliant silicone phantoms of large blood vessels, and modern optical measurement technology for quantifying complex three-dimensional blood flow fields. Our experimental approach is complemented by high-fidelity flow solvers for transitional to turbulent flow, which are coupled with finite-element models for soft tissue via the immersed boundary method. These models are optimized for high-performance computing platforms to provide unparalleled insight into the generation of turbulent blood flow past aortic valves.

Our research infrastructure enables us to perform ex vivo, in vivo, and in silico tests of different valve designs, and patient-specific modeling provides a tool for identifying the optimal personalized valve replacement therapy.

Mycocardial Infarction

The heart muscle is supplied with oxygen and nutrients through the coronary circulation whose complex network topology at different spatial scales (epicardial vessels, collaterals, coronary microcirculation) is a central factor in the outcome of myocardial infarctions (heart attacks).

Microvascular obstruction (MVO) of the myocardium is an underdiagnosed condition caused by heart attack, which may delay or even prohibit full recovery. In MVO, blood flow at the level of the cardiac microcirculation is partially blocked such that affected regions of the heart are insufficiently perfused.

A multi-scalebenchmark model of the coronary circulation 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 vessels of the cardiac microcirculation. It is used to study transport of substances (e.g., pharmaceutical agents) in the myocardium and to optimize infusion protocols for catheter-based treatment of MVO.

Dielectric Elastomer Augmented Aorta

Together with the Center for Artificial Muscles (CeAM) 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), the Dielectric Elastomer Augmented Aorta compresses and dilates a section of the aorta. This supports the function of the heart by reducing the afterload (aortic blood pressure) and by increasing the coronary perfusion. The device makes use of a dielectric elastomer that actuates the pump.

We are using an in vitro benchtop model and in vivo trials to optimize the design and actuation pattern of the device. Analysis of the experimental data and theoretical models of aortic pulse propagation provide novel insight into the mechanics of the beating heart.

Capillary Vasculature

Capillary vessels of the microcirculation are the smallest blood vessels (diameter 5 micrometers). Oxygen and nutrient exchange with the surrounding tissue takes place in the capillary networks. In contrast to blood flow in larger blood vessels, capillary blood flow follows different physical laws, which is related to the fact that capillaries are so small that red blood cells must squeeze through these vessels such that 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. We investigate how the network topology affects the heterogeneous distribution of red blood cells in the network and how the system reacts to local obstructions (e.g., micro-strokes). To study blood flow regulation mechanisms at the smallest scales, we have developed microfluidic valves to model pericyte cells that wrap around capillaries to locally dilate and construct the vessels.

Selected Publications

Chair for Image-Guided Therapy

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Group Members

Clinical Partners
Daniel Aeberhard, Director and Head of Department Radiation Oncology
Iris Bauernfeind, Director and Head of Department of Anesthesiology
Andreas Raabe, Director and Head of Department of Diagnostic, Interventional and Pediatric Radiology
Jan Graika, Director Institute of Diagnostic and Interventional Neuroradiology
Johannes Heverhagen, Director and Head of Department of Diagnostic, Interventional and Pediatric Radiology

Research Partners
SurgeonsLab AG, Bern, Switzerland
CASCINATION AG, Bern, Switzerland
MED-EL GmbH, Innsbruck, Austria

Group Members

Research Profile
Simulation and modelling, imaging and sensing, visualisation and robotics have reached sufficient quality and resilience to be introduced into clinical care. Research led by the Chair for Image-Guided Therapy leverages these developments to research technological innovations that could supersede the human operator inside the clinical environment. The investigations seek to (i) challenge current clinical procedures and (ii) conceive new procedures that provide treatment to the untreated, by setting the limits of novel clinical interventions according to technological capabilities, and not the limitations of human faculties. Translational aims for projects mean close relationships with partners, through clinical, academic and industrial collaborations.

Mapping and Modelling of Deep Brain Stimulation
(SNSF Ambizione 186142)

Brain Neuroradiology focuses on developing computer-assisted programming for deep brain stimulation (DBS). Finding therapeutic stimulation settings has become more complex with directional DBS and may take several hours of training. In one approach, stimulation maps that highlight effective stimulation regions are computed. In another approach, patient-specific tractography that highlight effective tracts in the brain are used. Both approaches can guide DBS programming. For DBS to treat Parkinson’s disease, the optimal stimulation level or contact are suggested with about 60% accuracy. For OES to treat psychiatric disorders such as treatment-resistant depression, preliminary work was performed to identify effective tracts.

Fighting Liver Cancer
(H2020 MSCA-ITN 722068 Innosuisse 37855.1 IP-LS)

For patients that suffer from non-spherical, larger, or critically located tumors, the success of thermal ablation treatment is not guaranteed, as the lesions potentially result being over-ablated, and the surrounding structures might be at risk. The aim is to remove these limitations, by providing an automated thermal ablation treatment model, using image-based planning and robotically assisted ablation, through simultaneous probe retraction and ablation energy modulation. An experimental prototype of a robotic system for thermal ablation was built and a proof-of-concept regarding its feasibility was conducted in a controlled environment using tissue mimicking specimens.

Virtual Histopathology of the Inner Ear by MicroCT

Anatomical investigations of the human cochlear architecture are challenging due to the organ’s helical shape and encasement in the petrous bone. The limitation of histopathological studies is that they do not allow for realistic isotropic perception or reconstructions. Novel 3D imaging techniques can improve the morphological assessment of cochlear structures before and after therapeutic procedures. With the aid of geometric enlargements, angular scanning, and noise reduction, micro-CT systems can provide focal spot sizes down to 200-500 nm.

Robotic Cochlear Implantation (ENF Project Number 176001)
The research from the recent years focused on robot-assisted cochlear implantation procedure was translated into a medical device. The investigation now continues in other aspects, such as the long-term fixation of the implant receiver-stimulator on the temporal bone, and a refined planning methodology for access to the inner ear. Particularly, for long-term fixation, the robotic system is proposed to be used along with intraoperative planning to mill a channel and an implant bed to store and protect the implant electrode and housing. An experimental study in a human ex-vivo model was conducted to investigate its safety and efficacy. Regarding inner ear access, the focus is on a refined planning strategy with automatic trajectory computation to reduce the impact of uncertainty in human decision-making on the consistency of the procedure.
Selected Publications


Robotic Spine Surgery
(Bridge Discovery 176498, Innosuisse 29836.1 IP-ENG)
Placement of pedicle screws to fuse vertebral segments is a challenging task for surgeons. In recent years, a robotic-assisted platform to drill pilot holes was developed. To verify the accuracy of the prototype platform, multiple phantoms were conceptualized and built, each focusing on different accuracy aspects within the present workflow. The most complex phantom supports dynamic dislocation in two degrees of freedom of the vertebra as a result of drilling manipulation. Multiple accuracy experiments were conducted to determine the platform’s performance.

High-Fidelity Neuroendovascular Simulator
(Innosuisse 51144.1 IP-LS, Herzstiftung FF20061)
Intracranial aneurysms are complex to treat. Recently, neurosurgical robots like CorPath GRX (Siemens Healthineers) have been used to treat patients found challenging to treat by accessing complex pathologies. To better prepare for the robotic endovascular interventions, neuroradiologists use the realistic 3D printed replica developed by our group and together with our spin-off SurgeonsLab AG (Figure 6) to sufficiently prepare for the procedure. The approach assists physicians in more accurate implants choice during the planning process. In addition, the 3D replica is coupled with a high-fidelity endovascular simulator to train residents and medical students preparing for their board certification and fellowship programs.
Computational Bioengineering

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- Prof. Georg Rauter, Department of Biomedical Engineering, University of Basel
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Group Members
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- Cael Buhglop
- Lopes Luís
- Remi Personel Marti
- Maritessa Nambiar
- Zhuolin-Bin Gao

Research Profile
The Computational Bioengineering Group tackles challenges in medical research with modern computer simulation tools. We focus not on the range of research topics. In addition to our core expertise in applying computational methods to simulate biomedical problems, we seek to improve surgical planning by developing numerical models of soft tissues, such as the cornea or arteries.

Personalized prediction of percutaneous coronary interventions
Cardiovascular disease is a global public health problem. The success of percutaneous coronary interventions (PCI) to restore blood supply in stenosed arteries may be limited in severely calcified lesions. In this project, we combine intra-arterial imaging and mechanical simulations to determine the outcome of PCI in patients with calcifications (Fig. 1) and compare the simulations to postoperative data. The results showed that in regions with many calcifications, the lumen area was correctly predicted by the model. However, the mechanical response of porcine aortas was only slightly affected by specimen orientation, consistent with a circular arrangement of the collagen network in pigs. This measurement protocol is now being used to characterize human samples, such as unused corneal grafts and lenticules removed from patients’ corneas during standard refractive procedures.

Instrumented indentation of untreated keratoconic corneas
Keratoconus (KC) is a progressive corneal disease caused by local mechanical weakening of the cornea. It is manifested by corneal protrusion, irregular astigmatism, and severe myopia. People in the Middle East and Asia have a strikingly high incidence of KC, which is considered an epidemic in these regions. If not properly treated, KC can lead to blindness. The few methods that have been introduced to mitigate or halt the progression of KC have demonstrated poor postoperative outcomes, often requiring multiple revision surgeries. A better understanding of the biomechanical condition of these patients is necessary to improve their treatment. However, to date, no detailed mechanical characterization of the KC cornea has been presented. Our goal is to provide a spatial characterization of KC and compare the biomechanics of KC with that of normal tissue. We quantify the biomechanical properties of the tissue using state-of-the-art nanindentation measurements (Fig. 3). Compared to other characterization techniques, nanindentation allows us to perform multiple local measurements on the sample, which is well-suited for characterizing very heterogeneous tissues such as KC. Mechanical characterization is of immediate importance for the treatment of KC patients, either for the proper selection of intracorneal ring implants or for the planning of corneal fusion by photo-chemical crosslinking.

Biomechanical characterization of ocular tissues
Stent deployment with a balloon in a coronary artery of a patient simulated using the finite element method.

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 arteries.

Research Partners
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- Prof. Alain Farron and Dr. Fabis Becce, Lausanne University Hospital, Lausanne
- Dr. Lorenz Räber, Dep. of Cardiology, Lausanne University Hospital, Lausanne
- Prof. Carol Hasler and Dr. Daniel Studer, Optimo Medical AG, Biel

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Research Profile
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Cardiovascular disease is a global public health problem. The success of percutaneous coronary interventions (PCI) to restore blood supply in stenosed arteries may be limited in severely calcified lesions. In this project, we combine intra-arterial imaging and mechanical simulations to determine the outcome of PCI in patients with calcifications (Fig. 1) and compare the simulations to postoperative data. The results showed that in regions with many calcifications, the lumen area was correctly predicted by the model. However, the simulations could not reproduce the clinical lumen gain in the highly stenosed regions where no calcifications were detected. In these sections of the artery, the simulation predicted under-expansion of the stent that was not observed after surgery, probably because of other plaque components that were not detected on the OCT images. Nevertheless, these other types of softer plaques appear to be less prone to stent under-expansion and could, therefore, be ignored to focus predictions on the calcified regions of the artery.

Instrumented indentation of untreated keratoconic corneas
Keratoconus (KC) is a progressive corneal disease caused by local mechanical weakening of the cornea. It is manifested by corneal protrusion, irregular astigmatism, and severe myopia. People in the Middle East and Asia have a strikingly high incidence of KC, which is considered an epidemic in these regions. If not properly treated, KC can lead to blindness. The few methods that have been introduced to mitigate or halt the progression of KC have demonstrated poor postoperative outcomes, often requiring multiple revision surgeries. A better understanding of the biomechanical condition of these patients is necessary to improve their treatment. However, to date, no detailed mechanical characterization of the KC cornea has been presented. Our goal is to provide a spatial characterization of KC and compare the biomechanics of KC with that of normal tissue. We quantify the biomechanical properties of the tissue using state-of-the-art nanindentation measurements (Fig. 3). Compared to other characterization techniques, nanindentation allows us to perform multiple local measurements on the sample, which is well-suited for characterizing very heterogeneous tissues such as KC. Mechanical characterization is of immediate importance for the treatment of KC patients, either for the proper selection of intracorneal ring implants or for the planning of corneal fusion by photo-chemical crosslinking.

Biomechanical characterization of ocular tissues
Selected Publications


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 disorders both in the hospital and at home. Core methodologies include telemonitoring, telerehabilitation, and virtual reality (VR) technology.

The research group partnered with the department of neurology (Claudio Bassetti) to establish the NeuroTec Loft, which is an instrumented apartment within the SITEM NeuroTec to monitor human behavior and to investigate how neurological disorders influence daily life.

Virtual reality stimulation for critically ill patients to reduce delirium

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

Following a series of studies conducted by our group, we can conclude that first, VR stimulation by using a HMD is safe to use within the intensive care unit, did not evoke any negative side effects, and was highly accepted by clinicians and patients. Moreover, the findings provided evidence that VR nature stimulation comforts critically ill patients. Second, it was found that the VR stimulation had a relaxing effect in the participants, as shown in a series of studies conducted by our group, we can conclude that VR stimulation has a relaxation effect in the participants, as shown in a series of studies conducted by our group, we can conclude that VR stimulation has a relaxation effect in the participants, as shown in a series of studies conducted by our group, we can conclude that VR stimulation had a relaxing effect in the participants, as shown in a second study in healthy participants revealed that the combination of auditory and tactile cues is the best combination (compared to audio or tactile only) to guide the patients’ attention back to the left side using different kind of stimuli.

In a first pilot study with a simple visual search task, a high usability and acceptance of the virtual reality system was shown in stroke patients as well as in young and elderly healthy participants. A second study in healthy participants revealed that the combination of auditory and tactile cues is the best combination (compared to audio or tactile only) to guide the patients’ attention back to the left side using different kind of stimuli.

Tele-monitoring for neurodegenerative diseases – the advancement of pervasive computing

Due to the advancements in technology in the past few years, pervasive technology has become more widely available. Small wearable sensors, such as smart watches, can track movement reliably through accelerometers and gyroscopes over extended periods of time, without disturbing the wearer. With the addition of photoplethysmogram (PPG) sensors, heartbeat and all derivative values can be monitored without the need for a full ECG. Sensors placed on or around objects, such as ferroelectric mats for under the mattress, can monitor heart rate and breathing patterns during the night without the need for any contact sensors. And finally, ambient sensors placed permanently, yet unobtrusively in participants’ homes, can track location and behavioral patterns throughout the home. Technology used for this include passive infra-red (PIR) sensors, magnetic door sensors, and radar-technology based sensors...
Unobtrusive, but continuous monitoring of health-related indicators has been shown to be both feasible as well as accepted by the target groups. Those groups include both the oldest as well as patients with neurodegenerative diseases, such as Parkinson’s disease.

In a study with people with Parkinson’s disease (PD), the acceptance and adherence to a set of ambient and wearable sensors was tested with very good feedback. The usage of wearable sensors is especially crucial for the monitoring of PD patients, as both the symptoms and the disease progress are highly individual in their manifestations. It’s imperative for the treating doctors and therapists to adjust medication and therapy to the needs of the patients. Current state of the art are self-reporting methods.

Wearable sensors, worn on the movement-dominant body parts can track typical PD-related motor symptoms, such as slowness of movement, tremors, rigidity, or the typical medication side effect – dyskinesias. Through a series of signal processing-based feature extractions and machine-learning-based symptom classification, we are working toward a more reliable symptom tracking system. This not only helps the doctors and therapists, but also increases quality of life for the patients by removing the burden of keeping a symptom diary.

Selected Publications


Physiological Role of the Spiral Shape of the Cochlea
(SNSF Grant No. 205321_200850)

Many believe that the spiral shape of the cochlea results from spatial constraints and that the coiling offers no particular advantages for hearing. However, this conclusion is based on studies that mainly focused on geometric curvature and neglected possible effects of torsion on sound propagation within the cochlea, especially secondary flow phenomena. This project aims to systematically investigate the role of geometric torsion on fluid mechanical processes in the cochlea. As part of the project, we are developing a shape parameterization method based on kinematic surface fitting that will enable unbiased classification of cochlear morphology. In addition, computational fluid dynamic simulations are performed to estimate secondary flow profiles.

Finally, we will conduct an observational study to correlate individual cochlear shape parameters obtained from high-resolution magnetic resonance imaging with the subject hearing performance.

Cochlear Implant Technology
We are working on the advancement of cochlear implants and implantation technology. Cochlear implants are hearing prostheses with an electrode array that is inserted into the inner ear to enable deaf people to hear again. Our group is developing new instrumentation for minimally invasive insertion of electrode arrays into the cochlea.

Cochlear implants can also be used as a measurement device. The technique is called telemetry and allows measurement of electrode impedances and responses of the sensory epithelium (e.g., ECochG) as well as nerve responses (e.g., ECAP). Our group has developed promising approaches to use telemetry data for clinical purposes. For example, telemetry-based impedance data can be used to estimate the position of electrode contacts in the cochlea or to monitor the degree of hearing preservation after surgery. Algorithms developed in our group can assist surgeons in inserting electrodes and provide them with feedback on the functional and structural integrity of the inner ear.

Smartwatches in Audiology
Loud noise at work or during leisure time can cause hearing loss or tinnitus. However, monitoring by professional sound level meters is not practical in everyday life. We are therefore, evaluating smartwatch-based applications for monitoring noise exposure. We believe that smartwatches will play an important role in the assessment of personal noise exposure and should be used as widely available and cost-effective means of hearing protection for clinical research. Ongoing work of our group is further focused on the use of smartwatches for clinical diagnostic purposes in tinnitus, hearing loss, and vertigo.
Selected Publications


Mechanical Design and Production

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CSL Behring AG
École polytechnique fédérale de Lausanne (EPFL)
CSL Behring AG
Department for Biomedical Research, University of Bern
Alveolix AG

Research Profile
The primary function of the Mechanical Design and Production (MDP) group is the 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), 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.

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.

This year we have had many changes in the staff. Fabio Spena left our workshop at the end of January to realize his career as a mountain bike cross country pro. We wish him much success and thank him for his excellent work and support in the MDP team in the last almost six years. We welcomed new employee Meret Ruch as a polymechanic with a workload of 60% on February.

For students of the department for machine engineering at ETH Zurich, it’s mandatory to have an industrial practical training for at least five weeks. This year, Clara Wittig performed her practical training during six weeks in our machine shop. The training was very instructive and successful. We wish her a lot of success with her studies.

Due to a high demand and heavy workload, we recruited a polytechnician, Sebastian Älgg, as an alternative civilian service employee. He performed administrative tasks and increased the productivity of our team. We thank him for the work he has accomplished in our workshop.

In 2020, we selected Piravin Jeyendran as our new apprentice, and he started his basic training on August 1, 2021 in the workshop of the physics institute of the University of Bern and will join us in the workshop in spring 2022. Our apprentice, Janosch Schär, completed his basic training exam at the end of the second year with a grade of 5.4 and we congratulate him.

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Research and Manufacturing As expected, the requirements of a machine shop supporting research in the biomedical engineering field are as diverse as the research field itself. The variety of subjects researched in the ARTORG yield a number of diverse design and production requests from prototype clinical and surgical tools to fixtures for mechanical, biological, and kinematic testing, as well as imaging system accessories and calibration equipment. The following illustration highlights one of this year’s projects.

ARTORG Cardiovascular Engineering Group: Test device for the exploration of the mitral valve
Simon Lüthi produced this device as a practical part of his exam. The device is suitable for clamping a mitral valve and then moving it radially as well as axially. The mitral valve functions as a check valve and connects the left atrium with the left ventricle of the heart. The entire device must be made of plastic and must not contain any metal components, so that the use of ultrasound can take place without interference during the examination of the function. The design was created by Michael Slucki (CIC Group).

Cranio-Maxillofacial Surgery Groups DBMR, Dental Plate Vertical
Since 2001, we have had a close collaboration with Nikola Soulasic from DBMR at the University of Bern to develop devices for bone growth studies. In 2018, we developed a horizontally functioning dental plate. This year we redesigned this device so that the function can be used in a vertical position. Again, the big challenge was to fabricate all of these very small parts and assemble them under the microscope. Some parts were cut out with a laser beam and welded together by an innovative partner company.

ARTORG Organ-on-Chip Group Chip Plate
This year, in collaboration with Rahim Ghasi as a technical employee in the ARTORG-DOC group, we were able to produce various chip plates. Thanks to the new acquisition of the Fehlmann machining center in 2020, we were able to produce these plates in many different designs. During the production we had two challenges at the same time. On one hand, the special plastic with a low melting point from which the plates are made and, on the other hand, the smallest hole to be produced was 8.0.2 mm “big”. Such projects help us in the workshop to get to know the limits of our machine park and also increase our special know-how.

ARTORG Bioengineering Group Cornea Three Finger Plates
Together with Shima Bahramizadeh Sajadi we have developed plates that are needed in the research of the cornea of the eye. With the help of all these three finger plates, she can easily determine the cornea properties on a microhardness testing machine and later perform laser tests with the cornea on the same plate on another machine. In this project, seven versions have been developed with different materials. In the end, we made all the required plates from the high-temperature-resistant thermoplastic PEEK (polyether-etherketone). The machining of PEEK is a challenge for tools to keep the tolerances because the abrasion of the tools is very high.

The MDP General view

Test device for the mitral valve

Dental plate vertical

Cornea three finger plate

The MDP General view

Test device for the mitral valve

Dental plate vertical

Cornea three finger plate

The MDP General view

Test device for the mitral valve

Dental plate vertical

Cornea three finger plate
Medical Image Analysis

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

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

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

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

Based on AI technologies, our group has developed methods and produced related translational technologies to automate the delineation of brain tumors. We have made these technologies available for the research community but also further developed them for future clinical use. In this regard, a unique feature of our translational developments has been in incorporating the capability of the technology to progressively adapt to changes in imaging modalities. In addition, the developed technologies feature an inclusive model, where state-of-the-art approaches worldwide can be fused to enhance performance and robustness.

Beyond lesion contouring, our current research activities lie on rethinking and challenging current AI technologies such that they are optimized to the clinical end goal. In these regards, in radiation oncology, we are investigating AI learnability approaches targeted directly toward metrics derived from the clinical end goal.

Radiomics is an emerging research area where image analysis methods are employed to mine imaging information to answer clinical questions. Our research in radiomics is focused in investigating patterns of robustness of radiomics-based imaging biomarkers in multi-center studies where imaging variability is inherent. We have highlighted current challenges to setup robust radiomics analysis in brain tumor imaging, and proposed methodologies to compensate these issues when models trained in single-center datasets are employed for multi-center radiomics analysis.

Due to the pandemic, our group joined efforts to investigate deep-learning-based radiomics analysis and radiomics strategies for the diagnosis and severity prediction of COVID-19 patients, employing a multi-omics approach. During 2022, our group tested the proposed AI solution on a multi-center study, with results superior to human performance.

Interpretability of Medical Image Segmentation Technologies Using Deep Learning Technologies
Our group is researching methodologies to enhance the interpretability of machine-learning models, so their decisions can be inspected (e.g., the machine capturing the relevant relation in the data?) and interpreted by human (opening of the "black box", e.g., If a system fails, why does it fail?). Enhancing interpretability of machine-learning methods is essential in medicine to build trust with these systems, but it is also very important in line with discussions pointing to decision-making and a "right to explain".

During 2022 our group moved beyond explorations to develop AI systems that employ interpretability information to gain accuracy and robustness.

Selected Publications
**Motor Learning and Neurorehabilitation Lab**

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

**Research Partners**
- **PD Dr. med. Kathleen Seidel**, Department of Neurosurgery, University Hospital Bern – Inselspital, Bern  
  - **Prof. Kenneth J. Hunt**, Bern University of Applied Sciences  
  - **Prof. Thomas König**, Psychology Department, University of Bern  
  - **PD Dr. med. Kathleen Sadal**, Department of Neurosurgery, University Hospital Bern – Inselspital, Bern

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- **Raphael Rätz**  
- **Edouard Hilke Steiger**  
- **Joannique Petitclerc André**  
- **Nicolas Merck**  
- **Othman Ebrahimi**

**Novel Clinical-Driven Robotic Devices for Sensorimotor Training**
Every year, millions of stroke survivors lose their functional autonomy due to upper-limb impairments. To recover upper-limb functions such as reaching and grasping, stroke patients should undergo highly intense, repetitive, and long-term training. This kind of training could potentially be provided by robotic devices. However, current robotic solutions are often cumbersome to set up and too complicated to be used in clinical practice. In addition, they mostly focus on the execution of movements and neglect the training of sensory functions, such as the sense of touch, even though research emphasizes its importance for recovery. We are developing a novel upper-limb rehabilitation robot that is easy to use and capable of fine haptic rendering. Haptic rendering is the physical simulation of interaction forces with virtual tangible objects. It can be used to make patients feel if they touch and interact with objects in the robotic computer games. Our novel device thus allows for simultaneous sensory and motor training and has the potential to improve the recovery of upper-limb functions.

**Immersive Virtual Reality to Enhance Neurorehabilitation**
The addition of virtual reality during robotic training has been shown to improve patients’ motivation. Yet, the virtual reality environments currently employed in rehabilitation practice are displayed on 3D screens. This transformation removes the focus of attention from the real movement and results in games that are cognitively too demanding for brain-injured patients. We explore how the use of augmented and immersive virtual reality can improve motor learning and neurorehabilitation.

**Robotic motor training with ARMin exoskeleton in immersive virtual reality**
Novel and commercially available head-mounted displays have great potential to realistically mimic the patient’s limb in a highly immersive training environment. In this immersive training environment, the symbolic virtual representation may become a self-representation (i.e., avatar), promoting the feeling of body ownership over the virtual limb. In the brain, body ownership and motor control share neural correlates. In an experiment with 10 participants, we evaluated how body ownership and congruency of multisensory information interact with motor performance in virtual reality. Our results suggest that VR-based motor tasks providing congruent haptic/somatosensory feedback and enforcing body ownership via visuomotor synchronies may best support motor training.

**Enhancing Touch Sensibility by Robotic Sensory Retraining**
Stroke survivors are commonly affected by somatosensory impairment, hampering their ability to interpret somatosensory information, critical to support movement execution. Yet, somatosensory training—in stark contrast to motor training—does not represent standard care in neurorehabilitation. To address this clinical need, we developed a virtual reality-based robotic texture discrimination task to assess and train touch sensibility. Our system incorporates the possibility of robotically guiding the participant’s hands during texture exploration. We ran a three-day experiment with 36 healthy participants who were asked to discriminate the odd texture among three visually identical textures, haptically rendered with the robotic device. Our results showed that participants significantly improved their task performance after training. In a follow-up experiment, we evaluated the potential of providing sensory electrical stimulation to further improve the training benefits of our robotic solution.

**Selected Publications**
Musculoskeletal Biomechanics

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Group Members
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Dr. Peter Varga, AO Research Institute (AO), Davos
Dr. Jakob Schwiedrzik and Dr. Johann Michler, EMPA, Thun
Prof. Michael Pretterklieber, Vienna University of Technology (VUT), Vienna
Prof. Dieter Pahr, University of Basel (UniBa), Basel
Prof. Kurt Lippuner, University Hospital Bern (IS), Bern
University Hospitals Geneva (HUG), Geneva

Research Partners
Prof. Viviane Chappuis, Dental Clinics of the University of Bern (ZMK), Bern
Prof. Serge Ferrari, University Hospitals Geneva (HUG), Geneva
Prof. Kurt Lipponer, University Hospital Bern (IS), Bern
Prof. Christian Meyer, University of Basel (UniBa), Basel
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Prof. Michael Pretterklieber, Medical University Graz (MUG), Graz
Dr. Jakob Schwiedrzik and Dr. Johann Michler, EMPA, Thun
Dr. Peter Varga, AO Research Institute (AO), Davos
Dr. Bettina Willie, McGill University (MGU), Montreal
Prof. Uwe Wolfram, Heriot-Watt University (HWU), Edinburgh

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 extra-cellular matrix to the organ level. Combined theoretical, experimental, and numerical approaches are applied to model, validate and simulate the mechanical behavior of bone tissue and bone-implant systems during growth, aging, disease and treatment. The group provides also biomechanical testing services and cooperates with local, national as well as international partners from academia, hospitals and industry to help reduce the burden of bone diseases and failure of the bone-implant interface.

Multiscale Mechanical Properties of Bone
(SNF grant #165510 with EMPA, MGU and HWU, ESKAS fellowship)
Bone is a complex material characterized by high strength and different toughening mechanisms at various length scale. A key in understanding its postyield behaviour is the mineralized collagen fibre embedded in an extracellular matrix. Combined micropillar compression and synchrotron X-Ray scattering were used to verify a 2D elastic-plastic model, and the experimental data was used to develop a 3D computational model of a unit cell to gain further insight into the influence of composition and architecture on the elastic and postyield properties. Further micromechanical and nanodentation experiments were conducted to investigate the bone extracellular matrix properties in Osteogenesis Imperfecta (OI). 

Fabric–elasticity Relationships of Tibial Trabecular Bone in OI and healthy individuals (SNF grant #200365 with MGU)
OI is an inherited form of bone fragility characterised by altered trabecular bone architecture and reduced bone mass. High resolution peripheral computed tomography (HR-pQCT) is a powerful method to investigate bone morphology at peripheral sites. In this project, trabecular morphology of distal tibiae with OI were compared to healthy controls with HR-pQCT. Mathieu Simon found the OI samples to have significantly lower bone volume fraction and trabecular number but no differences in trabecular thickness compared to control. After age and sex matching, relationships between trabecular architecture and stiffness on common regions of interest were compared between healthy controls and OI, showing that these relationships were similar for the two groups. With this work, Mathieu obtained the Student Award of the Swiss Society of Biomedical Engineering.

Experimental and Computational Approach to Investigate the Biomechanics of the Aging Human Femoral Neck (with VUT)
Aging of the population induces a higher number of fractures due to a loss of bone mass and an increasing falling risk. As the influence of aging on bone quality is unclear, micro finite element analysis (μFE) was used to assess the influence of aging on the mechanical properties of the femoral neck. Human femoral necks were prepared and loaded in compression to measure stiffness and strength. In parallel, μFE non-linear analyses based on microCT images were run on these neck samples. The μFE simulation was able to predict the experiment’s stiffness and strength, and the error did not reveal an age dependency.

AFFIRM-CT and Clinical Study
(SNF grant #183644 with HUG and IS)
Most hip fractures are caused by falls resulting in an impact force that exceeds the femoral bone strength. The AFFIRM-CT project aims to develop a new hip fracture risk model integrating a CT-based femoral bone strength. For model validation, a clinical study was conducted, starting with patient recruitment in March 2020. After the baseline visit assessing the risk of falling, the general health state and bone quality with HR-pQCT and DXA measurements, participants will be followed-up to record falls and fractures.

For the femoral bone strength estimate, a pipeline was developed that builds finite element models based on CT images. The pipeline was tested and validated using experimental data collected in an earlier study. It is now used to analyse different data sets to compare FE-based bone strength to other bone strength estimates and serves as a baseline for the development of personalized bad cases. Additionally, CT scanner stability was investigated. Using an existing dataset, the sources of intensity variations were examined, identifying potential parameters affecting calibration accuracy. Results showed that CT intensities were mostly affected by body volume and table height and should therefore be corrected for these parameters. In addition, a personalized fall rate estimate model was developed. Preliminary results show that prior experienced falls is a good predictor for future falls.

Linear regression between observed trabecular stiffness and predicted stiffness. Left: healthy controls. Right: OI.

Personnalised HR-pQCT-Based Homogenized FEA
(with IS and Unila)
Personalised in vivo assessment of bone strength estimated by finite element analysis (FEA) based on HR-pQCT becomes successful in identifying people at high risk of fractures. This year we published a unified pipeline, calibrated, and validated with experimental data sets of radius and tibia samples for the clinical use. Furthermore, we developed a method to personalising the loading conditions using Wolff’s law in trabecular bone adaptation and a simplified FES method. A clinical study applying HR-pQCT-based FEA on long-term type I diabetes is ongoing with our clinical partners.

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Biomechanical Testing and Simulation
(with ZMK)

Several projects could be conducted in the biomechanics laboratory. In a thesis aiming to test dental implants ex vivo, human mandibular and maxilla bone samples were cut, embedded, and scanned with the laboratory’s μCT system for morphological assessment. The primary stability of two dental implant sizes was quantified using an in-house testing protocol and the key morphological predictors were identified. On the simulation side, an explicit finite element methodology was applied to quantify insertion torque as well as stiffness and strength of distinct implant models in various loading configurations.

Selected Publications


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, called organ-on-chip. Such devices aim at reproducing the smallest functional unit of an organ, by mimicking the cellular composition and the cellular microenvironment. The group particularly focuses on modeling 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.

Breathing lung-on-chip (LOC)
We developed an advanced in vitro model of the lung alveoli, called “lung-on-chip”, which mimics the human lung alveolar barrier. In that system, the barrier is made of an ultra-thin, flexible polymeric membrane, on which lung cells are cultured on opposite sides. The polydimethylsiloxane (PDMS) membrane is porous (3μm pores), which enables the lung epithelial cells – top side of the membrane – and lung endothelial cells – bottom side, in contact with blood analog – to communicate. The actuation of the barrier – top side of the membrane - and lung endothelial cells – bottom side, in contact with blood analog – to communicate.

Second generation lung-on-chip
Although very innovative, the ultra-thin PDMS membrane used in the first-generation lung-on-chip is an artificial material, whose intrinsic nature, properties, and size differ from the extracellular matrix (ECM) of the distal airways. To circumvent these drawbacks, we developed a second-generation lung-on-chip with an array of in vivo like-sized alveoli and a stretchable biological membrane. The membrane is made of two proteins found in the lung ECM: collagen and elastin. Its fabrication process is very simple. The mechanical properties of the biological membrane could be easily adapted by modifying its composition or its fabrication process. It allows increasing an air-blood barrier without any artificial layer between the epithelial and the endothelial cells. This membrane opens the way to a new generation of lung-on-chip that enables mimicking of the biological barriers at a new level of complexity.

Microvasculature-on-chip
Vascular homeostasis is important to maintain the proper functioning of the organs, and interruption of this balance plays an initial role in many diseases. Engineered models of the blood vessels can contribute significantly to mimicking the pathology of vascular disease and proceed to drug development. We developed functional microvasculature platforms to study the biology of the blood vessel and answer mechanistic questions behind the pathology of vascular disease, drug testing, and endothelial mechanotransduction. Two different microvascular platforms have been developed. The first is a self-assembled complex microvascular network and the other is a simple microvessel exposed to cyclic forces. A three-dimensional microvasculature network was generated using a co-culture of human endothelial and mural cells within a 3D matrix of hy-
A dynamic perfusable microvasculature model incorporating a single/multiple vasculature/s within a hydrogel layer was designed and developed to investigate the effect of mechanical cyclic stretch on vascular remodeling.

Nanocellulose in biosensing devices
Lateral flow immunoassays (LFIA) are progressively important Point-of-Care devices in medical diagnostics. Standard LFIA strips are restricted due to the analysis of a limited sample volume, short reaction time, and a weak optical signal. In this project, we incorporated a novel cellulose nanofiber (CNF) aerogel material into LFIA strips to increase the sample flow time. The binding interactions between the analyte and the detection antibody increase and which in return improves the limit of detection (LOD). The presented optimization method offers a unique potential to transform lateral flow assays into highly sensitive, fully quantitative point-of-care diagnostics.

Illustrative comparison between a conventional LFIA strip design (A) and an aerogel-assisted LFIA strip design (B). This study was a joint project of the ARTORG Center and CSEM.

Selected Publications


Urogenital Engineering

Research Profile

The Urogenital Engineering (UGE) group focuses on the understanding and the treatment of diseases of urinary tract (UT) many of which have a significant impact on quality of life. Our translational projects address unmet clinical needs, which are identified and discussed with our clinical partners who are fully integrated in the project teams. Using innovative engineering approaches, the UGE group is developing new methods to improve the insight, diagnosis, and treatment of diseases of the urinary tract with special focus on urinary obstructions (e.g. kidney/ureteral stones), underactive bladder, overactive bladder, and incontinence. UGE and Cardiovascular Engineering (CVE) groups of ARTORG Center share experimental and computational research infrastructure/facilities. Next to computational tools and facilities, this includes our flow lab, which is equipped for bench experiments on biomedical flow systems and offers computer- controlled flow loops, pressure and flow sensors, high-speed cameras, and laser-based flow measurement systems.

Urinary Tract Modelling

The urinary tract includes the two kidneys, two ureters, a bladder, and one urethra. To achieve normal urination, all components of this system have to work in a synergic and correct way. A deep understanding of the normal UT function and its alteration due to pathologies is key to develop novel medical devices that can help patients. To this end, we have developed innovative platforms (combining in-silico, in-vitro and ex-vivo modelling) for biochemical and fluid mechanical studies within UT. These platforms aim at: (i) improving the insight into local fluid mechanics within UT, (ii) identifying the critical aspects of current medical devices, and (iii) testing new solutions. Our in-vitro platform has unique features as it consists of: (i) a roller pump (to simulate the production of urine from kidneys), (ii) a transparent ureter model, and (iii) a bladder compartment whose internal pressure can be controlled to simulate the physiological and pathological bladder pressures (during the filling and emptying cycles), and iv) an outlet tube (urethra). The platform can be combined with an index matched fluid to allow particle image velocimetry (PIV) measurements for full fluid mechanical characterisation and can be used to test various medical devices such as urine drainage devices (urethral stents and catheters), devices for incontinence (artificial sphincters), and urinary retention (see section “Non-invasive Solution for Urinary Retention”).

Non-invasive Solution for Urinary Retention

The UGE group is developing the world’s first non-invasive solution for urinary retention. Patients suffering from urinary retention are unable to empty their bladder because of either a weak bladder muscle or a bladder outlet obstruction (e.g. enlarged prostate in men). The main complaints from these patients are pain, urinary tract infections, continuous sleep disruption, the necessity to plan ahead for awareness of the location of toilets, impairment of social life, embarrassment, and reduced self-esteem. To date, catheters are the most 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 an unmet clinical need. Our patent-pending technology is based on an innovative pumping principle (impedance pump) which generates urine flow by applying an external intermittent compression on the urethra (the outlet tube of the bladder) such that direct contact with urine is avoided. This solution can drastically reduce urinary tract infections. This research has led to an external and handheld prototype. URODEA AG is a spin-off of the ARTORG Center and is focusing on bringing this technology to the patients.

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

Patients suffering from overactive bladder (OAB) live with a continuous urge to urinate even at low bladder volumes, often leading to incontinence. OAB has an enormous impact on the quality of life of affected patients. Despite the high prevalence, the understanding of the mechanism underlying OAB remains limited and, as 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. We developed an algorithm that generates alarms before the start of an unwanted bladder contraction. The algorithm was successfully

Schematic of the four analysed sections of ureteral stent retrieved from patient (left): renal pigtail, proximal straight part, distal straight part and bladder pigtail. Three dimensional µ-CT images of the renal pigtail and proximal straight part before (center images) and after (images on the right) segmentation, respectively. Luminal encrustations from the segmentation results are shown in orange. Stents are rendered semi-transparent for better visualisation.

Encrustations in Ureteral Stents

Ureteral stents are frequently used in clinical settings to maintain the drainage of urine in the presence of ureteral obstructions (e.g. stones, tumours). Once in place, ureteral stents extend along the whole ureter length, with side holes positioned at regular intervals. Encrustation and biofilm are considered the main causes of stent failure and it has been shown that their development in stented ureters is strongly influenced by local fluid mechanics (e.g. shear stresses). Ureteral stents, once implanted in patients, are exposed to complex fluid dynamic and chemical (bacteria, crystals) environments. Location and extent of encrustation in ureteral stents for different diseases may be informative for patient management and for the development of newer stent generations. In this context, current projects at UGE involve: (i) the use of micro-computed tomography (µ-CT) combined with a deep learning model to quantify the encrustation volume on ureteral stents, retrieved from patients, and (ii) scanning electron microscopy (SEM) combined with energy dispersive X-ray analysis (EDX) for morphological and chemical characterisations of the crystals. These investigations aim at: i) identifying the regions of the stents that are more prone to develop encrustation and ii) linking these regions to the local fluid mechanics.

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tested first in rats and then in patients using classical urodynamic signals. It could be used to warn the patient about an impending bladder contraction (to take action against incontinence) or to trigger conditional sacral nerve stimulation (i.e. stimulation of bladder nerves to inhibit the bladder contraction before incontinence). Moreover, our group has pioneered the use of cardiac catheters for minimally invasive electrophysiological investigations in the urinary tract. In a proof-of-concept study, we have shown that cardiac catheters can detect and track the propagation of electrical signals in the lumen of the ureter. Further investigations will apply this technology to bladder smooth muscle.

Selected Publications


Cardiovascular Center

Editorial
Inselspital, Bern University Hospital

Trans-professional research in the domain of biomedical engineering is firmly anchored at Inselspital, Bern University Hospital. Its interdisciplinary research aspirations connect clinicians, engineers, computer scientists, as well as data scientists in the largest University Hospital setting in Switzerland. At an institutional level, Inselspital maintains close ties to individual members of the Bern Biomedical Engineering Network (BBEN).

The links between Inselspital and biomedical engineering research institutes at the University of Bern foster strong and innovative multidisciplinary research activities. The majority of the departments presented in the following report work in close cooperation with the Faculty of Medicine at the University of Bern. They play a key role in supporting tertiary research and educational ambitions in their respective fields as well as taking part in different research clusters provided by the University of Bern.

As the founding partner of the Swiss Institute for Translational and Entrepreneurial Medicine (sitem-insel), Inselspital provides essential resources for translational activities. It hosts the Institute on site and therefore supplies enabling facilities such as the Translational Imaging Center Bern.

Within a clinical environment, biomedical engineering research at Inselspital focuses on both long-term and short-term research objectives. Joint research platforms and core infrastructure, enabled through support of the Inselspital, provide the means for effective fundamental and translational biomedical engineering research applicable to different academic research activities. The teams are involved in multicenter, randomized clinical trials as well as first-in-man human studies using innovative medical devices and pharmaceutical interventions. Some examples are listed below:

- Investigations of devices for the minimal-invasive treatment of coronary artery diseases, thrombembolic diseases, valvular heart diseases, vascular pathologies, novel surgical approaches (including congenital and pediatric procedures as well as extracorporeal circulation), and heart failure;
- Pharmacological therapies in the field of antithrombotic and lipid lowering drugs;
- Studies for the treatment of electrophysiological disorders and in the field of preventive cardiology;
- Novel imaging methodologies in the field of cardiovascular medicine.

Translational and preclinical research activities involve emerging technologies such as ex-vivo heart perfusion systems, novel cardiovascular imaging sequences, and innovative ablation therapy and cardiac pacing solutions.

The Cardiovascular Center is an active member of the Cardiovascular Research Cluster (www.cvc.unibe.ch).

Research Profile

The Cardiovascular Center at Bern University Hospital consists of the Departments of Angiology, Cardiology, Cardiac Surgery, and Vascular Surgery and maintains a broad range of clinical and translational research activities.

Main Research Partners
- Clinical Trials Unit, University of Bern
- University Hospitals Zurich, Basel, Lausanne, and Geneva
- ETH, CSEM, industry partners

Optimizing the duration of antiplatelet drug therapy after stent implantation in patients at high risk for bleeding

The appropriate duration of dual antiplatelet therapy in patients at high risk for bleeding after the implantation of a drug-eluting coronary stent remains uncertain. One month after they had undergone implantation of a stent, high-risk patients were randomly assigned to either discontinue dual antiplatelet therapy immediately (abbreviated therapy) or to continue it for at least two additional months (standard therapy). One month of dual antiplatelet therapy was non-inferior to the continuation of therapy for at least two additional months with regard to the occurrence of net adverse clinical events and major adverse cardiac or cerebral events. Abbreviated therapy also resulted in a lower incidence of major or clinically relevant non-major bleeding.

Abbreviated DAPT Standard DAPT

Abbreviated DAPT: A multicenter, randomized, open-label trial comparing one month of dual antiplatelet therapy with longer treatment after the placement of a drug-eluting stent in patients at high risk for bleeding. [1]
A robotic approach to reproducing physiological heart motions

We developed a novel robotic approach to reproduce physiological heart motions with high accuracy and repeatability to study their effect on implantable cardiac devices. This may benefit the device development process and offer the potential to increase safety and quality of next-generation implantable cardiac devices. This approach re-uses heart motion data repeatedly without sacrificing the life of animals, thereby promoting the 3R principles.

AI in medicine: AI tool development patterns and clinical evaluation

Artificial intelligence (AI) methods are playing an increasingly important role in the era of digital healthcare transformation and precision medicine. In a recent analysis, we identified significant variations in the patterns of AI tool development (training, validation, testing) and external (independent) validation leading up to their clinical evaluation in dedicated AI randomized controlled trials (AI-RCTs). In this early phase of novel AI-RCTs, trials are characterized by heterogeneous design and reporting. Data that would allow independent replication and implementation of AI tools were not available. Of note, most AI-RCTs do not test the AI tools in geographical areas outside of those where the tools were developed; therefore, generalizability remains largely unaddressed. As AI applications are increasingly reported throughout medicine, there is a clear need for structured evaluation of their impact on patients with a focus on effectiveness and safety outcomes, but also costs and patient-centered care before their large-scale deployment.

Selected Publications


Research Profile
The Insel Data Science Center (IDSC) is Insel Group’s interdisciplinary entity for digital data management. The IDSC’s mission is to organize all digital data from Insel Group and make it accessible and usable. We play a facilitating role at the interface between the University Hospital of Bern and the medical faculty of the University of Bern. Our main tasks include the development and operation of a data platform as well as of applications and data science activities building therein. In this context, we provide access to data from different sources, representing both patient-related and data science activities building thereon. In this context, we provide access to data from different sources, representing both patient-related and data science activities building thereon. In this context, we provide access to data from different sources, representing both patient-related

Research Products
Our specialized tools for researchers support the research strategy of the Insel Group. We enable researchers to enhance patient’s diagnostics and treatment. SearchBox - our cohort explorer for unstructured data that works like an internet search engine. The medical information from an electronic health record (EHR) can be extracted and used for research. All patient identifying data like first name, last name, address are replaced with random values to ensure anonymity. SearchBox is the primary tool for conducting a feasibility study and assemble a relevant cohort. The cohort definition can then be shared with IDSC to access further data needed for research.

Swiss Personalized Health Network
Swiss Personalized Health Network (SPHN) is a strategic program by the Swiss government that accelerates the digitalization, co-operation, and interoperability within the federal structures of the national health network. One outstanding example of SPHNs success is the Federated Query System (FQS). It enables researchers to search all five university hospitals for cohorts. The clinical data are fully anonymized and the hospitals remain in full control of their provided data. The system enables researchers to find out the number of patients in the university hospitals that may be relevant for a specific research question. The available include demographic data (age class, gender), diagnosis (ICD-10), procedures (CHOP), medication (ATC), and lab results (LUMS).

SPHN has co-ordinated and financed a network of high-performance computer nodes for easy data exchange and computation power to run nationwide studies. This unique infrastructure is kept in line with the latest security standards and sophisticated research algorithms.

SPHN fosters the establishment of personalized medicine in the hospital. Milestones for the development are defined in a so called “collaboration agreement” that sets goals to be met. The cohort explorer provided by the IDSC are two examples of SPHN-funded tools that are now in everyday use.

Selected Publications

Medicine
The product line medicine focuses on patients’ needs and aims for three main goals: increase quality of treatment, support physicians in their daily decision making, and enhancing transparency of data points relevant to patients.

A complete picture of a single patient is accomplished by linking the various data sources that contain person-specific data. The analysis of all patient data leads to an improved quality of assessment and treatment. Using intelligent algorithms on frequently updated data decision processes are supported. From quick overviews to in-depth representation of relevant indicators and a full range of tools for physicians is provided.

The IDSC was actively involved in several publications, including, among others e.g. VRE outbreak surveillance using hospital data and machine-learning techniques [1], the assessment and evaluation of acute and chronic kidney failure [2], the impact of nurse staffing on adverse outcomes [3] as well as classification propositions for coronarion section [4]. Also the interpretability of AI algorithms has been addressed in a comprensive review [5].

Management
The product line management develops structured applications that support management decision processes. Based on key performance indicators and blended with operational data, they ensure a 360 degree view on to Insel Gruppe’s business activities. The tools foster transparency across the entire organization and show the management on all levels the trends and the development of the specific data within their domain of responsibility.

The relevant data are updated daily to support the decision processes with a variety of charts and figures.

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Research Profile
In recent years, endovascular neurointerventional techniques have evolved significantly with an increasing spectrum of indications. This includes minimally invasive endovascular treatment procedures for acute ischemic stroke, intracranial aneurysms, and other cerebrovascular diseases such as aneurysm formation and fistulas as well as vascular syndromes of brain supplying vessels. The Interventional Neurovascular Research Group is focusing on the pre-clinical experimental evaluation of novel treatment approaches and the development of devices for endovascular treatment of neurovascular diseases. Furthermore, the improvement and development of pre-interventional neuroimaging and imaging-guided treatment monitoring are crucial components in the management of complex cerebrovascular diseases.

Acute Stroke Treatment
Acute ischemic stroke is a major cause of death and disability in industrialized countries. The management, diagnosis, and treatment approaches for acute ischemic stroke have enormously changed in the past decades. Initially, stroke management consisted solely of prevention, treatment of medical complications and symptoms, and rehabilitation, whereas nowadays endovascular treatment using mechanical thrombectomy has become the mainstay of stroke treatment due to large cerebral vessel occlusion. The most significant modifiable factors influencing the clinical outcome of patients are time span between symptom onset and revascularization, reperfusion and recanalization rate, and the occurrence of secondary complications such as symptomatic intracranial hemorrhage. Of those, reperfusion and recanalization have been shown to be the most crucial modifiable prognostic factors for favorable patient outcome. The Interventional Neurovascular Research Group has developed an in-vivo animal model for the pre-clinical evaluation and development of mechanical thrombectomy devices for the treatment of acute ischemic stroke. This model allows for a reliable evaluation of efficacy and safety as well as improvement of thrombectomy devices prior to their introduction into clinical use. Numerous experimental studies of the Interventional Neurovascular Research Group regarding mechanical thrombectomy for acute ischemic stroke treatment have been published in high-ranking journals and have paved the way for the transfer of the latest generation of mechanical thrombectomy devices, so-called stent retrievers, into clinical practice locally, but also on an international level. Furthermore, the group has gained international acceptance as an educational training model for mechanical thrombectomy device handling. Each year, the Institute of Diagnostic and Interventional Neuroradiology of the Inselspital Bern, in collaboration with the major neurological and neurosurgical European societies, organizes several distinguished international training courses dedicated to acute ischemic stroke treatment using this animal model (ISD-ESMINIT-ESNI Stroke Winter Schools).

Aneurysm Treatment
1. Device and material testing
A common indication for endovascular intervention is the treatment of unruptured and ruptured intracranial aneurysms. Since the ISAT-Trial (International Subarachnoid Aneurysm Trial), the majority of these aneurysms, around 50'000 annually worldwide, are treated endovascularly. Endovascular standard treatment is the occlusion of the aneurysms by deployment of platinum coils. New polymer-based endovascular devices (polymer strands, “plastic coils”) are currently under development as an adjunctive tool to platinum-based standard coils for endovascular aneurysm treatment. Conventional platinum coils cause imaging artifacts, reducing imaging quality and therefore impairing imaging interpretation on intra-procedural or non-invasive follow-up imaging. The results of the Interventional Neurovascular Research Group of in-vitro and in-vivo evaluation at different packing densities of these polymer strands showed significant reduction of imaging artifacts in fluoroscopy, CT, and MRI due to the lack of platinum compared to standard platinum coils. This might be advantageous for improved intra-procedural imaging for the detection of complications and post-treatment non-invasive follow-up imaging. Furthermore, applicability of the device under fluoroscopic guidance has been demonstrated in-vivo in a dedicated aneurysm model in rabbits which has been developed in collaboration with the Department of Neurosurgery.

2. Development of aneurysm models using additive manufacturing techniques (3D printing)
Further field of research is the development of in-vivo cerebral aneurysm models in collaboration with the ARTORG Center for Biomedical Engineering using different additive manufacturing techniques (3D printing). Patient-specific aneurysm models offer the possibility for pre-interventional planning of endovascular treatment procedures, especially for complex cerebral aneurysms using different treatment techniques. Pre-interventional in-vivo testing is helpful to determine the optimal treatment strategy and choice of devices in a specific patient to facilitate the treatment itself, to maximize treatment efficacy, and to minimize procedural risks. This approach has already been translated into clinical practice and is used on regular bases for interventional treatment planning. In addition, aneurysm models have been successfully introduced for hands-on training for complex endovascular aneurysm treatment and educational purposes. Furthermore, aneurysm models are used for the development, testing, and evaluation of novel endovascular devices and treatment approaches such as neurovascular robotics, as well as a model for measurements of different aspects of flow dynamics and their role in aneurysm formation and growth.

Successful retrieval attempt of a bifurcation thrombus in the animal model using opacified thrombus and a stent retriever device. Note retrieval of the side branch portion (arrowhead) and the straight position of the thrombus during mobilization and retrieval (arrow).
Developmental process of cerebral aneurysm models using additive manufacturing techniques (3D printing) based on patient-specific 3D imaging data sets for robotic-assisted neurointerventional procedures.

Selected Publications


Magnetic Resonance Methodology / DIN-DBMR

Research Profile

Magnetic resonance imaging (MRI) and spectroscopy (MRS) are powerful and extremely versatile methods for non-invasive studies and diagnostic examinations in humans. Our group is using MRI and MRS methods in close collaboration with clinical partners primarily in prospective studies of different organs. We also develop novel methods to suit pertinent needs to study physiology and pathology, together with the underlying mechanisms, in situ. Currently most MRI and MRS studies are performed in brain, kidney, muscle, liver, and heart, where the 3T and the high-field 7T scanners of the translational imaging center at stem-rod are used. In addition, high-resolution NMR studies are performed on biopsies, cell cultures, and body fluids in close collaboration with the Clinical Chemistry of the Inselspital and with numerous clinical and pre-clinical partners. The studies aim to detect metabolic disease biomarkers and improved physiological comprehension.

Methodology for MRI spectroscopy

In the framework of SNF grants and a European Innovative Training network (inspire-med), MRI spectroscopy methods and synergistic post-processing tools are developed that are tailored to the observation of brain metabolism, yet are also transferable to other organs. In collaboration with other Swiss and European centers, novel methods are developed, e.g. to study exchange processes between amides and water in human brain. Diffusion properties of brain metabolites are investigated with dedicated methodology to investigate brain, muscle, and prostate microstructure. For post-processing and quantification, traditional modeling and processing tools are developed that are tailored to the observation of brain metabolism.

Metabolic imaging to study glucose and lipid metabolism

Further work is aimed at the methodology for metabolic imaging of glucose metabolism in the liver and lipid storage and turnover in muscle, heart, liver, and kidney. Glucose turnover and integration into glycogen determination of potassium by %K MRI and MRS on the 7T MR Scanner. Low potassium intake associates with cardiovascular disease and mortality, while beneficial effects of higher potassium intake have been demonstrated. By using %K MRI for the first time, a non-invasive method for investigating K⁺ ion homeostasis in humans becomes possible.

High-Resolution Magic Angle Spinning NMR

High-resolution magic angle spinning (HR-MAS) NMR techniques were applied to correlate in vivo and in vitro NMR spectra of tissues but also from cell cultures and body fluids.

Several HR-MAS studies have been performed on biopsies as well as on cell cultures and analyzed by “metabonomical” methods. Funded by an SNF Grant, special emphasis is on investigation of OXPHOS deficient fibroblasts for separating different defect subgroups. In collaboration with the vendor Bruker, we established a perfused bioreactor system within the NMR spectrometer and performed feasibility measurements of living 3D cell cultures inside the NMR with changing conditions monitoring consequent metabolic and oxygenation cell responses.

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Renal function and potassium homeostasis

Renal function in native and transplanted kidneys has been investigated by multi-modal MRI and MRS. The functional MRI modalities such as diffusion weighted imaging, arterial spin labelling, and oxygen-dependent MRI differ in terms of sensitivity for cortical or medulary renal tissue and in their assessed determinants. In collaboration with the Nephrology Department, we aim at a better perception of the physiologic basis behind functional MR parameters and why they may be changed in renal disease. Recently, in collaboration with Siemens, an improved method for respiratory-triggered diffusion has been developed and evaluated. In clinical studies MRI measurements were performed for the Bernese renal biopsy registry, and the impact of functional kinking of iliac arteries on perfusion and oxygenation was investigated.

Funded by a stem-insel Support Fund and in collaboration with the Nephrology we are currently setting up studies for localized non-invasive in vivo measurement of potassium by %K MRI and MRS on the 7T MR Scanner. Low potassium intake associates with cardiovascular disease and mortality, while beneficial effects of higher potassium intake have been demonstrated. By using %K MRI for the first time, a non-invasive method for investigating K⁺ ion homeostasis in humans becomes possible.

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Selected Publications


Recently, our group developed a novel treatment planning process enabling the simultaneous optimization of modulated photon, electron, and proton beams for improved treatment plan quality in radiotherapy by means of benefitting from the different dosimetric characteristics of the three particle types. The framework is based on highly accurate dose calculation using Monte Carlo simulations. Dosimetric comparisons to currently available treatment techniques reveal the potential of TriB-RT. It is especially promising for cost-effective, single-room proton solutions with a fixed beamline in combination with a conventional linac delivering photon and electron fields.

Robustness Assessment and Robust Optimization

Robust assessment and robust optimization are important aspects in radiotherapy treatment planning as, for example, for mixed beam radiotherapy. This technique combines intensity-modulated photon beams with intensity- and energy-modulated electron beams. A robust optimization method was developed and experimentally verified. Robust optimized treatment plans were compared with conventional optimized plans demonstrating that robust optimization is a promising alternative approach for mixed beam radiotherapy.

Monte Carlo Simulation of X-ray Grating Interferometry

Phase-sensitive X-ray imaging techniques provide complementary contrasts in addition to absorption contrast used in conventional X-ray imaging. To understand the principles and limitations of this new imaging modality, it is important to establish virtual simulation frameworks. However, traditional simulation techniques such as wave optics methods and Monte Carlo particle transport fail to model both interference and inelastic scattering phenomena simultaneously. Therefore, we developed a new semi-classical Monte Carlo algorithm for efficient and simultaneous modeling of scattering and interference processes.

Dose distribution (left) and Dose Volume Histograms (right) of a 18 MeV electron treatment plan created for a left breast boost case.

Visualization of the highly non-coplanar dynamic trajectories for two different head and neck cases.

Dose contributions of photons, electrons, and protons resulting in the total TriB-RT dose distribution.
Selected Publications


Research Profile

Our aim is the improvement of our patients’ quality of life and survival. Our research focus is the improvement of surgical procedures, with special attention to highly translational or clinical problems. We collaborate intensively with medical technologies partners, both regionally and internationally. Our main research areas include deep brain stimulation, tumor resection, function monitoring, robotics, and an academic software suite.

Ability Academic Software Suite

Another main research project is the development of a personal learning environment. This new software will help physicians master the vast amount of medical information into valuable medical knowledge. It will enable users to search, find, catalog, process, and study documents that are of long-term interest. In clinical practice, it is common to encounter a range of valuable medical information from different sources, such as textbooks, images, PDFs, journal articles, etc. The software will allow users to cope with any such source. Medical knowledge is built-up layer by layer over the course of a career, beginning in the medical course, through residency and subspecialty training, and even as a consultant the knowledge is ever expanding. In most subjects, this knowledge needs to be available long term. In current practice, physicians either create a physical library of textbooks, hardcopy journals, and printed PDFs or increasingly build a digital library. Both, however, fail with time because of an ever-increasing volume of documents. There is also a need to share documents and communications between colleagues within such a system. Our aim is to provide a solution that is suitable for most medical subspecialties. Further applications may be found in life sciences and researchers in general.

Towards Intelligent Sensor-enhanced Neurosurgery

The malpositioning of pedicle screws is a common problem that can cause neurologic and vascular damage or result in non-fusion of the instrumented spine segment. A malpositioning rate of up to 35% is known from the literature. Using intraoperative navigation, the rate of misplaced screws could be lowered but remains a problem in spinal fusion surgery. Together with the ARTORG, we are addressing this challenge by an intelligent robotic system. By using the complexity of vertebral anatomy like a “sensor map,” the robotic drill is able to “feel” across the bone terrain and together with computer simulations of the activated tissue. Large data-sets are analysed group-wise by applying complex voxel-wise statistics to yield a probabilistic stimulation map with a stimulation “sweet spot” as illustrated below. Cross-validation of the data confirms the principal predictive value of such a map to predict effective stimulation parameters and the degree of postoperative stimulation success in individual patients.

HORAD Intra-operative Visualisation of Cerebral Fibre Tracts

The two major challenges in neuro-oncological surgery are the differentiation between tumorous and healthy tissue and the identification and localization of specific neuroanatomical functions during surgery. In search of a new, innovative approach to overcome these challenges, neurosurgeons at Inselspital explored new ways of science. The HORAD project started with a crowdfunding challenge followed by a subsequent crowdsourcing global competition in search of an out-of-the-box innovation. The competition led to a series of new ideas, and ultimately to a collaboration with the Laboratoire de physique des interfaces et couches minces at the École Polytechnique. The Paris. The new joint research team successfully tested a solution-based on Mueller Polarimetrie in a series of experiments and was awarded a research prize by an industry leader in medical technologies, as well as an extensive four-year SINECRIA Grant by the Swiss National Science Foundation (SNSF). The HORAD consortium – led by Prof. Kaspar Schindler (Neurosurgery) and consisting of the LPICM in Paris as well as the Departments of Neurosurgery and Neuropathology and the SCAN Lab at Inselspital – is currently performing experiments on a new prototype in the near-in-vivo Translational Lab at Inselspital, followed by advanced neuroanatomy analyses and machine-learning post-processing of polarimetric data. The ultimate goal is the full integration of PP-based real-time tractography and tumor identification into the microsurgical workflow.
Neuropathological Warning Criteria in Supratentorial Surgery

The resection of supratentorial tumors may be associated with functional morbidity. Postoperative functional deficits might be caused by different patients of injury. During surgery involving the insula, deficits are frequently caused by ischemic insult rather than mechanical injuries of the fiber tracts. During surgery in the paracentral region and close to the posterior limb of the internal capsule direct mechanical injury to the motor cortex (M1) and the corticospinal tract (CST) may be of major concern. Subcortical mapping techniques may allow for estimating the distance to the CST, thus providing functional guidance during tumor resection. Therefore, motor preservation requires both mapping of the M1 and the CST and continuous monitoring by motor-evoked potential (MEP) recordings.

Neuropathological warning criteria are essential to provide surgical guidance. In this project, the intra-operative electrophysiology team at Inselspital, led by Prof. Dr. med. Kathleen Seidel, sought to provide a comprehensive overview of the available evidence on MEP warning criteria in supratentorial surgery. To this, we used the emerging framework of a scoping review and visualized the data extracted from 68 heterogeneous studies. Collectively, MEPs perform well as diagnostic and surrogate biomarkers.

A rigorous quantitative evidence synthesis in the future necessitates consensus for definitions and a standardized terminology. This will facilitate training machine-learning models and applying artificial intelligence algorithms. A future strong collaboration between the department of Neurosurgery and the Bern Biomedical Engineering Network is essential.

Heat map. Diagnostic accuracy analysis of the 68 included studies. In general, specificity and NPV among various studies were high. That indicates that MEPs can reliably identify the true negative cases. Sensitivity and PPV varied across studies. However, the low and modest values are impacted by the low prevalence of reported motor deficits.
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Department of Nuclear Medicine – Inselspital Bern

Research Profile
The nuclear medicine group aims to develop new techniques to improve diagnosis and therapy in the setting of nuclear medicine. This theme encompasses several research focuses, including instrumentation, reconstruction, quantitative analysis, computer-aided diagnosis, dosimetry, and treatment planning. An artificial intelligence (AI) becomes increasingly valuable in different medical applications, achieving equal or even superior performance compared to human experts. Its integration in clinical practice is desirable and one of the group’s goals. The development of new image analysis methods employing artificial intelligence, simulation, or modeling and optimization, promises to unify physics, imaging, and therapy for the personalized practice of nuclear medicine. The group’s research portfolio has two main points of focus. The first is to optimize the nuclear medicine imaging for support of patient management at several clinics, including neurology, surgery, urology, and radiation oncology. The second is to improve treatment outcomes of targeted radionuclide therapy in several diseases, including neuroendocrine cancer and prostate cancer. The group cooperates with local, national, and international partners in medicine, neuroscience, and biomedical engineering and is intensively developing artificial intelligence methods for applications such as the early differential diagnosis of parkinsonism, pancreatic cancer, and lung lymph node. Oncology efforts target tumor lesion detection and segmentation, radiotherapy dose reduction, cross-protocol harmonization, image synthesis, and dosimetry prediction.

Early Parkinson’s Disease Diagnosis
Differential Diagnosis of Parkinson’s disease (PD) is the second most common neurodegenerative disorder and is characterized by a triad of motor symptoms: rigidity, tremor, and bradykinesia. Very similar clinical signs can appear in atypical parkinsonian syndromes, including multiple system atrophy (MSA) and progressive supranuclear palsy (PSP).

The early differential diagnosis is essential for the selection of disease-modifying treatment strategies and to achieve the best possible outcome for these patients. The research group has a long history in molecular imaging of PD, and has developed deep learning methods for differential diagnosis of parkinsonian syndromes. In collaboration with PET Center of Haasdonk Hospital, we established a 3D convolutional neural network (CNN) developed on FDG PET images of more than 1400 patient with parkinsonism and more than 1000 patients without parkinsonism for differentiation of Parkinson’s disease diagnosis. The network achieved sensitivities of 98.1%, 88.5%, and 94.5% and specificities of 90.1%, 89.2%, and 93.7% for the early diagnosis of PD, MSA, and PSP in a blind test.

As the final goal, we are currently trying to extrapolate the potential of this network to early stages. As rapid eye movement (REM) sleep behavior disorder (RBD) is considered a prodromal stage of synucleinopathies such as PD and MSA, a longitudinal RBD FDG PET imaging database was established to study the potential of deep learning in predicting disease conversion in these patients. For this purpose, the previous network was adapted to derive deep metabolic imaging (DMI) indices, which were used to determine predictive scores of longitudinal RBD data. Differences in baseline DMI indices of converted and non-converted RBD patients were assessed. The preliminary results show feasibility of the development of AI technologies for early RBD phenotype conversion. Further network improvements will be attempted with a larger RBD database.

Trajectory Inference of Tau Pathology in Alzheimer’s Disease
Neurofibrillary tangles (NFTs) are one of the key pathological features of Alzheimer’s disease (AD). NFTs are formed by the hyperphosphorylation and abnormal aggregation of tau protein. The abnormal tau pathology is related to cognitive dysfunction, and it predicts longitudinal change in metabolic imaging (DMI) indices, which were used to determine predictive scores of longitudinal RBD data. Differences in baseline DMI indices of converted and non-converted RBD patients were assessed. The preliminary results showed feasibility of the development of AI technologies for early RBD phenotype conversion. Further network improvements will be attempted with a larger RBD database.

The emerging technique of targeted radionuclide therapy (TNT) offers an effective treatment strategy for several advanced cancers, including metastatic castration-resistant prostate cancer (mCRPC) and neuroendocrine tumor. However, concerns of dosing effects and risks have also been raised. The individualization of the internal radiation dose is becoming a growing interest for novel radionuclides in nuclear medicine research. Meanwhile, the European council mandates that treatments should be planned according to the radiation doses delivered to individual patients. The lack of a database including parkinsonian patients and non-parkinsonian subjects with 18F-FDG PET images was established to support the potential of this network to early stages. As rapid eye movement (REM) sleep behavior disorder (RBD) is considered a prodromal stage of synucleinopathies such as PD and MSA, a longitudinal RBD FDG PET imaging database was established to study the potential of deep learning in predicting disease conversion in these patients. For this purpose, the previous network was adapted to derive deep metabolic imaging (DMI) indices, which were used to determine predictive scores of longitudinal RBD data. Differences in baseline DMI indices of converted and non-converted RBD patients were assessed. The preliminary results show feasibility of the development of AI technologies for early RBD phenotype conversion. Further network improvements will be attempted with a larger RBD database.

Treatment Planning for Targeted Radionuclide Therapy
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A database including Parkinsonian patients and non-Parkinsonian subjects with 18F-FDG PET images was established to support development of a 3D deep convolutional neural network for extraction of a deep metabolic imaging (DMI) biomarker.

Example of test results of [18F] FDG imaging from DMI (UCL Discovery M), mCT (Siemens, Biograph mCT), and Vision (Siemens, Biograph Vision). Of accepted methods to characterize the tumor burden and predict the dosimetry before RT can help realize the treatment planning. For the first time, we have developed a deep learning method, so called deep supervised residual U-Net to detect and segment autonomously prostate cancer lesions on PSMA imaging. This enables the characterization of a high number of lesions of heterogeneous size and uptake distribution in a variety of anatomical contexts with different background radioactivity. Furthermore, the group proposed a deep learning method for vesicle-wise prediction of post-therapy dosimetry from pre-therapy PET images. As the accuracy is still less satisfactory due to limited data, a physically based pharmacokinetic-PET model was integrated in the preprocessing of the deep learning methods to improve the prediction.

A second research focus is to study the feasibility of individual estimation of post-therapy dosimetry for 177Lu-PSMA I&T therapy. It is still debatable whether individualized dose should be applied for the emerging PSMA-targeted therapy management.

Cellular Nuclear Medicine Imaging System

The group is also active in the development of cellular nuclear medicine imaging systems. Conventional molecular imaging measures tracer uptake in living organs. As an alternative, we have built a continuously infused microfluidic radioassay (CIMR) system, which enables real-time measurement of the dynamic cellular uptake of tracers, with the estimation of cellular pharmacokinetics. The CIMR system consists of a high-sensitivity position emission detector positioned around the chamber holding the microfluidic slides. Perfusion medium containing tracer flows continuously into the cell chamber, while simultaneous measurement of a reference medium chamber avoids the calibration errors. By employing valid cellular compartmental models, the cellular pharmacokinetics of the tracer is robustly estimated from high-quality, real-time measurements. Our instrument was tested relative to mRNA expression of relevant enzymes using RT-PCR. Estimated ex vivo kinetic parameters were also consistent with literature values of kinetic parameters in vivo for cancer patients. The re-producibility, stability, and capability of the CIMR system for capturing pharmacokinetic parameters constitute a valuable tool for theranostic research.

Development of an On-Chip PET System

Organo-on-Chips (OCOs) are micro devices mimicking in-vivo organs that find growing applications in disease modeling and drug discovery. With the growing number of uses comes a strong demand for imaging capabilities of OOCs as modeling physiologic processes within OOCs is vital for the continuous improvement of this technology. PET would be ideal for OOC imaging due to its ability to retrieve in-vivo information about metabolism and molecular pathways. However, current imaging devices for measuring PET tracer uptake in either small animals or cell cultures are inadequate for the task of OOC imaging due to their limited spatial resolution. The group is currently developing an On-Chip PET system to make functional imaging of OOCs possible. We have optimized the design of the proposed system with a Monte Carlo simulation (MCST) and achieved a spatial resolution of 0.55 mm using a convolutional neural network (CNN) based scintillation position prediction and SART reconstruction.

Pharmacokinetic Modelling

Our group is also actively developing new technologies to improve the quantitative analysis of PET molecular imaging based on pharmacokinetic modelling. We have developed a physiological ground truth to improve the model selection and parametric image reconstruction. We have also developed a direct parametric image reconstruction (DPiR) method for estimating kinetic parameters and recovering single tracer information from rapid multi-tracer PET measurements. This approach has applications for dual acquisitions of different tracers. This entails integrating a multi-tracer model in a reduced parameter space (RPS) into dynamic image reconstruction along with introduction of an expectation-maximization surrogate function to incorporate a multi-tracer model for the optimization of the penalized log-likelihood. Furthermore, we have developed a new hierarchical pharmacokinetic modelling approach to improve the parametric image estimation by refining the setting of initial values as well as fitting boundaries hierarchically to reduce the local minima of nonlinear fitting. The methods were validated by both computational simulations and real data. The improved estimation of pharmacokinetic modelling can enhance the potential of PET imaging in diagnosis and therapy management.

Radio tracer Development and Preclinical Imaging

In keeping with the broader objectives of the department, aspirations for preclinical molecular imaging are the most recent topic of focus in the group. The research is centered around preclinical studies of neurodegenerative disease models such as PD and Alzheimer’s disease. This should be enabled by establishment of a facility for radiotracer development through concerted use of the on-chip/small animal PET, autoradiography in vivo, and radiomorphometric measurement of tracer metabolites formed in vivo.

Selected Publications


Research Profile

The translational imaging center (TIC) within sitenor is one of the central imaging labs on campus. Biomedical imaging plays an essential role in helping researchers and clinicians better understand disease processes. Research in this area involves using different imaging modalities to gather data on the structure and function of biological tissues and organs. This information is then used to develop new diagnostic tools and therapies.

Pulmonary function and radiological features four months after COVID-19: first results from the national prospective observational Swiss COVID-19 lung study

Group Members: Katharina Auer-Beigelman, Lukas Eber, Manuela Funke-Chambour, Christoph von Garnier, Christian Garzoni, Thomas K Geiser, Sabina Guler

Background: The infectious coronavirus disease 2019 (COVID-19) pandemic is an ongoing global healthcare challenge. Up to one-third of hospitalized patients develop severe pulmonary complications and acute respiratory distress syndrome. Pulmonary outcomes following COVID-19 are unknown.

Methods: The Swiss COVID-19 lung study is a multicentre prospective cohort investigating pulmonary sequelae of COVID-19. We report on initial follow-up four months after mild/moderate or severe/critical COVID-19 according to the World Health Organization severity classification. 113 COVID-19 survivors were included (mild/moderate n=47, severe/critical n=66).

Conclusion: Four months after severe acute respiratory syndrome coronavirus 2 infection, severe/critical COVID-19 was associated with significant functional and radiological abnormalities, potentially due to small-airway and lung parenchymal disease. A systematic follow-up of survivors needs to be evaluated to optimize care for patients recovering from COVID-19.

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AI-Powered Diagnosis and Management of Acute and Chronic Lung Diseases

Group Members: Andreas Christe; Lukas Eber; Stauroda Mougiakakou

For almost 10 years, our department, in close collaboration with the Artificial Intelligence (AI) in Health and Nutrition laboratory of the ARTORG Center, has focused on the diagnosis and management of interstitial lung disease (ILD) using state-of-the-art AI and computer vision technologies. While the last year we translated the research finding against COVID-19.

ILD are a heterogeneous group of more than 200 chronic overlapping lung disorders, characterized by fibrosis and/or inflammation of the lung tissue. ILD accounts for 15% of all cases seen by pulmonologists and can be caused by autoimmune disease, genetic abnormalities, infections, drugs, or long-term exposure to hazardous materials. Although ILD are a heterogenous group of histologically distinct diseases, most of these exhibit similar clinical presentations and their diagnosis often presents a diagnostic dilemma. However, early diagnosis is crucial for making treatment decisions, while misdiagnosis may lead to life-threatening complications.

The scope of our research is to develop a framework that allows the detection and diagnosis of the pathology, its prognosis, and finally the treatment personalization based on the AI-powered analysis of imaging, clinical laboratory, and patients history data as shown in Figure 1. Within this framework we introduce algorithmic approaches and a diagnosis support system able to (i) fully automatically segment the lung and the anatomical structures of the lung cavity and (ii) identify, characterize, and quantify different types of pathological lung tissues. The image analysis results along with the additional disease-related information are further analyzed to not only support the faster diagnosis, but also for the more efficient disease management in the sense of treatment selections and disease progression. The newly introduced algorithmic approaches are continuously validated within the framework of feasibility and clinical trials, while the integrated diagnosis support system was able to detect ILD with similar accuracy to a human reader.
Aortic stress imaging with new MR ergometer design

Adrian Auderset, Anil Aksöz, Dario Haeberli, Vladimir Maka

Our group receives funding from the Swiss National Science Foundation, -

analysis of imaging, clinical/laboratory, and patient’s history data. The sys-

festations, such as ground glass opacities, band consolidations, and re-

n= 55) and decompensated CSPH (dCSPH, as-

Manuela Pöllinger, Mauricio Reyes, Nicola Sverzellati)

Assessing severity and predicting a patient’s acute and chronic course

A systematic method was developed to implement the WHO clinical pro-

the similarity between manual and AI-aided lesion segmentation was evalu-

Experiments Procedures and Results: The first stage of the AssessNet-19

The second stage of the AssessNet-19 predicts the disease severity in CO-

results to predict the severity classification using the high-level WHO score.

Conclusion: Our study shows that the multi-class lesion segmentation al-

Manual segmentation and segmentation of five different lesion classes.

The first stage of the AssessNet-19 method inputs the multi-center CT

A multi-center dataset of one hundred forty CT

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Comparison among UNet3D, Scancovia model, and AssessNet-19 for lesion segmentation in COVID-19 patients. The AssessNet-19 method yielded a mean DC of 0.71 for GGO, 0.64 for CON, 0.57 for PLE, and 0.22 for BAN, compared to manual segmentation. A qualitative comparison among the AssessNet-19, a 3D-Unet model trained with the grand challenge dataset, and Scancovia** model for lesion segmentation in COVID-19 patients is also present. These two models fail in the segmentation of very dense lesions such as consolidation and pleural effusion, which occur in very severe COVID-19 patients.


Table 1. The WHO clinical progression scale and the three classes (high-level WHO score) were used to predict the severity of the COVID-19 patients.

<table>
<thead>
<tr>
<th>WHO clinical descriptor</th>
<th>Score</th>
<th>High-level WHO score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Uninfected, no viral RNA detected</td>
<td>0</td>
<td>—</td>
</tr>
<tr>
<td>Asymptomatic, viral RNA detected</td>
<td>1</td>
<td>Mild</td>
</tr>
<tr>
<td>Symptomatic, independent</td>
<td>2</td>
<td>Ambulatory</td>
</tr>
<tr>
<td>Symptomatic, assistance needed</td>
<td>3</td>
<td>Hospitalized Moderate</td>
</tr>
<tr>
<td>Hospitalised; no oxygen therapy*</td>
<td>4</td>
<td>Hospitalized</td>
</tr>
<tr>
<td>Hospitalised; oxygen by mask or nasal prongs</td>
<td>5</td>
<td>Moderate</td>
</tr>
<tr>
<td>Hospitalised; oxygen by nIF or high flow</td>
<td>6</td>
<td>High</td>
</tr>
<tr>
<td>Intubation and mechanical ventilation: p(\text{O}<em>2/F\text{I}</em>\text{O}_2 &gt; 200) or vasopressors</td>
<td>7</td>
<td>Critical</td>
</tr>
<tr>
<td>Mechanical ventilation p(\text{O}<em>2/F\text{I}</em>\text{O}_2 &lt; 200) or vasopressors</td>
<td>8</td>
<td>Severe</td>
</tr>
<tr>
<td>Mechanical ventilation p(\text{O}<em>2/F\text{I}</em>\text{O}_2 &lt; 150) and vasopressors, diuretics, or ECMO</td>
<td>9</td>
<td>Very severe</td>
</tr>
<tr>
<td>Dead</td>
<td>10</td>
<td>—</td>
</tr>
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</table>

Support Center for Advanced Neuroimaging (SCAN)

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Research Profile
The Support Center for Advanced Neuroimaging (SCAN) is a multidisciplinary imaging laboratory, where MR-physicists, computer engineers, neuroradiologists, neurologists, and psychologists investigate new applications for advanced neuroimaging together with specialized radiographers and technicians.

Ultra-High Field MRI
In 2019, the Translational Imaging Center (TIC) was established at the Campus of the Swiss Institute for Translational and Entrepreneurial Medicine (Innovo TEC AG). The TIC hosts a clinically certified 7 Tesla MRI system for basic and translational research and clinical investigation. In this context the research focus of the SCAN is the translation of 7T neuroimaging into patient care (Radojewski et al. 2021). We investigate the diagnostic yield of high-resolution clinical UHF imaging in neuromedicine (neurovascular disorders, presurgical epilepsy, neuroimmunology and degenerative disorders).

Applying machine learning to solve problems in brain image analysis, our research group works at the intersection of machine learning and neurology. Using deep learning and other techniques, we focus on model interpretability, uncertainty quantification, and model validation. In two recent projects, we implemented federated learning, a method that describes the training of machine learning models in a distributed fashion, across multiple data sites, without explicit sharing of information.

We provided data and segmentation architectures to the FETs project, a world-wide initiative to train models for glioblastoma delineation from the data of 6,314 glioblastoma patients from 71 geographically distinct sites. In the context of the Innosuisse project “Advanced Stroke Analytics Platform” we are exploring the potential of this technology to tools for acute stroke data analytics.

The Swiss-First Study
In an SNF-funded international SINERGIA project (https://www.swissfirst-project.com), we are currently monitoring approximately 500 patients who have experienced a first epileptic seizure. We analyze data at seven epilepsy centers in Switzerland. At the SCAN we make use of advances in MRI sequence development and signal analysis to quantitatively investigate abnormalities reflecting preexisting epileptogenesis and an increased risk for seizure recurrence. The development of new diagnostic tools based on EEG and MRI in combination with machine learning is expected to directly improve patient care. (Rebsamen et al., 2020, 2021).

Selected Publications

Federated learning enables training or local diffusion and perfusion models of acute stroke on data samples in multiple institutions. Parameters (weights and biases of a deep neural network) are exchanged between centers to generate a global stroke model shared by all centers.
Editorial

Biomedical Engineering Research at other Institutes of the University of Bern

At the University of Bern, along with the beforehand listed institutions specialized in biomedical engineering research, a variety of additional research institutions from different scientific angles also engage in targeted research activities in the field of biomedical engineering.

These additional viewpoints from diverse domains contribute to a productive research environment in Bern, owing to the very interdisciplinary nature of biomedical engineering research that greatly benefits from the specific expertise these technological and scientific institutes provide.

Research Profile

The Computer Vision group conducts research on the broad areas of machine learning, computer vision, image processing, and imaging and sensor design by employing models, algorithms, and analysis tools from optimization theory, probability theory, and applied mathematics. Our general aim is to extract high-level information from images by using digital processing. Such high-level information can be in the form of geometric or photometric quantities about objects in the scene, or semantic attributes such as their category, function, etc. To achieve this aim, we develop algorithms based on modeling and/or data-driven principles. Our model-based approaches describe the identification of unknown parameters of sensors and distortions of their measured signals, such as optical aberrations (defocus and motion blur), noise, spatial loss of resolution and quantization, as optimization problems. We also introduce novel optimization techniques, with a focus on computational and accuracy performance. In this domain, our efforts have been devoted to problems in: inverse imaging (deblurring, blind deconvolution, super resolution), 3D estimation (multi-view stereo, photometric stereo, coded aperture photography), motion estimation (structure from motion, tracking). Our data-driven solutions use large datasets to learn a model. Our focus is on unsupervised learning, i.e., on identifying key learning principles that allow a machine to learn without supervision/manual annotation. Manual annotation of data samples is quite costly, error-prone, time-consuming, in some cases ill-defined, and may introduce undesired bias into the training. Moreover, we look at machine-learning methods that map data samples to simpler representations that can be used effectively on tasks we have not trained on before. As shown recently, self-supervised learning methods, which avoid human annotation, can successfully build effective representations. The idea is to exploit the structure of the data as a form of annotation to define artificial learning tasks. These methods allow one to train models on data with very little labeling by first pre-training them on large datasets without labels.

Self-supervised Learning

Self-supervised learning is a novel paradigm in machine learning, where one can learn features without manual annotation. The main principle is to take the available data samples, split each sample into two parts, and learn to predict one part given the other as input. This principle allows a model to learn structure in the data. We have proposed a method that learns how to solve puzzles. We split images into a set of nine tiles (input) and the corresponding pixel coordinates of the center of each tile (output). By learning to arrange the tiles in the correct order, the model learns to distinguish object parts and how these object parts are typically arranged.

Disentangling Factors of Variation

We assume that visual data can be described by a finite set of attributes, or factors, such as the object identities, 3D shape, pose, viewpoint, and the global illumination. Computer graphics rendering engines are an example of how these factors can be used to generate images. We are thus interested in the inverse process, where we obtain these factors given an image. The collection of such factors is a feature vector that can be used efficiently for object classification, detection, and segmentation. We explore completely unsupervised methods as well as partly supervised methods, where only some factors (e.g., the object category) are specified.

Deblurring

If either the camera or objects in a scene move during the exposure, images will be degraded by an artifact known as motion blur. To remove this degradation we consider explicit models of blur (shift-invariant, camera shake, non uniform) and design energy minimization methods or machine learning methods that can be used to solve other visual tasks that require understanding the composition of objects.
data-driven methods (e.g., via deep learning) to retrieve the latent sharp image. Our approaches introduce priors for sharp images and models of the blurry image noise in an energy formulation. We then build novel iterative algorithms to solve the minimization task. In one of our recent works on deblurring, we presented a method to extract a video sequence from a single motion-blurred image.

Motion-blurred images are the result of an averaging process, where instant frames are accumulated over time during the exposure of the sensor. Unfortunately, reversing this process is nontrivial. First, averaging destroys the temporal ordering of the frames. Second, the recovery of a single frame is a blind deconvolution task, which is highly ill-posed. We present a deep-learning scheme that gradually reconstructs a temporal ordering by sequentially extracting pairs of frames. Our main contribution is to introduce loss functions invariant to the temporal order. This lets a neural network choose during training what frame to output among the possible combinations. We also address the ill-posedness of deblurring by designing a network with a large receptive field and implemented via resampling to achieve a higher computational efficiency. Our proposed method can successfully retrieve sharp image sequences from a single motion-blurred image and can generalize well on synthetic and real datasets captured with different cameras.
Department of Clinical Research

Complexity of clinical research has been growing steadily. The Department of Clinical Research provides an umbrella organization for facilities supporting clinical researchers both at the Faculty of Medicine and at Inselspital as well as small- to medium-sized companies. The department is currently comprised of CTU Bern and the Clinical Investigation Unit. While CTU Bern has its offices at Mittei lane 43, Clinical Investigation operates in the stem-mat building on the Inselspital campus. A full professor of clinical research will lead the department eventually.

Statistics and Methodology

The Statistics and Methodology division at CTU Bern offers professional services in research design and statistical analysis, supports Central Data Monitoring activities, and performs statistical analyses. The overarching aim of our consultancy work is to promote the use of appropriate study designs to address the question at hand, as well as methods of data analysis that provide coherent and relevant information while realistically acknowledging the uncertainty in the results. Services include consulting on designing and analyzing clinical trials and observational studies, sample size calculation, contribution to statistical parts of the study protocol, setting-up statistical analysis plans (SAPs), performing statistical analysis, preparing statistical reports, and support with manuscript writing. Ideally, our statisticians are involved early in the planning of a clinical study. Although not optimal we also support investigators after data collection is completed. In any case, successful work means that there is a close collaboration.

Data Management

CTU Bern provides and maintains a secure and up-to-date IT infrastructure. The servers hosting the study databases are stored in dedicated server facilities. CTU Bern Data Management ensures that all software required to run the servers is regularly updated. Backups of all study- and meta-data are made regularly according to a detailed back-up plan. The plan defines internal back-ups several times per day and daily back-ups on external disks. Our security measures have been checked by the "Datenschutzamt des Kantons Bern." The data management division (DM) at CTU Bern offers two different models of services and support during the setup of a clinical study database or register:

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

- Collaborative Setup
  - If an investigator wants to set up the study database mostly by her-/himself, we can introduce her/him to our EDC system REDCap, where studies can be set up independently (eCRFs, edit-checks, visit structure). CTU Bern will give as much support as requested. At the end, CTU Bern will review the implementation and set it productive, so that data entry can start.

Clinical Investigation Unit

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Electronic Data Capturing (EDC) Solutions

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

Clinical Study Management

Clinical Study Managers at CTU Bern oversee and coordinate the overall study and ensure that every aspect of planning and execution is taken proper care of, from study conception to close-out. We make sure that milestones are reached within pre-set deadlines and budget as well as personnel constraints, while complying with Good Clinical Practice, applicable national and international regulations, scientific guidelines and standards, standard operating procedures, and not the least the study schedule and protocol requirements.

By fostering an open and effective communication between stakeholders (e.g., teams at study sites, sponsor, and other CTU divisions), we ensure that everyone is up-to-date and motivated to allow a steady and flawless conduct of the project through all its phases.

Quality Assurance and Monitoring

CTU Bern offers quality control and assurance services (monitoring) to sponsors including sponsor-investigators working at Inselspital Bern or other interested parties for single-center or multi-center clinical studies. Our approach takes into account the risk of the individual study and that the monitoring strategy is risk adapted. We offer two interrelated services to support you in ensuring a high-quality study conduct:

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

Central and Statistical Data Monitoring

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

Quality Management

CTU Bern quality department is responsible for the internal quality management of the institute. Well-defined and documented procedures ensure that the legal foundations of conducting clinical research projects are met, while ensuring efficient, effective, and transparent processes are followed and continuously developed. In addition to managing the internal structures, the quality management division also offers its expertise to external customers and partners by providing consulting or support services to implement local quality assurance measures, develop procedures, or to establish comprehensive quality management structures. In addition, the quality management division can provide active support in the preparation for inspections, the writing of inspection reports, corrective and preventive action development and offers its auditing services to conduct an independent audit on your study or internal process structures.

Clinical Investigation Unit

Clinical Investigation is a service unit that offers professional services to investigators working at Inselspital Bern or to other interested parties engaged in single-center or multi-center clinical studies. These services

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Research Partners
All clinical departments of Inselspital Bern and institutes of the medical faculty of Bern as well as other Swiss hospitals and small- to medium-sized companies.

Annual Report 2020/21
BME Institutes of the University of Bern
Department of Clinical Research

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BME Institutes of the University of Bern – Department of Clinical Research

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include logistic support, planning, coordination, and execution of clinical studies from phases I to IV as well as observational studies.

The Clinical Investigation Unit is situated at University Hospital Bern in the site-insel building and runs a fully equipped outpatient clinic. Our facilities include:

- Fully equipped treatment rooms for outpatient study visits of patients and volunteers
- Access to the certified laboratories of the Inselspital Bern, including chemistry, hematology, microbiology, therapeutic drug monitoring, and other specialized investigations. Shipping to central study laboratories, if required
- Rapid access to emergency treatment via our own life support equipment and the University Hospital’s 24 h emergency center and resuscitation team
- Sample processing and controlled storage according to GCP guidelines (-20°C and -70°C)
- Controlled storage and handling of study medication, according to GCP and study guidelines
- Storage of study files (hardcopy and electronic data) for 15 years
- Working facilities for visiting study monitors

Selected Publications


Bone & Joint Program of the Department for BioMedical Research (DBMR)

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Group Members
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Research Partners
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Dr. Jérôme Nallely, ICN MedTech, Department of Information and Communication Technologies, Universitat Pompeu Fabra, 08018 Barcelona, Spain
Dr. med Michael Schär, shoulder team, Department of Orthopaedics & Traumatology, Inselspital University Hospital, Bern, Switzerland
Prof. Dr. M. Tryfonidou, Department of Clinical Sciences of Companion Animals, Faculty of Veterinary Medicine, Utrecht University, Utrecht, the Netherlands

Research Profile
The skeletal system is subject to traumatic conditions (fractures, large bone defects) and pathology due to degeneration (osteoporosis, osteoarthritis, intervertebral disc degeneration). The demand for improved and efficient treatments is increasing as the population of the elderly grows and wants to stay physically active. Surgical procedures for the repair of large bone defects or degenerated spinal discs, however, still need tremendous improvements. The regeneration of skeletal tissue is the focus of the Bone & Joint Research Program. This aims at strategies based on cells, materials, and growth factors that are currently employed ex vivo (2D/3D cell cultures, bioreactor) and in vivo. Pioneering orthopaedic surgery, which has been a long tradition in Bern, requires interactions between surgeons and scientists. The Bone & Joint Research Program will continue and extend this tradition and provide the clinicians with tools to improve the treatment of patients.

Intervertebral Disc Regeneration in Orthopaedic Research
There are currently four competitive funded research projects active in the field of intervertebral disc regeneration or in the field of improved spinal fusion. Two of these research projects are funded by the horizon H2020 framework, one in the field, one by the Swiss National Science Foundation, and one by the center of Applied science and Molecular Medicine – BCN MedTech, Department of Information and Communication Technologies, Universitat Pompeu Fabra, 08018 Barcelona, Spain

A second highlight is the investigation into engineered silk scaffolds for IVD repair. Here, a new project funded by the Swiss National Science has been started that targets regeneration of the IVD by using “cross-linked growth-factors and engineered” silk fibres and using knitting techniques developed by Dr. Michael Wöltje at the “Technische Universität Dresden, Institut für Textilmaschinen, und Textile Hochleistungswerkstofftechnik”, Dresden, Germany.

A third key topic was started in Nov 2020, which involves artificial intelligence, statistical shape modelling and finite element modelling, and organ culture models for IVD regeneration. The IFM E funded “DiscAll” project aims to tackle this issue through collaborative expertise of clinicians; computational physicists and biologists; geneticists; computer scientists; cell and molecular biologists; microbiologists; bioinformaticians; and industrial partners. It provides interdisciplinary training in data curation and integration; experimental and theoretical/computational modelling; computer aided design; tool generation; and model and simulation platforms to transparently integrate primary data for enhanced clinical interpretations through models and simulations. The consortium is led by the biomedical engineer

Specialized Bioreactor to apply compression and torsion for culturing entire units of bovine-derived intervertebral disc explants in organ culture under compression and torsion. Left: inside incubator, upper right: close-up view of culture chamber, lower right: Inside view of culture chamber with positioned bovine coccygeal intervertebral disc. This device is worldwide unique.

Profs. Jerome Nallely from the Universitat Pompeu Fabra (UPF) in Barcelona, Spain (https://upf.edu/web/discall). The DiscAll early-stage researchers will provide a new generation of internationally mobile professionals with unique skills for the development of new therapies in translational research applied to multifactorial disorders.

Finally, the fourth topic is the development of a coccygeal rat non-fusion model for the intervertebral disc. Here, in collaborative efforts with the RMS Foundation (Bettelach, SG), porous ceramics implants are currently being tested in an in vivo rat animal model for spinal fusion. This project has been awarded in Dec 2021 with the best-poster award at the German Spine Society Conference.
An overview of procedures of a newly established non-spinal fusion model. Spinal fusion in vivo animal model illustrating the concept of the procedure 1) discectomy of coccygeal intervertebral disc 2) placement of a ceramic of TCP that was coated with cytokines 3) Schematic view of operated Wistar rat with fixator extern that applies compression to induce spinal fusion.

Selected Publications


Bone Biology and Orthopedic Research

A further topic of interest in orthopedics is the healing of osteoporotic bone treated with bisphosphonates (BP), a class of drugs inhibiting osteoclastic bone resorption. In the past year, a mouse model of OVX and ßTCP-filled femoral critical size defects was applied to investigate whether treatments with BP affect defect healing and biomaterial turnover were impaired. After harvesting all the tissue samples and preparation of the RNA, presently the outcomes are assessed by histomorphometry and 3rd Generation Sequencing. This work is performed by Franziska Strunz, Ph.D. student, and supported by a grant from the Alfred & Anneliese Sutter-Stöttner Foundation. Gadolinium (Gd) is a component of contrast agents frequently used in clinical practice. Despite the frequent application, it is not clear, whether incorporation of Gd in tissues may cause negative long-term effects. In this project, the effects of injected Gd and of complexed Gd on the development and activation of bone cell lineages are investigated. This work is performed by Franziska Strunz, Ph.D. student, in collaboration with Prof. Rainer Egli (Clinic of Diagnostic and Interventional Radiology) and supported by a grant from the Inselspital. In collaboration with Prof. Philippe Krebs (Department for Pathology, University of Bern) the effects of a deficiency in the Inositol-Polyphosphate-5-Phosphatase (SHIP1) on osteoclast development and activity is being assessed. SHP1-deficient Styx mice are characterized by a low bone mass phenotype, and within this project, the cellular base for this phenotype is analyzed in vitro and in vivo.

Cranio Maxillo Facial (CMF) Research

The interest of the Saulacic Research Group is focused on translational research. Key topics within the field of bone regeneration are the development of new biomaterials, assessment of the biocompatibility, and the influence of the biodegradation on guided bone regeneration.

Bone Biology and Orthopedic Research

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The indication for a specific bone substitute material is related to the type and the stage of alveolar ridge resorption. Vertical bone defects are considered the most demanding for reconstruction. The feasibility of simultaneous vertical bone augmentation using block grafts (bone ring) and implant placement was established in collaboration with Advance Research Center, The Nippon Dental University School of Life Dentistry at Niigata, Japan. In terms of osseointegration, single-stage implant placement with autogenous bone has been demonstrated as useful to shorten an overall treatment period. Different biomaterials in block form have been developed to avoid the use of the autogenous block bone grafts.
Optoacoustic and Ultrasound Imaging

Optoacoustic (OA) imaging allows the display of optical contrast inside tissue based on detection of thermally induced ultrasound after tissue irradiation using nanosecond pulsed lasers. In combination with pulse-echo ultrasound, OA is promising to improve diagnostic accuracy via the display of small blood vessels and the local blood oxygen saturation within the anatomical context. For this purpose we developed a hybrid real-time multi-luminaum (MI) multispectral OA imaging setup with ultrasound (US) imaging capability; we trained gradient-boosting machines on MI spectrally colored absorbed energy spectra generated by generic Monte Carlo simulations, and used the trained models to estimate $sO_2$ on real OA measurements. These studies proved highly accurate and showed consistently good estimates on $sO_2$ values in humans. This proves that OA imaging method has the potential to be a robust tool enabling quantitative OA imaging in humans.

On the other hand, sound speed as a diagnostic marker has been of interest for many years due to the fact that sound speed can reveal changes in tissue and the interaction of laser radiation with soft and hard tissues, (2) laser-induced reversible and irreversible changes in optical properties of tissue response and the consequence of these changes on thermal and mechanical tissue damage and ablation (3) the development of laser and fiber-delivery systems optimized for specific medical applications; and (4) the development of novel biomedical optical and ultrasound imaging techniques. In particular, we concentrate on the development of two quantitative imaging techniques: polarimetric imaging of the human brain to determine the orientation and degree of alignment of nerve fiber bundles with the goal to visualize brain tumors and optoacoustic and ultrasound imaging to image tissue structures and function. Both imaging techniques have the potential to guide patient-tailored tumor therapeutics. Questions to be addressed are of applied and fundamental character: (i) What limits the image depth and resolution and how can both be increased? (ii) How does laser light interact with contrast agents? and (iii) How to improve multimodal imaging devices for clinical use simultaneously measuring echo and Doppler ultrasound, tissue elastography, speed of sound, and optoacoustic? Further main topics are two-photon imaging, fluorescence lifetime imaging, and interactions of ultrafast near infrared laser pulses with biological soft matter.

Polarimetry

With more than 200 various tumor types, malignant brain tumors are a particularly difficult disease to diagnose often because their exact borders is hard to precisely determine. The interaction of polarized light with matter can reveal features that are invisible to ordinary imaging techniques i.e. orientation of tissue structures. We are developing a polarimetric microscope that can measure cross- and auto-correlations between arbitrarily polarized incident and backscattered light (these correlations being commonly coded in the 4x4 Pome- Mueller matrix). Our research shows that polarimetry allows for sensitively defining the different degrees of alignment in healthy brain tissue in vivo without prior tissue preparation. On the other hand, it can be used to help accurate delineation of cancer tissue during resection. On the other hand, given the promising sensitivity of distinguishing tumors in degree of alignment inside white matter, it could also be used to guide resections by identifying axial nerve fiber trajectories by performing tractography of nerve fiber pathways in the brain. In addition to applications in the brain, the presented method has the potential to identify pathologies in other tissue types consisting of fibrous structures, such as the skin for diagnosing skin cancer or for monitoring the healing process after skin injuries. Recently, we added a 20 single photon counting camera that allows us to perform time-resolved measurements resulting in additional depth information and providing quantitative information about optical tissue properties. Our goal is to develop an instrument able to clinically differentiate tumours from healthy brain tissues to clearly determine tumour boundaries. In parallel, we want to thoroughly study the fundamentals of polarized light propagation in random media.

Respiratory Ciliary Clearance

Our research is directed on one hand towards a better understanding of the processes underlying the cilary motion. For example, we would like to understand how the characteristic motion pattern of individual cilium is related to the collective cilary motion pattern and how this can be influenced by medications. On the other hand, we would like to provide the physicians a tool to clearly diagnose primary ciliary dyskinesia (PCD). To this end, we developed a high-speed video reflection microscope and a software package for data analysis that allows us to characterize mucociliary function in vivo by means of quantitative observables, such as the cilary beating frequency, the velocity and wavelength of the metachronal wave, and the mucociliary transport. This system has the potential to become the gold standard for clinical diagnosis of PCD allowing for patient-tailored therapiesties. To this end we developed a high-speed video reflection microscope and a software package for data analysis that allows us to quantitatively determine cilary beating frequency, the velocity and wavelength of the metachronal wave, and the mucociliary transport.

Selected Publications

Center for Artificial Intelligence in Medicine

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Executive Team

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Research Partners
INSEL, SITEM-INSEL, UPD

Center for Artificial Intelligence in Medicine (CAIM)

The CAIM is a research, teaching, and translation platform that investigates AI medical technologies that can facilitate the work of doctors and nurses and bring better care to patients. CAIM capitalizes on the significant presence of scientific, healthcare, and medical technology industry players in the canton of Switzerland. It is a virtual center of the University of Bern’s medical faculty and the Inselspital, Bern University Hospital in partnership with the University Psychiatry Services (UPS) and the Swiss Institute for Translational and Entrepreneurial Medicine, sitem-insel. The University of Bern, the Inselspital, Bern University Hospital (“Digital Hospital”), and the Canton of Bern (“Engagement 2030”) have major, strategic digitalization efforts underway. CAIM provides tailored AI in medicine education for medical doctors and engineers through a portfolio of competitive and purposefully designed post-graduate programs to equip participants for Healthcare 4.0.

CAIM provides important insights, evaluation, and perspective for introducing novel AI technologies into clinical care by translating state-of-the-art research into tools for clinicians and healthcare professionals. Targeted educational programs and courses of the University of Bern provide AI researchers and clinicians with cutting-edge knowledge and qualifications in the field. This includes courses in “Digitalization and AI” for medical students, a dedicated master’s program for AI in Medicine (started fall 2021), and AI in healthcare-related postgraduate training and further education offerings.

MSc Artificial Intelligence in Medicine

Our newly established master’s program welcomed its first students in September 2021. The primary aim of the master’s program is to train the next generation of workforce and entrepreneurs with both theory and practical experiences in AI in health and medicine. The whole concept is based not only on the provision of insight information and knowledge about the algorithms and technologies, as offered by most of the AI post-graduate programs, but to complement them with first-hand experience from healthcare providers. The program is composed of 120 ECTS points over a period of 4 semesters. The entire program is taught in English. The program is designed for students with a bachelor’s degree in computer science, biomedical or electrical or mechanical engineering, physics, mathematics, or a related field. The program is built heavily on AI and healthcare including the following modules: AI, medicine, foundation and applied modules. There are also elective options, and a master’s thesis to be completed towards the end of the program. The uniqueness of the master’s program is that it is completely embedded in the faculty of medicine providing both theory and applications of AI courses, as well as an introduction to healthcare professionals into the medical content. Students are given the opportunity to visit various departments and university clinics, allowing them to dive deeply into clinical procedures and medical routines and apply their knowledge to identify these processes and procedures that can benefit from AI.

Research Profile

To take leadership in the direction of research and development of Artificial Intelligence (AI) in medicine, the University of Bern and the Inselspital, Bern University Hospital, together with partners from sitem-insel, the Swiss Institute for Translational and Entrepreneurial Medicine, and the University Psychiatry Services (UPS) have founded the Center for AI in Medicine (CAIM).

Bringing together world-class scientists and clinicians to join with collaborators in industry, patient advocacy, and medical ethics, researchers will enable the investigation and translation of advanced digital and robotic technologies to deliver a new generation of diagnostics, treatments, and interventions. CAIM started operations in January 2021 driven by the existing expertise in AI in medical research, engineering, and healthcare digitalization education within the Bern network to bring forward AI in medicine solutions with a positive impact for patients everywhere. During its first year, CAIM was nominated for the best 2022 AI in medicine center by the Alliance of Centers of Artificial Intelligence in Medicine (ACAIM). The CAIM is a research, teaching, and translation platform that investigates AI medical technologies that can facilitate the work of doctors and nurses and bring better care to patients. CAIM capitalizes on the significant presence of scientific, healthcare, and medical technology industry players in the capital of Switzerland. It is a virtual center of the University of Bern’s medical faculty and the Inselspital, Bern University Hospital in partnership with the University Psychiatry Services (UPS) and the Swiss Institute for Translational and Entrepreneurial Medicine, sitem-insel. The University of Bern, the Inselspital, Bern University Hospital (“Digital Hospital”), and the Canton of Bern (“Engagement 2030”) have major, strategic digitalization efforts underway. CAIM provides tailored AI in medicine education for medical doctors and engineers through a portfolio of competitive and purposefully designed post-graduate programs to equip participants for Healthcare 4.0.

CAIM’s activities are organized on four pillars:

Pillar I: Digitalization & AI Education
CAIM provides tailored AI in medicine education for medical doctors and engineers through a portfolio of competitive and purposefully designed post-graduate programs to equip participants for Healthcare 4.0.

Pillar II: Network & Dissemination
CAIM transmits, transfers knowledge on AI in medicine. This supports policy makers, educators, and the general public by shaping the current debates on AI in medicine with evidence-based information.

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

Pillar IV: Research Project Fund
CAIM promotes technological innovation by funding projects with strong potential to be groundwork-breaking clinical approaches and a realistic pathway toward patient benefit.

AI in Medicine – Fields of Research and Education

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

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

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

CAIM has been active in researching AI solutions for COVID-19 patients.

The vast amount of information in digital pathology is harnessing promising solutions to better mine disease patterns at multiple scales.
Editorial
Bern University of Applied Sciences BFH

Bringing specialists together, linking research and teaching, and providing the industry with well-trained professionals and close cooperation in the field of research and development: three ways that the Bern University of Applied Sciences BFH assumes responsibility and supports the medical hub of Bern.

With the aim of promoting healthy living and well-being, the BFH is committed to addressing societal challenges in healthcare in various locations and departments. Thus, the BFH Centre Health Technologies combines competences across three departments along the entire value chain, from medical technology and medical informatics to healthcare and sport.

In addition to bringing together experts, linking research and education is an important goal of the BFH. Many of the lecturers are simultaneously engaged in research, and the latest discoveries and methods are incorporated and actively implemented in teaching – especially in the context of semester papers and projects. Thus, students often contribute to the development of marketable products, particularly in cooperation with business partners and spin-off companies. This practice-oriented education prepares students both at the bachelor’s and master’s levels to become outstandingly qualified specialists and executives in the industry.

Medtech is an important branch of industry for Switzerland and has been able to grow steadily in recent years. The BFH is ready to further contribute to this positive development by providing the industry with well-trained professionals and close cooperation in the field of research and development. The BFH is well connected as a member of the Medical Cluster and the Competence Centre for Medical Technology – and a valuable partner in the Mittelland region, as well as throughout Switzerland and internationally.

Sebastian Wörwag, President
Bern University of Applied Sciences BFH

Research Profile
The BFH Centre Health Technologies as an interdepartmental collaboration between the School of Engineering and Computer Science, the School of Health Professions, and the Swiss Federal Institute of Sport Magglingen SFISM combines areas of expertise (see below) across the entire value creation chain from medical technology and medical informatics to healthcare and sports.

Various research institutes jointly foster technologies that improve the quality of life of patients and the health of society and enhance the performance of people who participate in sports. Applied interdepartmental research and development projects across the entire process chain from idea generation to innovative products or services as well as impact analysis are aimed at in a user-centric and participative way, incorporating relevant stakeholders in the fields of healthcare and sports.

Esophageal ECG System for 3D Pacemaker Lead Localization
The increase in cardiovascular diseases has led to a corresponding increase in pacemaker implantations worldwide. One of the risks that may occur during this procedure is the misplacement of stimulating pacemaker electrode leads. To overcome the limitations of state-of-the-art pacemaker lead localization methodologies, we are developing an innovative system.
for three-dimensional, minimally invasive, real-time pacemaker lead localization using esophageal ECG. The esophageal ECG system (esoECG), consisting of the esoECG-3D catheter and esoeLive analysis software, has been investigated for atrial arrhythmia applications and has demonstrated the ability to localize stimulations from various locations on the heart epicardium. Preliminary data analysis has shown the system can be applied to ventricle pathologies as well, a novel concept for esophageal ECG, which is historically considered limited to atrial applications. Innovative localization in the ventricle region makes the esoECG system available for use in a wider range of applications, such as localizing pacemaker leads during implantation surgery. The ability to locate leads in three dimensions in real-time should result in fewer misplacements, which would in turn improve the quality of life of patients and help save hospital resources.

The current research is highly interdisciplinary, including work on improved catheter designs, data acquisition device development, signal processing, and finally software development of the visualization tool. Overall, we aim to provide a fully integrated esoECG system as a surgical tool for pacemaker lead localization and other minimally invasive, real-time cardiac localization tasks using esophageal ECG.

This project is in close collaboration with the Department of Cardiology at the Bürgerspital in Solothurn and is currently funded by the BRIDGE program, jointly offered by SNSF and Innosuisse.

Tibial Translation

Injury to the anterior cruciate ligament (ACL) occurs frequently in physically active people. A rupture of the ACL results in joint instability and can eventually lead to knee osteoarthritis. For clinical decision-making about treatment modalities or to assess the rehabilitation progress, mechanical knee stability is evaluated during clinical examination by manually testing the passive knee displacement (Lachman Test, Drawer Test, Pivot Shift test) also described as anterior tibial translation. Mechanical knee stability during functional tasks, like standing or walking, is of utmost importance since knee stability is challenged in exactly these situations. The mentioned clinical knee stability tests are limited to passive situations and cannot directly be applied to weight-bearing situations. Therefore, a prototype of a measurement system to assess anterior tibial translation was recently developed in cooperation between the Biomedical Engineering Laboratory of the Institute of Human Centered Engineering at the BFH School of Engineering and Computer Science and the Bern Movement Lab at the BFH School of Health Professions.

The measurement system consists of a device with linear transducers on the tibia and patella and a data acquisition software with a graphical user interface that allows physiotherapists to measure the anterior tibial translation. On one hand, it currently covers the passive clinical testing condition for validation against the state-of-the-art. On the other hand, it supports a weight-bearing testing situation where the tibia is artificially perturbed and pulled forward by a distinct impulse while a test subject is standing in a regular pose. Validity and reliability have recently been evaluated in a cross-sectional study with 20 healthy test subjects. The evaluation has demonstrated a valid and clinically relevant measurement instrument to assess anterior tibial translation, which has the ability to detect the cutoff value of 3 mm described in the literature for the diagnosis of ACL-deficient knees. Further research is required to investigate ACL-deficient or hypermobile knees to gain more insight into the variability of the anterior tibial translation in different cohorts. The long-term goal is to measure the anterior tibial translation under dynamic loading like stair climbing, which is currently pursued within another bachelor’s thesis project.

Sprechende Bilder

Language barriers are the most common obstacles to emergency care for migrant children and young people, seriously impacting patient safety. Understandable communication in care is therefore essential for safe, high-quality, and equitable healthcare. The project “Sprechende Bilder” (Talking images) aims to address these challenges. A digital image-based tool was developed to support non-verbal communication in pediatric emergencies. The tool was developed in a participatory design process involving potential users (pediatric emergency nurses, migrant children, and parents) and an interdisciplinary team of BFH researchers from communication design, nursing research, and medical informatics. Requirements were collected through interviews and questionnaires shared with nurses. Besides requirement collection, the development process includes mockup testing, prototype development, usability testing, and user studies. During the entire development process, feedback from future users was collected. Key research questions were: How to design a communication aid for pediatric emergencies? How to design images that are understandable for people with diverse cultural backgrounds? Which features are useful for the daily practice?

Findings

The participatory design process enabled us to design images that are understandable for migrant parents and nurses. Participants confirmed that the images – even though kept simple – are extremely representative. Communicating visually is considered to be clear. However, we also learned that only image-based communication is insufficient for an empathic interaction in emergency situations. The interactions between parents and nurses also included mimicking and gestures to support the communication. There is great potential to extend the tool, for example regarding the follow-up procedures and regarding documentation facilities.
Institute for Medical Informatics I4MI

Research Profile
Knowledge management
We focus on activities in the field of decision-making support (clinical decision support), expert systems and terminology, semantics, and ontologies closely associated with them for applications in the field of pharmaceutical treatment safety and data management, for example, clinical studies or e-health.

Evaluation of medical IT applications
We possess expertise in the evaluation of medical IT applications – for example, clinical IT systems, decision-support systems, and active assisted living (AAL) installations – as well as in the assessment of quality initiatives and e-health infrastructures.

E-Health and telemedicine
We lead and support a variety of initiatives in the field of e-health and telemedicine, involving the development of the Swiss Electronic Health Record, Mobile Health, the establishment of integrated care processes, and telemedicine applications. We analyse aspects of technical and semantic interoperability, the integration of Active and Assisted Living (AAL) into healthcare, and the secondary use of data and Big Data.

Patient-centred applications
A key area of our research activities is patient-centred applications, such as personal mobile applications (mHealth), studies on patient empowerment and self-management, and support service activities. We also focus on personalised medicine as an area of application. Informed patient privacy consent plays a significant role here. An example of such an application is the development of a pollen allergy app (My Science) for a major pollen study, supported by the citizen science approach, based on the NEAT/A personal data and consent-management platform.

Information management and economic analysis of processes in the healthcare sector
Finally, another area we focus on is information management and the economic analysis of processes in the healthcare sector. We possess expertise in this environment for the analysis of treatment processes, the optimisation of treatment chains, the design of clinical pathways, including pathway cost calculations, and the working procedures for electronic order communication (Computerised Physician Order Entry (CPOE)).

Digitalisation and transmission of clinical information in nursing (digi-care)

Situation
According to an analysis by elisuisse Suisse, the use of information and communication technologies (ICT) in healthcare is essential, and nursing staff are increasingly confronted with the digitalization of work processes. This will also radically change the way clinical patient information is communicated by nurses and other healthcare professionals. It is therefore essential to promote the teaching of the relevant competencies in education and training, the exchange of good practice, and the development of effective teaching and learning methods.

Course of action
In the first phase, we will conduct an ethnographic study in six hospitals to understand the usual working method of radiologists resulting in technological solutions that support, not hamper, the daily work. The project will apply user-centered design methods to ensure an adequate user experience of the developed technologies. It will also help to understand the usual working method of radiologists resulting in technologies that support, not hamper, the daily work.

In exceptional cases for logistical reasons, The SMARAGD project aims to support the radiological reporting process using Natural Language Processing (NLP).

On one hand, the project will develop methods for automatically structuring radiology reports. Using a combination of an NLP pipeline and a novel template, reports written in German prose can be output in a structured, standardized, and comprehensible-check form. On the other hand, an automated chatbot will be developed to give patients an option of an anonymous conversation using a chatbot before the examination. The content, also processed via NLP, is fed to the radiologists during the reporting process.

The project will apply user-centered design methods to ensure an adequate user experience of the developed technologies. It will also help to understand the usual working method of radiologists resulting in technologies that support, not hamper, the daily work.

The entire software development cycle will be covered in the project. Starting with collecting requirements, the needs of physicians and patients will be collected. Building upon technologies from industry partners, the project will extend the existing methods and bring technologies together to create new products. Software development will be accompanied by comprehensive technical testing as well as user and usability testing. In addition, research will investigate the regulatory compliance of this AI-based medical device software.

Project partner
• Inselspital Bern, SITEM, ID Suisse AG, DFPA, mimacom, wemedoo, BFH
• Funding organization: Innosuisse

Selected Publications
[1] Tippenthaler, Kevin; Philipp, Marvin; Langdiger, Carlo R.; Sarnyai, Murat; Bühlke, Thomas (2020). “SMARAGD”: Supporting Radiology Reporting using Natural Language Processing. Radiology is a high-throughput medical discipline that serves different customer groups (referring physicians and patients). The high work pressure and economic constraints necessitate compromises in service. For example, referring physicians receive medical reports in prose, but would prefer a standardized and digitized form. Personal contact of physicians (radiologists) with their patients is only possible
Institute for Human Centered Engineering HuCE

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Research Profile
The Institute for Human Centered Engineering HuCE is a collaboration of six applied research and development laboratories, which provide a broad spectrum of engineering competencies focused on medical technology and industrial automation (see below). We aim to develop research-based technologies and foster their transfer into marketable products and services in close collaboration with industrial enterprises and hospitals.

The six laboratories presented on the subsequent pages are:
• Microelectronics Laboratory
• Optics Laboratory
• Biomedical Engineering Laboratory
• Laboratory for Computer Perception and Virtual Reality
• Robotics Laboratory
• Laboratory for Sensor Technology
The HuCE-microLab in a nutshell

We provide broad technology know-how in various disciplines ranging from microelectronics, signal processing, feedback control, high-speed hardware algorithms to microstructures and surfaces, which are tailored to novel smart medical devices. Our engineering competences are complemented by micro-assembly and packaging technologies as well as validation know-how of manufacturing processes in our in-house clean room, optimally equipped for medical device manufacturing enabling the bridge from research to small series production.

Windowed State Space Filters for Peak Interference Suppression in Neural Spike Sorting

In neural tissues, each firing neuron cell generates action potentials, which are observed as electric spikes on microelectrodes of a neural probe placed on the cortex. Multiple such spikes generated by a single neuron typically have a signature waveform due to the neuron cell geometry and orientation. For real-time neural decoding in brain implants, each detected spike must be linked back to the corresponding neuron, a process called spike sorting. Neural signals often originate from high-density, multi-channel probes with high data rates. Especially for recent neural probes with hundreds of channels, the computational effort of template matching with matched filters becomes substantial, as it scales linearly with the number of filter taps, channels, and patterns. Therefore, there is an urgent need to reduce the complexity of such filters.

In our approach, we use computationally attractive Autonomous Linear State Space Model (ALSSM) filters to substitute linear finite impulse response (FIR) filters. We approximate the impulse response of peak interference suppression filters by low-order ALSSMs and perform the signal convolution in the new, low-dimensional ALSSM feature space. We demonstrate our method on real neural recordings from array probes and conclude that our ALSSM substitution has an order of magnitude lower computational complexity and outperforms standard SNR-matched filters in detection quality.

Neonatal Echophaqal Signals Processing (NEO)

Premie infants, who account for more than 10% of all births worldwide, very often require cardiopulmonary monitoring on a neonatal intensive care unit due to autonomic dysregulation. Surveillance of the heart rhythm and respiratory rate, however, is cumbersome since surface ECG and EMG registrations suffer from relevant motion artifacts. The resulting high number of false alarms impedes care prioritization and optimal support of these neonates. Furthermore, accurate diagnostic tools that objectively assess and monitor precisely the level of maturation of neonates are lacking. Discharge of preterm infants from the hospital is only indicated once autonomic dysregulation is completely dissolved.

To overcome the limitations of state-of-the-art technology, we aim to develop a novel monitoring system for preterm infants. The neonatal echophaschal observation (NEO) system bases on echphagal signal recording, a technique that is widely known to provide high-quality electrocardiography and diaphragm electromyography. Based on recent technical advances in diagnostic catheter design and manufacturing, and achieved insights of esophageal signals, the NEO project proposes that vital signs and autonomic dysregulation may be monitored with a single esophageal catheter. The new catheter will integrate multiple sensors that, in combination with model-based signal and data processing based on machine learning, may provide accurate and robust measurements of heart rate, respiratory rate, swallowing/breathing coordination, temperature, and (SpO2). In addition, the multi-lumen catheter allows simultaneous enteral feeding.

The NEO approach is a scalable solution dedicated to low-income and highly developed countries. Basic and cost-effective cardiopulmonary monitoring may be achieved with a low-cost catheter version in combination with telemetric data exchange to remote hospitals serving as monitoring unit. On the other hand, a multisensory catheter in combination with advanced monitoring of perceived level of maturation and achievement states, personalized care may be possibly in more advanced hospitals. However, both solutions are expected to drastically reduce the number of false alarms in NICU monitoring and concurrently lower the monitoring burden on the result of lower resource allocation by the NICU and optimized NICU stay of preterm infants.

Smart Catheter Design and Manufacturing

The objective of the novel platform is to foster sustainable innovation in the development and production of smart diagnostic and therapeutic catheters through the patented design and manufacturing process. The design concentrates on thin-film, flexible printed electronic circuits (FPCB) with liquid crystal polymer (LCP) as biocompatible substrate, which integrates the multichannel and/or multimodal sensors or actuators as well as miniaturized amplifier or driving circuits. Analog-to-digital conversion placed closest to the sensor or multiple MCMs transducers are potential new features integrated into the next generation of active catheters. The
Microchip embedded in LCP

smart catheters will provide the interventionalist with new instruments that benefit from improved performance, higher resolution, and steel sensing and imaging capabilities. On the other side, the manufacturing process is based on a versatile thermobonding process that combines the LCP with the catheter tube. Complete encapsulation is possible with widely used medical-grade tube polymers, such as thermoplastic polyurethane or Pebax. Furthermore, the thermobonding process has been shown to allow a higher degree of automation compared to conventional catheter manufacturing, which will lower the production costs and consequently increase the rentability for legal or OEM catheter manufacturers, i.e. the principal customers of the LCP platform.

The goal of this research project is to extend the novel catheter platform with an enhanced LCP design process based on tailored FEM and CAD models, to increase the maturity of the thermobonding processes and consequently the manufacturing automation, and to announce the innovation in the research community and Medtech industry. A focus is also on the integration of catheters with active transducers into the platform as well as to the design and manufacturing of catheter demonstrators for representative clinical applications.

Packaging for a Microchip-based Multwell System

Available instruments for cell-based studies are not suited to exploit the potential offered by promising and recently introduced biotechnologies like human stem cells and 3D tissues, such as brain organoids, i.e. lab-grown miniature organs.

The goal of this project as research collaboration with 3Brain and CSEM is to develop a new platform that delivers unrivaled brain-on-chip phenotypic assays in 24-well format. Thanks to XCOO electrodes integrated per well and the BioSignal Processing Unit, the multiwell device features 24 simultaneous read-out sensors. The aspirated packaging based on Liquid Crystal Polymer (LCP) will fuse the microchip with the readout circuits and the well frames in a semi-automatic process that may reduce both electrical and leakage failures. While the environment will be controlled by the readout instrument (T, humidity, CO₂), new plate inserts will ensure precise sample positioning during both manual and automated operations.

The platform aims at revolutionizing preclinical drug discovery with a high-throughput microchip-based multiwell system. By integrating state-of-the-art microchips into each of the wells that make up a multiwell plate, the system will deliver in situ processing power and data intelligence. Integrated intelligence is a remarkable distinction from other products in the preclinical market, which are purely based on plastic passive plates. The new packaging based on LCP has the potential to reduce failure rates and consequently improve yield and cut production costs.

Capillary Driven Image Flow Cytometry for Blood Cell Analysis

Conventional flow cytometry is routinely used in clinical practice for counting total blood cells and in particular white blood cell sub-types to gain insight into the health of patients. We work on a point-of-care-based solution for image-based flow cytometry method to determine the complete blood cell count. A capillary-driven microfluidic chip is used, which has the advantage over conventional flow cytometry systems in terms of its small size, mechanical simplicity, and robustness, making it suitable for use in portable point-of-care devices.

Our approach measures WBCs without lysing the RBCs, enabling a different WBC count in whole blood, while investigating the RBC as well. To distinguish WBCs in the large bulk of RBCs, fluorescence microscopy methods typically applied to blood smears are used. Having algorithmically identified the individual WBCs, they are classified into three target WBC subgroups based on the difference in their fluorescent spectra and the different ratio of average red to green intensities, as can be done with the specific fluorescent acridine-orange staining that has been used. A scatterplot of the average red-green channel values for the detected cells of 2 μL of blood is shown. Three clusters can be seen, corresponding to the three WBC classes. The contours of the calculated three-component gaussian mixture model are superimposed.

Scatterplot of cell-averaged red and green values of all WBC detected in 2 μL of blood that has flown through the microfluidic channel. Contour lines represent a three-component gaussian mixture model that are superimposed to determine the three major sub-types of WBC.

Selected Publications


Optics Laboratory
Institute for Human Centered Engineering

Research Partners
Partner – SRT
Sebastian Wolf, Department of Ophthalmology, Inselspital, Bern University Hospital
Martin Zinkernagel, Department of Ophthalmology, Inselspital, Bern University Hospital
Chantal Dyal, Department of Ophthalmology, Inselspital, Bern University Hospital
Volker Enzmann, Department of Ophthalmology, Inselspital, Bern University Hospital
Boris Viktor Stanzel, Eye Clinic Sulzbach
Eric Odenheimer, Meridian AG
Tilmann Otto, Heidelberg Engineering GmbH
Partner – Corneal Collagen Fiber Distribution
H. Studer, Optimo Medical AG
Partner – Corneal Tissue Ablation
Ch. Rathjen, Ziemer Ophthalmic Systems AG
T. Feuser, Institute of Applied Physics, Bern University
M. Ayser, Institute of Applied Physics, Bern University

Research Profile
Optical Coherence Tomography and Laser Tissue Interaction
The Optics Laboratory of the HuC.E Institute focuses on optical coherence tomography (OCT) and laser tissue interaction. The laboratory equipment includes various OCT devices as well as a complete set of optoelectronic measuring equipment and opto-mechanical basic materials. Both spectral-domain (SD-OCT) and swept source (SS-OCT) systems at all common measuring devices to perform initial ex vivo experiments and to provide proof of concept.

The biomechanical properties of the cornea, such as the shape and the strength, arise largely from the precisely organized corneal collagen fibrils structure. The exact knowledge of collagen distribution in the cornea is crucial for accurate patient-specific modeling and surgery planning. Polarization Sensitive Optical Coherence Tomography, on the other hand, may have the capability to indirectly reveal the underlying highly organized collagen structure by detecting its birefringent properties. This information may serve as valuable patient-specific input for surgery planning.

Our research infrastructure and expertise enable us to develop dedicated measuring devices to perform initial ex vivo experiments and to provide proof of concept.

Pulsed Laser for Corneal Tissue Ablation
In ophthalmology, pulsed 4f (165 mm) or up-converted solid-state (210 mm and 235 nm) lasers are used for refractive surgery because the absorption coefficient of corneal tissue in the deep ultraviolet is very high. For this project, the main objectives are to develop a beneficial UV ablation laser based on different laser technologies then meanwhile establish for, and to investigate the impact of the temporal pulse shape on the ablation results.

Measuring Corneal Collagen Fibre Distribution Using Polarisation-Sensitive OCT
Today’s operation planning for arcuate keratotomy to correct astigmatism during cataract surgery depends on nomograms, statistical diagrams, and the assessment of the surgeon. Unfortunately, the patients are often not satisfied with the visual outcome and still require distance glasses. To overcome this issue, Opimo Medical AG developed the software Optimeyes for the patient-specific simulation, optimisation and planning of cornea surgeries based on a mechanical FEM model and unique algorithms.

Our research infrastructure and expertise enable us to develop dedicated measuring devices to perform initial ex vivo experiments and to provide proof of concept.

Pulsed Laser for Corneal Tissue Ablation
In ophthalmology, pulsed 4f (165 mm) or up-converted solid-state (210 mm and 235 nm) lasers are used for refractive surgery because the absorption coefficient of corneal tissue in the deep ultraviolet is very high. For this project, the main objectives are to develop a beneficial UV ablation laser based on different laser technologies then meanwhile establish for, and to investigate the impact of the temporal pulse shape on the ablation results.
Using different laser technologies allows also for achieving different laser wavelengths than the above mentioned. However, this implies that the optical properties at potential wavelengths are known, especially the corneal absorption coefficient, which is fundamental for the ablation processes. In the past, several groups have published measured absorption coefficients, yet the reported values vary by an order of magnitude. In order to 1) identify reasons for such large variations and 2) to provide the absorption coefficient at other than the three commonly used wavelengths, we first performed ellipsometry on porcine cornea in the wavelength range between 185 nm and 250 nm (Fig. 1). Specifically, we studied the temporal evolution of the absorption coefficient after enucleation for different storing and preparation conditions. We found that tissue degradation leads to a decreasing absorption coefficient irrespective of storage or preparation protocol. The almost linear decrease during the first nine hours post mortem allowed us to extrapolate the absorption coefficient to the time of death and to establish the in vivo absorption coefficient of porcine cornea between 185 nm and 250 nm. The findings will be published in the next issue of the Journal of Biomedical Optics.

For precise tissue ablation, a wavelength possessing a small optical penetration depth is required to confine the energy deposition to a small volume. However, to maximize the temperature, it is also required that thermal diffusion during the irradiation time is minimal (thermal confinement). Further, the ablation threshold will be decreased for minimal stress propagation during the irradiation time (stress confinement). Current ablation laser systems use a pulse duration of 10-20 ns. Accordingly, stress confinement for ablation lasers in the deep UV range is off by a factor of $>20$, while thermal confinement is undercut by a factor of $>150$. The impact of the UV pulse duration on the ablation result was never investigated for corneal tissue in the ns region, and an impact of the temporal pulse shape is expected as well, as demonstrated in literature for temporal Airy pulses in the ps region [N. Götte et al., Optica, 3(4), 389 (2016)].

The development of the UV ablation laser that allows for investigating these dependencies is in progress. The temporal pulse width and shape will be tuneable within 1 ns to 500 ns and a UV pulse energy $>0.5$ mJ is anticipated.

Selected Publications


Introduction

Orthosis System MOWA (modular walking)

We concentrate our development and research activities on system integration and electronic and software.

We have knowledge and experience in various engineering disciplines to develop specific solutions to challenges arising in medicine and biology. We concentrate our development and research activities on system integration and electronic and software.

Pascual Brunner, Medical Director MaschineMD, Head of Orthoptics, University Hospital Bern

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Pascual Brunner, CEO MovementSciences AG

The HuCE Biomedical Engineering Lab in a Nutshell

We have knowledge and experience in various engineering disciplines to develop specific solutions to challenges arising in medicine and biology. We concentrate our development and research activities on system integration and electronic and software.

Orthosis System MOWA (modular walking)

Introduction

People suffering from foot drop have an increased risk of falling. Often, limited movement in one joint is compensated for by excessive movement in other body parts. This can result in further complications due to overload. As a treatment, the foot is stabilized with a rigid orthosis at the cost of range of motion. The novel MOWA orthosis (Fig. 1) is less rigid and allows more freedom of movement while still providing enough support to the user for a smoother gait.

A novel 3D optical method, for example range stereophotogrammetry (RST), is a less expensive, non-ionizing technique that estimates deformity-related changes of the patient’s back using only light as a medium and thus allowing the investigation of the external shape and insights to the deformity of the spine. Figure 2 shows the assessment of the spine based on 3D surface measurements using the ScolioSIM tool, which outputs the spatial position and rotation of each vertebrae.

Today, however, there is no system available allowing for radiation-free, simple, fast, affordable, and dynamic (4D) measurements. Therefore, in this innovative project, the BFH researches the possible 3D scanning methodologies that can be used in such a device and develops a low-cost prototype for capturing 3D body images of the human back. In Figure 3, an evaluation test setup is shown in which different 3D measurement technologies are investigated for their suitability to scan the human back.

Surface Topography Measurements

The current gold standard for the clinical assessment of scoliosis, known as EOS imaging, involves X-ray imaging in the sagittal and frontal plane while the patient is upright standing. To monitor the progression of the pathology and to assess treatments or surgery outcome, patients often undergo repeated X-ray imaging, resulting in repeated exposure to potentially harmful ionizing radiation. A novel 3D optical method, for example range stereophotogrammetry (RST), is a less expensive, non-ionizing technique that estimates deformity-related changes of the patient’s back using only light as a medium and thus allowing the investigation of the external shape and insights to the deformity of the spine. Figure 2 shows the assessment of the spine based on 3D surface measurements using the ScolioSIM tool, which outputs the spatial position and rotation of each vertebrae.

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Moving Spine

Introduction

Musculoskeletal disorders in the spine are the main cause of age-related loss of autonomy and generate very high healthcare costs. The Moving Spine device is an intelligent and portable rehabilitation and diagnostic device on which the patient lies. It can then replicate the movements of walking in the spine and treat and document its rotational capacity. Based on its diagnostic function, it collects and analyzes data, self-regulates in real time, and thus digitizes and personalizes the rehabilitation of the spine, leading to an increase in autonomy and a decrease in healthcare costs.

Methods

We monitor and process several device-specific parameters in order to automate, personalize, and individualize the treatment with Moving Spine. We further develop and implement a novel pressure sensor matrix, which enables an additional monitoring of the pressure distribution in real time to draw valuable diagnostic conclusions and adapt the treatment accordingly.

Outlook

The novel hardware and software will be implemented in a new prototype. A number of trials will follow to test and optimize the treatment further.

The modular MOWA orthosis for patient-specific care

BIOSKOP – 3D body imaging

The novel hardware and software will be implemented in a new prototype. A number of trials will follow to test and optimize the treatment further.

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The modular MOWA orthosis for patient-specific care

BIOSKOP – 3D body imaging

The novel hardware and software will be implemented in a new prototype. A number of trials will follow to test and optimize the treatment further.
Selected Publications


In the Computer Perception and Virtual Reality Lab, we deal with the analysis and synthesis of 2D and 3D digital images and their use in robotics and human-machine interaction. Our research lab focuses on applied research and development on image and video data analysis as well as 3D data visualization and interaction in virtual space. With the latest visualization techniques, complex data can be processed in a novel way and made intuitively accessible. Among other things, we use these methods to simplify human-machine interactions.

**Agile Robotic System for High-Mix Low-Volume Production**

Traditional automation is not profitable for high-mix low-volume production. The project’s goal is to develop an intuitive yet flexible automation system that allows companies to develop their own automation solutions in a profitable way.

**Situation**

In Switzerland, a lot of work is still done manually. In many cases, automating these tasks would decrease production costs and allow prices to compete. However, although technically possible, traditional, fixed automation solutions for assembly tasks are not economically viable for companies with a high-mix low-volume production, meaning the lot sizes are small, with a large product diversity and high-quality requirements. In addition, the system needs to be rapidly reallocated to new tasks according to production needs and flexible enough to allow for the integration of new products. Instead of relying on these traditional high-end solutions requiring external expertise, the company involved in the research project wishes to develop their internal know-how to be able to develop ad hoc, flexible automation solutions.

**Course of Action**

To keep the flexibility of manual work in the automation solution, a production system needs to be developed that is, in this case, a smart human-machine interface (HMI) that enables workers to efficiently use the robotic solution according to their needs to improve productivity. Since the worker is no robotic expert, the system needs to be smart; it needs to be able to translate human-defined goals into actual robotic trajectories. To achieve this, the researchers propose developing a digital twin of the workspace. Since the robotic system needs to be flexible, the workspace is unknown and needs to be modeled online according to sensory information and a priori knowledge. The digital twin is generated in real-time based on the fusion of sensory information (cameras and lidar) and a priori information (e.g., CAD files, process descriptions, etc.). A probability model is associated with the different recognized objects, and active perception is used to improve performance. An interface allows the user to add new objects and define the parameters of a set of pre-defined algorithms for object recognition and localization. In order to simultaneously address the question of flexibility and intuitiveness, the HMI is based on a three-layer architecture. The architecture allows for programming of new tasks without coding, but also automatically creates the associated intuitive interface for operators.

**MuscleModel**

This project led by the division of physiotherapy aims at developing an artificial intelligence-based approach for the automated extraction of patient-specific information on spinal muscle morphology from medical images. The successful treatment of spinal pathologies depends on well-founded knowledge of the disease mechanisms. Unfortunately, many spinal pathologies are not sufficiently well understood, and treatment effects are controversial. This is partially due to the fact that relevant biomechanical parameters such as segmental compressive forces can only be measured in vivo using highly invasive approaches. Due to these technical advances in the past two decades, this can now be achieved using complex digital technologies such as musculoskeletal (MSK) modeling.

However, MSK modeling is only accurate if the models are patient-specific, particularly in terms of muscle properties. To adjust such parameters, we usually rely on manually segmented CT scans, but these processes are highly time-consuming and therefore not applicable for research on larger samples or for everyday clinical practice.

One possible way to speed up these processes might be to use an artificial intelligence (AI) approach such as deep learning, which uses biologically inspired neural networks that enable computers to learn from observational data. A well-trained neural network could reduce the time needed for image segmentation from several hours to a couple of seconds per patient.

**Research Partners**

Samuel Hilger, CDO, Bien-Air Dental SA
The HuCE Robotics Lab in a Nutshell

We have knowledge and experience in robotics and mechatronics to develop specific solutions to challenges arising in medicine, rehabilitation, everyday life with disabilities, and manual industrial production. We concentrate our development and research activities on system integration and development of functional prototypes, in particular in the area of collaborative robotics.

Body Motion Analysis with 6D Tags and 2D Cameras

Three-dimensional Motion Capture (MoCap) can be useful in various stages of the rehabilitation process, as well as in diagnostics, sport sciences, and ergonomic analysis. Gait assessment is the most widely used application. MoCap also allows for objective, more informed decision-making. High costs are the primary factor preventing a broader application in clinical routine. Therefore, it is desirable to develop more affordable alternatives.

In this project phase, an affordable application was developed based on printable tags and regular 2D cameras. The application is capable of analysing a squat knee flexion and a hop-test and was evaluated against a state-of-the-art 3D MoCap system from Vicon. Further development will enable the application to run on hand-held tablets and smartphones and be extended to general gait analysis and arm motions.

A Hand Exoskeleton for Somatosensory and Motor Training

A hand exoskeleton was built that provides enough range of motion and force to move the fingers and execute common hand gestures, such as grasping an object or tapping the fingers on a flat surface. It provides finger position tracking to analyse the finger movements and recreate the hand in a 3D environment, where the patient could grasp virtual objects and feel them pushing back. The device may be used in combination with electrical stimulation and is hence made to be electrically noise-proof. The weight and volume of the device are minimized to provide a seamless experience to the patient and is quick to equip and remove it. Finally, the device covers as little surface of the hand's palmar side as possible to maximize natural somatosensory feedback. The focus was set on building a functional prototype with mechanical, electronic, data processing, and comfort aspects that could be improved upon.

Selected Publications

[1] Lara Piers (Master Thesis, BME)
Towards Gait Analysis with 6D Tags and 2D Cameras:
Setup and Analysis of a Hop Test
Supervisors: Gabriel Gruener, Patric Eichelberger, Heiner Baur
Institutions: Bern University of Applied Sciences, Institute for Human Centered Engineering
Examiners: Patric Eichelberger, Gabriel Gruener

Development of a Hand Exoskeleton for Somatosensory and Motor Training
Supervisors: Gabriel Gruener, Laura Marchal-Crespo
Institutions: Bern University of Applied Sciences, Institute for Human Centered Engineering
Examiners: Gabriel Gruener, Laura Marchal-Crespo
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The HuCE Sensors Lab in a nutshell (150–200)
Our laboratory develops sensor systems in the medical, sports, and industrial fields. We can integrate existing sensors into your application. In some cases, when no industrial sensor is available, we design sensors to best suit your application. We focus on mechanical sensors, i.e., force, pressure, tactile, and distance sensors, accelerometer, gyroscope, magnetic sensors, or IMU sensors. We also perform critical measurement for quality control or production monitoring, for example with a 2D laser Doppler vibrometer.

The group also has a strong expertise in applied mathematics, for example hyperspectral imaging, deep learning, machine learning, partial differential equations, or inverse problems.

Load Sensor for in vivo Data Acquisition
The Ligamys implant used for anterior cruciate ligament (ACL) rupture healing was successfully introduced in the medical device market by Mathys Ltd. in 2012. Despite the clinical success, a growing need for a smaller implant is reported from the market. To further decrease implant size and optimize the rehabilitation process, in vivo data of the healing process is needed. Therefore, the goal of the QuaLiHeal project (Innosuisse 28867.1 IP-LS) was to find the right sensor principle to be integrated into an instrumented Ligamys. The Sensors Laboratory together with the Switzerland Innovation Park Biel/Bienne and the research group Biomechanical Engineering (BME) at ZHAW were involved in the development of various innovative solutions in the minimal space available within the implant. The developed sensor system is now ready to be integrated within an ACL-healing implant and will be capable of measuring in vivo loads wirelessly. Once the verification and validation are completed, it can be used in a clinical study to generate the necessary data to better understand and improve the ACL healing and rehabilitation processes, as well as minimize the implant size.

Sensor system capable of measuring in vivo loads wirelessly

2D Hand Grip Sensor
A cylindrical sensor has been developed to accurately measure position and pressure of all fingers of a complete hand. Very detailed studies about the biomechanics of the hand are now possible. This hand grip sensor can be used for diagnostics as well as a control tool after a hand operation to measure the rehabilitation process. It provides a much more detailed picture of the biomechanical activity and of the hand and all fingers than the actual devices on the market. A high-resolution tactile sensor and a dedicated readout electronic have been developed, allowing 3,000 pixels representing a hand imprint to be delivered in real time. This wireless device transmits data to a smartphone or other smart device for direct analysis. It can also be shared or stored. Data analysis algorithms have also been developed to facilitate the diagnosis. This project has been performed with EoSwiss Ltd. in Geneva. A patent application for this device has been submitted, and a clinical study is ongoing.

Laser Doppler Interferometer
The Laboratory for Sensor Technology and Applied Mathematics has a high-end PSV-500 Scanning Vibrometer that allows non-contact vibration mapping and analysis of vibrating structures. This laser Doppler vibrometer allows for determination of vibrating velocity or displacement over areas ranging from mm² to m². It has applications in acoustics, structural dynamics, and ultrasound measurement, for example.
The Institute for Rehabilitation and Performance Technology (IRPT) uses methods and technologies from sports and exercise physiology to improve rehabilitation outcomes for people after they have experienced accidents or illness. The IRPT specializes in the areas of cardiopulmonary and neurological rehabilitation after stroke or spinal cord injury. Feedback control for physiological systems, as well as automation and control of training equipment, is essential for the rehabilitation of people with various neurological problems including stroke and spinal cord injury.

The IRPT has an excellent infrastructure for research including a dedicated lab within Reha Rheinfelden. Robotics-assisted devices, including gait-rehabilitation robots and tilt tables, have been extended to facilitate application for cardiopulmonary rehabilitation. This involves biofeedback of patient effort, volitional control of mechanical work rate, together with automatic feedback control of physiological outcome variables, including heart rate, oxygen uptake, and metabolic work rate. A key feature of the group's work is the employment of methods from sports and exercise physiology and the adaptation of these protocols to the rehabilitation setting. Working closely with key clinical collaborators, these approaches are applied in the clinic for rehabilitation of people with various neurological problems including stroke and spinal cord injury.

The IRPT has an excellent infrastructure for research including a dedicated lab within Reha Rheinfelden. Robotics-assisted devices include exoskeletons (Lokomat, Hocoma AG) and end-effector (G-EO System, Reha Technology AG), and a robot-assisted tilt table (H. Rigo, Hocoma), and an adaptive leg robot (Allergo, Dynamic Devices AG). The institute also has modern cardiopulmonary monitoring systems.

The Sports Engineering Group focuses on interdisciplinary research on advanced feedback control methods for treadmill and cycle-ergometer automation and on basic research in the area of physiological heart rate variability (HRV). The work builds on multidisciplinary expertise in engineering, neurosciences, sports and exercise science, and medicine. This allows professionals to address prevention and management of the progressive secondary complications of spinal cord injury, stroke, and a wide range of further neurological conditions. This approach promotes neurological recovery for improved motor control, sensation, and autonomic function.

The Rehabilitation Engineering Group develops new technical devices and extends the functionality of existing products. Recent developments include novel rehabilitation devices for adults and children with neurological impairment, involving close collaboration with the BFH SCI-Mobility Lab and the company GBY AG. The group develops recumbent cycling systems for people with complete lower-limb paralysis. These systems use functional electrical stimulation (FES) of the paralyzed muscle groups. The IRPT participated in the FES Bike Race at Cybathlon 2016 (bronze medal winner) and 2020 (fourth place).

The following selection of research and development projects gives an overview of the spectrum of research activities of the Sports Engineering Group:

- Investigation of the characteristics of heart rate variability, dynamics, and control during exercise, currently funded by the Swiss National Science Foundation (SNSF).
- Feedback control of heart rate, oxygen uptake, or metabolic work rate during treadmill and cycle-ergometer exercise.
- Automatic position control for walking and running on a treadmill.

The IRPT labs are equipped with high-performance treadmill (Fenius and Pulsar, Hypnosys sports and medical gmbh) and cycle-ergometer (LCT, Monark Exercise AB) technology. Various position monitoring sensors, including ultrasound and laser, and a real-time communication protocol give complete control over the treadmill/ergometer through a computer. The institute also has modern cardio-respiratory monitoring systems for online breath-by-breath monitoring, ECG recording, and HRV analysis.

The IRPT team at the FES Bike Race, Cybathlon 2016.
Selected Publications


Movement Biomechanics and Physiotherapy

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Technical Head of Bern Movement Lab
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Institute Members

Clinical & Research Partners
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Philippe Bächler, HARVARD Center, University of Bern, Bern
Carol-Claudius Zander, Orthopaedic Department, UNIBE, Basel
Moritz Demi, Department of Orthopedic Surgery, Bern University Hospital, Bern
Emanuel Liechti, Department of Orthopedic Surgery, Bern University Hospital, Bern
Jasmin Busch, DIPR, Bern University Hospital, Bern
Dennis E. Anderson, BEPMG, Harvard Medical School, Boston, MA, USA
Lennart Scheys, IROIT, KU Leuven, Leuven, Belgium
Philipp Henle, Knee Surgery & Sports Traumatology, Sonnenhof Orthopaedic Center Bern
Anja Hirschmüller, Athlus Swiss Spinecenter, Rheinfelden
Annette Kuhn, Department of Gynaecology and Obstetrics, University Hospital Bern
Andreas Reinhard, Ortho-Team AG Bern
Martin Verra, Department of Physiotherapy, University Hospital Bern

Research Profile
The Applied Research and Development Physiotherapy of the School of Health Professions at the Bern University of Applied Sciences focuses on movement biomechanics in a physiotherapy context. We analyse human movement in relevant daily life activities and situations. The Bern Movement Lab is equipped with essential kinematic, kinetic, and neuromuscular analysis methods to provide an excellent environment for the Bern Movement Lab. Simulating spinal loading using motion capture-driven biomechanical parameters.

Neuromuscular Control (Heiner Baur)
The lower extremity is involved in all movements of daily life and physical activity. We focus on the influence of internal (age, gender, etc.) and external factors like training parameters or pathological conditions on dynamic movement patterns. The general methodological paradigm combines the pure biomechanical view with a focus on the organization and adaptation of the neuromuscular system. Currently, the group is working on the acute and long-term tolerance of anterior cruciate ligament (ACL) injury on knee stability and knee function in general to develop rehabilitation strategies and preventive measures. Beside mechanical stability, adequate neuromuscular control secures necessary joint stability and protection. The evaluation of sensorimotor control in functionally relevant situations may therefore serve as a key element in functional diagnostics. The extraction of objective outcomes can help to rate rehabilitation progress or return-to-sport decisions after rehabilitation. The methodological setup can potentially be used to check the effects of orthotic devices or to investigate the effects of different surgical reconstruction techniques.

Spinal Movement Biomechanics (Stefan Schmid)
The Spinal Movement Biomechanics Group focuses on the identification of biomechanical parameters that help clinicians better understand musculoskeletal spine disorders and develop new or more effective prevention and treatment strategies. Using optical motion capture, surface electromyography, and personalized musculoskeletal modeling techniques, we are conducting laboratory-based experimental research to investigate kinematics, segmental loading, and individual muscle forces of the spine during functional activities in different patient populations. Our current focus lies on spinal deformities and non-specific chronic low back pain (CLBP).

Foot Biomechanics and Technology (Patric Eichelberger)
The Foot Biomechanics and Technology Group is concerned with gaining a better understanding of foot biomechanics and related complaints and evaluating or developing therapy options with a focus on applying current technology to the assessment and therapy of the locomotor system and orthotics. It’s part of our mission to bring the lab to patients, physiotherapists, clinicians, or orthopedic technicians. We aim to apply the latest technological developments to transfer objective assessment of movement biomechanics and neuromuscular control from the laboratory into the clinical routine to further build evidence in physical therapy. Currently, the group is working on the topic of relationships between plantar pressure, foot and lower extremity kinematics and associated complaints with the overall goal of optimizing foot orthotics and physiotherapeutic interventions.

Pelvic Floor and Continence (Irene König)
The mean prevalence of stress urinary incontinence (SUI) in women is 37%. SUI is clearly underestimated by public opinion, mainly because in a taboos subject. Two thirds of women suffering from SUI reported a negative impact on quality of life since the involuntary urine leakage affects their physical and psychosocial well-being while putting a burden on their economic situation. Even young women are affected, often in sports, but especially after delivery. From a scientific point of view, physiotherapy is the first-line treatment in this field, as its effectiveness has been thoroughly evaluated. In our Pelvic Floor and Continence Group we want to further improve and optimize physiotherapy related to SUI. We investigate diagnostic techniques, interventions, and therapy plans regarding patient information, perception, and movement as well as strengthening of the pelvic floor muscles (PFM) in isolated contractions and complex whole-body movements. Specifically, we focus on the neuromechanical aspects of PFMs, i.e., the activation and contraction behavior during voluntary and involuntary, reflexive contractions, which are essentially important to guarantee continence.

Public Health and Physiotherapy-Related Health Economics (Jan Taeymans)
The group currently focuses on a joint collaboration (GFW·WEAVE) with the University of Applied Sciences and Arts of Southern Switzerland (SUPSI) and the Vrije Universiteit Brussel (Belgium) where the project’s focus is on chronic low back pain. The group focuses on the effects of different surgical reconstruction techniques.

Foot Biomechanics and Technology
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and physical exercises) to current best evidence rehabilitation (pain neuroscience education plus cognition-targeted exercise therapy) for overweight or obese people with CLBP. An international, multi-center randomized controlled trial comparing a behavioral weight reduction program combined with pain neuroscience education and cognition-targeted exercise therapy versus pain neuroscience education and cognition-targeted exercise therapy alone will be conducted. The primary outcome is pain and the primary endpoint was chosen at 12 months follow-up; secondary outcomes include healthcare use and daily functioning. More specifically, it includes innovative research targeting chronic low back pain rehabilitation as well as a health economic evaluation. The results of this study will apply to rehabilitation practice, public health, and health economics.

Work Disability Prevention (Maurizio Trippolini)

This group’s research focuses on disability prevention strategies, enhancing recovery in musculoskeletal disorders, healthcare effectiveness, work disability, and methods to achieve safe and sustained return to work. Specific topics include healthcare for workers with musculoskeletal injury in compensable settings, development and evaluation of self-reported assessments, and performance-based tests that measure physical functioning and psychosocial factors. Research methods include quantitative, qualitative, and mixed-methods of observational studies in primary care or rehabilitation. Implementation of findings from clinical research into practice and continuing professional education are at the core of our motivation.

Selected Publications


Structure of Courses

Structure of Courses in the Master’s Program

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

As of fall semester 2008, all courses were grouped in a strictly modular way to enhance both the clarity and flexibility of the curricular structure. The new curriculum seeks to guide the students through their studies in a better way by adding an elective part to the major modules, which formerly had consisted exclusively of mandatory courses. Besides, the curriculum was expanded by a number of new specialized courses as well as an additional major module called “Image-Guided Therapy.”

Adaptations in the legal framework of the master’s program now offer more flexibility in the design of courses and modules, thus providing the basis for a second fundamental restructuring of the curriculum as of fall semester 2013. In particular, a module called “Complementary Skills” was introduced. In addition, the list of mandatory courses in both basic and major modules was revised. More recently, in fall semester 2017, a module “Preparation Courses” was created. The courses in this module are intended to fill gaps regarding prerequisites for basic and advanced courses in the master’s program Biomedical Engineering.

After the above preparation, the curriculum was again restructured as of fall semester 2021. The focus is now on a more practice-oriented education, which is achieved primarily through the newly created “BME Laboratories.” These will be conducted in the second semester in the research laboratories of the Institute of Biomedical Engineering at the University of Bern (IBME) and the Swiss Laboratories for Materials Science and Technology (Empa). In addition, thanks to the great commitment of the Institute of Biochemistry and Molecular Medicine, practical laboratories are now included in the course “Biological Principles of Human Medicine,” which illustrate and complement the theoretical lectures.

The Curriculum

Duration of Studies and Part-Time Professional Occupation

The full-time study program takes four semesters, which corresponds to 120 ECTS credits, one ECTS credit being defined as 25-30 hours of student workload. It can be extended to a maximum of six semesters. When a student decides to complete the studies in parallel to a part-time professional occupation, further extension is possible on request. To support regular part-time work, mandatory courses take place (with rare exceptions) on only three days per week.

Preparation Courses

Diving into the interdisciplinary nature of the BME master’s program, our students come from various fields of study. Especially students with a non-engineering background – for example in medicine – do not fulfill all prerequisites for the courses of the master’s program. Therefore, introductory courses in MATLAB C++, programming, Electrical Engineering, Engineering Mechanics, and Material Science as well as the tutorial-based course “Selected Chapters in Mathematics” were introduced and allow us to create a tailor-made curriculum for these students. Students with a background in engineering, on the other hand, can select these courses freely if they feel the need to refresh some of the knowledge provided.

Basic Modules

The basic modules provide students with the necessary background to be able to fully understand the complex subject matter in the specialized courses. All students have to complete all courses in the Basic Modules Human Medicine, Applied Mathematics, and Biomedical Engineering. In the first semester, all mandatory courses belong to this group, whereas in the second semester, the courses from the basic modules make up approximately 20%.

Major Modules

The choice of one of three major modules Biomechanics, Electronic Implants, or Image-Guided Therapy after the first semester constitutes the first opportunity for specialization. Approximately one third of the major modules consist of mandatory courses. In the elective part of the major module, the student is allowed to select every course from the list of courses in the master’s program, giving rise to a high degree of diversity and flexibility and allowing for numerous course combinations. However, this freedom makes it somewhat difficult for the student to make reasonable choices regarding professional prospects. This is why the responsible lecturers developed a recommended study plan to guide the students through the course selection process and to avoid organizational problems such as overlapping courses. If a student follows the recommended path, he or she can be sure to establish a sound professional profile.

Module “Complementary Skills”

Apart from the rapid development of technology itself, today’s biomedical engineers are increasingly challenged by complementary issues like ethical aspects, project planning, quality assurance and product safety, legal regulations and intellectual property rights, as well as marketing aspects. Language competence in English is of paramount importance both in an industrial and academic environment. This situation has been addressed for by the module called “Complementary Skills” where students are required to complete two mandatory courses (Innovation Management; Fundamentals of Quality Management and Regulatory Affairs) as well as 2-4 ECTS credits from the elective courses (Ethics in Biomedical Engineering; Scientific Writing in Biomedical Engineering; Clinical Epidemiology and Health Technology Assessment).

Master’s Thesis

The last semester is dedicated to a master’s thesis project on an individually suited topic in an academic research group at the University of Bern or the Bern University of Applied Sciences or, for particular cases, in an industrial research and development environment. As a rule, all 80 ECTS credits from the course program have to be completed, thus ensuring that the student is able to fully concentrate on the challenges imposed by existing research activities. The master’s thesis includes the thesis proposal, a thesis presentation and defense, as well as a one-page abstract for publication in the Annual Report of the master’s program.
The respiratory, cardiovascular, and musculoskeletal systems are the transport and structural bases for our physical activities, and their health have a profound influence on our quality of life. Lung diseases, cardiovascular diseases, musculoskeletal injuries, and pathologies are costly ailments facing our healthcare systems. Both in terms of direct medical costs and compensation payments related to loss of work.

In this module, students will gain a comprehensive understanding of the multi-scale organisation of the respiratory, cardiovascular, and musculoskeletal systems, combining knowledge from the cell, tissue, organ, to the body level. They will learn how to apply engineering, biological, and medical theories and methods to resolve complex problems in biomechanics and mechanobiology. Students will learn to draw connections between tissue morphology and mechanical response, and vice versa. Students will also gain the required expertise to apply their knowledge in relevant, practice-oriented problem solving in the fields of pneumology, cardiology, cardiovascular surgery, orthopaedics, dentistry, rehabilitation engineering, and pharmaceuticals. Most of the major companies in the fields of cardiovascular technology, orthopaedics, dentistry, rehabilitation engineering, and pharmacueticals are strongly represented within the Swiss medtech industry and have an ongoing demand for graduates of this major module. At the interface between biomedical engineering and clinical applications, graduates may also pursue careers related to the evaluation and validation of contemporary health technology, a cornerstone for future policies on the adoption of these new methods in the highly competitive healthcare domain.

Knowledge gained during the coursework highlights the multidisciplinary nature of this study focus area, encompassing the cell to body, the idea to application, and the lab benchtop to the hospital bedside. This knowledge is applied during the final thesis project, a project often with a link to a final diagnostic or therapeutic application. Examples of recent master thesis projects include lung alveoli array on chip, development of an in-vitro model of the lower urinary tract, personalized prediction of preterm newborn interventions, setup and analysis of a hop test, and development of a device for sensorimotor hand training.

Career prospects are numerous. Many students proceed to further postgraduate education and research, pursuing doctoral research in the fields of biomechanics, tissue engineering, lab-on-chip, or development of biomaterials.
Electronic implants are devices such as cardiac pacemakers and cochlear implants. Due to miniaturization and other developments, many new applications have become feasible, and this exciting area is growing rapidly. For example, cochlear implants provide people a sense of sound. These people were previously profoundly deaf or severely hard of hearing. Recently, researchers demonstrated that electronic retinal implants allow the blind to read large words.

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

In this module, students will gain a comprehensive technical and application-oriented understanding that will allow them to select, use, design, and optimize electronic implants and similar biomedical systems. Since the work on such complex systems is usually done in interdisciplinary groups, another important goal is that graduates are able to work and communicate in teams consisting of, for example, engineers, scientists, and medical doctors.

Specifically, students will learn about technology basics including intelligent implants and surgical instruments, biomedical signal processing and analysis, low-power microelectronics, wireless communications for medical devices, biomedical sensors, and microsystems engineering including MEMS technology. Application-oriented elective courses are also taught, e.g., cardiovascular technology, biomedical acoustics, biomedical laser applications, ophthalmic technologies, and diabetes management.

Students may already apply their knowledge as a part-time assistant in an institute and/or during their master's projects. After finishing the degree program, a wide variety of career paths is available ranging from research and development to project and product management. Many companies in Switzerland work in this field, and "traditional" implants manufacturers have recently become interested in electronic implants, for example, to measure forces in knee implants.

This major is open to all students in our master's program. However, typically, students have an engineering-related background such as electrical engineering, microtechnology engineering, systems engineering, mechatronics engineering, mechanical engineering, or computer science. Students have recently become interested in electronic implants, for example, to treat Parkinson's disease, obesity, depression, incontinence, hydrocephalus, pain, paraplegia, and joint diseases.

The Ligamys implant used for anterior cruciate ligament (ACL) rupture healing has been instrumented to be able to measure in-vivo loads wirelessly. This work was part of an Innosuisse project. The BFH (HUCE-SensorLab) together with the Swiss Innovation Park Biel and the HAFL were involved in the development of this innovative solution.

Image-Guided Therapy

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

Students of the IGT module will study the clinical and technical fundamentals of image-guided therapy systems. They will develop an understanding of currently applied clinical standards as well as an overview of the latest advancements in research. Successful students will be enabled to develop novel clinic-technological applications for complex medical procedures as well as improve existing approaches. This will be the foundation for successful careers both in the industrial and academic sector.

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

University of Bern
Christiane Albrecht, Prof. Dr.
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Claas Breidenbach, Prof. Dr.
Julia Bühler, PD Dr.
David Bormens, Prof. Dr.
Dieter Brzoska, Prof. Dr.
Philippe Büchler, Prof. Dr.
Jürgen Burger, Prof. Dr.
Ramona Duerer, Dr.
Peter Büllecker, Prof. Dr.
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Roch-Philippe Charles, PD Dr.
Marina Deng, Dr.
Sigrun Lick, Prof. Dr.
Pinho Fasano, Prof. Dr.
Cristian Fernández Palomo, Dr.
Gian Ferrari
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Nicolas Gerber, Dr.
Stephan Gerber, Dr.
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Olivier Guenat, Prof. Dr.
Walter Martin Senn, Prof. Dr.
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Alexandra Spörri, Dr.
Hubert Steinke, Prof. Dr.
Jürg Street, Prof. Dr.
Raphael Stern, Prof. Dr.
Mabio Vlamincka, Dr.
Stefan Weber, Prof. Dr.
Nicola Ween
Wilhelm Wimmer, Dr.
Soheila Zemati, Dr.
Marcel Zhuk, Prof. Dr.
Sandra Zyprek, Prof. Dr.

**Bern University Hospital (Inselspital)**
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Roland Wiel, Prof. Dr.

**Bern University of Applied Sciences**
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Christian Arnold, PD Dr.
Laura Marchi-Crespo, Prof. Dr.
Ines Markou, Dr.
Beatrice Minder
Stavroula Mougiakakou, Prof. Dr.
Aileen Naf
Tobias Net, Prof. Dr.
Samira Nienyde, Dr.
Dennis Noer, Prof. Dr.
Ludovica Parisi, Dr.
Christine Pfeiffer, Dr.
Jean Pascal Pflister, Prof. Dr.
Leonardo Pietrasanta
Clemens Raabe, Dr.
Raphael Raetz
Manfred Reyes, Prof. Dr.
Jean-Sébastien Rieutort, PD Dr.
Anne Rutjes, Dr.
Shahriar Saghazian, PD Dr.
Katerina Sahinoukova, PD Dr.
Norayn Schätz

**Number of New Students and Graduates**

![Number of New Students](image)

![Number of Graduates](image)

**Profession after Graduation: Activity after 1 (inner circle) and 5 years**

![Profession after Graduation](image)
### Completed Master's Theses in 2021

<table>
<thead>
<tr>
<th>Name</th>
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<th>Supervisor(s)</th>
<th>Institution(s)</th>
<th>Examiners</th>
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<td>Eylem Akalp</td>
<td>Modality Dependent Accuracy Analysis of Patient-Specific 3D Anatomy Modelling</td>
<td>Dr. Kate Gerber, MSc Hanspeter Hess</td>
<td>University of Bern, Stem Center for Translational Medicine and Biomedical Entrepreneurship</td>
<td>Dr. Kate Gerber, Dr. Guozong Zeng</td>
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<tr>
<td>Cyril Albrecht</td>
<td>Trajectory Planning for Robotic Thermal Ablation with overlapping Volumes</td>
<td>PKMs Bubisovici, Dr. Ivan Pasulczu</td>
<td>ARTORG Center for Biomedical Engineering Research, University of Bern</td>
<td>PKMs Bubisovici, Prof. Dr.-Ing. Stefan Neber</td>
</tr>
<tr>
<td>Raphael Andonie</td>
<td>Time-Adaptive Algorithms for Low-Power Medical Devices</td>
<td>Prof. Dr. ac. ETH, Dr. med. Reto Wildhaber</td>
<td>Bern University of Applied Sciences, Institute for Human Centered Engineering HUCIE</td>
<td>Prof. Dr. Marcel Jacomet. Prof. Dr. ac. ETH, Dr. med. Reto Wildhaber</td>
</tr>
<tr>
<td>Martin Bertsch</td>
<td>Targeted Drug Delivery in Ovoidontoma Mouse Models</td>
<td>Prof. Dr. Roch-Philippe Charles, MSc Javier Pareja</td>
<td>University of Bern, Institute for Biochemistry and Molecular Medicine</td>
<td>Prof. Dr. Roch-Philippe Charles, MSc Javier Pareja</td>
</tr>
<tr>
<td>Benjamin Bircher</td>
<td>Middle Ear Laser Doppler Vibrometry Assessment for improved Electroocochrography</td>
<td>Prof. Dr. Bertrand Dutuit, Klaus Schürch</td>
<td>Bern University of Applied Sciences, HUCIE, University of Bern, ARTORG Center for Biomedical Engineering Research</td>
<td>Prof. Dr. Bertrand Dutuit</td>
</tr>
<tr>
<td>Martin Boschbacher</td>
<td>Effect at Angiopoietin-1 and Angiopoietin-2 on Human (h) Progenitor Cells</td>
<td>Prof. Dr. Benjamin Gantenbein, Dr. Julián Guerrero</td>
<td>University of Bern, Department for Biomedical Research</td>
<td>Prof. Dr. Benjamin Gantenbein, Dr. Julián Guerrero</td>
</tr>
<tr>
<td>Pavel Boušek</td>
<td>Ex Vivo Validation of an Implantable Continuous Cardiac Monitor</td>
<td>Prof. Dr. Thomas Niederhauser, Svet Krause</td>
<td>Bern University of Applied Sciences, Institute for Human Centered Engineering HUCIE</td>
<td>Prof. Dr. Thomas Niederhauser, PD Dr. med. phil. Andreas Härberlin</td>
</tr>
<tr>
<td>Thomas Buchegger</td>
<td>Speech Recognition for Parkinson Patients in an Instrumented Apartment</td>
<td>Prof. Dr. Stephan Gerber, Pascal Reuse</td>
<td>University of Bern, ARTORG Center for Biomedical Engineering Research</td>
<td>Prof. Dr. Tobias Nef, Dr. Stephan Gerber</td>
</tr>
<tr>
<td>Linard Büchler</td>
<td>Assessment of Cell Viability and Metabolic State using Autofluorescence Spectroscopy inside Cell Bulk</td>
<td>Karl-Heinz Seibmann, Prof. Christopher Meier, Prof. Dr. Torsten Ochsenreiter</td>
<td>Bern University of Applied Sciences, Institute for Human Centered Engineering Bern University of Applied Sciences, Institute for Human Centered Engineering Bern University of Applied Sciences, Institute for Human Centered Engineering Bern University of Applied Sciences, Institute for Human Centered Engineering</td>
<td>Karl-Heinz Seibmann, Prof. Christopher Meier</td>
</tr>
<tr>
<td>Nina Chatelain</td>
<td>Mechanical and Biological Validation of a Novel Microvascularite-on-Chip Device</td>
<td>Prof. Dr. Mauricio Reyes</td>
<td>Bern University of Applied Sciences, Institute for Human Centered Engineering Bern University of Applied Sciences, Institute for Human Centered Engineering Bern University of Applied Sciences, Institute for Human Centered Engineering</td>
<td>Prof. Dr. Mauricio Reyes. PD Jahn Anderson-Garcia Henao</td>
</tr>
<tr>
<td>Carolina Duran</td>
<td>Confounder-Free Deep Learning Training for Brain Tumour Segmentation</td>
<td>Prof. Dr. Mauricio Reyes</td>
<td>Bern University of Applied Sciences, Institute for Human Centered Engineering Bern University of Applied Sciences, Institute for Human Centered Engineering Bern University of Applied Sciences, Institute for Human Centered Engineering</td>
<td>Prof. Dr. Mauricio Reyes. PD Jahn Anderson-Garcia Henao</td>
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<tr>
<td>Lukas Geisshäuser</td>
<td>In-Vivo Setup for Temporal Interference Stimulation</td>
<td>Prof. Dr. Thomas Niederhauser, MSc Elisa Maria Kaufmann</td>
<td>Bern University of Applied Sciences, Institute for Human Centered Engineering HUCIE</td>
<td>Prof. Dr. Thomas Niederhauser, PD Dr. med. Andreas Härberlin</td>
</tr>
<tr>
<td>Katrin Gfeller</td>
<td>Design of an End-Effector Based Arm-Swing-Device for Gait Training</td>
<td>Prof. Dr. Kenneth Hunt, Dr. Juan Fang</td>
<td>Bern University of Applied Sciences, Institute for Rehabilitation and Performance Technology</td>
<td>Prof. Dr. Kenneth Hunt, Dr. Juan Fang</td>
</tr>
<tr>
<td>Rafael Gfeller</td>
<td>A Bionically Transplantation Device for Reduction of Complications after Pressure Injuries Surgery</td>
<td>Prof. Dr. Jivko Stoyanov Ph.D, Dr. Alessandro Bertolo Ph.D.</td>
<td>Swiss Paraplegic Research, Nottwil</td>
<td>Prof. Dr. Jivko Stoyanov Ph.D, Prof. Dr. Benjamin Gantenbein Ph.D.</td>
</tr>
</tbody>
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Michael Herrman  
Deep Learning based Segmentation and Fat Fraction Analysis of the Shoulder Muscles using quantitative MRI  
Supervisors: Dr. Nicolas Gerber, MSc. Hanspeter Hess  
Institution: University of Bern, sitm Center for Translational Medicine and Biomedical Entrepreneurship  
Examiners: Prof. Dr. Kate Gerber, Dr. Nicolas Gerber

Eco Su Ildiz  
Lack of Endothelial PECAM-1 Enhances Extravasation of Brain Seeking Melanoma Cells Across the Blood-Brain Barrier in vivo  
Supervisor: Prof. Dr. Ruth Lyck  
Institution: University of Bern, Theodor Kocher Institute  
Examiners: Prof. Dr. Ruth Lyck, Dr. Giuseppe Locatelli

Marc Ilic  
Development of Stentless Coronary Arterial Phantom for a Coronary Artery bench Simulator  
Supervisors: MSc Cornelia Amstutz, Prof. Dr. Jürgen Burger  
Institution: University of Bern, sitem Center for Translational Medicine and Biomedical Entrepreneurship  
Examiners: MSc Cornelia Amstutz, Prof. Dr. Jürgen Burger

Camille Kaufmann  
Development of an Ultrasonic Scalar for Dental Calculus Removal  
Supervisor: Martin Hofmann  
Institution: University of Bern, sitm Center for Translational Medicine and Biomedical Entrepreneurship  
Examiners: Prof. Dr. Jürgen Burger, Martin Hofmann

Simon Krebs  
A Novel Device to Measure Applied Forces During Minimal Invasive Coronary Interventions  
Supervisors: Dr. Adrian Zuruchbun, MSc. Cornelia Amstutz, PD Dr. med. Dr. phil. Andreas Häberlin  
Institution: University of Bern, sitm Center for Translational Medicine and Biomedical Entrepreneurship  
Examiners: Dr. Adrian Zuruchbun, Prof. Dr. med. et phil. nat. Rolf Vogel

Christian König  
Lung Atheros Array on Chip: Reproduction of Atherosclerotic Structure in vivo Using  
Stiffness Gradient  
Supervisors: Prof. Dr. Olivier Guenat, MSc Dario Ferrari  
Institution: University of Bern, ARTORG Center for Biomedical Engineering Research  
Examiners: Prof. Dr. Olivier Guenat, MSc Dario Ferrari

Caio Leitchy  
Development of High-Throughput Platform for IPF-on-Chip Model  
Supervisors: Prof. Dr. Olivier Guenat, Dr. Pauline Zamprogo  
Institution: University of Bern, ARTORG Center for Biomedical Engineering Research  
Examiners: Prof. Dr. Olivier Guenat, Dr. Pauline Zamprogo
Editorial

Networking

Our innovative capacity is only as strong as our network. For this reason the BBEN supports networking of members right from the start.

The annual Biomedical Engineering Day (BME Day) provides an irreplaceable hub for prospective and current students, alumni and industry partners to connect. It offers students the opportunity to make valuable contacts and become actively involved in the Biomedical Engineering Club to lay the corner stones for their future careers. Participants can explore the potentials of academic-commercial collaborations via industry-driven project proposals, also leveraging on the skills and knowledge of the research community. New partnerships and commercial networking of medtech and life science companies in our region have more than once arisen from this occasion. Even in a virtual format, the event has succeeded in forging new collaborations.

The Biomedical Engineering (BME) Club is a non-profit Alumni organisation from the University of Bern that aims to provide and promote networking events among its interdisciplinary members. We are a constantly growing group of biomedical engineers, scientists, past and present students and medical technology corporate eager to bring together the fields of engineering, biology, and clinical medicine. The BME-Club accomplishes these goals by networking and hosting events, in particular, information sessions to learn about cutting-edge research fields of bioengineering, attendance of national/international conferences, and visit plans to industries and laboratories. The BME Club has been recognized as an official Alumni association of the University of Bern under the umbrella organization – Alumni UniBE. A dedicated executive committee within the BME-Club follows the principles of our constitution. We are an enthusiastic and versatile group that performs diverse activities including:

- Regular visits to Swiss medical and engineering companies
- Organization of the annual MEDICA trip
- Information on career opportunities for Masters levels
- Organization of the annual Welcome event for new students of the BME Master program
- Organization of an annual Alumni gathering for networking purposes
- Sponsorship of the best Master thesis award at the annual BME day
- Sponsorship of 2 Travel Grants to International conferences
- Joint membership for former students of the University of Bern
- Offering (optional) joint membership with Swiss Society for Biomedical Engineering

Taken together, the BME club represents a unique platform for professional, lifelong communication and networking events.

Further details on the BME-Club are available on our website:
> [http://www.bmeclub.ch](http://www.bmeclub.ch)
> [... our LinkedIn appearance](https://www.linkedin.com/company/biomedical-engineering-club/)
> [... and frequently added posts of the Instagram profile of the BME-Master course](https://www.instagram.com/bme_unibe/)

How to Join

Becoming a BME member is easy! Simply join at any BME Club event or sign in at our website. We are looking forward to seeing you.
On May 7, 2021, the first virtual Biomedical Engineering Day in 13 years was held. The master’s program in Biomedical Engineering of the University of Bern organized this event for the 12th time.

The event is an efficient platform in Switzerland for networking of master’s and Ph.D. graduates and Swiss and international medical technology companies. This year’s companies introduced themselves through oral presentations in a Zoom webinar and gave insight into their commercial activities and their company philosophies as well as showed their demands on junior employees. Students had the opportunity to get to know potential employers and contact them directly during the virtual coffee break organized in the virtual town “gather city.”

The BME Day offered great opportunities for the Bernese biomedical researchers, too. The ARTORG Center for Biomedical Engineering Research and the Bern University of Applied Sciences, a partner within the master’s program, used the opportunity to present current research projects to more than 200 virtual participants. Interestingly, master’s and Ph.D. students play an important role in many of these projects. Thereby, this event was a demonstration of scientific achievements, too. In addition to company representatives, scientists, researchers, and young academics, medical doctors participated in this year’s event as well.

For the first time, young researchers presented their projects in a humorous way during a “my thesis in 180 seconds” session. One highlight of the morning was definitely the successful live surgery during the lung resection due to cancer.

Awards

The following awards for excellent academic achievements in the field of Biomedical Engineering at the University of Bern were presented:

• Swiss Engineering Award for the best master’s thesis (innovation): Maxime Chiarelli (Estimation of the Energy Loss through Turbulence in an Aortic Stenosis Model Using Backlight Particle Tracking Velocimetry in a Silicone Ascending Aorta Phantom)
• Swiss Engineering Award for the best master’s thesis (basic science): Giuditta Thoma (Lung-Alveoli-on-Chip: Mechanical Characterization of a New Biological Membrane)
• CCMT Award for the best Ph.D. thesis: Serife Kucur (Exploration and Exploitation of Visual Fields: from Acquisition to Prediction of Glaucoma)
• BME Club Awards for the best master’s thesis abstract:
  1st place: Simone Poncioni (Optomechanical Simulations of Laser Refractive Surgeries)
  2nd place: Nathan Egger (Contactless Detection of Gait and Gait Abnormalities)
  3rd place: Martin Bertsch (Targeted Drug Delivery in Glioblastoma Mouse Models)
• RMS Award for the best GPA in the MSc Biomedical Engineering: Adrian Ruckli (GPA 5.77)

The first virtual BME Day was a great success
Acknowledgements

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