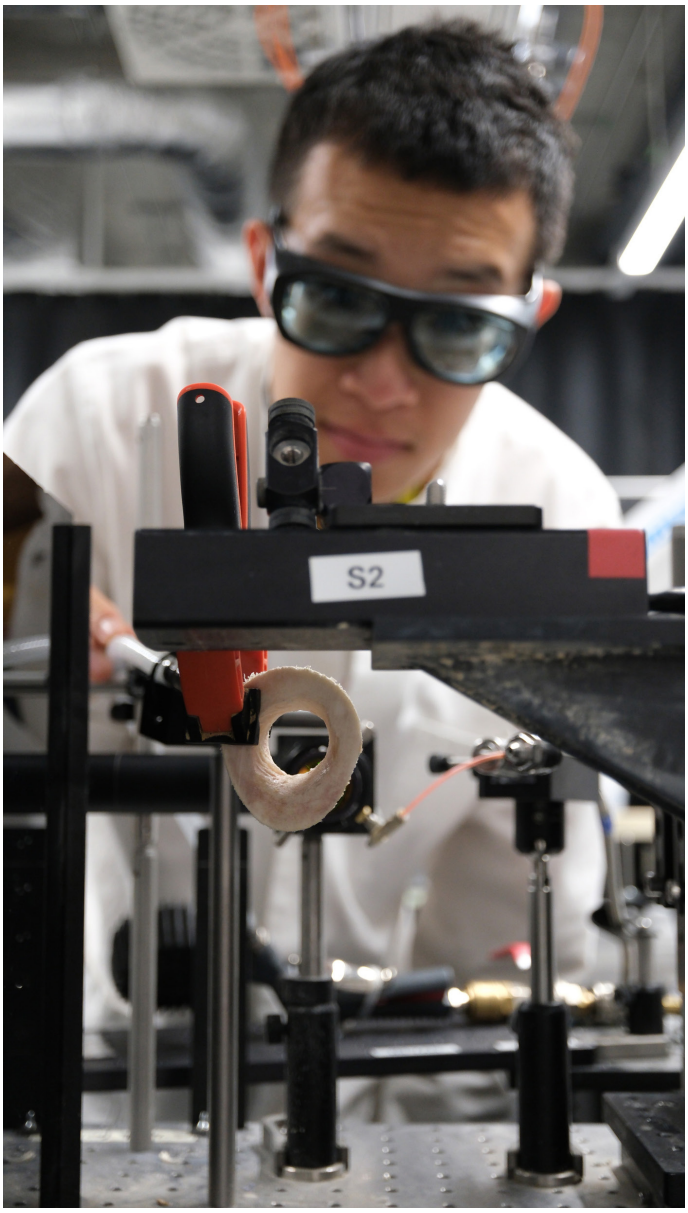
University of Basel

Department of Biomedical Engineering

Department of Biomedical Engineering

PhD & Master's Thesis 2024

Completed PhD Thesis



Working in CIO's laser lab (picture: R. Wendler)

In 2024, 11 PhD students defended their theses at our department and started new carreers. They include:

Memory-Efficient Deep Learning Methods for Brain Image Analysis

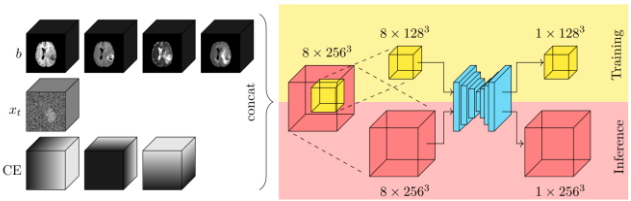


Figure 1: A CT-scan of a patient with an intraparenchymal- and subdural hemorrhage from the CQ500 study (1), along with the heat map of our proposed unsupervised anomaly detection model (2). (Picture: F. Bieder).

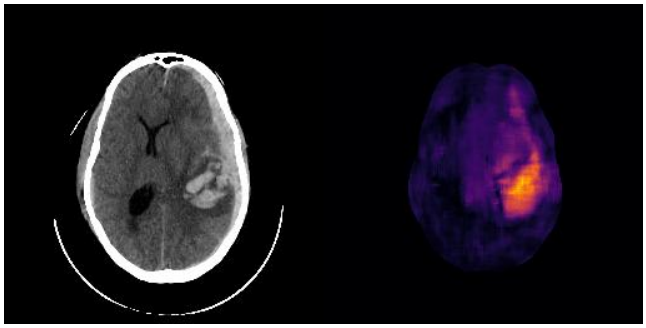


Figure 2: Overview of our memory-efficient 3D denoising diffusion model (3). Due to a fully convolutional architecture and a coordinate encoding (CE) we can train on smaller patches extracted from the full volume, and reduce the memory consumption during training by a factor of eight. (Picture: F. Bieder).

PhD Thesis by Florentin Bieder (Department of Biomedical Engineering, University of Basel) at CIAN.

The diverse array of imaging modalities currently in use has profoundly impacted the practice of medicine. In particular, X-ray computed tomography (CT) and magnetic resonance imaging (MRI) have the capacity to record a three-dimensional image of the body with great detail. As a consequence of their widespread use, the amount of available data is continuously increasing at an unprecedented rate. This presents an opportunity to apply machine learning and, in particular, deep learning. Deep learning is a subfield of machine learning that is particularly well-suited to train on large quantities of data and to capture complex features in high-dimensional data. Currently, deep learning methods rely on graphics processing units (GPUs) to be evaluated with any reasonable speed. However, GPUs with high-performance characteristics – which are directly linked to their memory capacity – contribute significantly to the high implementation costs of deep learning methods. To enable an easier access and a more widespread adoption, it is crucial to reduce this barrier of entry. In this work, we explore the potential of deep learning methods for a range of tasks involving brain imaging data, with a focus on reducing the GPU-memory consumption. This is particularly relevant for methods that process MR and CT scans, as they inherently are three-dimensional. We explored various techniques to minimize the resource consumption in diverse problem settings.

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References:
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Advanced MRI in Multiple Sclerosis: Disentangling Aging and Pathology Effects

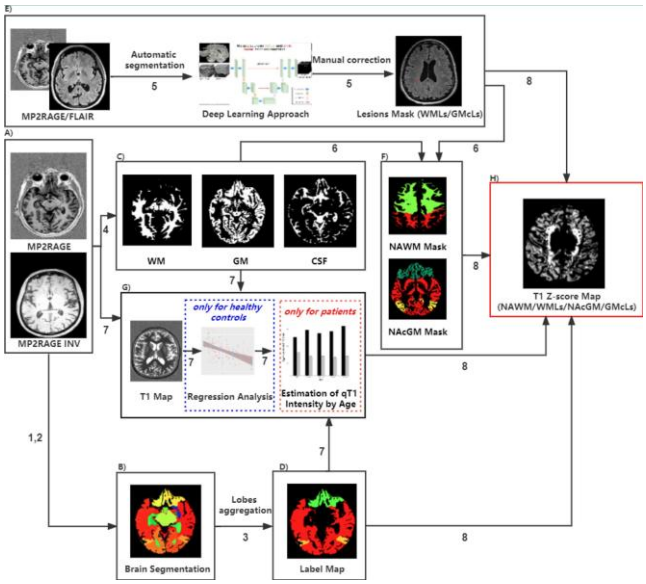

Figure 1: Advanced MRI (quantitative T1) mapping reconstruction for quantifying multiple sclerosis-isolated pathology. (Picture: X Chen).

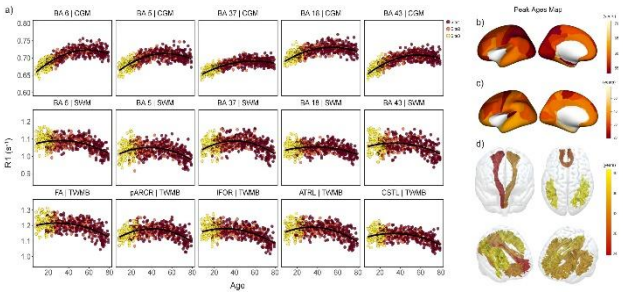

Figure 2: Model brain normative age trajectories with advanced MRI techniques (quantitative T1). (Picture: X Chen).

PhD Thesis by Xinjie Chen at ThINk Group (Department of Biomedical Engineering, University of Basel).

Multiple sclerosis (MS) is a chronic neuroinflammatory disease characterized by demyelination, axonal loss, and neurodegeneration in the central nervous system. Both normal aging and MS pathology contribute to neurodegeneration, making it challenging to distinguish the effects of normal aging from disease-specific pathology.

To address this, we developed a framework using advanced MRI techniques to investigate MS-specific pathology and MS-related aging. We modeled the influence of age on quantitative MRI measures to isolate MS-specific pathology by adjusting for age dependency (1). We also derived normative age trajectories of MRI measures in healthy individuals to better understand the effects of aging on brain microstructure and brain maturation patterns (2). Building on this, we applied machine learning methods to predict MS patients' brain age using morphological and quantitative data. The results strongly link predicted deviations from chronological age and disease progression.

These findings offer new insights into the interplay between aging and MS pathology and the mechanisms underlying clinical worsening. This thesis, therefore, establishes a foundation for future therapeutic strategies targeting pathological aging in MS patients.

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References:
(1) Chen, Xinjie, et al. "Personalized maps of T1 relaxometry abnormalities provide correlates of disability in multiple sclerosis patients." NeuroImage: Clinical 37 (2023): 103349.

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Volume Rendering for Surgical Planning in Virtual Reality

Figure 1: Pedicle screw tract palpation using a 6-DoF haptic force feedback device and a virtual reality headset. (Picture: B. Faludi, E. Zoller)

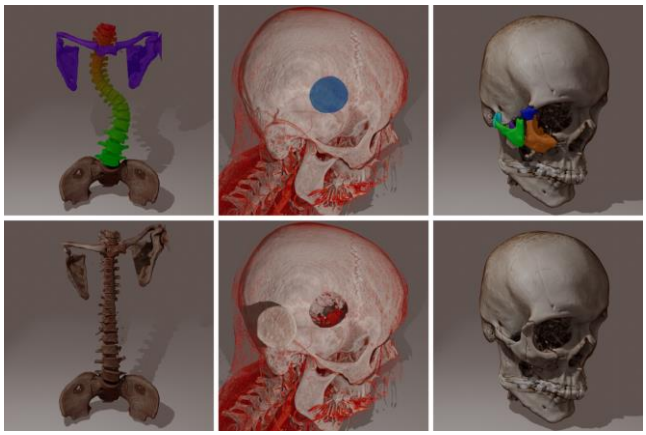

Figure 2: Three datasets rendered with our ray-marching-based multi-volume renderer. Left: Spinal fusion for scoliosis surgery. Middle: Sylvian keyhole approach for aneurysm clipping. Right: Zygomatic arch fracture reduction. The top row shows possible segmentations within each dataset. The segmentations can be created ad-hoc, serve only to divide each dataset into sub-volumes, and are not needed for the visualization. The bottom row shows the same segments extracted into separate volumes and moved within the scene. (Picture: B. Faludi)

PhD Thesis by Balázs Faludi (Department of Biomedical Engineering, University of Basel) at CIAN Research Group.

Surgical planning of complex cases is typically done using volumetric medical images, such as computed tomography (CT) scans or magnetic resonance imaging (MRI) data sets. This thesis explores the use of direct volume rendering (DVR) and virtual reality (VR) for surgical planning, preparation, and training purposes. DVR techniques, such as ray marching, allow immediate visualization of raw data without time-consuming preprocessing. Combining this with virtual reality enhances depth perception and spatial understanding, offering unique benefits for surgeons.

In a collaboration with Esther I. Zoller, we combined DVR with haptic force feedback using a novel rendering method that could simultaneously visualize a volumetric data set and compute haptic force feedback without requiring a segmentation [1]. We applied this method to build a VR simulation of the palpation of pedicle screw tracts using a pedicle probe (Figure 1) [2].

Subsequently, I worked on extending our volume rendering pipeline to improve its flexibility and allow more dynamic visualizations. I implemented a new acceleration method that enabled real-time changes of the transfer function at a performance adequate for a VR application [3]. Next, I extended the renderer to support the visualization of overlapping volumes with correct occlusion, which is needed for the preparation of cases that require the movement of bones, such as spinal fusion or fracture fixation (Figure 2).

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References:
(1) B. Faludi et al. Direct visual and haptic volume rendering of medical data sets for an immersive exploration in virtual reality. In MICCAI, 2019.
(2) E. I. Zoller et al. Force quantification and simulation of pedicle screw tract palpation using direct visuo-haptic volume rendering. In IJCARS 2020.
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Bio-Inspired Compliant Actuation for Safer Robotic Neurosurgeries

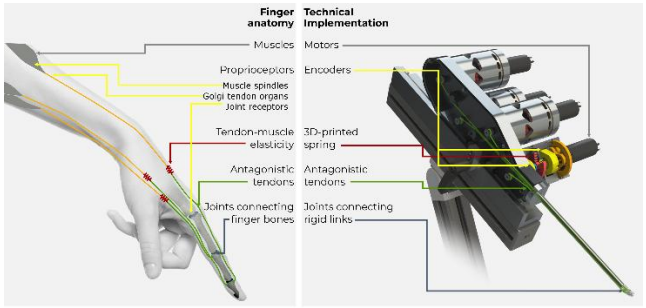

Figure 1: Bio-Inspired system design: The movement is generated remotely by electric motors and is transmitted through antagonistic tendons to the endoscope joint. Similar to the musculoskeletal actuation of the finger, the transmission was deliberately designed to be elastic, which reduced force peaks due to contacts with the environment (figure composition: L. Fasel, published in [5]).

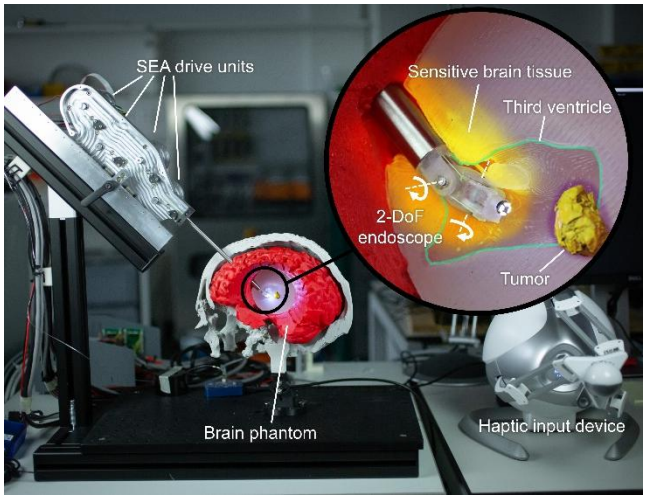

Figure 2: Safer robotic neurosurgeries: The novel actuation reduces contact forces between the robotic endoscope and sensitive brain tissue, thus avoiding tissue damage. Pathologies such as tumors in the posterior third ventricle, which are currently not accessible by conventional endoscopy, could be treated in a safe way (photos: L. Fasel).

PhD Thesis by Lorin Fasel (DBE, University of Basel) at BIROMED-Lab.

Robotics could increase maneuverability in minimally invasive neurosurgical procedures, but current systems face unsolved safety concerns.
In my PhD thesis, I addressed this scientific challenge for more safety by reducing potentially harmful instrument-tissue contact forces.
Inspired by musculoskeletal actuation (Figure 1), I developed a more compliant tendon-driven actuation concept for endoscope joints [1] and built several iterations of robotic endoscope prototypes based on series elastic actuation.
The design offered inherent compliance [2], reliable state estimation and control [3,5], force sensing [4,5], stable force control [2,5], and variable stiffness [5].
These features could enable a more complete yet safe treatment of pathologies in the brain (Figure 2).
Further, the actuation concept holds potential for robotic procedures in other surgical disciplines where a safe interaction between the robot and the tissue is required.

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References:
[1] L. Fasel, N. Gerig, and G. Rauter, "Endodevice," International patent application WO2022096624A1, Nov. 6, 2020.
[2] L. Fasel, N. Gerig, P. C. Cattin, and G. Rauter, "Tendon force control evaluation for an endoscope with series elastic actuation," in *New Trends in Medical and Service Robots (MESROB 2020)*.
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Unraveling the Heterogeneity of Multiple Sclerosis Pathology in the Brain through Quantitative MRI

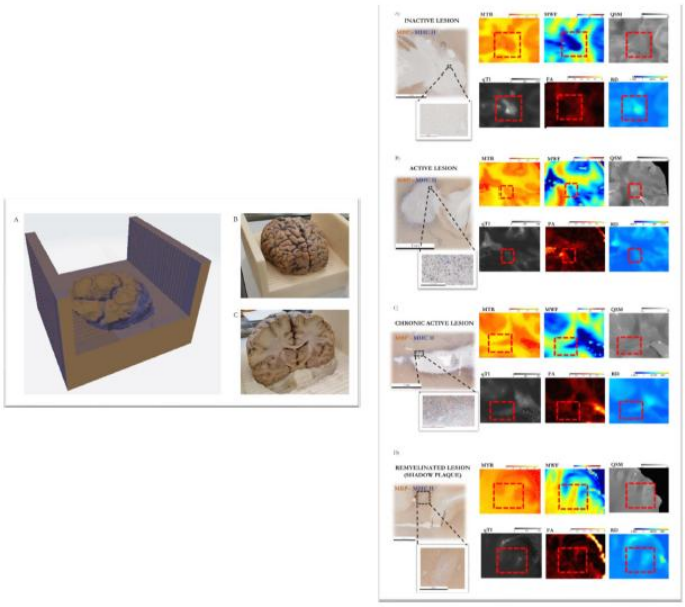

Figure 1: On the left, 3D model of an individualized cutting box (A), 3D print of the same model (B) and intermediate stage of the cutting process (C). On the right, examples of histopathological lesion types and their correspondent qMRI (pictures: R. Galbusera).

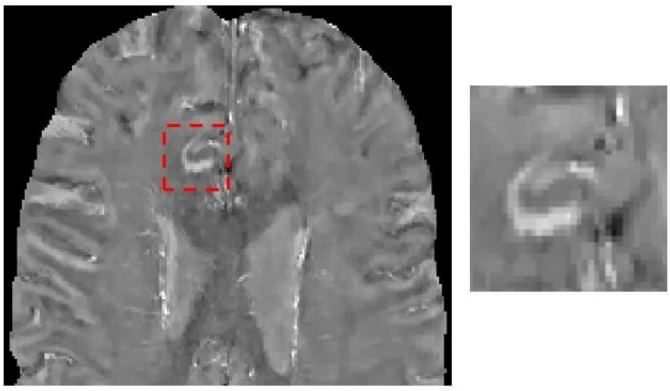

Figure 2: In vivo qMRI (Quantitative Susceptibility Mapping) of a patient with MS showing one juxtacortical paramagnetic rim (pictures: R. Galbusera).

PhD Thesis by Riccardo Galbusera (Department of Biomedical Engineering, University of Basel) at the Translational Imaging in Neurology (ThINk) Basel group.

Multiple sclerosis is an immune-mediated disease of the central nervous system that affects more than three million people worldwide. The clinical severity is highly variable and the heterogeneity likely results from a varying balance between inflammation, neurodegeneration and repair mechanisms. Estimating the underlying pathological changes and measuring repair processes of each individual in vivo would pave the way to tailored therapy strategies.

This doctoral thesis aimed at investigating the potential of quantitative MRI (qMRI) in disentangling the miscellaneous tissue changes in MS brains by using postmortem multiparametric qMRI of 8 formalin-fixed whole human brains as an experimental model. After imaging, the exploitation of a 3D-printed, personalized cutting box for each brain enabled a very good registration between the MRI slices and the tissue slabs and facilitated the MRI-histology comparison (Fig. 1).

The data we obtained emphasizes the usefulness of qMRI measures in unraveling the tissue alterations that characterize MS. Our data support the use of magnetization transfer ratio (MTR) and myelin water fraction (MWF) for the identification of remyelinated lesions in the white matter and the use of these metrics in clinical trials testing remyelinating compounds should be further encouraged (1). Moreover, we investigated the cerebral cortex and found that, among all the myelin-sensitive qMRI metrics considered, qT1 was most sensitive in detecting cortical remyelination (2). Last, we described a novel MRI feature present in about 10% of the MS patients, the juxtacortical paramagnetic rim, which could be a potential novel biomarker for cortical lesion detection, for disease prognostication and also for patient's stratification in clinical trials (3).

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References:

(1) Galbusera, R., Bahn, E., Weigel, M., Schaedelin, S., Franz, J., Lu, P. J., ... & Granziera, C. (2023). Brain Pathology, 33(6), e13136.

(2) Galbusera, R., Weigel, M., Bahn, E., Schaedelin, S., Cagol A., Lu, P. J., ... & Granziera, C. In Preparation.

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Intuitive Control for Hand-guiding Surgical Tools with Macro-robots

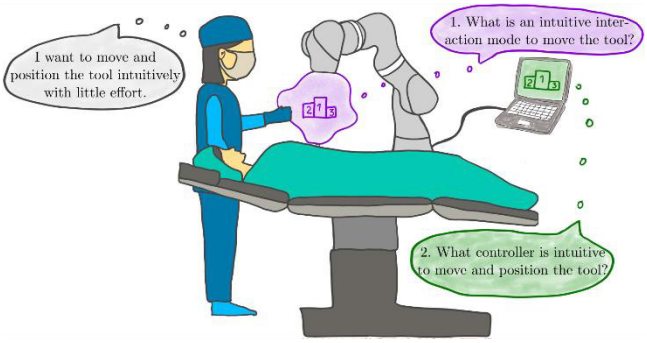

Figure 1: The goal of the work is to allow surgeons to move tools intuitively by hand while the robot bears the tool's weight and maintains the desired tool pose until changed by the surgeon. The two research questions on the right side resolve challenges in achieving the goal (Picture: M. Karnam).

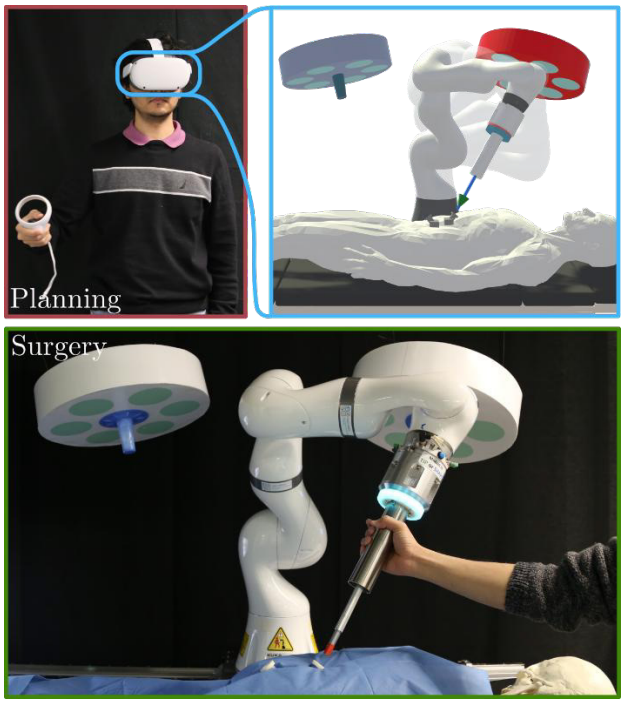

Figure 2: The thesis outcome allowed users to hand-guide a robot-mounted tool and simultaneously reshape the robot to avoid obstacles (below) based on user-taught inverse kinematics in VR (above) (Picture: M. Karnam).

PhD Thesis by Murali Karnam (Department of Biomedical Engineering, University of Basel) at BIROMED-Lab.

Surgeons typically teleoperate robot arms in robot-assisted surgeries. Surgeons are nevertheless trained and skilled to move tools directly with their hands in both open and minimally invasive surgeries. Recent collaborative robot arms allow physical human-robot interaction and come with a benefit – the arm can be reshaped while moving the tool as desired. The robot's shape can be changed to avoid obstacles such as operating room lamps. This PhD project aimed to develop intuitive control for collaborative robots that is safe for surgeons, patients, and other equipment in operating rooms.

We developed and implemented a real-time framework to control off-the-shelf robot arms such as the KUKA LBR iiwa additionally equipped with a linear axis (8th degree-of-freedom). In a user study, four admittance controllers were evaluated to intuitively hand-guide robot-mounted surgical tools. The one hand-guidance control was extended to simultaneously move the tool and reshape the robot in null space (redundant degrees of freedom) as hand-taught by the user (Figure 2). This was a proof-of-concept to control any redundant robot with one or more redundant degrees-of-freedom. Augmented and Virtual Reality interaction methods were implemented to extend the usability of the controllers and potentially reduce the time necessary to use the robot in an operating room.

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References:
(1) Karnam M., et al. *Learned task space control to reduce the effort in controlling redundant surgical robots.* 161-168 (MESROB, Springer, 2020).

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Multi-Parametric Brain Tissue Characterization Using Magnetic Resonance Imaging

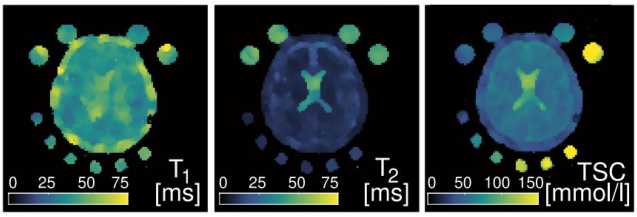

Figure 1: Sodium T_1, T_2 and tissue sodium concentration (TSC) maps obtained from a phase-cycled bSSFP acquisition (picture: J. Schäper).

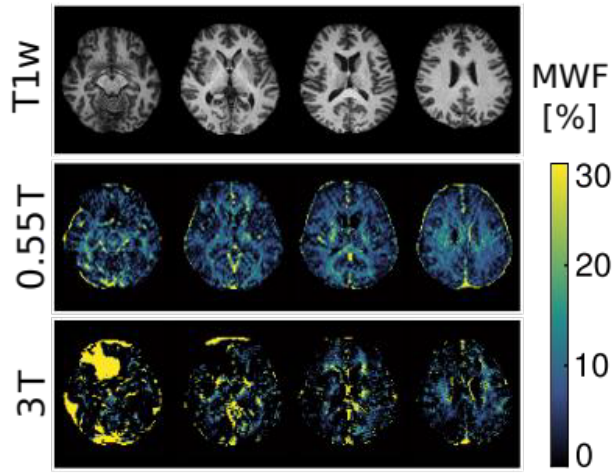

Figure 2: Comparison of an example slice of the myelin water fraction (MWF) at 3T and 0.55T together with an MP-RAGE anatomical reference (T1w) (picture: J. Schäper).

PhD Thesis by Jessica Schäper at the Magnetic Resonance Physics and Methodology Group of the University of Basel.

One of the biggest disadvantages of conventional MRI is the fact that images do not obey an absolute scale but rather show relative gray values which strongly depend on imaging and device parameters. However, it is highly beneficial to look at multiple facets and quantitative parameters of the brain tissue. This thesis was focused on improving some of the existing methods which provide some insight into brain tissue beyond conventional MRI.

First, features of the balanced steady-state free precession (bSSFP) sequence were investigated for fast, simultaneous quantification of the tissue relaxation parameters T_1 and T_2 (1).
The bSSFP quantification was also applied to sodium MRI, where it could offer a more efficient alternative to the commonly used methods.

Moreover, the magnetization-prepared rapid gradient echo (MP-RAGE) sequence, which serves as a powerful tool in volumetry by offering fast T_1-weighted images, was optimized for the new generation of clinical 0.55T scanners (2).

Furthermore, myelin water fraction (MWF) imaging was implemented and tested at 0.55T and compared to 3T in order to demonstrate its advantages at lower field strengths and its viability (3).

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(1) Schäper J et al. "Pure balanced steady-state free precession imaging (pure bSSFP)", Magn Reson Med. 2022;87:1886-93.
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Challenges of Mixture Deconvolution using DEPArray™ Technology – Establishing Single-Cell Analysis in Forensics

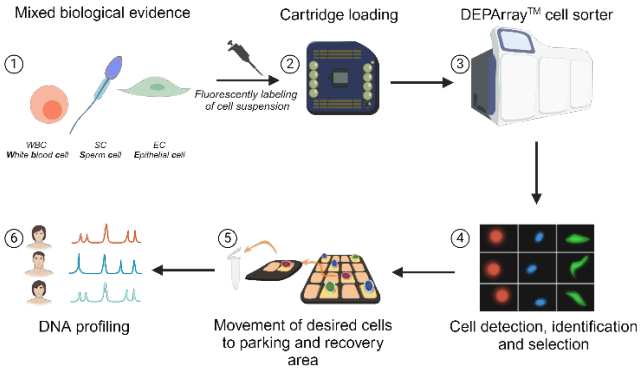

Figure 1: Isolation of leucocytes, spermatozoa, and/or epithelial cells using the DEPArray™ system. The cells are labeled with specific dye-conjugated antibodies targeting white blood, sperm, and epithelial cell markers (1). Cells are loaded in a dedicated cartridge (2), separated by a dielectrophoresis (DEP)-based microfluidic system and visualized by fluorescence microscopy (3). High-quality images are provided for size, shape, and fluorescence intensity evaluation (4). Desired and selected cells are moved to a parking area using DEP forces and recovered as single or pooled cells (5). Successful isolation and subsequent genetic downstream analysis results in a single DNA profile that can be assigned to its corresponding cell type and donor (6). Created by Caravaku Life Design, Switzerland and adapted with BioRender.com. Picture: Janine Schulte

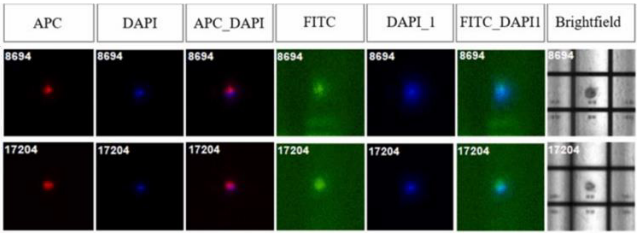

Figure 2: Examples of spermatozoa detected 96 hours after consensual sexual intercourse using DEPArray™ technology. APC = Allophycocyanin (conjugated dye on intracellular SC marker), FITC = Fluorescein isothiocyanate (conjugated dye on intracellular EC marker), DAPI = 4′,6-diamidino-2-phenylindole (conjugated dye on nuclei marker), BF = Brightfield and their respective overlays. Picture: Janine Schulte

PhD Thesis by Janine Schulte (Institute of Forensic Medicine, Forensic Genetics, University Basel)

In forensic DNA analysis, identifying mixture components and assigning them to a person of interest remains challenging, especially for cell-like mixtures (e.g., blood-blood). With an increased number of contributors, the interpretation of mixtures becomes more difficult or even impossible. Separating distinct cell populations or collecting single cells prior to genetic analysis is, therefore, promising.[1]

The thesis attempted to optimize, validate, and implement a cell-sorting strategy, such as the DEPArray™ technology (Fig. 1), with the aim to successfully separate mixed forensic evidence into its identifiable cellular components and perform genetic analysis down to the level of a single cell.[2]

In a systematic approach, we optimized and validated the methods technically and genetically for forensic purposes. A descriptive study on simulated sexual assault samples was conducted to compare the performances of conventional cell enrichment (i.e., differential extraction [DE]) and capturing techniques (i.e., laser capture microdissection [LCM]) to the more advanced DEPArray™ system.

Epithelial, blood, and sperm cells were reliably detected, quantified, and genotyped, highlighting the device's cell detection, identification, and separation capabilities (Fig. 2). We concluded that advanced image-based technologies could help extend standards by enabling accurate cell type identification and overcoming their limits. Our research outlines the technology's initial, practical use, laying the groundwork for future deployment, and improvements.

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References:
(1) K. Anslinger and B. Bayer, "Whose blood is it? Application of DEPArray™ technology for the identification of individual/s who contributed blood to a mixed stain," *Int. J. Legal Med.*, vol. 133, no. 2, pp. 419–426, 2019.
(2) V. R. Williamson, T. M. Laris, R. Romano, and M. A. Marciano, "Enhanced DNA mixture deconvolution of sexual offense samples using the DEPArray™ system," *Forensic Sci. Int. Genet.*, vol. 34, no. March, pp. 265–276, 2018.

Eye and Heart Synchronisation: Development of Time-Resolved Optical Coherence Tomography with Electrocardiographic Coupling

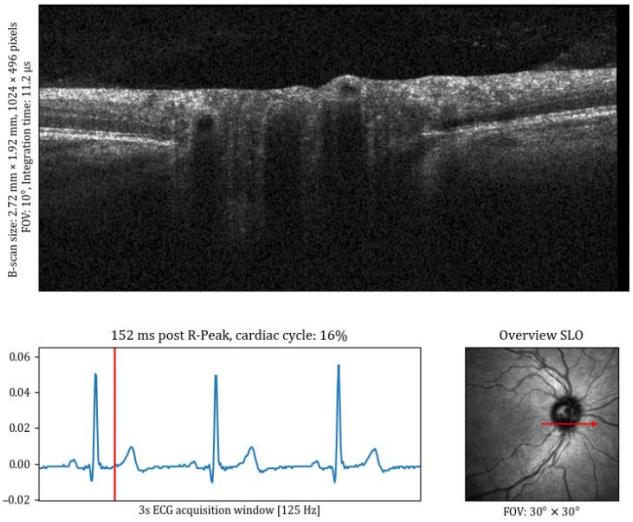

Figure 1: Time-resolved optical coherence tomography (OCT) with synchronised retinal and electrocardiographic data acquisition. (Image: P. Valmaggia).

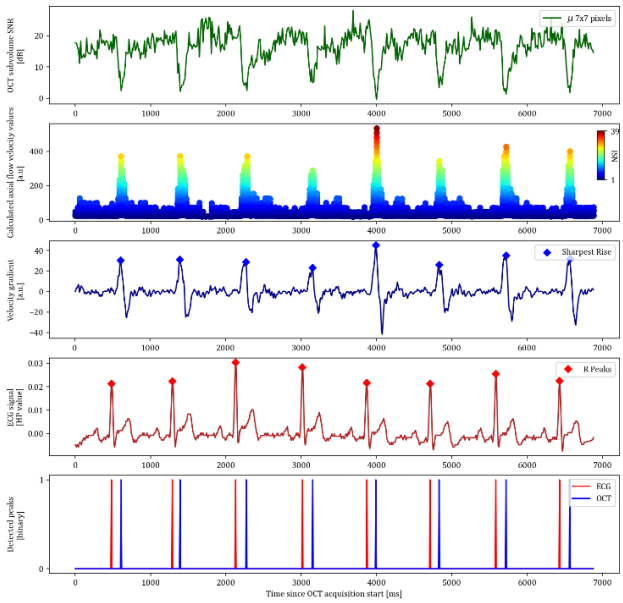

Figure 2: Heart-retina time analysis based on electrocardiographic R-peaks and pulse arrival calculated by the retinal blood flow profiles (Image: P. Valmaggia).

Funding:

FNSNF
Fonds National Suisse
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Fondo Nazionale Svizzero
Swiss National Science Foundation

AlumniMedizin Basel

Janggen-Pöhn-Stiftung

MD-PhD Thesis by Philippe Valmaggia at the Center for medical Image Analysis & Navigation (CIAN).

Optical coherence tomography (OCT) is a non-invasive imaging technique that can provide depth-resolved images of the retina with a micrometre resolution. In clinical settings, the images are static, which does not allow for the visualisation of changes over time.

To overcome this, we developed methods to generate time-resolved OCT images, enabling the visualisation of blood flow dynamics in the eye. We estimated retinal blood flow profiles based on quantitative fringe washout analysis, allowing us to analyse the intravascular blood flow dynamics in vessels close to the optic nerve head. Additionally, we built a coupler to synchronously acquire OCT and electrocardiogram (ECG) data. This approach enabled the calculation of the blood flow propagation from the heart toward the eye. This time is presented as the heart-retina time (HRT) and proposed as a potential biomarker for cardiovascular health. Using classical computer vision techniques and deep learning algorithms, this research further aimed to automate the segmentation of blood vessels and pigmented choroidal lesions, previously unexplored entities of automation in OCT data.

Overall, this research has explored novel dynamic, quantitative, and automated analyses of OCT data. We introduced methods to visualise retinal blood flow dynamics, to calculate the heart-retina time and to segment retinal structures and tumours automatically.

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References:

[1] Valmaggia P, et al. Feasibility of Automated Segmentation of Pigmented Choroidal Lesions in OCT Data With Deep Learning. *TVST* 2022.

[2] Valmaggia P, et al. Time-Resolved Dynamic Optical Coherence Tomography for Retinal Blood Flow Analysis. *IOVS* 2024.

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Therapeutic Monitoring in a Pediatric Clinical Setting via Breath Analysis by High Resolution Mass Spectrometry

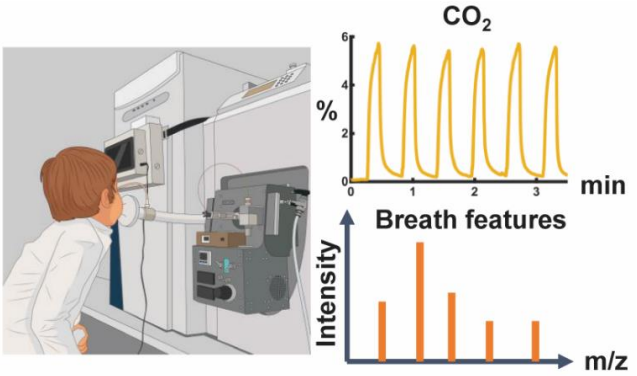

Figure 1: Real-time breath measurement whereby CO_2 along with metabolites are detected non-invasively by high-resolution mass spectrometry (Picture: J.Zeng).

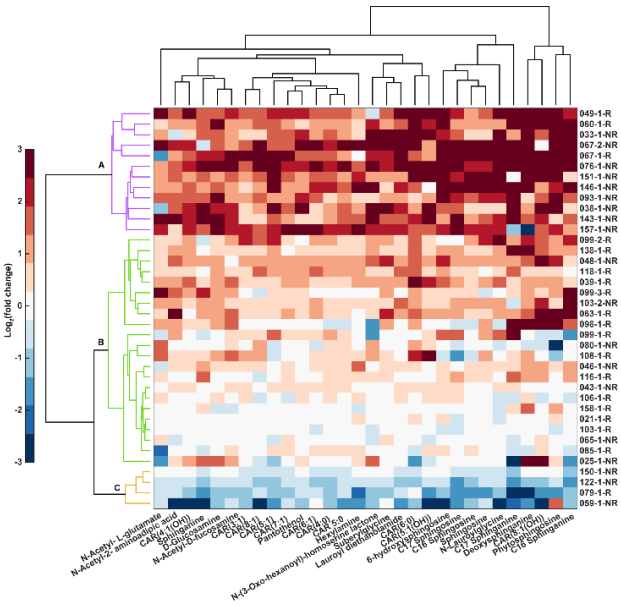

Figure 2: Cluster analysis of breath metabolite profiles in salbutamol responders and non-responders.The heatmap shows log_2 fold changes in exhaled metabolite levels, with red indicating upregulation and blue indicating downregulation post-salbutamol inhalation. Patient codes follow the format: Patient ID-Visit number-Responder status (R for responder, NR for non-responder). Three distinct clusters are observed: Cluster A (75% NR vs. 25% R) displays an overall upregulation of metabolites; Cluster B (68% R vs. 32% NR) shows moderate changes in metabolite levels between pre- and post-treatment; and Cluster C (75% NR vs. 25% R), a smaller group, shows a trend toward downregulation. Dendrograms on both axes indicate hierarchical clustering of patients and metabolites based on their metabolic responses. (Picture: : J.Zeng)

Funding:

fondation BOTNAR

FNSNF Swiss National Science Foundation

PhD Thesis by Jiafa Zeng (Department of Biomedical Engineering, University of Basel) at the Translational Medicine Breath Research.

Pharmacometabolomics is an emerging approach that supports therapeutic monitoring by providing insights into metabolites altered by pharmaceuticals or those that influence clinical outcomes.[1,2] Pharmacometabolomics through breath analysis holds particular promise for therapeutic monitoring.[3] In this thesis, we evaluate this approach by integrating a breath analysis platform into a real-world pediatric hospital setting. We hypothesize that breath analysis (Figure 1) can offer a comprehensive layer of metabolic information to better characterize patient heterogeneity and clinical responses to therapeutic interventions.

We assessed metabolic changes by analyzing exhaled breath before and after salbutamol inhalation in 38 asthmatic children. Significant alterations in over 200 breath mass spectral features were detected following salbutamol administration. Enrichment analysis highlighted sphingolipid metabolism and arginine biosynthesis as significantly affected pathways. Additionally, 30 metabolites associated with these pathways were linked to patient heterogeneity and metabotypes of poor salbutamol responsiveness (Figure 2). In a separate clinical application in the operating room, offline breath analysis using sample bags demonstrated the potential to monitor actual blood propofol concentrations in patients undergoing total intravenous anesthesia.

In conclusion, pharmacometabolomics via breath analysis has potential utility for therapeutic monitoring, allowing for the quantification of medication responses and prediction of drug concentrations.

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References:
(1) Vermeire, S.; et al., *How, When, and for Whom Should We Perform Therapeutic Drug Monitoring?* 18, 1291-1299 (Clin Gastroenterol Hepatol, 2020).

(2) Everett, J. R.; et al, *Pharmaco-metabonomics and Personalized Medicine*, 50, 523-545 (Annals of Clinical Biochemistry, 2013)

(3) Bruderer, T.; et al, *On-Line Analysis of Exhaled Breath*. 119, 10803-10828 (Chemical Reviews, 2019)

Completed Master's Thesis

Studying Biomedical Engineering (picture: R. Wendler).

In 2024, numerous Master's students were involved in DBE's research projects. They include:

Investigating the Relationship Between the Morphometric Data of MS Patients and a Selected Cognitive Game

Figure 1: *Numbers* game screenshots from the DreaMS application. This game features two modes: Numbers Game Mode (NGM) (left) and Numbers Test Mode (NTM) (right). In NGM, patients are tasked to complete as many rounds as possible in 60 seconds. In NTM, the time taken to complete all rounds is measured with no time limit (picture: RC2NB's DreaMS application).

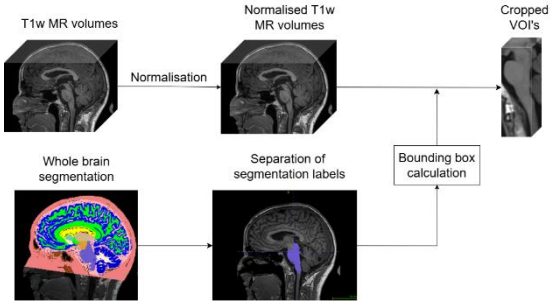

Figure 2: General overview of image pre-processing pipeline (picture: A. Bah).

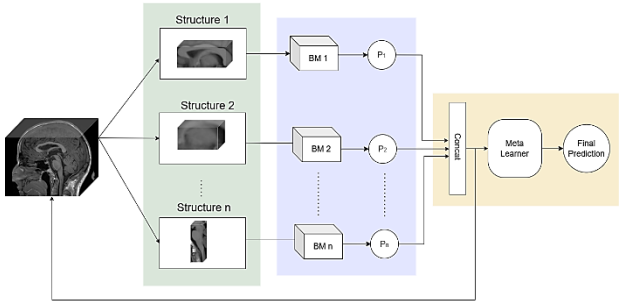

Figure 3: Overview of the stacked ensemble model: Cropped MR volumes from different brain structures are input into their corresponding base models (BM). The output predictions from these base models are concatenated and fed into a meta-learner, which generates the final patient-level predictions (picture: A. Bah).

Master's Thesis by Aaisha Bah (Department of Biomedical Engineering, University of Basel) at Translational Imaging in Neurology (ThINk) Basel Group

Multiple sclerosis (MS) is a disease of the central nervous system that is characterized by demyelination and neuronal damage. Volumetric MRI changes in MS patients over the disease progression show a strong correlation with cognitive performance, which can be assessed using traditional neuropsychological evaluations and digital tools. Researchers at the Research Center for Clinical Neuroimmunology and Neuroscience (RC2NB) developed, *Numbers*, a cognitive game of number assortment, designed to measure information processing speed.

This thesis investigates the correlation between performance features derived from the *Numbers* game, traditional cognitive assessments, and volumetric measurements of 25 brain regions in 153 patients. Deep learning models were used to predict the game features and stacked ensemble models were developed to provide patient-level predictions.

The findings show that deep grey matter structures such as the putamen, thalamus, and pallidum, along with the cerebral cortex volume are strongly associated with standard cognitive assessments and key game features like the number of successful touches and completion time, which are both indicators of the patients' cognitive performance. The ensemble models are able to effectively learn from patient specific features to provide improved final predictions.

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(1) J. A. Cohen and A. Rae-Grant, "Handbook of multiple sclerosis: Second edition," Handbook of Multiple Sclerosis: Second Edition, pp. 1–88, Jan. 2012.

(2) N. Bergsland et al., "Localized atrophy of the thalamus and slowed cognitive processing speed in MS patients," Multiple Sclerosis, vol. 22, no. 10, pp. 1327–1336, Sep. 2016.

Development of a self-assembled osteochondral construct using 4D technology

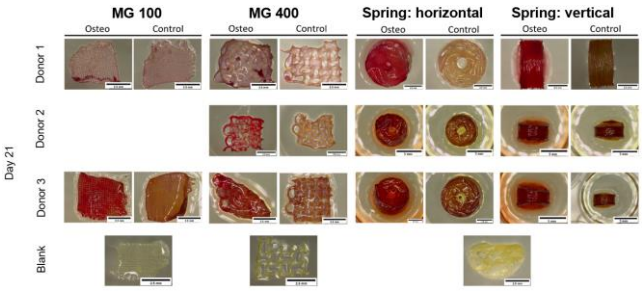

Figure 1: Alizarin red staining on medical grade (MG) PCL scaffolds seeded with NC from three donors and exposed or not to osteogenic medium. Red staining is proportional to calcium deposition. The blank does not contain any cells (scalebar = 2.5 mm) (picture: G.Borer).

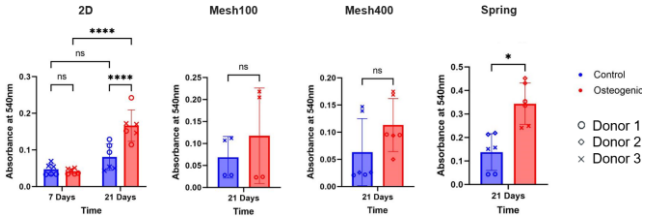

Figure 2: Absorbance values of alizarin red on monolayer (2D), Mesh100, Mesh400, and Spring after 21 days. Data are expressed as Mean ± SD vs. the control group (N = 3 donors, * $p \leq 0.05$, **** $p \leq 0.0001$) (picture: G.Borer).

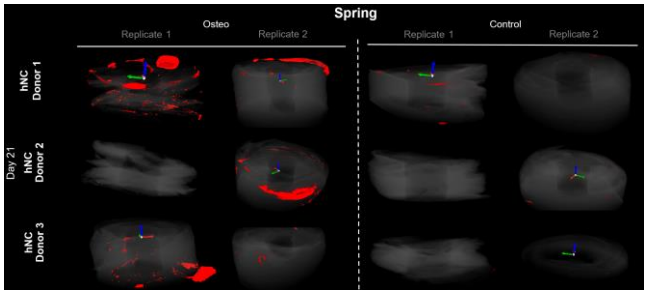

Figure 3: Localization of mineralized areas within the Spring (according to an applied threshold filter). Areas that correspond to high X-ray absorption values are highlighted in red and are compared to the control group (picture: G. Borer).

Master's Thesis by Borer Géraldine at Swiss Medical Additive Manufacturing Group (Department of Biomedical Engineering, University of Basel).

The limited regenerative capacity of the temporo-mandibular joint (TMJ) poses a treatment challenge due to the inability of cartilage to regenerate (1). This work aimed to engineer an osteochondral tissue mimicking the TMJ interface by culturing nasal chondrocytes (NC) on a 4D polycaprolactone (PCL) scaffold overlaid with GelMa hydrogel. It is hypothesized that integrating NC into this Spring scaffold and combining it with bioprinted GelMa layers, will yield a stable osteochondral structure with enhanced bone formation due to osteogenic differentiation medium compared to control scaffolds (2).

Human NC from three donors were cultured on various dimensions (2D, 3D Mesh, and the innovative 4D Spring) under osteogenic (0.1 mM ascorbic acid, 10 mM *β*-dexamethasone and 5 mM glycerol phosphate) or control conditions for 21 days (2,3). Scaffolds were made of melt electrowritten (MEW) PCL medical grade. The analysis included qPCR for bone and cartilage-related genes, immunofluorescence for specific proteins, and investigation of potential calcification using alizarin red staining and µCT imaging.

The NC adhered immediately and spread evenly over the PCL scaffolds within 7 days. Analysis after 21 days demonstrated increased calcification in the osteogenic group. Cell growth led to more compact and stiffer structures, enhancing construct maturation over time.
This study demonstrates osteogenic differentiation of NC on PCL scaffolds. The osteogenic group, particularly the 4D PCL Springs, showed increased mineralization suggesting potential for TMJ regeneration.

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(1) Chung, C. and Burdick, J.A. *Engineering cartilage tissue.* 60(2):243-262. (Advanced Drug Delivery Reviews, 2008).

(2) Pippenger, B. E., et al. *Bone-forming capacity of adult hNC.* 19(6):1390-1399. (Journal of Cellular and Molecular Medicine, 2015).

(3) Della Bella, E. et al. *Dexamethasone Induces Changes in Osteogenic Differentiation of hMSC via SOX9 and PPARG, but Not RUNX2.* (Intern. Journal of Mol. Sciences, 2021).

University of Basel

Department of Biomedical Engineering

Associations between paraspinal muscle fatigue, paraspinal muscle endurance and patient-reported function in patients with lumbar spinal stenosis

Master's Thesis by Thomas Braunwarth (Karlsruhe Institute of Technology) at the Functional Biomechanics Laboratory (University Hospital Basel).

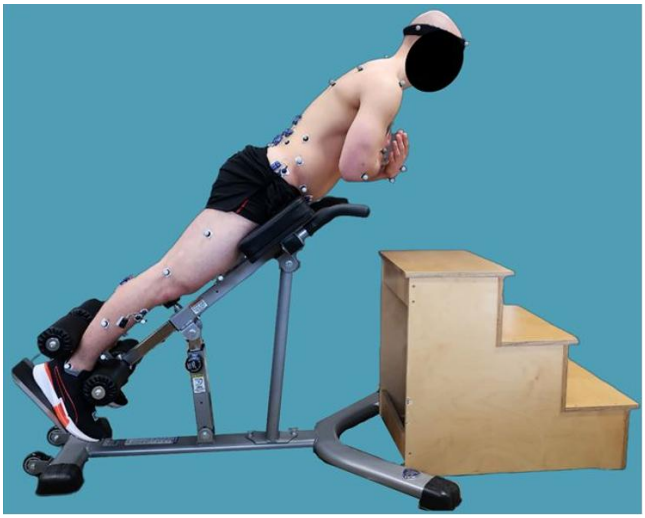

Figure 1: Modified version of the Biering-Sorensen test.

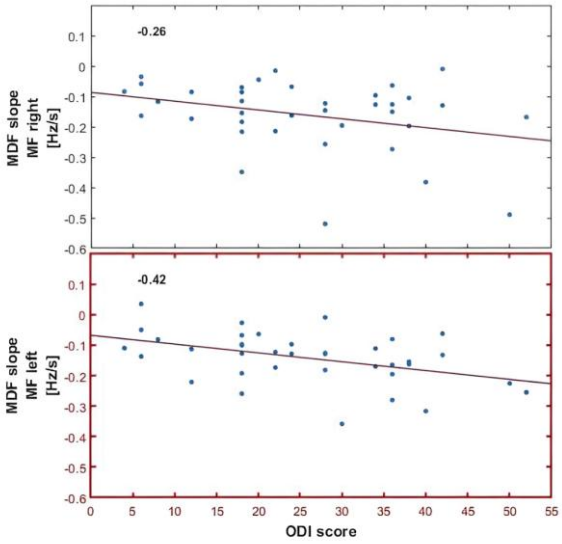

Figure 2: Correlations between patient-reported function and muscle fatigue parameters in the multifidus muscle; ODI = Oswestry Disability Index; MDF = median frequency; MF = multifidus (Thomas Braunwarth).

Lumbar spinal stenosis (LSS) is a spine disorder that may result in severe disability[1]. Although LSS is common among the elderly, there is a lack of research on the relationship between function of the paraspinal muscles[2] and patient-reported disability. The aim of this thesis was to assess associations between paraspinal muscle endurance, paraspinal muscle fatigue and patient-reported function in patients with LSS.

A modified version of the Biering-Sorensen test (Fig. 1) was used to assess muscle endurance and to induce fatigue in the paraspinal muscles in 37 patients with symptomatic LSS. Bilateral electromyography (EMG) of three paraspinal muscles (m. longissimus, m. iliocostalis, m. multifidus) was used to assess muscle fatigue defined as the slope of the median frequency from start to end of the modified Biering-Sorensen test. Patient-reported back-specific disability was assessed using the Oswestry Disability Index.

Correlation analysis showed moderate to strong correlations between muscle endurance and fatigue (R=0.340 R=0.520). Greater muscle endurance was associated with lower muscle fatigue. No systematic correlations between patient-reported disability muscle endurance and fatigue were found, our data indicated a trend for an association between muscle fatigue of the m. multifidus and the ODI score, where greater muscle fatigue was associated with greater disability (Fig. 2).

According to our results, muscle fatigue might limit muscle endurance performance. Future research should consider the relationship between morphological and physiological parameters of paraspinal muscles among patients with LSS.

Funding:

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[1] Lurie, J., & Tomkins-Lane, C. (2016). Management of lumbar spinal stenosis. *The BMJ*, *352*, h6234. https://doi.org/10.1136/bmj.h6234

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Dynamic Compensation in Spinopelvic Alignment in Patients with Symptomatic Lumbar Spinal Stenosis

Master's Thesis by Nicola Büttiker (Department of Health Science and Technology, ETH Zurich) at the Functional Biomechanics Laboratory (University Hospital Basel).

Figure 1: Study Flow Chart (Nicola Büttiker).

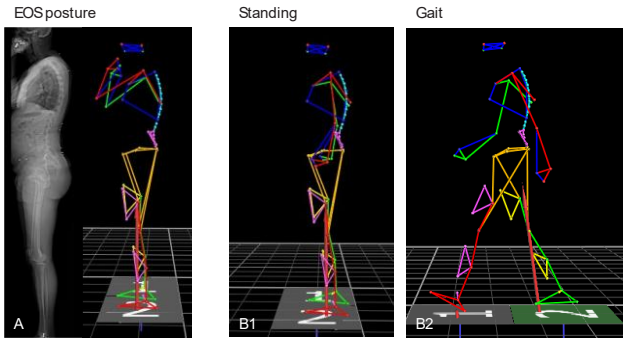
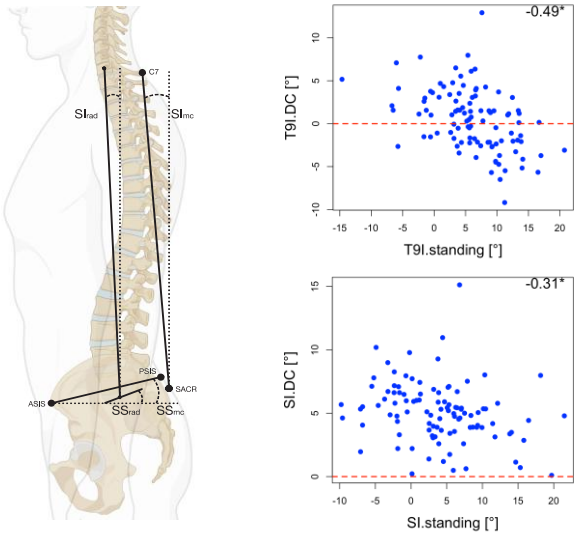


Figure 2: Conceptual overview. A: Correction of the motion capture angles to the true anatomical angles of the EOS. B1 and B2: Modeling of the true anatomical angles during stance and gait (Nicola Büttiker).



Left: Exemplary association of radiological and motion capture sagittal spinopelvic alignment (Modified from [1]); Right: Scatterplots (standing vs. dynamic compensation) T9 Inclination and Spine Inclination (Nicola Büttiker).

This study investigated the compensatory mechanisms of sagittal spinopelvic alignment during standing and walking in patients with symptomatic lumbar spinal stenosis (sLSS) [2]. Traditional approaches focus on static sagittal spinopelvic balance assessed using standing radiographs, which do not capture the compensatory adjustments that occur during walking [3]. To address this gap, this study combined radiological imaging with motion capture analysis to dynamically model true sagittal spinopelvic alignment.

Biplanar EOS full-body imaging was performed to assess sagittal spinopelvic alignment using various positional parameters. Marker-based motion analysis was conducted during standing and walking (Fig 1, Fig 2). The spinopelvic alignment derived from the motion analysis was corrected to reflect the true anatomical sagittal alignment. Spearman correlation analysis was used to investigate the relationships between sagittal alignment during standing, compensatory mechanisms during walking, and self-reported disability as measured by the Oswestry Disability Index (ODI).

Significant correlations were found between dynamic compensation and standing alignment for T9 inclination, spine inclination, and pelvic tilt. ODI scores correlated weakly but significantly with dynamic sacral slope and pelvic tilt compensation (r = -0.23; r = 0.23).

These findings suggest that standing postural parameters influence adaptive strategies during gait and highlight the relevance of pelvic dynamics in understanding functional impairments in patients with sLSS.

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References:

[1] *BioRender*©. (2024). https://www.biorender.com

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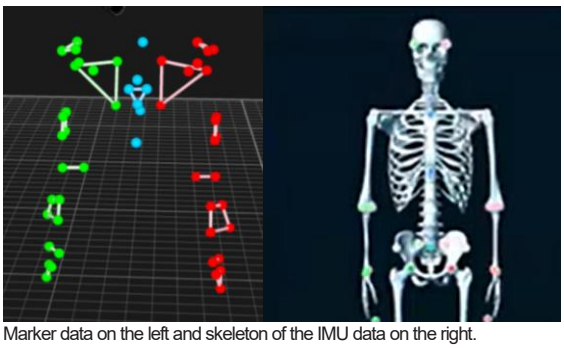
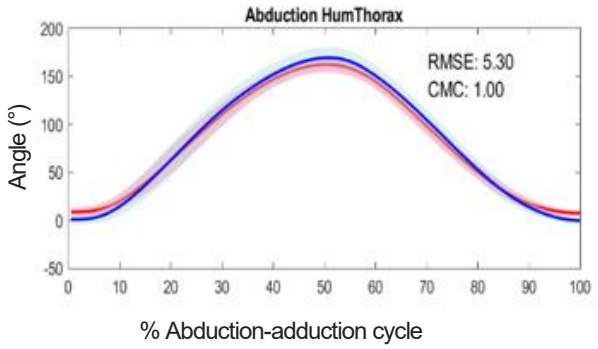
Department of Biomedical Engineering

Comparison of shoulder kinematics during arm abduction between inertial measurement unit-based and marker-based motion capture



Marker data on the left and skeleton of the IMU data on the right.



Mean and standard deviation the abduction angle during full abduction movement in the scapular plane from marker-based (red) and IMU-based (blue) motion capture. RMSE, root mean square error; CMC, coefficient of multiple correlations.

Master Thesis by Won Wook Chung (Department of Biomedical Engineering, University Basel) at the CADENCE Laboratory.

Shoulder kinematic analysis can help to understand shoulder musculoskeletal disorders. Compared to the gold standard motion capture system, inertial measurement unit (IMU)-based motion capture systems require less time and are more feasible for outside-of-laboratory assessments [2]. Hence, this study aimed to compare shoulder kinematics between marker-based and IMU-based (Noraxon Ultium Motion, Noraxon USA Inc., Scottsdale, AZ) motion capture systems during full arm abduction in the scapular plane in 20 healthy subjects.

Good agreements were found for the humerothoracic abduction angles and scapulothoracic upward rotation, where the root mean square errors were below 7.1°. Kinematic trajectories in the other planes for the humerothoracic and scapulothoracic joints between the two systems presented large differences, with root mean square errors ranging from 22.5° to 43.0°.

The use of IMU sensors for assessing shoulder kinematics is still not adequate for a clinical use and improvements are still needed to increase their applicability for upper extremities. Furthermore, analyses should be extended to other movements.

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References:

(1) Lahkar, et al (2022). Frontiers in Sports and Active Living, 4, 939980. https://doi.org/10.3389/fspor.2022.939980

Artificial neural networks for the detection of lung functional abnormalities in preterm infants

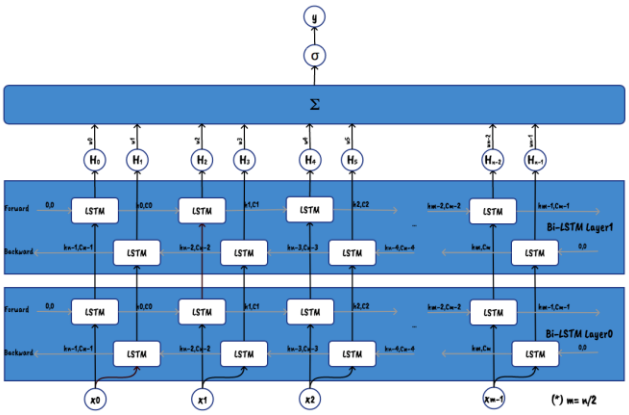

Figure 1: General Architecture: Based on two layers of Bi-LSTM and a fully connected layer. (Picture: A. Falhi)

Infants without BPD	Infants with BPD	Training accuracy [%]	Validation accuracy [%]	Test accuracy [%]
197	132	94	96	96

Accuracy [%]	Specificity [%]	Precision [%]	Sensitivity [%]	F1-Score [%]
96.88	100	97.62	95.83	96.61

Figure 2: Accuracy of the best fold of the model trained with Inselspital data sets vs Test majority vote metrics of the model folds trained with Inselspital data sets. (Picture: A. Falhi)

Master's Thesis by Abdessamad Falhi (DBE – University of Basel) at Computational Physiology & Biostatistics lab.

Preterm infants are susceptible to chronic lung disease of infancy (CLDI), also known as Bronchopulmonary dysplasia (BPD), requiring a special care since their lungs are not fully developed as the term infants. The detection of the breathing difficulties in the preterm infants is a challenging topic because these infants cannot respond to medical staff requests or follow instructions to perform breathing operations during monitoring procedures. Therefore, the tidal breathing monitoring, in conjunction with capnography or the multiple-breath washout technique, is commonly employed for diagnosing respiratory anomalies in this case. In this work, the classification of a given infant's tidal breathing as either normal or abnormal is addressed using machine learning paradigms. Based on Long Short-Term Memory (LSTM) networks, the proposed architecture of the model and the techniques used in this work have shown high test scores (above 96% for accuracy, specificity, and sensitivity) on a given data set.

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csem

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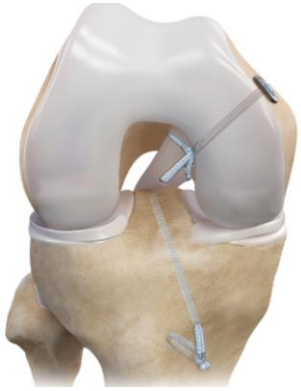
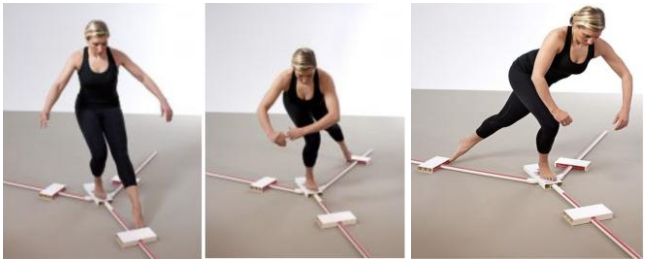
References:
(1) Fousaz Et al., Volumetric capnography in infants with bronchopulmonary dysplasia, 164(2):283-8.e1-3., J Pediatr., 2014.

(2) Fousaz Et al., Breath-to-breath variability of exhaled CO2 as a marker of lung dysmaturity in infancy, 123(6):1563-1570 J Appl Physiol, 2017

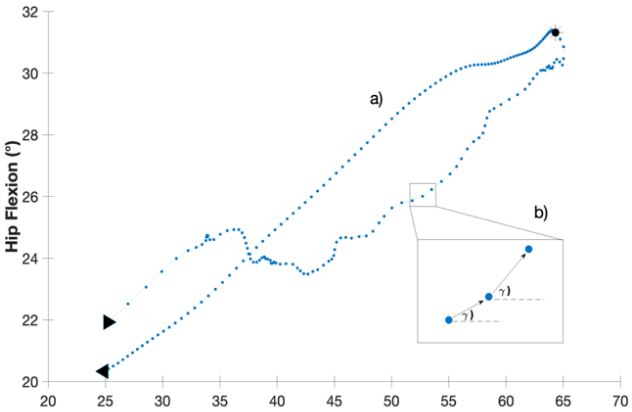
Inter-joint coordination during the Y-Balance Test: Comparison between patients 2 years after ACL repair with InternalBrace vs. ACL reconstruction vs. healthy controls



ACL primary repair with InternalBraceTM. Courtesy: Athrex GmbH



Y-Balance test in anterior (l.), posteromedial (m.) and posterolateral direction (r.). Courtesy: FunctionalMovement.com



Calculation of coupling angles according to the modified Vector Coding Technique derived from angle-angle plot of hip and knee joint during YBT anterior reach. Courtesy: Kathrin Fiedler

Master Thesis by Kathrin Fiedler (Department of Sports Science, University of Freiburg) at the Functional Biomechanics Laboratory (University Hospital Basel).

Kinematic changes in lower limb joints after anterior cruciate ligament reconstruction (ACL-R) are observed during various functional[1] and during dynamic postural control tasks[2]. Recently, ACL repair with InternalBrace™ augmentation (ACL-IB; Fig.1) has gained attention due to ligament preservation and omission of donor-site harvesting compared to ACL-R[3]. While clinical results are promising, data on kinematics[4] and coordination after ACL-IB are limited. We aimed to compare lower limb inter-joint coordination during the Y-Balance Test (YBT) between patients 2 years after ACL-IB (n=29), ACL-R (hamstring grafts; n=27), and sex- and aged-matched healthy controls (n=29).

Kinematic data were recorded during YBT in all directions (Fig.2) using a motion capture system (Vicon, UK). Inter-joint coordination of sagittal plane hip-knee and knee-ankle joint pairs was analyzed using the modified Vector Coding Technique in maximum reach trials for each YBT direction and compared between groups.

No significant differences were found in inter-joint coordination between all groups and YBT directions. ACL-IB yields similar coordination of the lower limb joints during dynamic postural control task.

These results suggest that neuromuscular knee function is restored 2 years postoperatively in both ACL groups and highlight the equivalence of ACL-IB as an alternative to ACL-R with hamstring grafts.

Funding:

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References:
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(3) Heusdens et al. (2018). Arthrosc Tech 7, e747–e753.
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High-resolution spectrograms as a decision support system for clinicians without background in sleep medicine

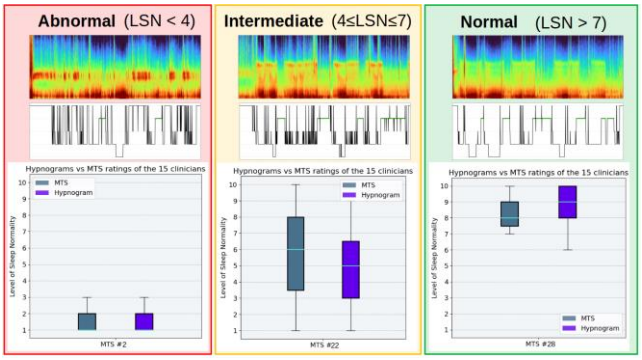

Figure 1: Example of abnormal, intermediate and normal HRS and hypnogram regarding the Level of Sleep Normality (LSN) scoring. Abnormal for LSN < 4, Intermediate for 4 ≤ LSN ≤ 7 and Normal for LSN > 7. (Picture: [D.Ferré]).

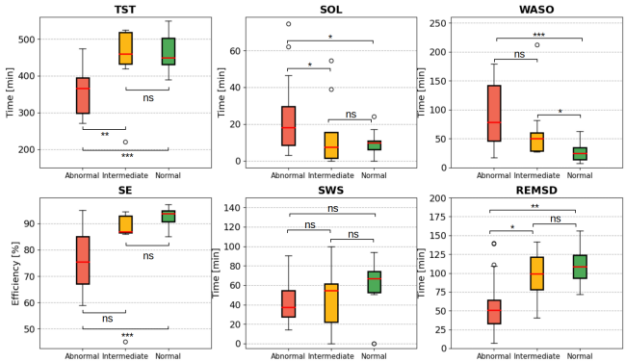

Figure 2: Sleep architecture features (TST, SOL: Sleep Onset Latency, WASO, SE, SWS and REMS), for the respective HRS grouped by abnormal, intermediate and normal by all clinicians. P-values between groups: (ns): p≥0.05, (*):p<0.05, (**):p<0.01, (***):p<0.001. P values obtained with Post-hoc Dunn test for Kruskal Wallis Test.. (Picture: D.Ferré).

Master's Thesis by David Ferré López (Department of Biomedical Engineering, University Basel) at Rekonas GmbH.

Quantifying sleep is crucial in clinical medicine. Clinicians without sleep-medicine expertise (nonSC) are interested in assessing sleep, although the diagnosis of sleep disorders is made by clinicians with sleep-medicine expertise (SC). It is hypothesized that pathological sleep can reliably be identified by nonSC using high-resolution spectrograms (HRS). NonSC may potentially gain important initial insights into sleep architecture (slow wave sleep (SWS), Rapid Eye Movement Sleep (REMS), Wake After Sleep Onset (WASO)).

A remote digital trial of three experiments was performed by 15 clinicians (SC: n=8; nonSC: n=7). (**I**) Clinicians independently scored 40 HRS and their corresponding hypnograms on a scale from 1 (abnormal) to 10 (normal), and (**II**) manually extracted hypnograms from 10 HRS. (**III**) To quantify potential learning effects and test-retest reliability, (**I**) was repeated. Multitaper spectrogram (1) method was used to obtain the HRS.

Perceived abnormality in the HRS was linked significantlly to sleep efficiency (SE) ($p<0.001$), REMS ($p<0.01$), WASO ($p<0.001$) and total sleep time (TST) ($p<0.001$). These findings provide evidence that HRS can enable nonSC to reliably identify pathological sleep architectures with a similar accuracy to clinical scored hypnograms.

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References:
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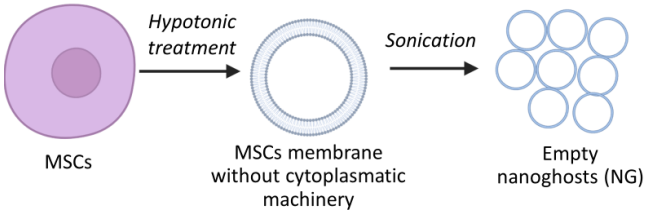
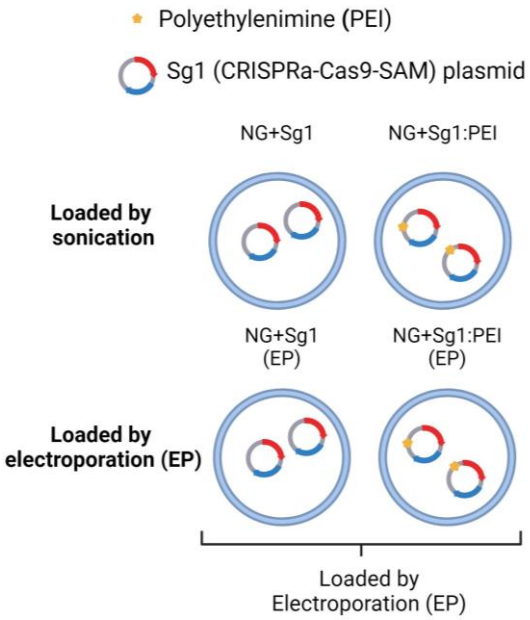
Optimization of nanoghosts (NG) loading and cell delivery for gene therapy applications



Visual representation of nanoghosts (NG) fabrication from Mesenchymal Stromal Cells (MSCs). The removal of cytoplasmatic machinery is done by a hypotonic treatment followed by a process of sonication. Image created using BioRender.com



Groups of loaded NG considered during this thesis. These include NG loaded by electroporation or sonication, as well as plasmid complexation with Polyethylenimine (PEI). Image created using BioRender.com

Master's Thesis by Ximena Forero (University of Basel) at Cartilage Engineering Group

Nanoghosts (NG) are delivery vehicles produced from the lipidic membrane of Mesenchymal Stromal Cells (MSCs) that maintain the biocompatibility and immunomodulatory capacity of this cell type and allow the loading of genetic material for gene therapy applications [1]. We hypothesized that NG could be used in-vitro for the modulation of GDF-5 gene, crucial in cartilage degenerative diseases [2], which could promote cartilage regeneration in chondrocyte cells in-vitro. For this a CRISPRa-Cas9-SAM plasmid [3] was previously designed and verified for the activation of GDF-5 gene.

First, the NG loading with the plasmid was verified considering two different loading methods (electroporation and sonication) as well as plasmid complexation with polyethyleneimine (PEI). Second, NG were applied on target cells (Nasal chondrocytes, Nucleus pulposus cells and C28-I2 established cell line) to evaluate GDF-5 gene expression. Last, plasmid concentration loaded in NG was modified to determine the optimal number of plasmids per NG to achieve gene expression.

NG loading parameters were optimized as well as the technique for confirmation of NG loading. This includes the selection of plasmid marker, sample concentration, beyond others. Additionally, the capacity of loaded NG to produce GDF-5 modulation in chondrocyte established cell line C28-I2 was confirmed, performance was limited on primary cells.

Multiple steps for further optimization were identified and include the quantification of NG during intermediate steps and further functionalization of NG membrane.

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[1] L. Kaneti et al., "Nanoghosts as a Novel Natural Nonviral Gene Delivery Platform Safely Targeting Multiple Cancers," Nano Lett., vol. 16, no. 3, pp. 1574–1582, Mar. 2016, doi: 10.1021/acs.nanolett.5b04237

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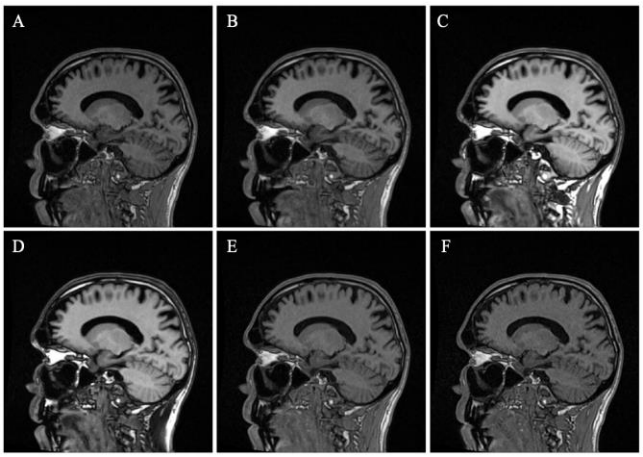
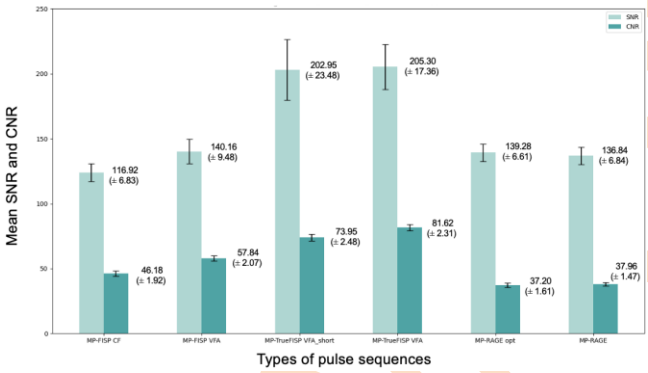
Flip Angle Optimization for MP-RAGE



Visual results of optimized pulse sequences on 0.55 T. The images from A-F correspond to the following order of pulse sequences: MP-FISP$_{CF}$, MP-FISP$_{VFA}$, MP-TrueFISP$_{VFA_short}$, MP-TrueFISP$_{VFA}$, MP-RAGE$_{OPT}$, and MP-RAGE. (Silvan Furrer)



The resulting mean values of the signal-to-noise and contrast-to-noise ratios for each inspected pulse sequence and their respective standard deviations are enclosed in brackets. They highlight the differences between continuous and variable flip angle implementations as well as the choice of pulse sequence type. (Silvan Furrer)

Master's Thesis by Furrer Silvan (University of Basel) at Magnetic Resonance Physics & Methodology.

Background: Magnetic Resonance Imaging (MRI), a non-invasive technique leveraging the differential relaxation times of tissues, plays a crucial role in this endeavor. While high-field MRI scanners prevail, low-field devices offer cost-effective alternatives with specific benefits. Consequently, there exists a considerable gap in the development of pulse sequences of low- and high-field applications.
Purpose: To improve the grey/white matter contrast of magnetization-prepared rapid gradient echo (MP-RAGE) and to demonstrate the feasibility of implementing variable flip angles on a low-field 0.55 T MR scanner for brain imaging.
Methods: Eight healthy volunteers underwent brain imaging using six protocols on a 0.55 T MR scanner. The protocols employed a Cartesian k-space trajectory in all sequences. For the three pulse sequences with variable flip angles (VFA), a pyramid-like ramp structure was used for RF excitation. The optimization process was facilitated by utilizing an extended phase graph (EPG) simulation. Signal-to-noise and contrast-to-noise ratios were used to compare the resulting protocols.
Results: Comparative analysis across eight participants showed robust results, with an average difference margin of approximately 1.37%. MP-FISP with continuous flip angle demonstrates a contrast improvement of 24% compared to manufacturer sequences. Employing VFA contributes to an additional contrast improvement of 32% for MP-FISP and 53% for MP-TrueFISP. Banding artifact formation in MP-TrueFISP was effectively addressed through parameter adjustments.
Conclusion: This study shows promising results in low-field brain imaging, introducing two enhanced pulse sequences suitable for clinical applications — MP-TrueFISP (short TR) and MP-FISP, featuring variable flip an-

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Identification of 9.4T MRI sequences for enhanced cellular visualization of MS lesions

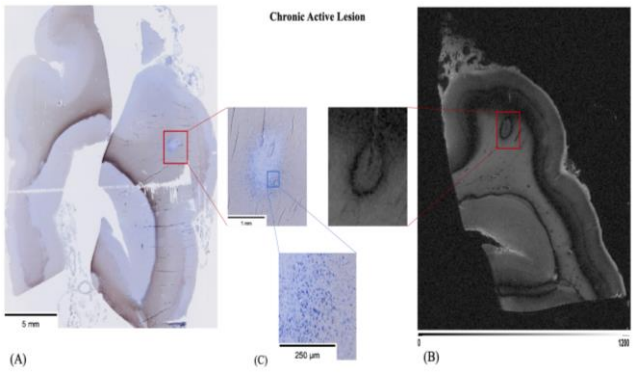

Figure 1: Example of immunohistochemical (IHC) and MRI images used in the study. IHC image (A) and 9.4T MRI FLASH contrast (B) of a brain block presenting a chronic active MS lesion. The characteristic rim of microglia of the lesion is highlighted in (C). (Pictures A,C by Institute of Neuropathology of the University Medical Center Göttingen; Picture B by Preclinical Research Imaging Center of the University Medical Center Freiburg; Figure by E.Giacomelli)

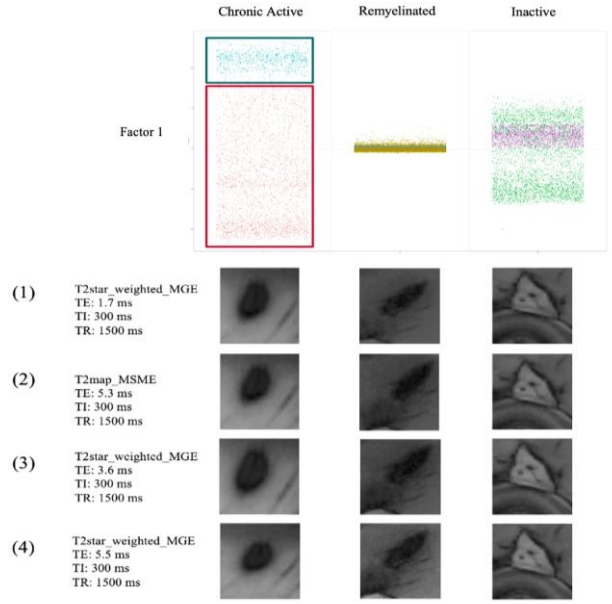

Figure 2: Example of the results from the Factors analysis of the MOFA+ model. (Top) In the scattered plots for the factor 1 the clusters from the NAWM, in aquamarine, and lesion, in red, are shown for three different MS lesion types. (Bottom) The four most enhancing MRI contrasts detected by the model to explain the variance for factor 1 are shown. (Plots by E.Giacomelli; MRI contrasts by Preclinical Research Imaging Center of the University Medical Center Freiburg; Figure by E.Giacomelli)

Master's Thesis by Elisabetta Giacomelli (Department of Biomedical Engineering, University of Basel) at ThINK Group.

Magnetic resonance imaging (MRI) at ultra-high-field (UHF, 7T or higher) offers a higher signal-to-noise ratio and enhanced susceptibility effects compared to MRI at clinical fields (eg. 3T), leading to an improved visualization of some pathological hallmarks in complex neurological disorders, like Multiple Sclerosis (MS) (1). This advanced technology might potentially help discovering novel pathophysiological mechanisms associated with mechanisms of damage and repair in MS. When UHF MRI is applied postmortem and is associated with histological analysis of a given tissue, it is possible to establish the direct relationship to changes in MRI signals and pathological features of different MS lesion types.

In this study, Multi-Omics Factor Analysis v2 (MOFA+) [2], a statistical framework for comprehensive integration of multi-modal data, was applied to dissect the spatial signature of 9.4 T MRI measures, related to the presence of specific tissue characteristics in a sample of lesions collected from patients with MS (Figure 1). The model explored the features of MRI scans to learn a low-dimensional representation of complex data, which presented a combination of factors, capturing technical sources of variability, and their respective weights, representing the MRI scans' importance in explaining the tissue diversity corresponding to different lesion types. As a result of the factors' analysis, the most informative T_2 and T_2^*-weighted MRI sequences for distinctive lesions and, therefore, different cellular contents were detected. In addition, the learned factors enabled the identification of sample clusters between damaged tissue and normal appearing white matter (NAWM) for different lesion types (Figure 2).

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References:

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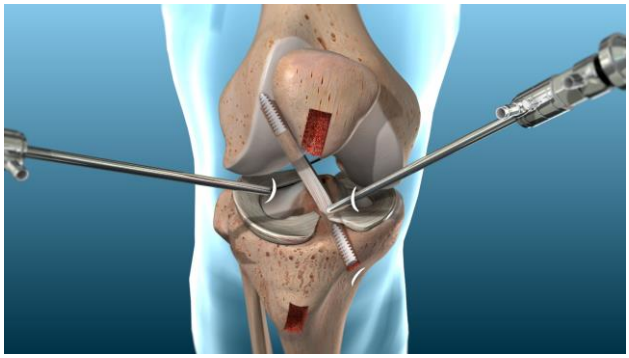
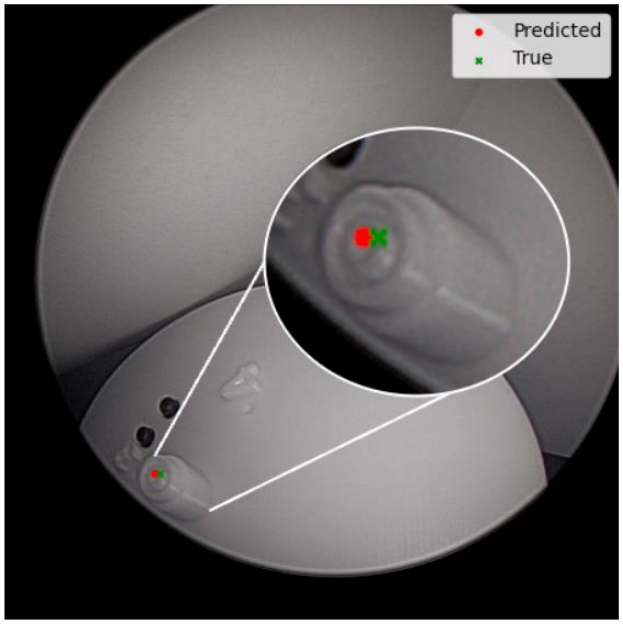
A Deep-Learning Approach for Navigated Anterior Cruciate Ligament Surgeries



A graft is obtained by resecting the patellar tendon and used in the reconstructive surgery of the damaged ACL along with the arthroscope (picture: Willis Knighton Health) (1).



The trained model shows good performance on the test set (picture: M. Giorgi).

Master's Thesis by Martino Giorgi (Department of Biomedical Engineering, Universität Basel) at CIAN.

The anterior cruciate ligament is frequently subject to injury in the human knee, often necessitating reconstructive surgery. Research indicates that the precise location of the ACL femoral fixation point significantly influences the success of surgical interventions and subsequent rehabilitation.

This Master's Thesis introduces an innovative approach to support surgeons in ACL surgery, addressing existing limitations in available navigation solutions. The proposed solution utilizes a deep learning approach to estimate the ideal fixation site of the ACL from a video feed. To obtain the training data for the machine learning model, a complex pipeline of transformations is used to derive 2D pixel coordinates of a specific location on the image of the patient, such as the ACL fixation site from a 3D CT scan.

The promising results affirm the functionality of the proposed proof-of-concept, suggesting the feasibility of conducting further experiments on real knees with an expectation of similar positive outcomes.

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References:
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Smart OCT ystem as a tool for time-resolved dehydration detection in biological tissues: Investigating the potential and limitations

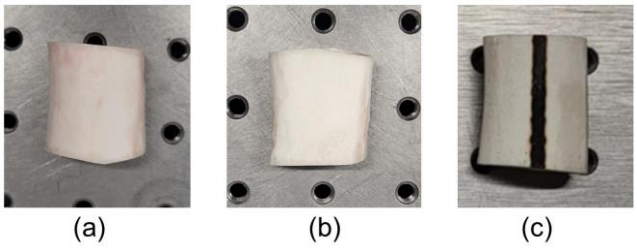
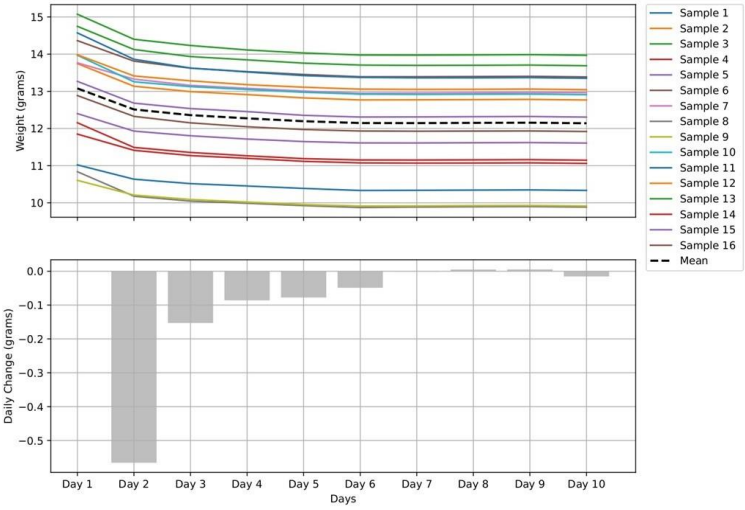


Figure 1: Photos of three bone samples at the fresh (a), dehydrated (b), and calbonized (c) stages.



	ResNet-18	ResNet-50
ACC	97.33 %	96.03 %
F1	97.32 %	96.03 %
AUROC	97.33 %	96.00 %
AUPR	96.22 %	94.00 %

Figure 2: Plot of the weight from each bone sample for 10 days (above), plot comparing the mean weight value with the mean value from the previous day (middle). Performance results of the ResNet-18 and ResNet-50 models in classification between fresh and dehydrated bones (accuracy (ACC), area under the receiver operating characteristic curve (AUROC), and area under the precision-recall curve (AUPR)) (bellow).

Master's Thesis by Aikaterina Grava at the Center of Intelligent Optics, University of Basel.

Optical coherence tomography (OCT) is widely acknowledged medical imaging modality, providing non-invasive, three-dimensional images which closely resemble histological representations of biological tissues [1]. In recent years, OCT has demonstrated promising results as guidance system for laser surgery [2]. This project aims to enhance precision and safety of laser surgery on bone tissue (laser osteotomy) by developing deep learning-assisted OCT to detect the hydration stages of bone. This study was designed to observe different hydration stages of bone, mimicking laser ablation process. The goal is to prevent thermal damage and optimize tissue removal efficiency during laser osteotomy based on the findings of this study.

For this experiment, a swept-source OCT system is utilized. First, OCT volume images of 13 bones in different stages (fresh, dehydrated, and carbonized) were acquired, and a ResNet50 deep learning model was used to differentiate between these stages based on the OCT images (Fig. 1). Our model achieved an accuracy of 0.912 in detecting differences among fresh, dehydrated, and carbonized bones. However, to assign dehydration correctly in the deep-learning model, we focused on the transition between fresh and dehydrated bones at room temperature. For this, OCT images and weight measurement is performed in the period of 10 days (Fig. 2). Based on the weight measurements, the dehydration threshold was estimated and used as label for the deep learning model. Subsequently, both ResNet18 and ResNet50 models were used, achieving accuracies of 0.973 using the ResNet18 model and 0.96 using the Res-Net50 in distinguishing between fresh and dehydrated bones (Fig. 2). In conclusion, this project represents a progressive stride towards safer and more precise surgical interventions, leveraging and advancing the established capabilities of OCT.

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References:
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Deep Learning for Automatization of Video-Analysis for Malaria Vector Behavioral Studies

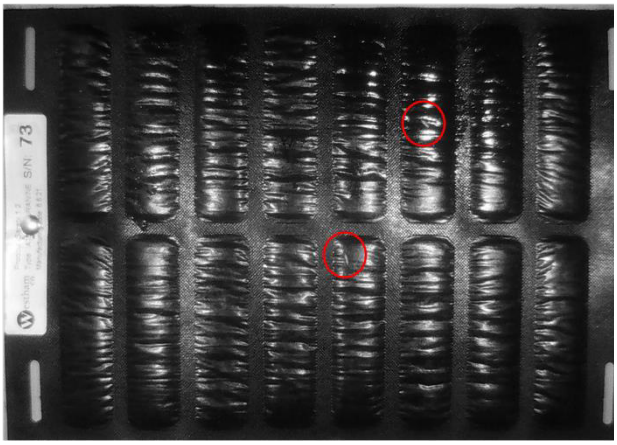

Figure 1: Sample image of an Attractive Toxic Sugar Bait with two mosquitoes on it. These images were used to train the models used in this thesis. (Picture: SwissTPH, Tenywa Frank).

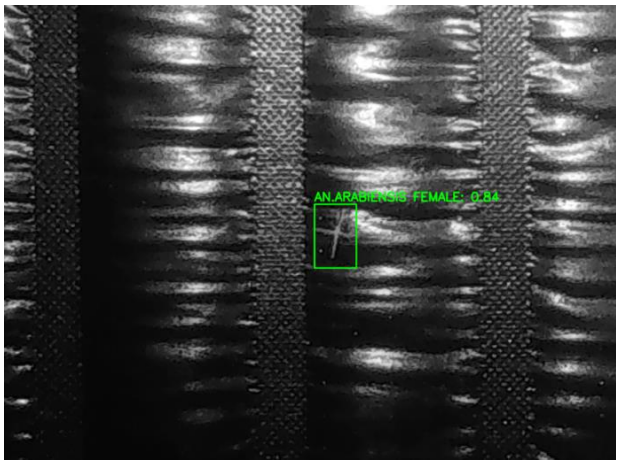

Figure 2: A resulting output of the working YOLOv8m algorithm that detects mosquito species and sex. (Picture: Juval Gutknecht).

Master's Thesis by Juval Gutknecht (Department of Biomedical Engineering, University of Basel) at the Center for medical Image Analysis & Navigation (CIAN).

Malaria is caused by a parasite that is transmitted through the bite of infected mosquitoes. In 2022, about 249 million cases of malaria were recorded. If untreated, malaria can cause death, which happened to 608'000 people in 2022 (1). The goal of this master's thesis was to develop a series of Deep Learning models to support mosquito behavioral studies and vector control strategies, particularly through the use of attractive toxic sugar baits (ATSB). These baits attract mosquitoes, which consume the toxic sugar, fly off, and ultimately die due to the insecticidal properties of the ingested solution (2).

The data consisted of 24-hour series of images of the ATSBs taken every minute and labels indicating whether mosquitoes were present, and if so what their gender and species were. Using this data, a series of models were trained to solve two tasks: mosquito detection and mosquito classification.

First, an Inception-ResNet-v2 was deployed as a binary classifier on the pre-processed image series. The resulting model achieved F1 scores up to 0.93. For the detection and classification task, bounding box labels were created. This enabled the training of a YOLOv8 model. It reached mAP scores up to 0.83 on the test set. Finally, a second YOLOv8 model was developed that could tackle species and sex classification tasks. And achieved mAP scores of up to 0.9. This performance might be due to the small size of the dataset.

The results of all the models are promising, but to achieve more generalized models, larger labeled datasets are required.

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Association between severity of stenosis, fat infiltration of the paraspinal muscles and trunk flexion during gait in patients with lumbar spinal stenosis

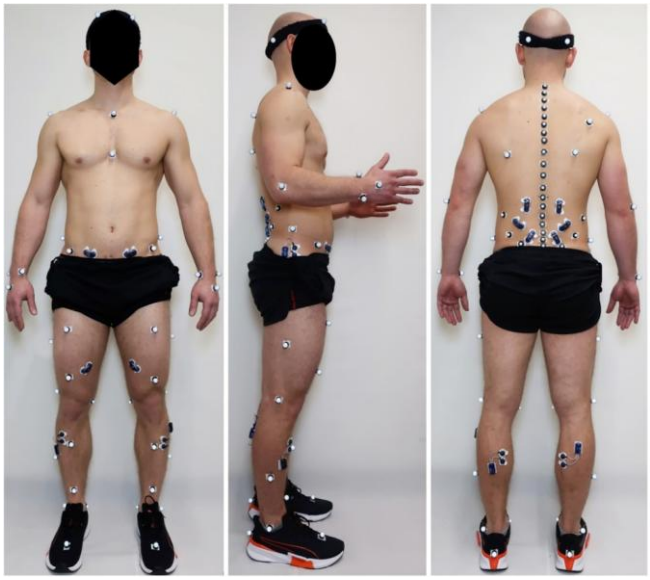

Figure 1: Placement of retroreflective markers for the biomechanical assessment (Koch et al., 2023).

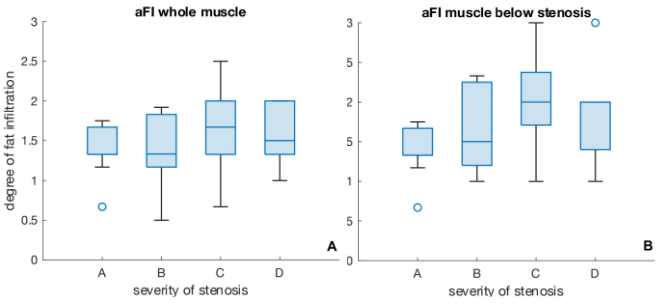

Figure 2: **A**: Boxplot showing degree of stenosis and degree of fat infiltration of the paraspinal muscles using the aFI over the whole; **B**: Boxplot showing degree of stenosis and degree of fat infiltration of the paraspinal muscles using the aFI over the muscle parts below the highest degree of stenosis. aFI = average fatty infiltration (Maxine Gygax).

Fat Infiltration (Goutallier)

	L1		L2		L3		L4		L5		S1	
	left	right	left	right	left	right	left	right	left	right	left	right
Patient 1	n.a.	n.a.	1	1	2	2	3	2	4	2	4	3
Patient 2	1	1	1●	1	2	2●	2	2●	2	3●	2	2
Patient 3	1	1	1	1	1	2	2	2	2●	2	3●	2
Patient 4	1	1	1	2	2	2●	2	2	3	2	3●	2
Patient 5	1	1	1▲	1	1	1	1	2	1	2●	2	2●

Figure 3: Qualitative summary of the patients with side-to-side differences in fat infiltration of the paraspinal muscles. Blue dots indicate the side with the higher degree of foraminal stenosis, the triangle indicates a higher degree of lateral recess stenosis (Maxine Gygax).

Funding:

Swiss National Science Foundation

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Universitätsspital Basel

Department of Spine Surgery

Master's Thesis by Maxine Gygax (Department of Health Science and Technology, ETH Zurich) at the Functional Biomechanics Laboratory (University Hospital Basel).

With the aging population, lumbar spinal stenosis (LSS) is becoming an increasingly important issue as the disease is associated with age-related changes in the spine [1]. Research shows a mismatch between radiological and clinical findings in patients with symptomatic LSS (sLSS) [2] and has often overlooked lateral manifestations. Furthermore, while patients report reduced pain in a flexed posture, the relationship between stenosis severity and bent posture remains unclear [3]. This study investigated associations between the radiological severity of stenosis, fat infiltration of the paraspinal muscles and trunk flexion during gait.

Sagittal and transversal images of the lumbar trunk of 54 patients were collected and rated for central, lateral recess and foraminal stenosis, as well as fat infiltration of the paraspinal muscles. Gait analysis was performed using a Vicon motion capture system (Fig. 1). Spine flexion angle and thorax tilt were extracted for six gait cycles for each patient, and their maximum was computed and averaged.

A significant correlation was found between the average fat infiltration (aFI) of the paraspinal muscles below the stenotic segment and the severity of stenosis ($r = 0.372$, $p = 0.008$) but not between spine flexion or thorax tilt and severity of stenosis or aFI of the paraspinal muscles below the stenotic segment. Side-to-side differences in fat infiltration of the paraspinal muscles have been found in 10% of the patients or 3.4 % of all analysed levels (Fig. 3).

LSS appears to primarily affect the muscle morphology below the stenotic segment. A qualitative analysis of side-to-side differences in fat infiltration of the paraspinal muscles promises interesting results for further studies with a larger patient cohort or a finer grading scheme. The lack of association between trunk flexion and radiological signs of LSS may be due to patients using different pain alleviation strategies to relieve their symptoms.

Therefore, it may be worthwhile to investigate different pain relief strategies and their association with (quantitative) morphological parameters in patients with sLSS.

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References:

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University of Basel

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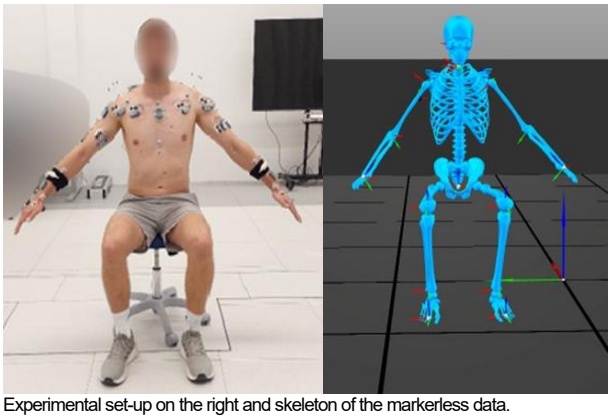
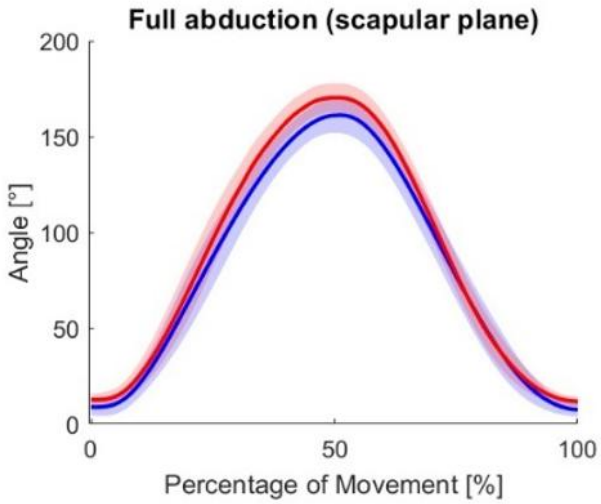
Comparison of shoulder kinematics between marker-based and marker-less motion capture



Experimental set-up on the right and skeleton of the markerless data.



Mean and standard deviation the abduction angle during full abduction movement in the scapular plane from marker-based (blue) and markerless (red) motion capture.

Master Thesis by Christoph Künzel (Department of Biomedical Engineering, University Basel; Department of Sport and Sport Science, University of Freiburg) at the CADENCE Laboratory.

Kinematic analysis can significantly enhance clinical examinations for detecting rotator cuff tears. This study aimed to compare shoulder kinematics between marker-based and markerless (Theia 3D, 1) motion capture systems during full arm abduction in both the frontal and scapular planes, as well as during full arm flexion in healthy subjects.

Qualitatively, the average waveforms of joint angles exhibited similar patterns across all movements between the two systems. Root mean square errors ranged for abduction from 5.9° to 9.1°, for flexion from 8.7° to 12.1°, and for internal rotation from 16.5° to 24.1°. Correlation of multiple correlation were good to very good for all angles.

The use of markerless motion capture for shoulder kinematics seems promising, but improvements are still needed to achieve better concordance with marker-based motion capture, especially for the internal rotation angles.

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References:

(1) Lahkar, et al (2022). Frontiers in Sports and Active Living, 4, 939980. https://doi.org/10.3389/fspor.2022.939980

Large Language Model Approach for Analysing Medical Information from the Internet

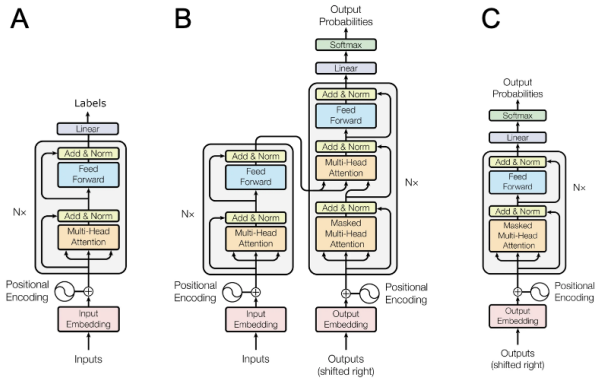

Figure 1: Transformer based natural language processing model architectures. [A] Encoder-only architecture with a linear classification layer. [B] Original transformer by Vaswani et Al. [C] Decoder-only architecture used by large language models (Sébastien Muheim adapted from Vaswani et Al. (3))

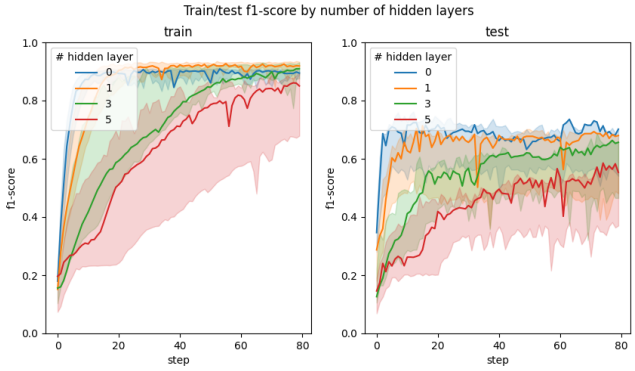

Figure 2: F1-score evolution by number of hidden layers of a grid search. The F1-score ranges for all parameter combinations of the grid search are are shown over the training epochs (step) for training (train) and validation (test). The solid lines are the scores of the set of parameters that achieved the best f1-score at epoch 19 during validation. All other sets of parameters reached f1-scores within the shaded area. The colours differentiate the parameter sets per number of hidden layers of the classifier head. (Sébastien Muheim)

Master's Thesis by Sébastien Muheim (Department of Biomedical Engineering, Universität Basel) at CIAN-Lab.

Improving health literacy of the general public is one of the goals set by the Swiss Federal Council's health policy strategy 2020–2030 (1). This thesis examines the use of large language models to evaluate the quality of medical information found on the internet. The quality of the texts was assessed based on the criteria from the Ensuring Quality Information for Patients score. The rating capabilities of state-of-the-art pre-trained generative models such as GPT-4 and the results from fine-tuned classifiers were compared to the ratings of experts. The results show that the GPT-4 model has an average of 71% accuracy with high disparity between the questions evaluated. This variation is attributed to a refinable alignment between the rating criteria from the experts and the model. The fine-tuning of specialised classifiers showed promising results on the individual paragraphs of the website with 95% accuracy and a 0.68 micro averaged f1-score. The exploration of models trained longer with less influence of regularisation techniques is advised. It is concluded that the natural language processing capabilities of transformer-based models are suited to assess the quality of medical information and will be of use to improve health literacy.

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(1) FOPH, F. O. of P. H. The Federal Council's health policy strategy 2020–2030. https://www.bag.admin.ch/bag/en/home/strategie-und-politik/gesundheit-2030/gesundheitspolitische-strategie-2030.html.

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(3) Vaswani, A. et al. Attention Is All You Need. Preprint at http://arxiv.org/abs/1706.03762 (2023).

3D Printed Bone-Like Realistic Anatomical Models For Surgical Simulation

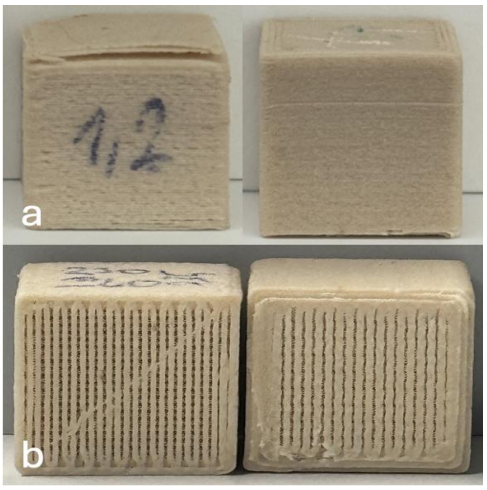

Figure 1. Comparison of 3D-printed cube structures, illustrating external (a) and internal (b) parts printed with initial (left) and optimized (right) printing parameters. (Credits: A. Ozsoy)

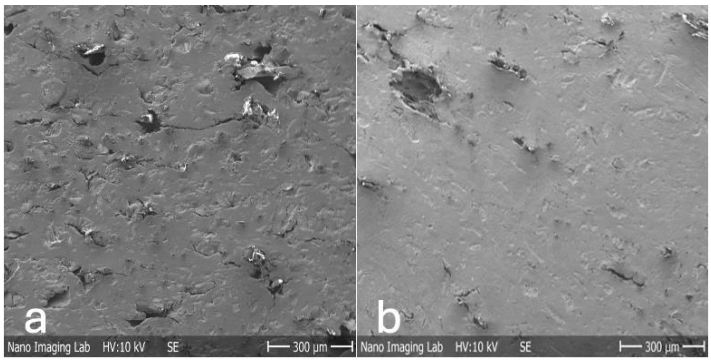

Figure 2. Scanning Electron Microscopy images of FibreTuff PAPC samples printed at different temperatures (a): 255°C; (b):260°C (Credits: A. Ozsoy)

Master's Thesis by Ataberk Ozsoy (Department of Biomedical Engineering) at the Medical Additive Manufacturing (Swiss MAM) Research Group.

Surgical simulation plays a vital role in medical education and training. However, the limited availability and high costs associated with cadaver bones present challenges. This situation underscores the need for cost-effective alternatives such as 3D-printed anatomical models that closely mimic the properties of real bone. These models offer a realistic and reusable solution for surgical simulation, addressing the current constraints and enhancing the learning experience for medical professionals. [1,2].

This study aimed to assess the suitability of FibreTuff polyamide, polyolefin, and cellulose (PAPC) as a material for 3D-printed bone-like anatomical models for surgical training. The research involved optimizing 3D printing parameters to ensure durability and quality, followed by a comparison between different infills (percentage and patterns variables) of FibreTuff PAPC and PolyTerra Polylactic acid (PLA). Mechanical tests including tensile, flexural, and compressive assessments were performed, along with drilling observations and CBCT scans to assess radiodensity behavior.

The results indicated that FibreTuff PAPC exhibited weaker mechanical properties and higher radiolucency compared to PLA. Specifically, the 90% gyroid infill, resembling bone structure, showed weaker properties compared to 100% rectilinear infill.

In conclusion, despite similarities in tactile response to drilling, FibreTuff PAPC does not exhibit sufficient bone-like behavior for use in realistic anatomical models for surgical simulation.

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Three-dimensional hard X-ray micro-tomographic imaging of the human palatal anatomy and gracilis muscle

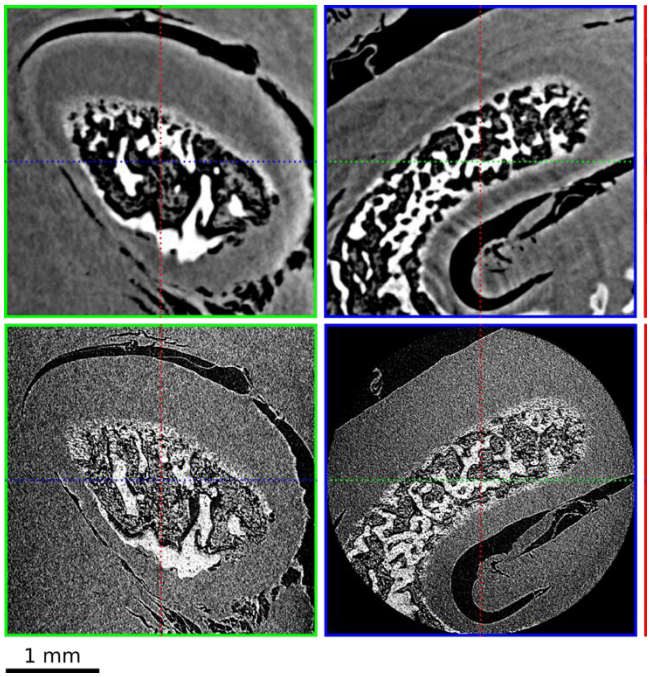

Figure 1: Comparison of soft-tissue contrasts in synchrotron radiation-based (top) and laboratory-based (bottom) micro computed tomography of the pterygoid hamulus (Picture: D. Schönegg).

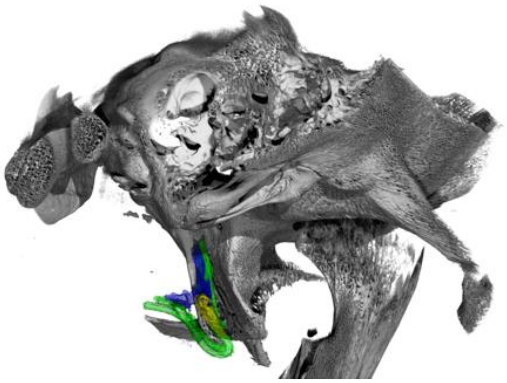

Figure 2: 3D rendering of the local anatomy around the pterygoid hamulus illustrating the muscle sling formed by the two heads of the tensor veli palatini muscle (lateral head: green; medial head: yellow) and the levator veli palatini muscle (blue) (Picture: D. Schönegg).

Funding:

University of Basel
Department of Biomedical Engineering

diamond

Master's Thesis by Daphne Schönegg (Department of Biomedical Engineering, University of Basel) at the Biomaterials Science Center (BMC)

Palatoplasty in infants with cleft palate aims to reconstruct the anatomy and restore the velopharyngeal function. This interdisciplinary project used micro tomography (µCT) to non-destructively visualize human muscle microanatomy, extending existing knowledge from dissection and histological studies. A detailed understanding of the anatomy is critical for optimizing surgical procedures and improving functional outcomes.

The right half of a plastinated infant head and an ethanol-dehydrated, unstained segment of a human gracilis muscle were examined using laboratory-based and synchrotron radiation-based µCT. Images were rigidly registered and analyzed. Automated threshold-based bone segmentation and manual segmentation of soft tissues including muscles, tendons, and aponeurosis allowed for the visualization of their 3D topographic relationships and of the muscle fiber architecture with sub-micrometer voxels (1).

Laboratory-based µCT systems proved suitable for virtual histology of unstained soft tissues, allowing visualization of subcellular structures therein. Synchrotron radiation-based µCT with phase retrieval provided enhanced contrast within the plastinated soft tissues (1).

Tapered fibers identified in long muscles may alter biomechanical behavior. The palatal muscles form a complex sling around the pterygoid hamulus. This underscores the importance of preserving this bony prominence during cleft palate repair (2).

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References:
(1) D. Schönegg et al.: *Three-dimensional hard X-ray micro-tomographic imaging of the human palatal anatomy and gracilis muscle* Proc. SPIE **13152** (2024) 1315229.

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Evaluation of OA Synovium's Response to Anti-inflammatory Cytokines and NC-IL-1Ra Chondrogenic Potential

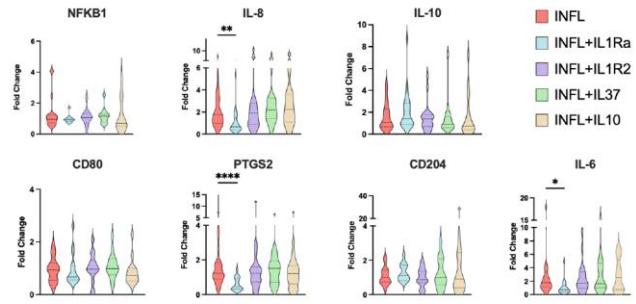

Figure 1: Comparison of the efficacy of different anti-inflammatory cytokines on OA synovial explants (Picture: K. Sovdagarova).

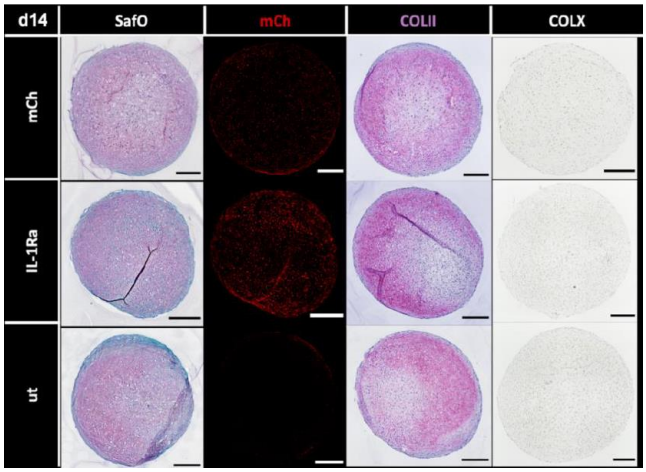

Figure 2: Histological analysis of NC-mCh, IL-1Ra-mCh and ut on d14 of NCs pellet culture (Picture: K. Sovdagarova).

Master's Thesis by Ksenia Sovdagarova in Tissue Engineering group at DBM.

Osteoarthritis (OA) is a prevalent degenerative joint disorder characterized by articular cartilage degradation, subchondral bone remodelling, and synovial inflammation. Current treatment modalities primarily focus on symptom management and fail to address the underlying pathophysiology effectively.

Interleukin-1 Receptor antagonist (IL-1Ra), an endogenous cytokine receptor antagonist, has emerged as a promising therapeutic agent due to its ability to counteract the pro-inflammatory effects of interleukin-1 (IL-1), a pivotal mediator in OA progression. Nasal Chondrocytes (NCs) possess unique properties, including robust regenerative capacity and immunomodulatory properties, making them an attractive candidate for tissue engineering and regenerative medicine approaches.

This study aims to elucidate the synergistic potential of NCs transduced with IL-1RA in the long-term treatment of OA. Several anti-inflammatory cytokines were assessed for their potential in mitigating inflammation in OA synovial explants. IL-1Ra has shown the best performance in downregulating the key inflammatory markers. Therefore, it has been chosen for genetically engineering NCs by lentiviral transduction. This potentiation was later confirmed to have no undesirable effects on the chondrogenicity of the NCs.

By comprehensively evaluating the synergistic interactions between IL-1Ra and NCs, this research seeks to advance our understanding of their potential as therapeutic mechanisms and pave the way for the innovative and potent treatments for OA, offering new hope for patients suffering from this debilitating condition.

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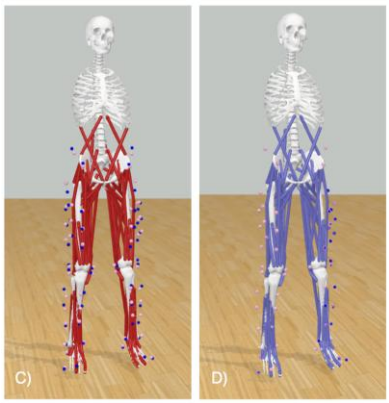
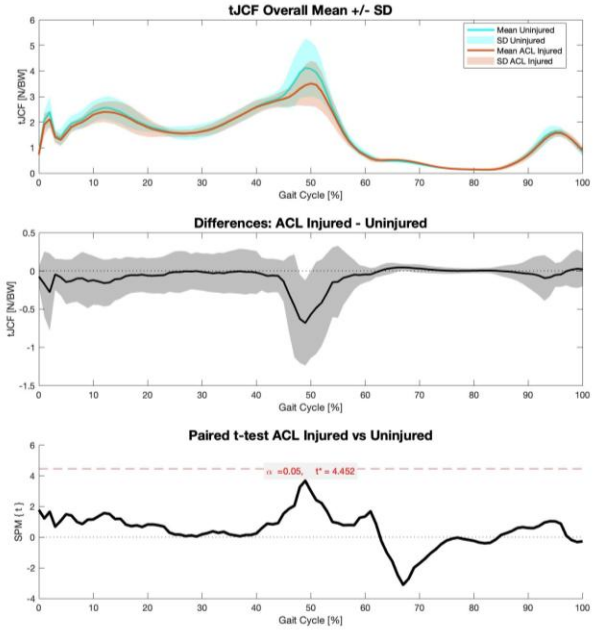
Tibiofemoral Joint Contact Forces in ACL Injured and Uninjured Legs – Implementation of the OpenSim Workflow and Pilot Comparisons



Measurement-based scaling process: C) Scaling: computation of scaling factors and scaling of bodies by comparison of distances between marker pairs; D) Registration: adjustment of the virtual markers to the experimental data (pink and blue markers at the same locations).



Mean tibiofemoral joint contact forces (solid line) ± SD of the ACL injured knees (red) and the uninjured knees (blue, top subplot), differences [N/BW] between the knees (middle subplot), and statistical parametric mapping (SPM) analyzes between the knees (paired t-test and statistical critical value (t), bottom subplot).

Master Thesis by Lea Schweiker (Karlsruhe Institute of Technology (KIT)) at the Functional Biomechanics Laboratory (University Hospital Basel).

ACL injuries significantly impact individuals and healthcare systems, increasing the risk of post-traumatic knee osteoarthritis (OA)[1]. Understanding altered gait mechanics, including joint contact forces (JCFs), is crucial.

This study implemented an automated OpenSim workflow to estimate JCFs in individuals with ACL injuries. Ten females (20–30 years) with unilateral ACL injuries 2–10 years prior were analyzed. The Gait2392 model was used to estimate knee angle trajectories, knee flexion moments, and tibiofemoral JCFs. These outputs were assessed for plausibility and compared between injured and uninjured knees using statistical parametric mapping (SPM).

The results showed that the estimated knee trajectories, flexion moments, and tibiofemoral JCFs were physiologically consistent and aligned with existing literature. Injured knees exhibited lower flexion moments and tibiofemoral JCFs than uninjured knees, though SPM analysis revealed no statistically significant differences.

This proof-of-concept study supports the feasibility of OpenSim for estimating JCFs non-invasively with data measured in the Functional Biomechanics Laboratory. Future studies should focus on refining models, improving scaling, increasing sample size, and incorporating variables such as muscle forces to further understand JCFs and their role in developing post-traumatic OA after ACL injury.

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References:
1) Chen, T., Wang, S., Li, Y., Ai, C., Jiang, F., & Chen, S. (2019). Radiographic Osteoarthritis Prevalence Over Ten Years After Anterior Cruciate Ligament Reconstruction. International Journal of Sports Medicine, 40(11), 683–695. https://doi.org/10.1055/a-0902-8539

Predicting the Ground Reaction Force from Pressure Data

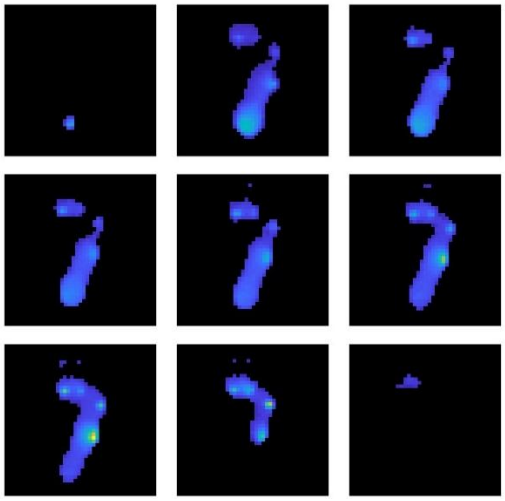

Figure 1: Example of plantar pressure distribution sequence during walking (Picture: P. Rudolf von Rohr).

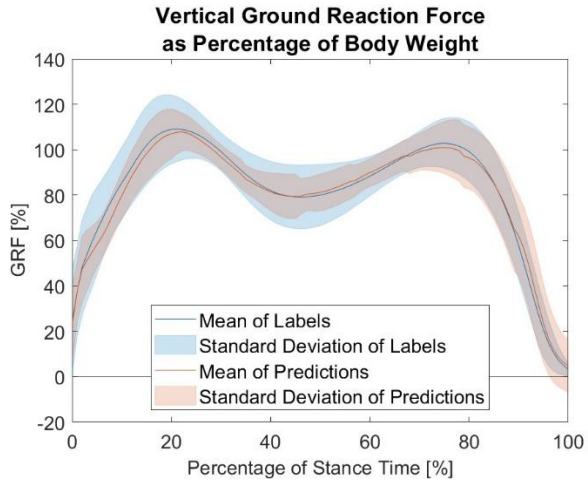

Figure 2: Comparison of the vertical GRF component of the GRF measurement (blue) and the model predictions (orange) (Picture: P. Rudolf von Rohr).

Master's Thesis by Pascal Rudolf von Rohr (Department of Biomedical Engineering, University of Basel) at the Gait Lab of UKBB.

Gait analysis is a key element of clinical biomechanics, where the patient's kinematics is measured during walking. A central quantity, which is acquired with the use of force plates, is the Ground Reaction Force (3-dimensional vector). With the help of the GRF, the inverse dynamics approach can be applied to determine the kinetics of gait.
It would be useful to have outdoor measurements of gait, where the patients follow their everyday life, to have a more natural loading case. However, it is very difficult however, to determine the GRF directly outside, but the pressure distribution of the foot can be measured with the use of pressure measuring insoles placed inside the patients' shoes. By implementing an adequate model, which is trained on patients' data, the GRF may be predicted from the pressure data.
The goal of this project was to create such a model and to investigate the feasibility of the concept and the models' prediction accuracy. The evaluation of the accuracy was done by calculating the normalized root mean squared error of the predictions with respect to the measured range of each GRF component. The best result was achieved by a model, which was based on a CNN-LSTM architecture (a long-short-term-memory model, which takes the output of a convolutional neural network as input) and trained on data of the patient of whom it was predicting the GRF.
The model showed a mean error of 5.63 % for the anterior-posterior component, 18.51 % for the medial-lateral component, and 6.36 % for the vertical component.

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Diffusion Models for Contrast Harmonization of Whole Head Magnetic Resonance Images

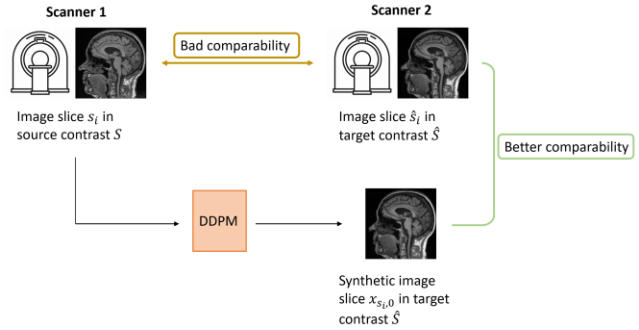

Figure 1: Graphic representation of the contrast harmonization method (picture: E. Winnips).

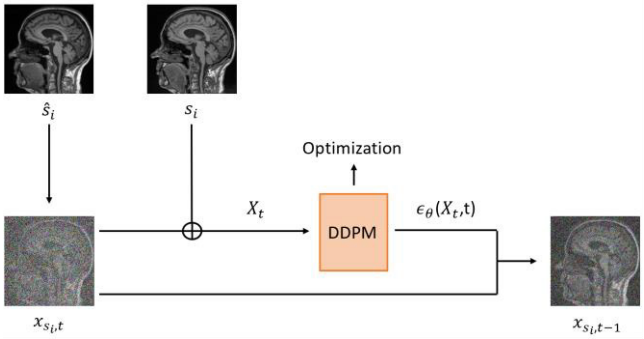

Figure 2: Graphic representation of the model training. The noisy groundtruth image at target contrast is concatenated with the baseline of the source contrast, giving anatomical information to the model. The model uses the concatenated image to predict noise levels at timestep $t-1$ (picture: E. Winnips).

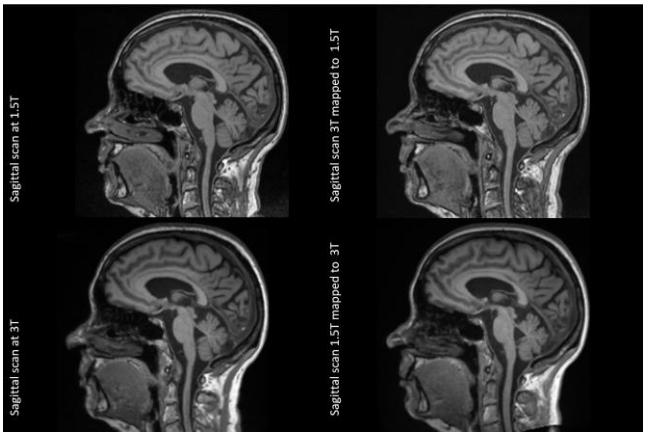

Figure 3: Sagittal view of original images (right) and the respective mapped contrast (right) (picture: E. Winnips).

Master's Thesis by Eva Winnips (Department of Biomedical Engineering, University Basel) at the Center of medical Image Analysis & Navigation (CIAN).

Magnetic resonance (MR) imaging is an imaging technique prone to variabilities, originating from differing scanner models or acquisition protocols. Diseases, such as Multiple Sclerosis, require longitudinal monitoring, which can be impaired by such variabilities.
Contrast differences and resulting issues in the subsequent comparison of the scans were observed during the Swiss Multiple Sclerosis Study [1] as a scanner change from 1.5T to 3T magnetic field strength took place.

This work presents a Denoising Diffusion Probabilistic Model (DDPM), developed to harmonize contrasts of skull-stripped brain MR images acquired at the two different field strengths [2], extended to work with whole-head images. It managed to map contrasts from 1.5T to 3T and from 3T to 1.5T. The mapped images show increased comparability to scans of the target contrast, reducing biases during automated downstream tasks, arising when comparing the original scans acquired at different field strengths.

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