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Institute for Surgical Technology
and Biomechanics

Annual Report 2018

INSTITUTE FOR SURGICAL TECHNOLOGY AND BIOMECHANICS

Contents

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INSTITUTE FOR SURGICAL TECHNOLOGY AND BIOMECHANICS

EDITORIAL

In 2003, the former M.E. Müller (MEM) Institute for Biomechanics founded in 1981 was restructured to form the MEM Center for Orthopaedic Surgery. As part of the MEM Center the Institute for Surgical Technology and Biomechanics (ISTB) has grown over the past 15 years into a highly interdisciplinary translational biomedical engineering research unit. Together with clinical partners our international multidisciplinary team has realized a unique concept for an integrated research continuum from the bench (basic science) to the bedside (clinical application). In 2008, the ISTB also became the nucleus of the newly founded Artificial Organ Center for Biomedical Engineering Research (ARTORG). Effective January 1, 2019 the ISTB and the ARTORG Center for Biomedical Engineering Research have joined forces as a center of excellence in Biomedical Engineering under the ARTORG brand. We are preparing the ISTB's move to the Insel campus later this year, also in close neighborhood to our collaborating partners at the Bern University Hospital (Inselspital).

We are very proud to present this last annual report of the Institute of Surgical Technology and Biomechanics. In 2018, 4 students earned their PhD degrees in Biomedical Engineering in the frame of the Graduate School for Cellular and Biomedical Sciences (www.gcb.unibe.ch) with an excellent research output and well-attended presentations. The ISTB contributed again substantially to the Master's Program in Biomedical Engineering (www.bme.master.unibe.ch) with hundreds of teaching hours and numerous master theses.

On the research side, our publication record reached 32 peer-reviewed journal and conference publications. In addition, members of the ISTB team have edited 2 books throughout the past year. Our IPMI group head Guoyan Zheng has been elected as member of the board of directors of the Medical Image Computing and Computer Assisted Intervention Society (MICCAI), recognizing his high level contributions to the field and his continuous services to the organization. Congratulations for this remarkable accomplishment. Several awards and prizes were also obtained, among others, the Best Paper Award on Machine Learning in Medical Imaging at MICCAI and the Ypsomed Innovation Award (2nd).

External funding was maintained at a high level. Our five research groups continued to be successful in convincing national and international funding agencies, NGOs, and the Medtech industry to support our research and development activities with appropriate funds. In particular three new projects were granted by the Swiss National Science Foundation and two from the Federal Innovation Promotion Agency Innosuisse. Our teams have been successfully involved in organizing and co-organizing national and international workshops and conferences striving themes such as bone biomechanics, spinal interventions, repair and regeneration of interconnecting soft tissue and medical image computing.

In 2018, masterly organized by Julia Spyra the ISTB and ARTORG had a joint summer excursion in the region of the lakes Neuchâtel and Murten. At the Laténium the largest Swiss Archaeology museum we were taught 50´000 years of regional history. A boat took the merry group to Sugiez, starting point for an extended hike through the vineyards of Mont Vully, enjoying the superb view over the Lake Murten region. A t the end of the day in Môtier at the Le Petit Château vinery the owner family Simonet introduced us to the secrets and joys of viticulture.

We would like to welcome our new coworkers who initiated their PhD thesis, postdoc and administrative, technical or scientific jobs in the course of the year. Despite the ongoing challenges in biomedical engineering, we hope they will enjoy the friendly and international atmosphere of our research organization and wish them an excellent start.

Our special thanks not only go to the funding agencies for their ongoing support, but especially to our research partners for their faith in our competences and their efforts towards our common goals. Finally, we would like to acknowledge our group heads and their teams for their unyielding strive in teaching, research and translational medicine.

We wish you a captivating report

Lutz-P. Nolte, Director ISTB

Philippe Zysset, Co-director ISTB

INSTITUTE FOR SURGICAL TECHNOLOGY AND BIOMECHANICS

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E. Gnahoré

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G. Zheng
Information Processing in Medical Interventions

M. Reyes
Medical Image Analysis

Ph. Zysset
Musculoskeletal Biomechanics

B. Gantenbein
Tissue and Organ Mechanobiology

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Research Profile

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

Together with our collaborators, we constitute a strong team covering a wide spectrum of research topics ranging from direct support of surgical patient treatment to basic tissue properties. Besides our core expertise in applying finite element analysis to study skeletal biomechanics, we are seeking to improve planning of computer aided interventions by developing and applying refined numerical techniques into the field of computer aided surgery. Another important research focus of the group is the development of numerical models of soft tissues such as corneal or peripheral arteries.

Mathematical Modeling of the Biomechanical Forces causing Brain Tumor Mass-effect

Brain tumors present with different growth phenotypes, ranging from invasive lesions without notable 'mass effect' to strongly displacing lesions that induce mechanical stresses and result in healthy tissue deformation, midline shift or herniation. Biomechanical forces, such as those resulting from displacive tumor growth, shape the tumor environment and are known to affect tumor growth and evolution. Likewise, tumor growth drives physical changes in the micro-environment that affect tissue solid and fluid mechanics.

We develop mathematical models to study the biomechanical impact of brain tumor growth and possible treatment implications. We use these models to investigate determinants of tumor shape, such as the influence of tissue structure and growth location, and to evaluate quantitative image-based measures of tumor mass effect. Along with these models, we develop approaches for identifying patient-specific growth characteristics from clinical imaging data (Figure 1).

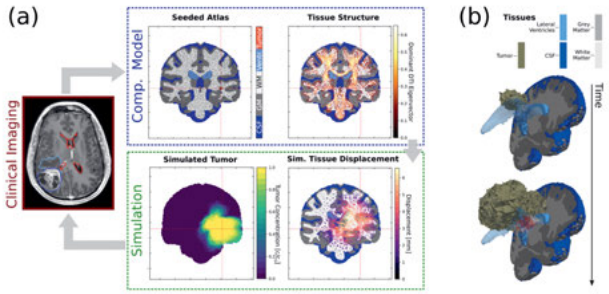

Figure 1. (a): Computational models are initialized from clinical imaging data. The simulation predicts tumor invasion and mechanical stresses induced by tumor growth. Simulation results are compared to imaging findings. (b): Simulated time evolution of 3D tumor growth and tissue deformation.

Planning of Refractive Interventions

Refractive interventions are widespread techniques for vision correction such as myopia or astigmatism. The cornea of the patient is reshaped by surgical intervention like incisions and laser ablation of stromal tissue. The amount of tissue to remove is traditionally estimated based on experimental nomograms or geometrical approaches. Unfortunately, the change of corneal power is frequently over- or under-estimated.

We proposed an opto-mechanical simulation framework to quantify the optical outcome induced by alteration of the corneal biomechanics. Our models rely on the precise shape of the anterior and posterior surfaces of the cornea measured pre-operatively. However, new tools are required to characterize the biomechanics of the patient's cornea and inform this personalized planning platform. Non-contact tonometry (NCT) represents an appealing approach for the in-vivo characterization of corneal biomechanics. This technique relies on a short

air pulse to induce a deformation of the cornea. However, before being able to derive mechanical information from these measurements, the actual load applied on the cornea by the strong air-jet must be quantified. The problem is complex as it involves the calculation of the air-flow around a rapidly moving structure. We showed that the standard approach that neglects the corneal deformation when calculating the pressure on the tissue, induces an error of up to 200%. This finding is expected to greatly impact the mechanical characterization of the cornea in-vivo from tonometric measurements (Figure 2).

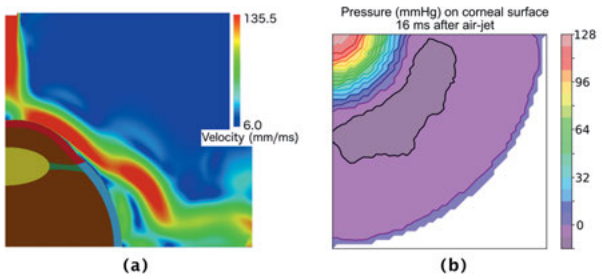

Figure 2. Fluid-structure simulation of the air-puff used to deform the cornea during non-contact tonometry. The fluid velocity on the deformed corneal surface (a) induces a complex distribution of air pressure on the cornea surface (b).

This numerical framework was used to perform personalized simulations of different surgical procedures such as corneal ring implantation and arcuate keratotomy. For example, arcuate keratotomy is a surgical technique used to correct astigmatism following cataract interventions. Our numerical simulation framework could estimate the outcome of different planning options before the surgery. Based on this numerical approach, we were also able to propose optimization algorithms to automatically determine the surgical parameters optimal for each specific patient. The patient-specific optimization of the surgery proved to better control the outcome of the intervention, leads to more reliable postoperative astigmatism, and limits the risks of overcorrection (Figure 3).

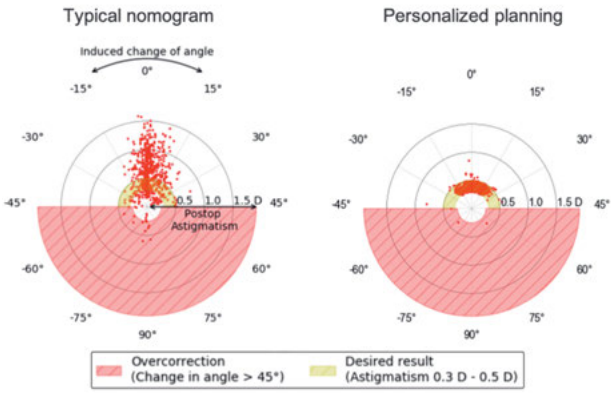

Figure 3: The outcome of personalized arcuate keratotomy simulations on more than 600 patients. The outcome of the intervention is shown using polar plots; the distance from the center represents the postoperative astigmatism while the polar position describes the rotation of the steep meridian induced by the surgery. The surgical procedure must reach a final astigmatism of 0.4D (yellow area) while absolutely avoid inducing overcorrection (red area). Results show that the outcome of existing nomogram exhibit a large variability across patients, while the personalized optimization of the surgical parameter leads to more reliable postoperative astigmatism, and limits the risks of overcorrection.

Finite Element Analysis of Peripheral Arterial Disease

Endovascular therapy in patients suffering from peripheral arterial disease show high rates of restenosis. We hypothesized that restenosis following revascularization is associated with hemodynamical markers derived from blood flow during leg flexion. Therefore, we performed personalized computational fluid dynamics (CFD) analyses of patients, who underwent routine endovascular femoro-popliteal interventions. The CFD analyses were conducted using 3D models of the arterial geometry in straight and flexed positions, which were reconstructed from 2D angiographic images (Figure 4). Based on restenosis rates reported at 6 months follow-up, statistical analyses were performed to quantify the relationship between hemodynamical parameters predicted by the numerical simulations and clinically-observed restenosis. Results showed that unphysiological arterial deformations induced postoperatively by the flexion of the leg led to adverse hemodynamic conditions that may trigger restenosis. Statistical models based solely on hemodynamical markers showed a prediction accuracy of more than 75%, which indicates that flow parameters are sufficient to predict restenosis. This approach, based on the immediate post-operative configuration of the artery, has the potential to identify patients at increased risk for restenosis. Based on this information, clinicians could take preventive measures and more closely follow these patients to avoid complications.

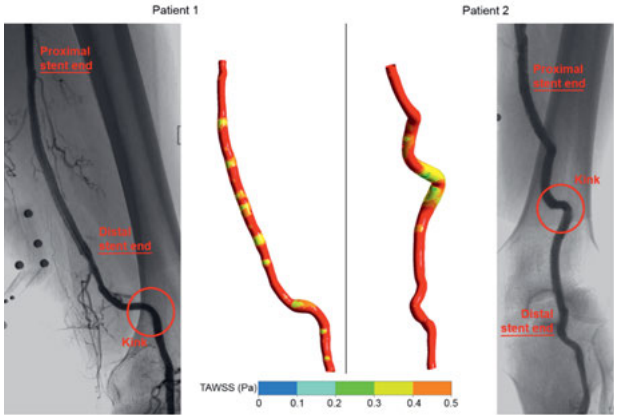

Figure 4: The distribution of shear tress (TAWSS) in two stented arteries that exhibited arterial kinking during leg flexion. The X-ray images show the locations of the stented regions and the arterial kinks. The location of the atheroprone areas were concentrated around the vicinity of the kinks. Additional areas affected by adverse flow conditions were within the stented segments, in which leg flexion resulted in the intermittent pinching of the artery along the length of the stent.

Selected Publications

1. Lieger O, Schaub M, Taghizadeh E, Büchler P. How Symmetrical Are Bony Orbits in Humans? J. Oral Maxillofac. Surg. [Internet]. 2018 Aug 28;9. Available from: https://www.sciencedirect.com/science/article/pii/S0278239118309832doi:10.1016/j.joms.2018.08.018
2. Brusa T, Abler D, Tutuian R, Gingert C, Heverhagen JT, Adamina M, et al. Anatomy and mechanical properties of the anal sphincter muscles in healthy senior volunteers. Neurogastroenterol. Motil. [Internet]. 2018;(October 2017):e13335. Available from: http://doi.wiley.com/10.1111/nmo.13335doi:10.1111/nmo.13335
3. Ariza-Gracia MÁ, Wu W, Calvo B, Malvè M, Büchler P, Rodriguez Matas JF. Fluid–structure simulation of a general non-contact tonometry. A required complexity? Comput. Methods Appl. Mech. Eng. [Internet]. 2018 Oct;340:202–215. Available from: https://doi.org/10.1016/j.cma.2018.05.031doi:10.1016/j.cma.2018.05.031
4. Balmer TW, Vesztergom S, Broekmann P, Stahel A, Büchler P. Characterization of the electrical conductivity of bone and its correlation to osseous structure. Sci. Rep. [Internet]. 2018 Jun 5;8(1):8601. Available from: http://www.nature.com/articles/s41598-018-26836-0doi:10.1038/s41598-018-26836-0
5. Abler D, Berger S, Terrier A, Becce F, Farron A, Büchler P. A statistical shape model to predict the premorbid glenoid cavity. J. shoulder Elb. Surg. [Internet]. 2018 Oct 26;27(10):1800–1808. Available from: https://doi.org/10.1016/j.jse.2018.04.023doi:10.1016/j.jse.2018

INFORMATION PROCESSING IN MEDICAL INTERVENTIONS

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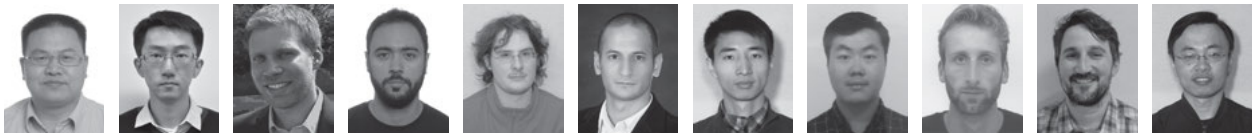

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Research Profile

Information Processing during medical interventions, including medical image computing and computer assisted interventions, has been playing an increasingly important role in diagnosis and treatment of various diseases. Specifically, medical image computing ensures the derivation of optimized parameters from the acquired multimodality medical images, allows for exploitation of the image-derived parameters, and facilitates the development of anatomical and associated physiological models which can further help in understanding different disease mechanism. Recently the breakthroughs in Artificial Intelligence (AI), especially those based on deep learning, has led to medical applications which are now having a profound impact on personalized therapy. In collaboration with national and international experts from both industry and academia, IPMI group actively embrace such a technical trend, reflected by the development of medical image computing algorithms that achieved state-of-the-art performance on multimodality medical images. Another focus of the group is on translational research, aiming to improve healthcare delivery to patients.

Current Research Areas

Bayesian VoxDRN for whole heart segmentation (SNSF Grant 169239)

We proposed a probabilistic deep voxelwise dilated residual network, referred as Bayesian VoxDRN, to segment the whole heart from 3D MR images. Bayesian VoxDRN can predict voxelwise class labels with a measure of model uncertainty, which is achieved by a dropout-based Monte Carlo sampling during testing to generate a posterior distribution of the voxel class labels. Our method has three compelling advantages. First, the dropout mechanism encourages the model to learn a distribution of weights with better data-explanation ability and prevents overfitting. Second, focal loss and Dice loss are well encapsulated into a complementary learning objective to segment both hard and easy classes. Third, an iterative switch training strategy is introduced to alternatively optimize a binary segmentation task and a multi-class segmentation task for a further accuracy improvement. Experiments on the MICCAI 2017 multi-modality whole heart segmentation challenge data corroborate the effectiveness of the proposed method.

Fig. 1. The architecture of our Bayesian VoxDRN

Fully automatic segmentation of paraspinal muscles from 3D Torso CT images (JSPS Fellowship)

We proposed a novel learning-based method for fully automatic segmentation of paraspinal muscles from 3D torso CT images. Multi-scale iterative random forest classifications with multi-source information were employed to speed up the segmentation to improve the accuracy. Here, multi-source images include the original torso CT images and later also the iteratively estimated and refined probability maps of the paraspinal muscles. Validated on 20 torso CT images, the presented method achieved a mean Dice coefficient of 93.0%.

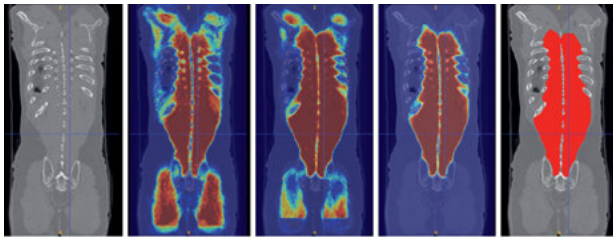

Fig. 2. A segmentation example

Fully automatic segmentation of lumbar vertebrae from CT images (SNSF grant 157207)

We present a method for automatic segmentation of lumbar vertebrae from a given CT image. More specifically, our automatic lumbar vertebrae segmentation method consists of two steps: affine atlas-target registration-based label fusion and bone-sheetness assisted multi-label graph cut which has the inherent advantage of automatic separation of the five lumbar vertebrae from each other. We evaluate our method on 21 clinical lumbar spinal CT images with the associate manual segmentation and conduct a leave-one-out study. Our method achieved an average Dice coefficient of 93.9 ± 1.0% and an average symmetric surface distance of 0.41 ± 0.08 mm.

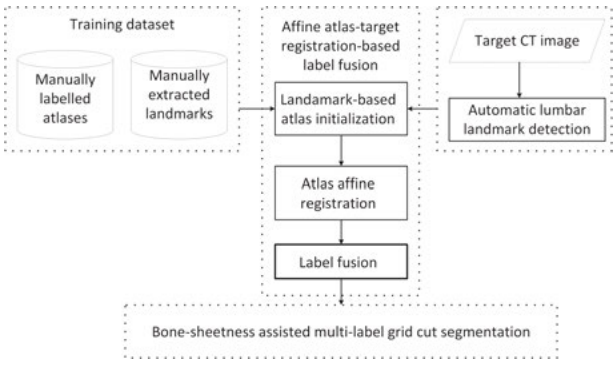

Fig. 3. A Schematic view of the fully automatic segmentation approach

Multi-modal image computing for computer assisted interventions (SNF grant 163224 and Insel-Ortho-IPMI Cooperation)

This project focuses on developing an efficient method to generate 3D anatomical models using CT-free imaging protocols that are used in clinical routine in order to support computer-assisted diagnosis and surgical planning of femoroacetabular impingement (FAI). The project aims for development of a fully automatic approach based on multi-modal images combining 2D X-ray radiograph with 3D MR images acquired with small field of view. In year 2018, we developed a multi-level latent shape space constrained 3D U-net which we named as Latent3DU-net for automatic segmentation of the proximal femur from radial MRI of the hip.

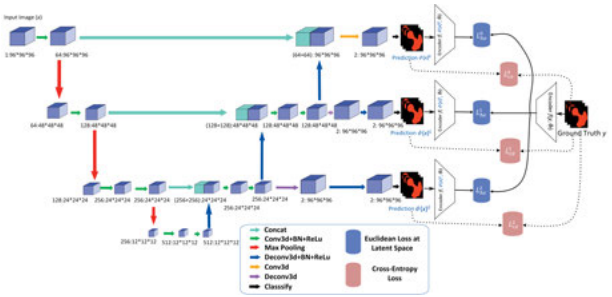

Fig. 4. A Schematic view of the Latent3DU-net

Selected Publications

Edited Book

1. G Zheng, W Tian and X Zhuang (eds.): Intelligent Orthopaedics – Artificial Intelligence and Smart Image-guided Technology for Orthopaedics. Springer, 2018. ISBN: 978-981-13-1396-7.

Selected Peer-reviewed Papers

1. L Maier-Hein, M Eisenmann, A Reinke, S Onogur, M Stankovic, P Scholz, T Arbel, H Bogunovic, A P. Bradley, A Carass, C Feldmann, A F Frangi, P M. Full, B van Ginneken, A Hanbury, K Honauer, M Kozubek, B A. Landman, K März, O Maier, K H Maier-Hein, B Menze, H Müller, P F. Neher, W Niessen, N Rajpoot, G Sharp, K Sirinukunwattana, S Speidel, C Stock, D Stoyanov, A Aziz Taha, F van der Sommen, C-W Wang, M-A Weber, G Zheng, P Jannin, A Kopp-Schneider. Why rankings of biomedical image analysis competitions should be interpreted with care. ***Nature Communications,*** 9(1):article5217, 2018.
2. N Kamiya, J Li, M Kume, H Fujita, D Shen and G Zheng. Fully automatic segmentation of paraspinal muscles from 3D torso CT images via multi-scale iterative random forest classifications. ***International Journal of Computer Assisted Radiology and Surgery,*** 13(11):1697 – 1706, 2018.
3. X Li, Q Dou, H Chen, C-W Fu, X Qi, D.L. Belavy, G Armbrecht, D Felsenberg, G Zheng and P-A Heng. 3D multi-scale FCN with random modality voxel dropout learning for intervertebral disc localization and segmentation from multi-modality MR images. ***Medical Image Analysis,*** 45:41-54, 2018
4. G Zheng, H Hommel, A Akcoltekin, B Thelen, J Stifter, G Peersman. A novel technology for 3D knee prosthesis planning and treatment evaluation using 2D X-ray radiographs: a clinical evaluation. ***International Journal of Computer Assisted Radiology and Surgery,*** 13:1151-1158, 2018.
5. H Yun, WS Murphy, DM Ward, G Zheng, B Hayden, SB Murphy. Effect of Pelvic Tilt and Rotation on Cup Orientation in Both Supine and Standing Positions. ***The Journal of Arthroplasty,*** 33:1442-1448, 2018.
6. S Pflugi, R Vasireddy, T Lerch, TM Ecker, M Tannast, N Boemke, K. Siebenrock, G Zheng. Augmented marker tracking for peri-acetabular osteotomy surgery. ***International Journal of Computer Assisted Radiology and Surgery,*** 13:291-304, 2018

MEDICAL IMAGE ANALYSIS

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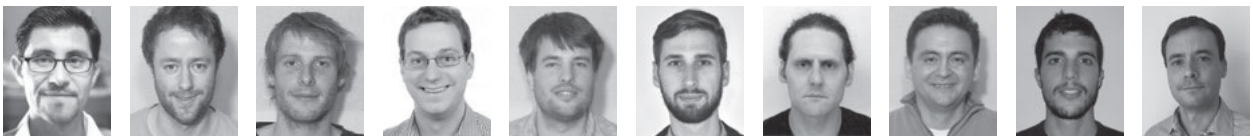

Mauricio Reyes | Simon Habegger | Alain Jungo | Yannick Sutter | Fabian Balsiger | Tobias Rothen | Urspeter Knecht | Waldo Valenzuela | Adriano Pinto | Michael Rebsamen

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Research Profile

The Medical Image Analysis group develops advanced medical image analysis technologies, and related translational biomedical engineering technologies, to quantify, diagnose, and follow-up disorders related to the central nervous system (e.g. glioblastomas, stroke, multiple sclerosis, etc.).

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

The developments revolve around the vision of scalable, adaptable and time-effective machine learning algorithms developed with a strong focus on clinical applicability. The group further supports these developments with dedicated techniques for super-resolution imaging, aiming at bridging information from low and high levels of image resolution, and fast and robust human-machine interfacing, designed to leverage the communication between computer algorithms and expert domain knowledge. The MIA group joins in 2019 the newly launched Insel Data Science Center, and takes the lead of the Imaging A.I. lab to develop state of the art technologies aiming at enabling a scalable, sustainable and safe medical imaging A.I.

Accurate Quantification and Radiomics Analysis for Brain Lesions

Magnetic Resonance Imaging (MRI) and its variants are a powerful imaging modality that encompasses rich anatomical and physiological information at a high resolution. In neurosciences, these modalities have become a standard in clinical practice. However, the interpretation of the images requires the combined use of different modalities, which leads to the need of computer-assisted technologies. The group has developed several methodologies to analyze MRI images with focus on multimodal image segmentation for brain image lesion analysis studies. These developments are driven by clinical requirements such as computation speed, robustness, and use of standard clinical imaging protocols.

Accuracy is particularly paramount for an image-guided brain lesion quantification technology. Through a strong interdisciplinary collaboration with the department of neuroradiology, at the University Hospital, Bern, our interdisciplinary group has developed over the years accurate and clinically-relevant (i.e. in line with clinical requirements) solutions based on machine learning methodologies for automated brain tumor segmentation, stroke lesion segmentation, and multiple-sclerosis lesion segmentation, which have ranked among top-approaches at MICCAI (Medical Image Computing and Computer-Assisted Interventions) challenges, top-venue of the medical image computing field. Our seminal work on automated brain tumor volumetry was awarded the Young Scientist Publication Impact Award 2016, in recognition for being the most-impactful MICCAI work of the last five years, as well as the Ypsomed Innovation Award 2016.

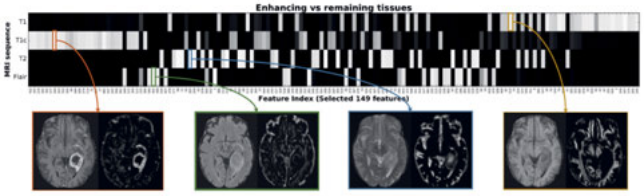
Automated brain lesion quantification technologies are now used for Multidimensional Response Assessment in Glioma Patients, which is an interdisciplinary effort aiming at developing longitudinal radiomics technologies and non-invasive biomarkers providing a better assessment of disease progression and patient response to therapy.

Uncertainty and Interpretability of Medical Image Segmentation Technologies using Deep Learning technologies

Next to accuracy, the robustness of computer-assisted technologies is fundamental for their effective deployment and integration in medicine. Particularly, it is crucial to develop technologies that can cope with computer errors stemming from the large heterogeneity of medical images, the complex pathophysiology of disease, among other factors. To this end, our group is developing algorithms that check the reliability of machine learning's results by yielding uncertainty estimations of computer-generated results, which can be used to change the paradigm, so medical experts are no longer executioners of the task (e.g. brain tumor delineation) but use this information to monitor and correct them in a time-effective manner. In addition, as the amount of collected medical image information is rapidly growing, it is vital to develop Human-Machine Interfacing technologies (HMI) to ensure scalability of time-effective monitoring and correction technologies of computer-generated results.

Our group is researching methodologies to enhance the interpretability of machine learning models, so their decisions can be inspected (e.g. is the machine capturing the relevant relation in the data?), and interpreted by human (opening of the "black box", e.g. If a system fails, why does it fail?). Enhancing interpretability of

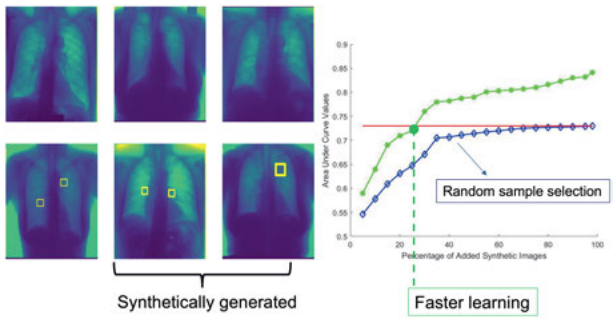
machine learning methods is essential in medicine, so to build trust with these systems, but it is also very important in line with discussions pointing to decision-making and a "right to explanation". Motivated by the current decoupling between the design of medical image sequences, and their exploitation through machine learning algorithms. In collaboration with MRI physicists from the academic and private sectors, our group is researching machine learning methodologies that are being applied at the image formation process stage, with the overarching goal of designing the best combination of MRI sequences and machine learning algorithms.



Global interpretability of deep learning features to segment enhancing tissue. Features are sorted from most to least important (left to right). Brighter means higher squared L2-norm of the weights connecting the hidden unit of a given feature to a given MRI sequence. Bottom) examples of pairs of MRI sequences (left) and feature maps (right). Source: Pereira et al. Medical Image Analysis, 2018.

Efficient Focused Active Learning for Evolutive Deep Learning in Medical Image Analysis

We develop techniques for focused active learning, enabling fast learning rates of deep learning technologies for image segmentation and image classification. The approach utilizes measures of uncertainty of computer-generated results to focus on difficult learning areas of an image. The focused learning is coupled with smart a data augmentation approach that synthetically generates similar data samples around the data point of current focus. Experimental results on medical images show the ability of the approach to learn at faster rates than traditional active learning systems, while enabling a better usage of the available training set.



Focused Active Learning. Exploiting sample informativeness and synthetic data augmentation enables a faster learning (see slope of green curve) versus standard active learning approaches (blue curve), and an improved use of the information compared to the performance obtained when training with all available data at once (red line).

Towards Streamlined and High-throughput Data Curation Processes

Our group is establishing technologies for automatic quality assessment of curated data, as well as the reliability of the machine learning models produced with curated medical image information. On the one hand, automatic quality assessment of curated data is essential for high-throughput data curation of a highly heterogeneous and error-prone human interaction process of medical image information in the clinical routine. On the other hand, it is crucial to research and develop technologies that can inspect the reliability of machine learning models derived from this data.

We initiated a Swiss-wide initiative to create infrastructure and technologies for a local and distributed radiomics platform, which features a data curation workflow occurring within the daily clinical routine. By leveraging the daily clinical workflow with human-machine intelligence technologies, we aim at creating a rich and sustainable symbiosis between their daily clinical needs, and the data curation process needed for biomedical research, therapy assessment (e.g. clinical trials), and in general for the improvement of data-driven biomedical engineering technologies.

Selected Publications

1. Mahapatra D., Bozorgtabar B., Thiran J.P., and Reyes M. Efficient Active Learning for Image Classification and Segmentation using a Sample Selection and Conditional Generative Adversarial Network. Medical Image Computing and Computer-Assisted Intervention -- MICCAI 2018, Lecture Notes in Computer Science, In Press, 2018.
2. Jungo A., Meier R., Ermis E., Blatti-Moreno M., Herrmann E., Wiest R., and Reyes M. On the Effect of Inter-observer Variability for a Reliable Estimation of Uncertainty of Medical Image Segmentation. Medical Image Computing and Computer-Assisted Intervention -- MICCAI 2018, Lecture Notes in Computer Science, In Press, 2018.
3. Chandran V., Maquer G., Gerig T., Zysset P., and Reyes M. Supervised learning for bone shape and cortical thickness estimation from CT images for finite element analysis. Medical Image Analysis, 52, 42 - 55, 2019. http://www.sciencedirect.com/science/article/pii/S1361841518308612
4. Pinto A., Pereira S., Meier R., Alves V., Wiest R., Silva C., and Reyes M. Enhancing clinical MRI Perfusion maps with data-driven maps of complementary nature for lesion outcome prediction. Medical Image Computing and Computer-Assisted Intervention -- MICCAI 2018, Lecture Notes in Computer Science, In Press, 2018.
5. Barros N., Meier R., Pletscher M., Stettler S., Knecht U., Herrmann E., Schucht P., Reyes M., Gralla J., Wiest R., and Slotboom J. On the relation between MR spectroscopy features and the distance to MRI-visible solid tumor in GBM patients. Magn Reson Med, 2018. https://doi.org/10.1002/mrm.27359
6. Suter Y., Rummel C., Wiest R., and Reyes M. Fast and Uncertainty-Aware Cerebral Cortex Morphometry Estimation Using Random Forest Regression. ISBI 2018: Proceedings of the 2018 IEEE international conference on Biomedical imaging, In Press, 2018.
7. Pereira S., Meier R., McKinley R., Wiest R., Alves V., Silva C., and Reyes M.. Enhancing interpretability of automatically extracted machine learning features: application to a RBM-Random Forest system on brain lesion segmentation. Med Image Anal, 44, 228--244, 2018. https://dx.doi.org/10.1016/j.media.2017.12.009
8. Balsiger F., Konar A., Chikop S., Chandran V., Scheidegger O., Geethanath S., and Reyes M. Magnetic Resonance Fingerprinting Reconstruction via Spatiotemporal Convolutional Neural Networks. International Workshop on Machine Learning for Medical Image Reconstruction, 39-46, 2018.
9. Jungo A., Meier R., Ermis E., Herrmann E., and Reyes M. Uncertainty-driven Sanity Check: Application to Postoperative Brain Tumor Cavity Segmentation. 1st Conference on Medical Imaging with Deep Learning (MIDL 2018), In Press, 2018.
10. Pereira S., Meier R., Alves V., Reyes M., and Silva C. Automatic brain tumor grading from MRI data using convolutional neural networks and quality assessment. Understanding and Interpreting Machine Learning in Medical Image Computing Applications, 106--114, 2018.

MUSCULOSKELETAL BIOMECHANICS

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Research Profile

Motivated by prevention, diagnosis and treatment of degenerative diseases the research of the musculoskeletal biomechanics group focuses on multi-scale structure-function relationships of bone from the extracellular matrix to the organ level. A combined theoretical, experimental, and numerical approach is applied to model, validate and simulate the mechanical behavior of bone tissue in the course of growth, aging, disease and treatment. The group provides also biomechanical testing services and cooperates with local, national as well as international partners from academia, hospitals and industry to help reduce the burden of bone diseases and failure of the bone-implant interface.

Current Research Areas

Micro-meso scale transition of bone strength (SNF grant #165510 with EMPA)

A micromechanical tensile setup was designed and optimized to test focused ion beam (FIB) fabricated samples on the length scale of a single lamellae (3-7 um) inside a scanning electron microscope (SEM). The tensile response of ovine osteonal bone was characterised in both axial and transverse orientations. The micro-tensile tests revealed a clear size effects and anisotropy of the mechanical properties at this length scale (Figure 1). Both axial and transverse samples revealed higher strengths than the ones measured on the macroscale by a factor of 2.5, highlighting the hierarchical organization of bone tissue. Interestingly, the anisotropy was found to be more pronounced in tension than in previous compression tests.

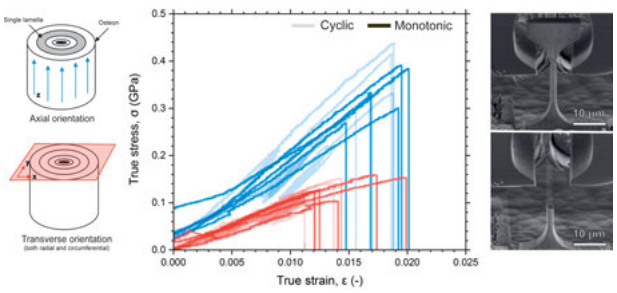

Figure 1. Micro-tensile stress strain behavior of ovine osteonal bone (left), high resolution secondary electron image of a micro-tensile specimen before and after loading (right).

An Explicit Micro-Finite Element Model of Trabecular Bone (with RMS)

The ability to simulate the post-yield behavior of trabecular bone under large deformations would help in predicting damage in osteoporotic bones and at bone-implant interfaces. For this purpose, an explicit micro finite element (µFE) approach was adopted and an isotropic, elasto-plastic model with distinct yield and ultimate strains was implemented. Element deletion was triggered after reaching the ultimate strain criterion, which produced damage in the form of a stiffness reduction. The method was applied to 3 human trabecular bone samples of different BV/TV using 13 monotonic load cases. An apparent quadric strength surface for trabecular bone was successfully fitted in a normalized stress space.

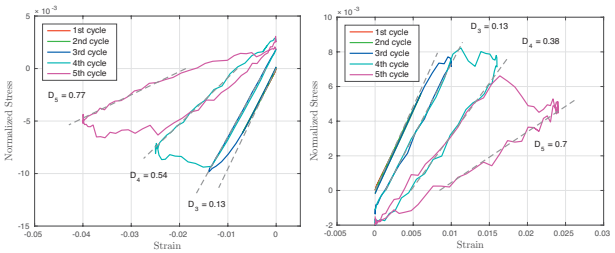

Figure 2. Cyclic normalised stress-strain curves for trabecular bone in compression and tension using explicit finite element analysis.

Normative Database of HR-pQCT-Based Bone Strength Assessment by Homogenized FEA in the Healthy Swiss Population (with EUT, PO and VUT)

High-resolution peripheral quantitative computed tomography (HR-pQCT) reconstructions enable the application of finite element analysis (FEA) to compute bone strength, which is clearly associated with fragility fractures in postmenopausal women. Recently, a new homogenized FEA approach was developed to

reduce evaluation time by improving the computation of fabric and the superposition of material properties in mixed elements. The current project aims to determine *in vivo* precision of the methodology using a calibration phantom, but a clinical study (NODARATIS) providing a normative database for radius and tibia strength in the healthy Swiss population is currently conducted by our clinical partner (PO).

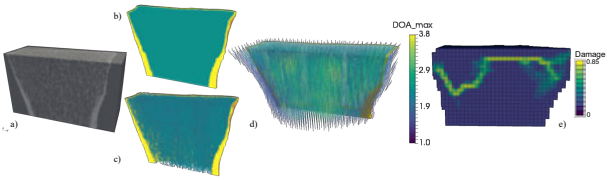

Figure 3. HR-pQCT image (a) with segmentation of cortex (b) and trabeculae (c) to extract main orientation or fabric (d) and finite element analysis to estimate failure load of the wrist.

Strength of Metastatic Vertebral Bodies (SNF grant #165510 with HMS)

Metastatic bone disease can lead to pathological fractures which are, especially in the spine, a major clinical concern. Only little is known about the material properties of bone tissue in the vicinity of metastatic lesions. In addition, clinical grading scales were shown to have limited sensitivity in estimating fracture risk of metastatic vertebrae. Accordingly, the aim of this project is to analyze the mechanical properties of metastatic bones at the tissue (nanoindentation) and organ (bio-mechanical test of entire bones) level. With the insight gained from the experiments, micro-CT based finite element models are generated and validated. These models can potentially be used in the future to identify metastatic bones at risk of fracture and thus help to induce the appropriate treatment.

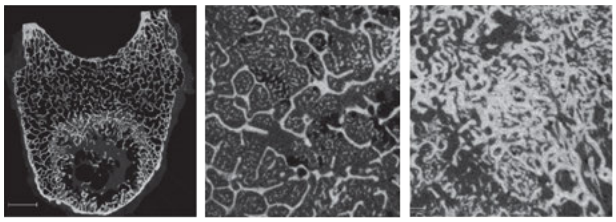

Figure 5. Lytic (left), normal (center) and blastic lesions (right) in metastatic vertebrae.

Non-Linear Models of Mineralized Collagen Fibril Arrays (with HWU)

Recent small-angle X-ray scattering (SAXS) and wide-angle X-ray diffraction (WAXD) experiments revealed small mineral and collagen strain ratios with respect to the apparent strain during micropillar compression of mineralized turkey leg tendon (MTLT). The aim of this starting project is to develop 1D analytical and 3D finite element models of mineralized collagen fibrils embedded in a mineralized matrix of non-collagenous proteins that deliver an apparent elastic modulus, ultimate stresses and constituent strain ratios that are compatible with experimental observations. Results aim to provide further insights for computational fracture risk prediction of bone tissue.

Peripheral Trabecular Bone Compaction and Primary Stability of Dental Implants (with NB)

Primary stability is a key metric to decide upon immediate or postponed loading of a dental implant after surgery. To assess primary stability, understanding of the biomechanics of the bone-implant interface becomes indispensable. Different drilling protocols and various design features of a dental implant were investigated in bovine trabecular bone. The pilot holes were drilled and the implants were inserted with instrumented tools. The bone-implant systems were imaged with µCT and tested mechanically to quantify primary stability. The µCT images revealed the spatial extent of trabecular bone compaction, while both stiffness and strength were clearly dominated by the surrounding bone volume fraction (BV/TV).

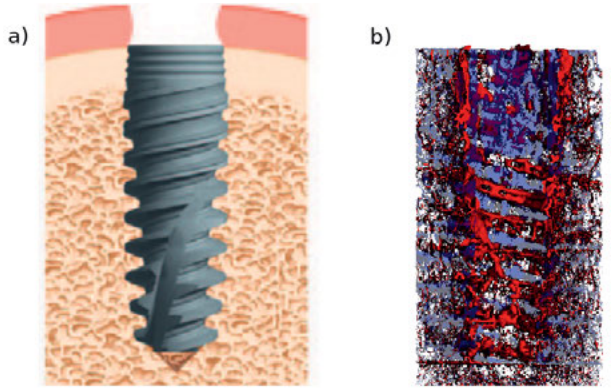

Figure 7. Compaction of trabecular bone around a dental implant using subtractive µCT imaging.

Biomechanical Testing

Several biomechanical experiments were conducted in the laboratory for internal projects and industrial contract research. To help improve treatment of scoliosis, we tested the material of an experimental 3D printed corset with different mesh sizes in tension. This nylon PA 12 material was stiffer and reached higher ultimate forces than the standard polyethylene material. Biomechanical tests were also performed within a master's thesis with the aim to validate mutually the location and intensity of microdamage between a bone overloading experiment and its simulation by non-linear micro-finite element analysis (microFE). The results supported the hypothesis that a weak but statistically significant relation exists between them.

Selected Publications

1. Chappuis Vivianne, Maestre Laura, Bürki Alexander, Barré Sébastien, Buser Daniel, Zysset Philippe, Djonov Valentin and Bosshardt Dieter, "Osseointegration of ultrafine-grained titanium with a hydrophilic nano-patterned surface", Biomater Sci, 6(9):2448-2459, 2018.
2. Panyasantisuk Jarunan, Dall'Ara Enrico, Pretterklieber Michael, Pahr Dieter, Zysset Philippe, "Mapping anisotropy improves QCT-based finite element estimation of hip strength in pooled stance and side-fall load configurations", Med Eng Phys, 59:36-42, 2018.
3. Ovesy Marzieh, Voumard Benjamin and Zysset Philippe, "A non-linear homogenized finite element analysis of the primary stability of the bone-implant interface" Biomech Model Mechanobiol, 17(5):1471-1480, 2018.
4. Stadelmann Marc, Maquer Ghislain, Voumard Benjamin, Grant Aaron, Hackney David, Vermathen Peter, Alkalay Ron and Zysset Philippe, "Integrating MRI-based geometry, composition and fiber architecture in a finite element model of the human intervertebral disc", J Mech Behav Biomed Mater 85:37-42, 2018.
5. Feldmann Arne, Wili Patrik and Zysset Philippe, "The thermal conductivity of cortical and cancellous bone", Eur Cells and Mater, 35:25-33, 2018.
6. Ahmad Sufian, Hirschmann Michael, Voumard Benjamin, Kohl Sandro, Zysset Philippe, Mukabeta Takura, Evangelopoulos Dimitrios, Ateshrang Atesch, "Adjustable loop ACL suspension devices demonstrate less reliability in terms of reproducibility and irreversible displacement", Knee Surg Sports Traumatol Arthrosc 26:1392-1398, 2018.
7. Joda Tim, Voumard Benjamin, Zysset Philippe, Bragger Urs and Ferrari Marco, "Ultimate force and stiffness of 2-piece zirconium dioxide implants with screw-retained monolithic lithium-disilicate reconstructions", J Prosthodont Res, 62:258-263, 2018.

TISSUE AND ORGAN MECHANOBIOLOGY

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Research Profile

The Tissue & Organ Mechanobiology (TOM) Group of the Institute for Surgical Technology and Biomechanics (ISTB), University of Bern, conducts translational research in the intersection of tissue engineering, biology and applied clinical research. The group's primary aim is to understand the cellular response onto biomechanical stimuli and how cellular communities are affected *in situ* using 3D tissue and organ culture models. Our research can be divided into two main foci: On the one hand the group investigates causes of low back pain due to intervertebral disc (IVD) degeneration and on the other hand the group focuses on the human knee where they aim to identify cell-based solutions for the non-healing or delayed ruptures of the anterior cruciate ligament (ACL). The common focus of the TOM group is to advance *in vitro* organ culture models, which match closely the human situation and where regenerative therapy strategies, such as novel biomaterials and cells, can be tested in a most authentic *in vitro* set-up.

Low Back Pain and Intervertebral Disc Degeneration and Regeneration

The TOM group conducts research in two main directions: i) IVD research in the area of regeneration using biomaterials and stem cells[1-4] and ii) in the area of non-successful spinal fusion and possible involvement of pseudo-arthrosis[5]. For the first research area we use a combination of 3D tissue and organ culture approaches. The research of the second focus is the understanding of the balance between BMP agony and antagony. Besides the investigation of the exogenous stimulation of BMP antagonists on mesenchymal stem cells (MSC) and osteoblasts, the main focus lies on the observation of the interaction between IVD cells and osteoblast, by performing co-cultures[1].

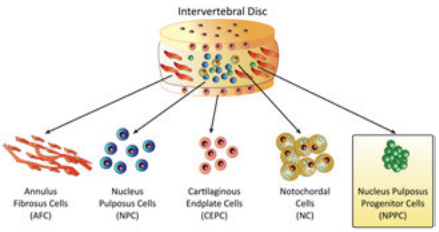

Figure 1. Image illustrating the four "classical" cell populations previously characterized in the intervertebral disc. In yellow on the right are the newly detected Tie2+ nucleus pulposus progenitor cells (NPPC).

In a Gebert Rüf financed project a fiber-reinforced hydrogel was tested in a physiologically clinically relevant organ culture model by cross-linking the fibrin mesh with genipin[1]. Therefore, a healthy control, an injured IVD (2 mm biopsy punch) and the repaired IVD were tested, and histology was performed to visualize the injury and integration of the novel silk and fibrin hydrogel. These results were recently reported in the Journal of Functionalized Biomaterials[1] and in the European Spine Journal[3].

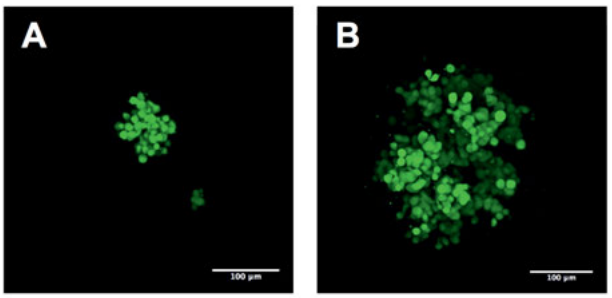

Figure 2. Confocal Laser Scanning Microscopy of A) nucleus pulposus progenitor cells (NPPC) and B) nucleus pulposus cells (NPC) after seven days of colony unit forming assay in a viscous medium. NPPC do result in more dense and spherical colonies whereas NPC form more lose and wider spread colonies. Cells were stained with a live dye in green. Scale bar = 100 µm.

Recently, autochthonous progenitor cells were detected in the human IVD, which could lead the path to cell therapy (Figure 1). Here, we concentrated on the most suitable isolation protocols to "fish" nucleus pulpous progenitor cells (NPPC) from the total population of cells in the bovine coccygeal disc. We also focused on their multipotency capacity and their application for IVD repair (Figure 2). Future research is to understand how these cells can be best isolated and whether these cells can be maintained *in vitro* to regenerate the IVD[4]. Furthermore, it would be highly desirable to investigate how induced multipotent stem cells (iPSC) could be used for IVD repair. This is the main aim in an upcoming Horizon 2020 Project named "iPSpine" starting in 2019 for three years in collaboration with internationally well-known scientists and experts in the field of engineering, biomaterials and biomechanics.

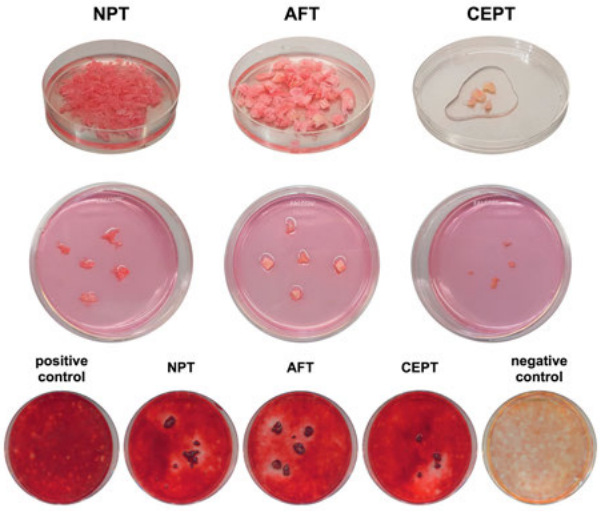

Figure 3. Human mesenchymal stromal cells (hMSC) were seeded in 100 mm Petri dishes and cultured until they reached 90% of confluency. Human intervertebral disc (IVD) explants (tissue of the nucleus pulposus (NPT), annulus fibrosus (AFT) or cartilaginous endplate (CEPT), 2-5 mm3) were cultured in direct contact with the hMSC in osteogenic medium (lacking bone morphogenetic protein 2). Top row: preparation of tissue. Middle row: Contribution of human NPT, AFT and CEPT on the top of hMSC monolayer. Bottom row: Alizarin red staining of direct culture after stimulation of 21 days with osteogenic medium (except negative control) and co-cultured with NPT, AFT and CEPT. Proof-of-concept of inhibitory effects (N = 1).

Biological Repair of the ruptured Anterior Cruciate Ligament

In Switzerland, the incidence of ACL ruptures is estimated at 32 per 100,000 in the general population and even more than double in the sports community. The current gold standard for ACL repair is reconstruction using an autograft, however, this approach has shown some limitations. Here, cell-based approaches using collagen patches or the application of platelet-derived plasma (PRP) are of interest for the clinical application.

Reducing the Senescence in Mesenchymal Stem Cells

Stem cell therapy faces the problem of the necessity to rely on fetal bovine serum (FBS) for cell expansion, which proved to have major disadvantages for application in the clinics. Additionally, MSC undergo senescence during expansion *in vitro*, which impairs their therapeutic potential. Here, alternate serum-free media formulations were investigated in terms of cell proliferation and differentiation potential, which could make their way to a GMP-compliant solution.

Selected Publications

1. Frauchiger DA, May RD, Bakirci E, Tekari A, Chan SCW, Wöltje M, Benneker LM, Gantenbein B, Frauchiger D, May R, Chan S, Benneker L (2018) Genipin-Enhanced Fibrin Hydrogel and Novel Silk for Intervertebral Disc Repair in a Loaded Bovine Organ Culture Model. J Funct Biomater 9(3):40. doi: 10.3390/jfb9030040
2. Frauchiger DA, Heeb SR, May RD, Wöltje M, Benneker LM, Gantenbein B. Differentiation of MSC and annulus fibrosus cells on genetically engineered silk fleece-membrane-composites enriched for GDF-6 or TGF-β3. J Orthop Res 2018; 36:1324-1333 DOI: 10.1002/jor.23778.
3. Frauchiger DA, Chan SCW, Benneker LM, Gantenbein B (2018) Intervertebral disc damage models in organ culture: a comparison of annulus fibrosus cross-incision versus punch model under complex loading. *Eur Spine J*: doi: 10.1007/s00586-018-5638-5
4. Sakai D, Schol J, Bach FC, Tekari A, Sagawa N, Nakamura Y, Chan SCW, Nakai T, Creemers LB, Frauchiger DA, May RD, Grad S, Tryfonidou MA, Gantenbein B (2018) Successful fishing for nucleus pulposus progenitor cells of the intervertebral disc across species. *JOR Spine* 2018e: doi: 10.1002/jsp2.1018
5. May RD, Frauchiger DA, Albers CE, Benneker LM, Kohl S, Gantenbein B (2018) Inhibitory Effects of Human Primary Intervertebral Disc Cells on Human Primary Osteoblasts in a Co-Culture System. *Int J Mol Sci* 19(4): doi: 10.3390/ijms19041195
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Selected Conference Contributions

1. Bakirci E, Hugi A, Ahmad S,Kohl S, Guenat O & Gatenbein B. Optimization of 3D Bioprinted Hydrogels with Primary Anterior Cruciate Ligament Cells for Tissue Engineering Applications. *International Conference on Biofabrication* 2018, 28-31 October, Wuerzburg Germany.
2. Caliò M, Wuest SL, Wernas T, Tanner S, Giger-Lange C, Wyss F, Ille F, Gantenbein B, Egli M. Influence of mechanical unloading on articular chondrocyte dedifferentiation, in eCM Online Periodical, 2018, *eCM Conference Abstracts, 2018 eCM XVIII: Cartilage & Disc: Repair and Regeneration, 25-28 June* 2018, Davos.
3. Frauchiger DA, Chan SCW, Benneker LM, Gantenbein B. Comparison of two annulus fibrosus injury models investigated in a loaded bovine intervertebral disc organ culture format, in eCM Online Periodical, 2018, eCM Conference Abstracts, 2018 eCM XVIII: Cartilage & Disc: Repair and Regeneration, 25-28 June 2018, Davos.
4. Frauchiger DA, May RD, Zhang X, Stoyanov J, Bertolo A, Benneker LM, Grad S, Tryfonidou MA, Gantenbein B. Comparing three cell isolation techniques for "fishing" angiopoetin-1 (Tie 2) positive progenitor cells from the nucleus pulposus, in eCM Online Periodical, 2018, *eCM Conference Abstracts, 2018 eCM XVIII: Cartilage & Disc: Repair and Regeneration, 25-28 June* 2018, Davos.
5. Gantenbein B. Invited Keynote: Repair of the Intervertebral Disc using Biomaterials and Progenitor Cells, in *Proceedings of Biospine Asia Pacific, 26-28 April* 2018, Seoul, South Korea.
6. May RD, Frauchiger DA, Benneker LM, Gantenbein B. Comparison of gene expression of discs from Diffuse Idiopathic Skeletal Hyperostosis (DISH) and trauma patient, in *Proceedings of Biospine Asia Pacific, 26-28 April, Poster Presentation* 2018, Seoul, South Korea.
7. May RD, Frauchiger DA, Benneker LM, Gantenbein B. Osteoinductive Stimulation of Intervertebral Disc Cells with Bone Morphogenetic Protein 2 or Osteogenic Medium, in *Proceedings of Biospine Asia Pacific, 26-28 April, oral Presentation 2018,* Seoul, South Korea.
8. Gantenbein B. Oral Presentation: Mechanical loading under compression and torsion of bovine coccygeal intervertebral discs, in *Proceedings of the 8th World Conference of Biomechanics, 8-12 July* 2018, Dublin.

MECHANICAL DESIGN AND PRODUCTION

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Lukas Rufener

Group Profile

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

Training & Education

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

In 2018 we made one trial apprenticeship and elected Janosch Schär as our new apprentice and he will begin his 4-year training next year on 1st of August as a Polymechanic EFZ apprentice.

For students at the ETH-Zürich on the department for machine engineers, it's mandatory to have an industrial practical training at least for five weeks. This year we performed this training with Dominic Seibold and Alexander Macpherson. It was a very instructive and successful training and we wish them a lot of success in their studies.

Due to a high demand of workload, we recruited, Dominic von Ah, Daniel Germann and our former apprentice Lukas Rufener as alternative civilian-service employees. They performed administrative tasks and increased the productivity of our team and we thank them for the work they have accomplished in our workshop.

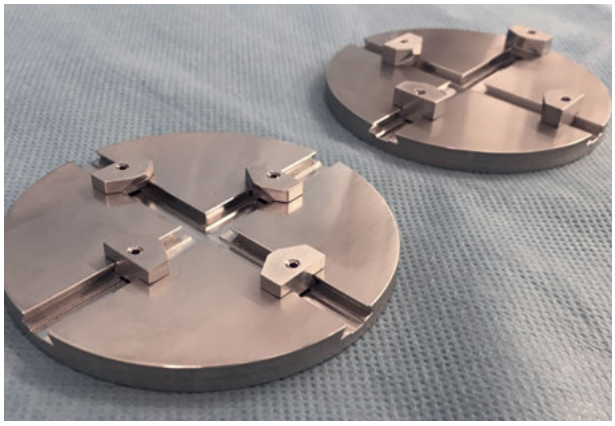
Research Equipment Design & Manufacturing ISTB

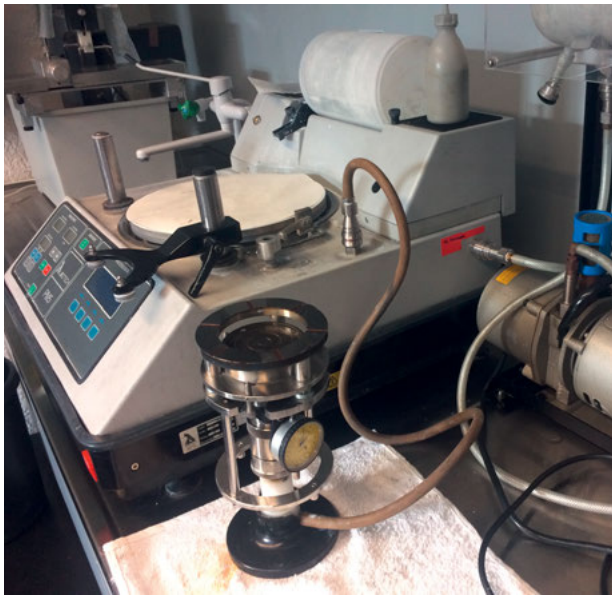
As expected, the requirements of a machine shop supporting research in the biomedical engineering field are as diverse as the research field itself. The variety of subjects researched in the ISTB yield a number of diverse design and production requests from prototype clinical and surgical tooling to fixtures for mechanical, biological and kinematic testing, as well as imaging system accessories and calibration equipment. The following illustrations highlight a few of this year's projects.

This highlight of this year projects is shown in the following illustration.

Project: MB-Group, Additional Equipment for the Lap-machine

The Musculoskeletal Biomechanics group has bought a lap-machine and they need some special additional equipment. For example this two clamping devices they make it possible to clamp different samples to the machine and to treat the surface in a very fine roughness and flatness. The device plate ground surface must have the same roughness and flatness as later the samples have, and must be plane-parallel 0.005mm, (5µ) because the sample holder of the lap machine is working with a vaccum system.

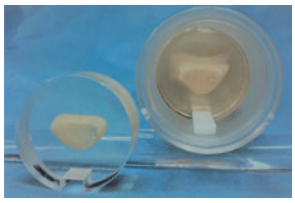


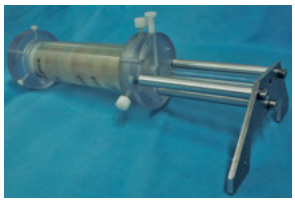


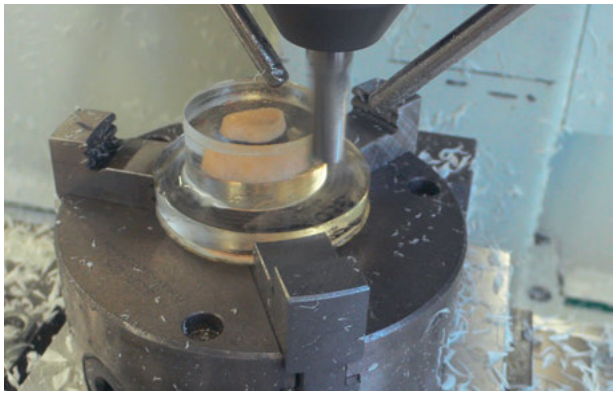
Project: MB-Group, Calibration Phantom for Radius Bone Samples

The calibration phantom was developed in cooperation with Denis Schenk from the musculoskeletal biomechanics group and was manufactured in our machine shop. The phantom can contain up to six samples. With the CNC milling machine each sample got an indentation fitting the bar fixed within the tubular sample holder to always ensure correct repositioning of the samples. The correct repositioning is important because the phantom shall be send to other centers in Switzerland or abroad to compare the results or calibrate different HR-pQCT* scanners.

**High-resolution peripheral quantitative computed tomography*

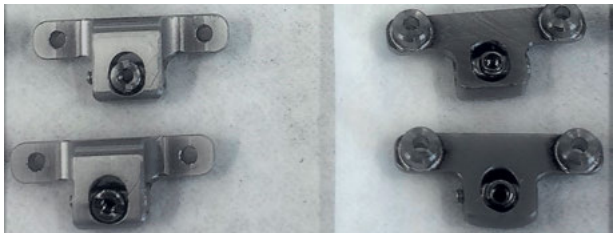


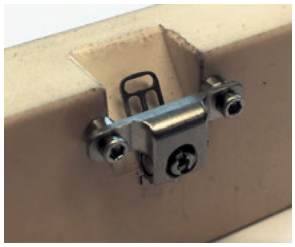




Project: DBMR Cranio-Maxillofacial Surgery Groupe, Dental Plate

Since 2007 we have a strong collaboration with Nikola Saulacic from the DBMR at the University of Bern, to develope devices in different shapes for studies in the field of bone growing. This year we developed some devices for the jawbone growing research. The big challenge was it to manufacture all this very small parts also to assemble them under the microscope. Some parts were cut out with laser beam and laser welded together in a partner company.



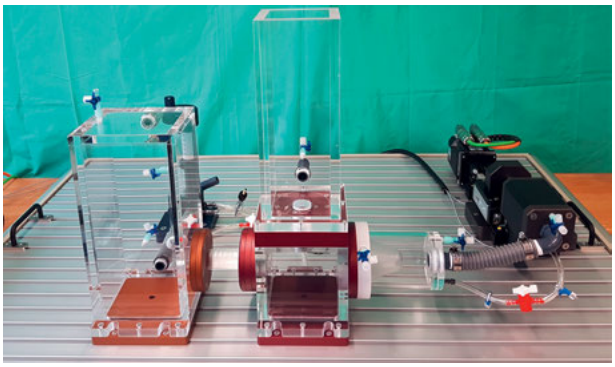


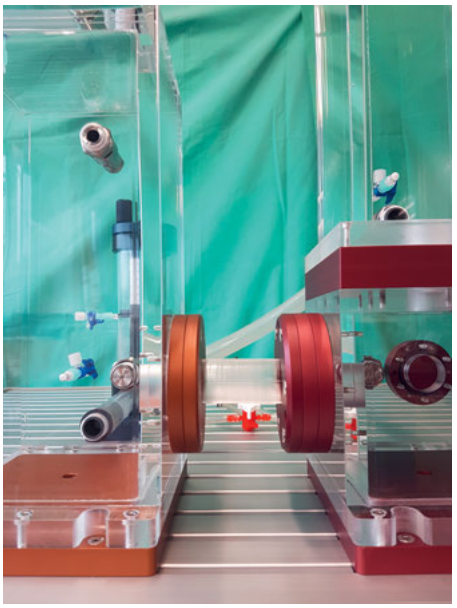
Mechanical Design & Production ARTORG

The workshop at the ARTORG Center was managed by Danaël Gasser as a full time polytechnician. He manufactured some different project-parts, mainly for the CVE (Cardiovascular Engineering) and IGT (Image Guided Therapy) groups.
His function was it to design parts of devices himself and to manufacture these parts afterwards. The ARTORG workshop pursues many of the same aims as the MDP group at the ISTB. The partnership between the two groups was growing and strengthened as a “core facility” sharing work and knowledge.

Project CVE: Flow loop system

In collaboration with the EPFL (L’Ecole polytechnique fédérale de Lausanne) at Neuchatel we developed a new artificial blood flow loop system and a new pump device. The existing flow loop and its pump in our lab had some problems with the piston guidance and was leaking. For this reason we developed a new pump piston guide concept with success. The hole system mounted on a plate can be transported and moved in a easy way. A new type of tube connection for different artificial aortas allows it to chance them in an easy way and the two chambers are longitudinally displaceable to adjust different lengts of aorta tubes.





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- We graciously and specifically would like to thank the Swiss National Science Foundation (SNSF) for their support and Innosuisse for providing R & D matching funds.
- We would also like to thank all of our research partners for their collaboration and cooperation.
- In addition, support in the form of equipment, donations, or finances provided by various foundations and companies for a large number of specific research projects is gratefully acknowledged.
- Finally, we would like to thank all the members who dedicated their time and talent to the ISTB in 2018.

COMPLETED DISSERTATIONS

Daniela Frauchiger, *"Engineered Silk, Reinforced Hydrogel and Progenitor Cell Therapy for Intervertebral Disc Repair". PhD in Biomedical Engineering, Medical Faculty, GCB University of Bern, 2018.*

Simon Habegger, *Quantitative Measures for Stroke Recovery and Outcome. Co-supervised by Roland Wiest. PhD in Biomedical Engineering, Medical Faculty, GCB University of Bern, 2018.*

Marc Stadelmann, *"Finite Element Modeling of the Human Spine: Applications on Metastatic Vertebral Bodies and Intervertebral Discs". PhD in Biomedical Engineering, Medical Faculty, GCB University of Bern, 2018.*

Simon Wüest, *"Cartilage Tissue Engineering and Electrophysiological Recordings on Microgravity Platforms", PhD in Biomedical Engineering, Medical Faculty, GCB University of Bern, 2018.*

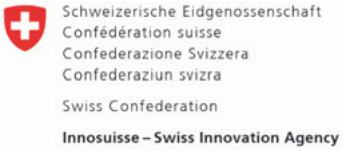
AWARDS & PRIZES 2018

Second best accuracy in the 2012-2017 analysis of BRATS results. Miccai 2018.
Awardee: Alain Jungo

BME Club Award for the best master's thesis abstract: Indentation Properties of Metastatic Vertebral Bone
Awardee: Christopher Lenherr

SICAS Award for the best PhD thesis: Thermal and Drilling Properties of Bone
Awardee: Arne Feldmann

FUNDING AGENCIES & PARTNERS



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