INSTITUTE FOR SURGICAL TECHNOLOGY & BIOMECHANICS

Contents

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INSTITUTE FOR SURGICAL TECHNOLOGY AND BIOMECHANICS

EDITORIAL

It is our pleasure to present the annual report 2014 of the Institute for Surgical Technology and Biomechanics (ISTB). Our institute comprises a multidisciplinary team of about 50 co-workers. It is also closely integrated into the Bern Bioengineering Network (www.bbn.ch), which is an inter-faculty and inter-institutional activity, forming a large collaborative research network from the university hospital, Inselspital Bern, institutes of the University of Bern, the University of Applied Sciences of Bern and various external partners.

In 2014, our group heads Philippe Büchler (Computational Bioengineering) and Mauricio Reyes (Medical Image Analysis) were both appointed Associate Professor at the Medical Faculty. By this the University of Bern recognized their outstanding research, teaching and service over the past years. In our machine shop, another poly-mechanic apprentice, Patrick Moser, graduated after 4 years of job education. In addition, we continued our activities in training undergraduates, graduate students, and postdoctoral fellows for future leadership roles in research, teaching and industry. Our Master of Science in Biomedical Engineering program (www.bme.master.unibe.ch) attracts students nationally and internationally. In addition, many students from the ISTB are currently enrolled in the interdisciplinary doctoral program in Cellular and Biomedical Sciences (www.gcb.unibe.ch).

External funding was maintained at a high level through both governmental funding and non-governmental organizations as well as our industrial partners. Key collaborative projects with the Swiss MedTech industry continue to be developed through funding from KTI/CTI, the Innovation Promotion Agency of the Swiss Federal Office for Professional Education and Technology.

We were also proud to have our research and development efforts recognized by several awards. Most notably Jakob Schwiedrzik, who not only published part of his thesis work in Nature Materials but also obtained the 2014 award of the Swiss Society of Biomedical Engineering for the best PhD research. For the third year, we continued to rank among the top-three in the MICCAI brain tumor segmentation challenge. This was complemented by various media appearances nationally and internationally.
In the past year, the ISTB contributed to the organization of several scientific meetings, most notably, the SHAPE 2014 conference on statistical shape modelling, the MICCAI brain tumor segmentation challenge and the 2014 Biomedical Engineering Day. With support of the Swiss Institute for Computer Assisted Surgery (www.sicas.ch) we continued to expand our Virtual Skeleton Database (www.virtualskeleton.ch).

Among the highlights of this year, we would like to mention our summer excursion to CERN, the European Organization for Nuclear Research, and in particular our dive into the guts of the ATLAS detector that was kindly coordinated by our colleague Prof. Antonio Ereditato and his doctoral students from the Albert Einstein Center for Fundamental Physics (AEC) of the University of Bern. We were deeply impressed by the achievement of these thousands of physicists and engineers concentrating their efforts on the function of this essential instrument for the detection of Higg's boson. We could not avoid the analogy with the virtual physiological human paradigm that would similarly require thousands of biomedical engineers to achieve an exhaustive understanding of the multiple biomechanical functions of the human body. We strongly believe that a better coordination of these efforts would accelerate the development of surgical technologies and bring numerous and objective improvements in health care.

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Research Profiles

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 bone 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 novel statistical finite element methods for the incorporation of uncertainty in bone shape and mechanical properties in to the evaluation of bone biomechanics.

Superficial Femoral Artery

In-stent restenosis remains a significant problem in Femoropopliteal (FP) arteries. One of the main reasons is suggested to be arterial wall damage during and post stenting. With self-expanding Nitinol stents being used for the treatment, clinicians tend to select large stents to ensure optimal wall contact and prevent stent migration. However, this oversizing can cause trauma in arteries and may be the cause for restenosis.
A better description of the biomechanical implications of oversizing on arterial tissues is necessary to understand the mechanisms responsible for restenosis and help the clinicians in selecting the appropriate stent size during intervention. During the past year, numerical models have been developed to evaluate the mechanical effects of Nitinol stent deployment (fig. 1). Our results showed that stent oversizing increases the risks of chronic irritation of the structural and hemodynamic properties of the popliteal arteries. The damage inflicted onto the arterial walls and resulting continuous degradation of critical flow parameters may create circumstances for restenosis. The numerical model indicates that a maximum oversizing ratio of 1.1 is recommended for the FP arterial tract to reduce the risk of restenosis.

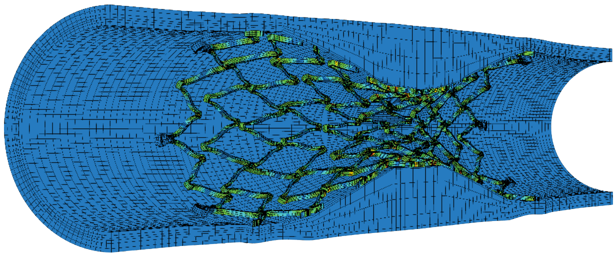

Fig. 1 Numerical simulations were used to describe the mechanical effect of the deployment of Nitinol stents in healthy and diseased arteries.

Bone Trabecular Orientation

Patient-specific models can be used to evaluate bone strength. The models are built from clinical CT scans, which allow assigning bone mechanical properties according to the spatial distribution of bone intensities. However, it has been shown that bone density is not sufficient to accurately estimate bone strength and that adding information about the trabecular orientation improves such calculations. One of the limitations of this approach is that high-resolution scans are required to obtain the bone orientation, which can only be used *in vivo* for a few bones at the extremities. To improve the accuracy of strength calculations from finite element models, we proposed to rely on a reference map of bone anisotropy that can be adapted to each patient.
The approach used to predict the trabecular bone structure relies on image registration. The patient's clinical CT is registered to the template dataset. This process results in a high-resolution image with the outer shape of the patient's bone and with the trabecular structure adapted from the template. Validation of the registration procedure showed a good correspondence of the microstructure between the reference and target images (fig. 2). The mechanical assessment of this registration approach showed improved bone strength predictions with the estimated bone orientation compared to the assumption of bone isotropy. The work indicates that the morphing of a template trabecular orientation can be used as part of a pre-clinical tool to estimate bone strength.

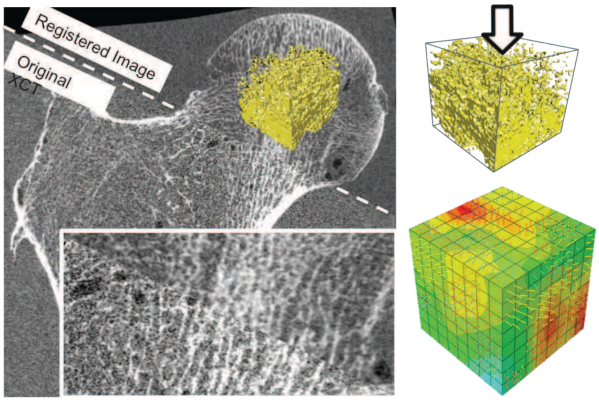

Fig. 2 Image registration was used to adapt the trabecular orientation from a template bone to the patient's clinical CT scan. Evaluation of the method showed a good correspondence of the registered microstructure as well as improved prediction of the bone strength calculated with finite element models.

Bone Electric Conductivity

Direct cochlear access (DCA) is an attractive approach to place electrodes into the cochlea while limiting the invasiveness of the surgery. This minimally invasive technique should replace the mastoidectomy currently used. However, DCA can only be done under robotic guidance, as the trajectory of the drilling passes at only 0.5mm away from the facial nerve and other critical structures in the inner ear. In the case of DCA, an adapted facial nerve (FN) monitoring procedure can help determining the distance to the nerves at risk. However, this technique requires a deeper understanding of the propagation of the electrical signals within the bone to ensure reliable measurements.

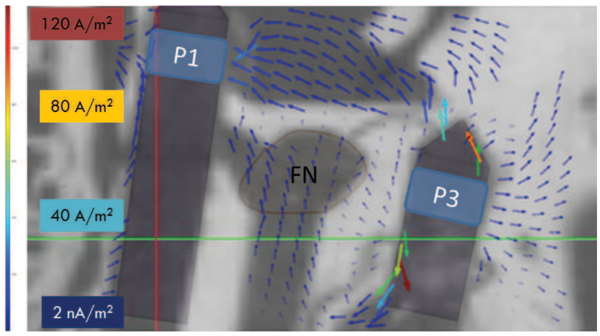

Fig. 3 Bone electric impedance has been measured *in vivo*. Numerical calculations were used to reproduce the experimental measurements and model propagation of the electric currents in the tissue at the microscopic scale.

A setup for measuring electric properties in facial nerve monitoring (FNM) was developed and used to evaluate the FN monitoring procedure on five sheep at the veterinary hospital of the University of Bern. Bone impedance was measured *in vivo* for various voltage frequencies and intensities. In addition, an *ex vivo* test setup has been developed to quantify the electric properties of bone samples. These measurements will allow understanding the individual elements contributing to the bone conductivity and will improve our comprehension of the data collected *in vivo*. Numerical models were also developed to determine the parameters responsible for the bone conductivity at the microscopic scale (fig. 3).

Biomechanics of the Scoliotic Spine

Spinal fusion is the treatment of choice when the thoracic curve of an adolescent idiopathic scoliosis patient is expected to reach at least 50° by skeletal maturity. Accurate planning of surgery requires a good understanding of both patient-specific spinal morphology and stiffness. Spinal morphology is usually obtained from medical imagery such as X-ray radiographs, but the surgeon has only limited information on the mechanical behavior of the patient's spine. Current clinical tests solely rely on the displacement of the spine without taking force information into account. Only reducibility (displacement of the spine) can be evaluated by these methods, not mechanical stiffness.
To overcome this issue, a new preoperative method has been developed to quantify the three-dimensional stiffness of the spines of adolescent idiopathic scoliosis patients. The technique combines a novel clinical test – the spinal suspension test (fig. 4) – with numerical optimization of a finite element model of the patient's spine. A pilot study conducted on five patients showed that the model was able to provide accurate 3D reconstruction of the spine's midline and predict the spine's stiffness for each patient in flexion, bending, and rotation. Statistically significant variation of spinal stiffness was observed between the patients. This result confirms that spinal biomechanics is patient-specific, which should be taken into consideration to individualize surgical treatment.

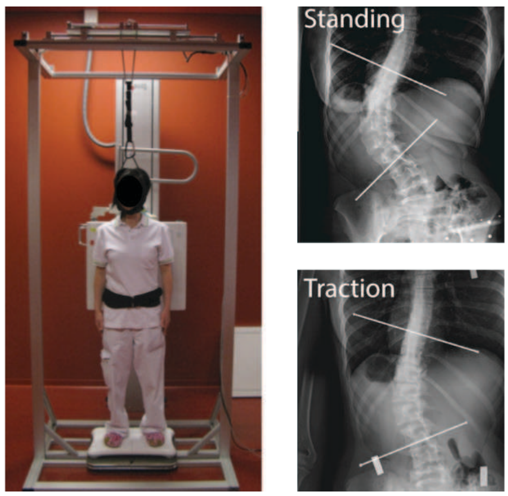

Fig. 4 The spinal suspension test has been designed to ensure an axial loading of the patients' spine. A platform allows rotating the patient to acquire orthogonal radiographic images before and after elevation with a force equivalent to 30% of the patient's weight. The radiographs before and after traction enabled to quantify the correction of the curve induced by the test and are used to assess the spinal stiffness.

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Information Processing in Medical Interventions

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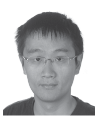
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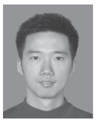
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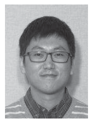
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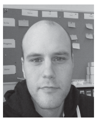
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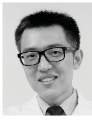
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Research Profile

IPMI group focuses on the development of medical image-based quantitative-analysis applications (Fig. 1). This is done by translating established or developing new imaging technologies to robust and innovative software for clinical trials with the ultimate goal to improve healthcare delivery to patients. In recent years, the group has focused strongly on translational research in different stages of medical interventions. Typically examples include the automatic segmentation of meaningful regions in medical images for treatment planning, the accurate derivation of 3D patient-specific anatomical models from 2D medical images (e.g., X-ray images), the precise calibration of intra-operative imaging devices and surgical instruments for medical interventions, the rigid/non-rigid registration of medical images to patient's physical space, and the image-based measurement and quantification of anatomical and clinically meaning parameters.

iJoint: X-ray Radiograph Based True 3D Planning and Evaluation System for THA

Supported by the Commission for Technology and Innovation (CTI), a personalized X-ray reconstruction-based planning and post-operative treatment evaluation framework (Fig. 1, middle-left) called iJoint was developed for THA. Based on a patented X-ray image calibration cage and a unique 2D-3D reconstruction technique, iJoint can generate accurate patient-specific models of hip joint by non-rigidly matching statistical shape models to the X-ray radiographs, whose acquisition is part of the standard diagnostic and treatment loop. As part of the system, a 3D model-based planning environment provides surgeons with hip arthroplasty related parameters. With this newly developed system, we are able to provide true 3D solutions for computer assisted planning of THA using only 2D X-ray radiographs, which is not only innovative but also cost-effective.

iBack: Fully-Automatic Lumbar Intervertebral Disc (IVD) Segmentation from MR Images

The recent shift of the disc pathology treatment paradigm from surgical procedures towards treating the underlying aetiologic process has changed the clinical requirement of disc degeneration diagnosis. One of the difficulties with current MRI-based evaluation approaches is that the analysis of the MR images is done manually. Thus, such an evaluation is susceptible to inter- and intra-observer variability. Supported by the Swiss National Science Foundation (SNSF), we have developed methods for fully-automatic localization and segmentation of 3D IVDs from both T2-weighted turbo spine echo MR images and multimodality MR spinal images acquired with Dixon protocol (Fig. 1, top-left) by exploiting information from both training data and geometric constraints. The problem is formulated in a unified objective function which is then solved globally and efficiently.

iLeg: X-ray Radiograph Based True 3D Planning and Evaluation System for Lower Extremity Interventions

Supported by the SNSF, in this project we developed a system called "iLeg" that allowed reconstructing a patient-specific 3D models of the complete lower extremity in a weight-bearing situation from clinically available X-rays for true 3D planning and evaluation of surgical interventions of the lower extremity (Fig. 1, bottom-left). Supported interventions include lower extremity osteotomy (LEO) and total knee arthroplasty (TKA). A recent validation study on 12 cadavers (24 legs) demonstrated a mean pose+shape reconstructing accuracy of 1.3 mm, taking surface models derived from the associated CT scan as the ground truth.

Patient-specific Periacetabular Osteotomy (PAO) Planning with Biomechanical Optimization

Supported by a cooperation with the Department of Orthopaedic Surgery, Inselspital, we have developed a comprehensive system for computer assisted planning and navigation of periacetabular osteotomy (PAO) with range of motion optimization (Fig. 1, middle-right). In order to investigate the optimal acetabulum reorientation after PAO, we extended our system with a patient-specific finite element prediction of cartilage contact stress change before and after PAO treatment. Our experi-

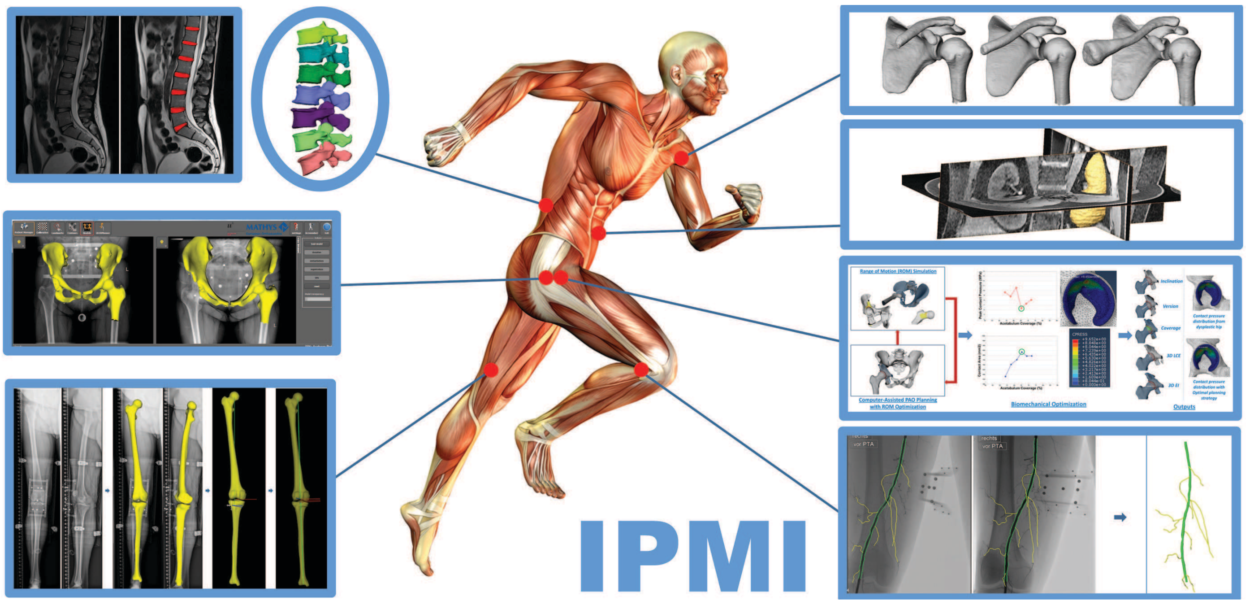

Fig. 1 An overview of selected on-going projects. See main text for details.

mental results showed that an optimal position of the acetabulum can be achieved, which maximizes contact area and at the same time minimizes peak contact pressure in pelvic and femoral cartilages.

A Technique for 3D Reconstruction of Arteries from Angiographic Projections

Peripheral arterial disease (PAD) is a relatively common disease affecting many adults worldwide. PAD is the presence of lower extremity artery obstructions and is mainly associated with a cramping leg pain. In severe cases, PAD can lead to myocardial infarction and ischemic stroke. A common treatment of PAD relies on the insertion of stents to improve blood flow and to prevent recurrent obstructions. But as stents are subject to failure and can cause arterial wall damage, restenosis is frequently observed. For a reduction of the restenosis risk, the selection of the stent needs to be optimized in terms of shape and material properties. In order to select the optimal stent, a three-dimensional, patient-specific model of the artery is required. We have developed a semi-interactive framework to construct such a model from two angiographic images (Fig. 1, botton-right). Strarting from image calibration with our patented calibration cage, we first extract the main arterial branch and its side branches from the acquired images. This information is then used to perform a three-dimensional reconstruction of the arterial tree. Currently, a clinical study is running in order to assess the overall accuracy of our framework

Radiographic Reconstruction of Fractured Tibia Bones: A First Trial

Conventionally, tibial fractures are first surgically aligned and then postoperatively reduced by distraction osteogenesis using external fixators. Over a specific period of time, these external fixators constantly apply tension stress to the bone fragments to stimulate its regeneration. In order to supervise this regeneration process, the patient has to regularly undergo x-ray examinations. These recurrent x-ray acquisitions are associated with repetitive radiation exposures and high costs for the healthcare system. We have developed a solution based on our existing 2D-3D reconstruction framework to recover the rotational relationship between proximal and distal bone fragments. A statistical shape model of both fragments is matched to two calibrated x-ray radiographs to reveal the underlying transformation. The validity of our proposed system was demonstrated on a customized mockup by simulating different fractured scenarios using synthetic bone models.

Selected Publications

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Medical Image Analysis

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Research Profile

The Medical Image Analysis group conducts theoretical and applied research in image processing, computer vision, and artificial intelligence for the analysis of medical image datasets. The focus of our research relies on the paradigm of evidence-based image modeling and personalized medicine, which aims on the one hand to understand the natural anatomical and physiological variability encountered in a population and, on the other hand, to use this understanding to overcome imaging limitations hindering patient treatment.

During the last years our group has focused on three major questions that align with the paradigm of evidence-based modeling and personalized-medicine:

- *How to effectively combine Magnetic Resonance Imaging information for a comprehensive spatial and temporal characterization of brain lesions?*
- *How to design planning and post-operative simulation algorithms and systems to assist cranio-maxillofacial and oral surgeons?*
- *How to effectively encompass anatomical and physiological variability for the understanding of musculo-skeletal diseases, the design of orthopaedic devices, and less-invasive, yet more effective orthopaedic surgical approaches?*

Computational Anatomy for Orthopaedic Research

Computational anatomy enables analysis of biological variability throughout a population. Using statistical mathematical techniques, models can be built to represent the typical shape of an anatomical structure and its predominant patterns of variability across a given population. During 2014 we have used these techniques to improve the design of cochlear electrodes, used to reestablish hearing on patient suffering from moderate to severe hearing loss, as well as to support the complex surgical planning procedure. Our research also supports the efforts in prediction of bone fractures, by developing methodologies to segment and model bone microstructure and algorithms to quantify complexity and organization of biological tissues.

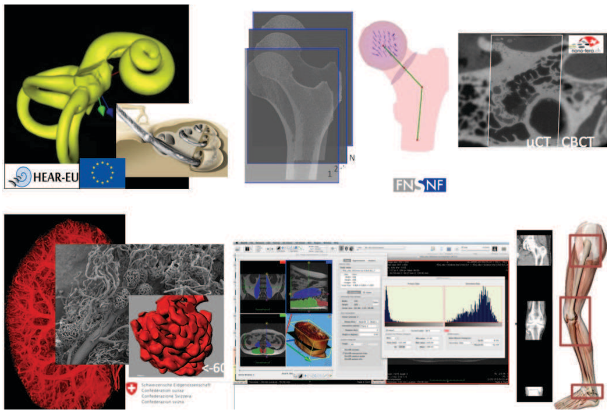

Fig.1 Modeling anatomical variability and its application to applications such as cochlear surgery, bone fracture prediction, Sarcopenia and characterization of organ complexity.

Oral and Cranio-Maxillofacial Surgery

Our group develops algorithms and systems to perform prediction of soft-tissue deformations after cranio-maxillofacial surgery. The algorithms have been developed with a strong emphasis on its clinical usability (i.e. compliance to imaging protocol, computation speed and usability). The simulation framework features high accuracy by incorporating non-homogeneous and anisotropic tissue properties as well as sliding contact considerations. During 2014 we focused on developing a dedicated software for soft tissue simulation in CMF interventions, termed Sotirios MxFx (Soft Tissue Reconstruction for Intra-Operative Simulation - Maxillofacial). Through a multicenter study, the software is currently being evaluated. On the basic research, we have presented with our partners an innovative approach to deal with metal artefacts or similar image deteriorations and allow a robust segmentation of bone structures. In addition, our developments jointly incorporate functional and anatomical considerations, such as dental occlusion, desired aesthetic outcome, etc.

Brain Image Analysis

Magnetic Resonance Imaging (MRI) and its variants are a pow-

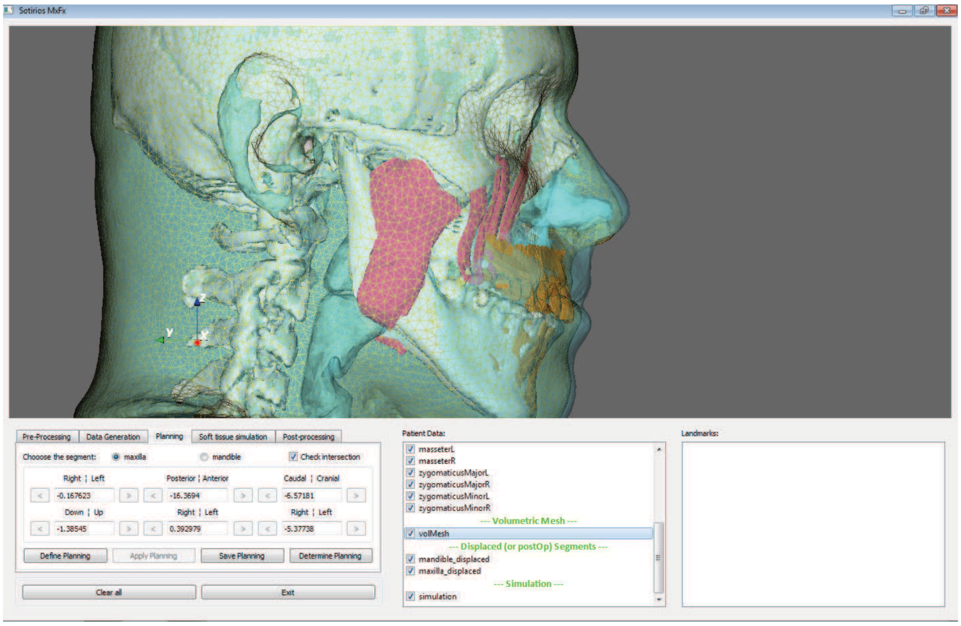

Fig.2 Sotirios MxFx Software: "Soft Tissue Reconstruction for IntraOperative Simulation- Maxilofacial". Sotirios enables a fast and accurate simulation of postoperative skin deformation for CMF surgery.

erful 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 lesoin analysis studies. These developments are driven by clinical requirements such as computation speed, robustness, and use of standard clinical imaging protocols. During 2014 we have further developed algorithms to automatically segment glioblastomas grade III and IV from multimodal images (i.e. T1, T1c, T2, FLAIR) and for longitudinal studies. Frthermore, we have proposed an algorithm to segment post-operative images, which is very important to assess extent of resection and tumor volume redisual. The algorithms are based on supervised and unsupervised classification techniques tailored to the clinical scenario.

We have performed technology transfer to our clinical collaborators and deployed a software for multimodal brain tumor image analysis, termed BraTumIA (Brain Tumor Image Analysis), which was during 2014 clinically evaluated. BraTumIA has been made available to the community for research purposes. The underlying technologies are being extended to deal with other brain lesions, notably, acute infarct stroke and multiple sclerosis.

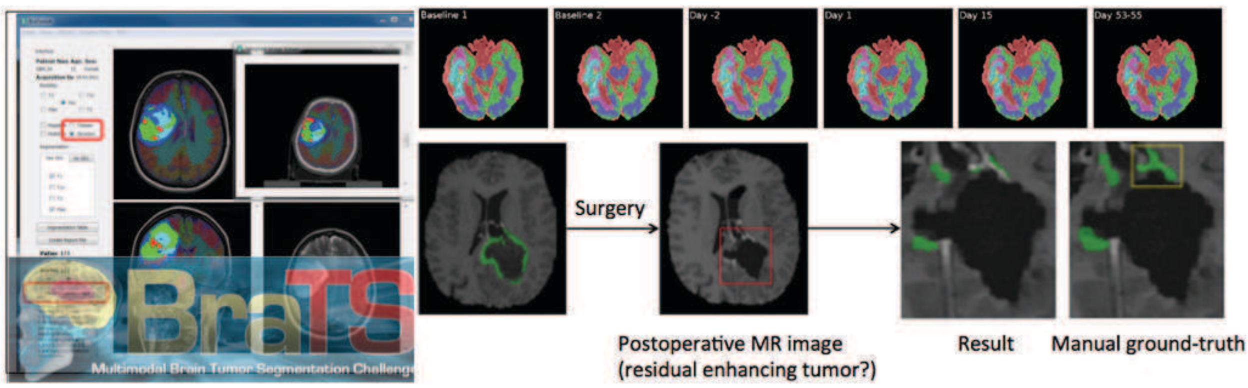

Fig. 3 Brain Tumor Image Analysis- BraTumIA. BraTumIA is a software tool that enables full segmentation of Glioblastomas from Multimodal Images and stems from our research in multimodal brain tumor segmentation. Top right shows results of a longitudinal brain tumor segmentation. Bottom right, postoperative brain tumor segmentation for assessment of tumor resection.

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Musculoskeletal Biomechanics

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Research Partners

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Prof. Dieter Pahr, Vienna University of Technology
Prof. Moritz Tannast, Division of Orthopedic Surgery and Traumatology, Inselspital

Research Profile

Motivated by prevention, diagnosis, treatment and follow-up of degenerative diseases, the research of the musculoskeletal biomechanics group focuses on multi-scale structure-function relationships of bone and intervertebral disc tissue 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 musculoskeletal tissues in the course of growth, aging, disease and treatment. The group provides also specialized biomechanical testing services and cooperates with local, national as well as international partners from academia, hospitals and industry to help reduce the burden of osteoporosis and other degenerative diseases.

Bone Indentation

Instrumented indentation is used routinely in our laboratory to measure heterogeneous and anisotropic elastic properties of bone tissue at the micron and submicron level in both dry and wet conditions. However, numerical studies failed to extract unique post-yield properties of bone from single indentation experiments. As a further attempt to explore the post-yield behaviour of the bone matrix, atomic force microscopy (AFM) was used to determine the shape of the residual imprint in copper, polymethyl-methacrylate (PMMA), human and ovine bone. Statistical shape analysis of the imprints revealed that no pile-up occurs in bone and that the achieved surface preparation is of high quality.

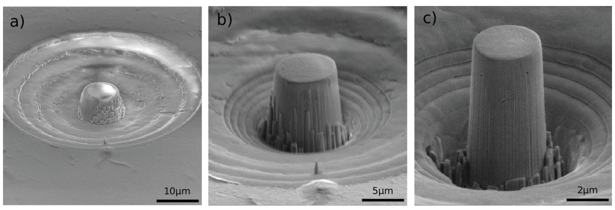

Fig. 1 Manufacturing of a bone micropillar in a scanning electron microscope using a focused ion beam (FIB).

Bone Damage

Fractures of the femoral neck usually occur after an overload along a direction of impact, which does not coincide with the typical physiological load direction and, thus, generates non-physiological loading stresses. This project aims at investigating the loading mode dependent damage accumulation in bone tissue and its role in femoral fracture risk.

Loading mode dependent damage accumulation was quantified experimentally in osteonal bone biopsies. A new material model that is able to describe the coupling of bone damage accumulation between different loading modes for repetitive cycles was developed based on the obtained experimental results and is currently extended to 3D. Furthermore, novel synchrotron micro-computer tomography protocols have been developed to analyze microcrack families in bulk osteonal samples.

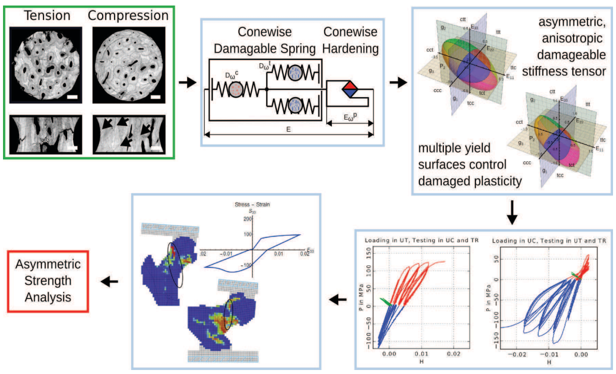

Fig. 2 Coupling of damage in different loading modes of human compact bone: visualization with synchrotron tomography, constitutive modelling in 1D and 3D, multistep mechanical testing and finite element analysis.

Bone Drilling

The research of bone drilling is relevant for many surgical procedures. Thermal elevation of the drilling process can lead to bone necrosis and possibly inhibit bone implant ingrowth. Another important application is robotic drilling of the human skull. High temperature elevation of the drilling process might lead to facial nerve damage and reduced motor control of the face.

Our research focuses on computer modeling of the drilling process and on validation experiments with a state of the art experimental setup. Drilling forces and temperatures are analyzed and drill bit geometry will be optimized. A deeper understanding of the tool/ material interaction is necessary to solve thermal and mechanical problems and to improve the surgical outcome.

Spine Research

Computer tomography (CT)-based biomechanical models assess vertebral strength better than the usual diagnostic tool. Intervertebral disc degeneration and loading conditions are overlooked. MRI and CT data were recently combined in spinal unit models. Loading over a degenerated disc was compared to a loading via embedded endplates, the experimental paradigm. Compression and lifting were simulated, load and damage pattern were evaluated at failure. Osteoporotic vertebrae with degenerated discs are consistently weaker - especially under lifting, but clinical assessment of strength is possible without extensive disc modeling. Our current aim is to improve the discs models by including MRI-based fiber orientation and fiber damage.

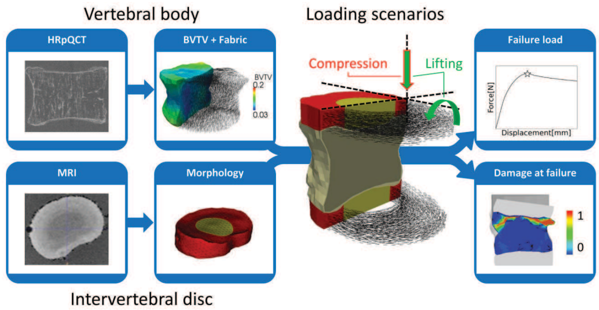

Fig. 3 Modeling of a the human vertebral body strength using high-resolution computer tomography of the bone and MRI scanning of the intervertebral discs.

Finite Element Analysis of the Proximal Femur

In homogenization analysis of non-periodic media, the results strongly depend on the type of applied boundary conditions (BCs). Therefore, this study investigated the role of the widely used kinematic uniform BCs (KUBCs) and a new set of mixed uniform BCs, namely periodicity-compatible mixed uniform BCs (PMUBCs). KUBCs or uniform displacement BCs constraint every node on boundaries to displace homogeneously. PMUBCs are combinations of uniform displacement and uniform traction BCs. The two boundary conditions were compared using micro FE to analyze 167 femoral trabecular bone biopsies. Three uni-axial and three shear loading cases were applied on each biopsy to obtain its elastic properties. As expected, PMUBCs delivered more compliant results than KUBCs. Unlike KUBCs, PMUBCs were sensitive to heterogeneity of the trabecular bone samples. The two boundary conditions should be further investigated in yield and in whole bone analyses.

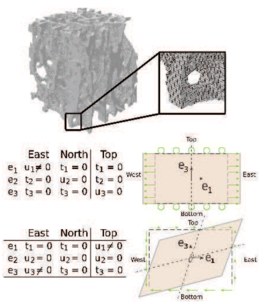

Fig. 4 Micro-finite element models of trabecular bone cubes: uniaxial elongation and pure shear load cases using periodicity-compatible uniform boundary conditions (PMUBCs).

Strength of the Distal Radius

Homogenized finite element (hFE) models, which are based on high-resolution peripheral computed tomography (HR-pQCT) reconstructions, enable fast and accurate prediction of *in vitro* fracture load of the distal radius. Upon proper validation, this low X-ray dose technique may help improve diagnosis of osteoporosis and allow regular follow-up of radial strength.

For this purpose, twelve pairs of human cadaver forearms were scanned intact using the high and the low-resolution protocols (61 and 82 µm voxel size) of the new generation XtremeCT2 scanner of SCANCO Medical AG. The most distal radius sections were dissected out of the forearms and tested in compression up to failure. Sample-specific hFE models of the sections were generated from the grey level images and our non-linear material model of bone predicted their strength accurately with an excellent short-term reproducibility. Following adequate software implementation, this study will make this technique mature for clinical use.

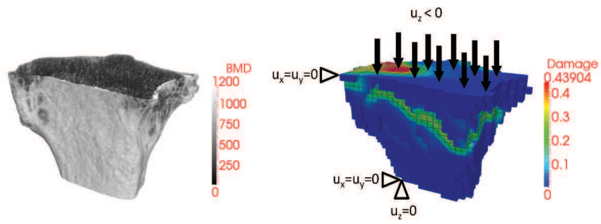

Fig. 5 MicroCT image and homogenized finite element models of a distal radius section: finding a compromise between accuracy and computing time.

Biomechanical Testing

Biomechanical experiments were performed for industrial contract research, clinical projects and internal research. For instance, measurements of the mechanical properties of dental abutments for dental reconstructions according to industrial testing standards were conducted. Regarding musculoskeletal applications, a sheep model for femoro-acetabular impingement (FAI) was investigated to assess biomechanical stability. This project was devised by the department of Orthopaedics and Traumatology of the Insel Hospital in Bern. In collaboration with the VetSuisse faculty, degeneration of the canine atlanto-axial joint was investigated. Several new types of implants for treatment of the defect were evaluated by exploratory *in vitro* biomechanical testing.

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Tissue & Organ Mechanobiology

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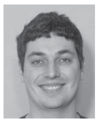
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Research Profile

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 tissues and organ culture models. Their 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 develop *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.

Intervertebral Disc Degeneration and Low Back Pain

The year 2014 has been a year of exploration of the new two degree of freedom bioreactor to test the importance of complex loading. The TOM group investigated further into the understanding of complex forces such as compression and torsion onto IVD cells *in situ in organ* culture. Here, we investigated towards the understanding of duration of mechanical loading for IVD cells. The team explored the effect of increased cell death by application of a duration of 8h of dynamic compressive loading. The group developed a strong *ex vivo* model using bovine IVD organ culture. This model has been used to explore fast and reliable models for disc degeneration using non-clinical relevant enzymes such as papain.

Furthermore, the group explored non-viral gene therapy as an option for IVD regeneration using growth and differentiation factor 6 (GDF6 = BMP13) as a primary target for differentiating human mesenchymal stem cells towards IVD-like precursor cells. Here, new approaches to deliver plasmid to target cells are under investigation.

In a Gebert Rüf financed project a novel type of silk material is currently being investigated for IVD repair. This futuristic sounding project attracted the attention of media, such as 20min.ch.

Silk is a very old and interesting biomaterial with high elastic properties and low allergenic potential once the amino acid sericin has been removed. The TOM group started to investigate into new growth-factor-enriched silk, which is produced from genetically transducted silk worms (*Bombyx mori*), which covalently link the growth factor of interest directly into the silk. The new biomaterial will be tested *in vitro* on disc cells and mesenchymal stem cells but also in their 3D organ culture model using the bioreactor for applying complex loading protocols.

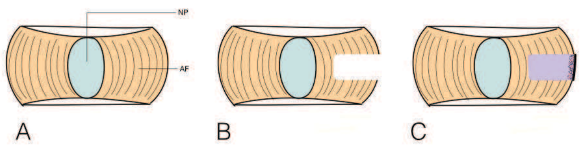

Fig. 1 Overview of disc repair approach using a hydrogel and silk fleece membrane composite. A. Intact disc with annulus fibrosus (AF) forming the outer fibrous ring and nucleus pulposus (NP) as gelatinous core. B. Round circular AF defect introduced by a biopsy punch. C. Defect filled with a fibrin based hydrogel and sealed with a silk fleece membrane composite.

Biological Repair of the Ruptured Anterior Cruciate Ligament (ACL)

ACL injuries are very common; in Switzerland the incidence of ruptures is estimated at 32 per 100,000 in the general population and in the sports community this rate increases more than double. Current gold standard for ACL repair is reconstruction using an autograft. However, this approach has shown some limitations. A new method has been heralded by the Knee Team at the Bern University Hospital (Inselspital) and the Sonnenhof clinic called Dynamic Intraligamentary Stabilization (DIS) which keeps ACL remnants in place in order to promote biological healing and makes use of a dynamic screw system. Here, cell-based approaches using collagen patches or application of platelet derived plasma (PRP) are of high interest. The aim of this study was to investigate the use of collagen patches, in combination with the application of platelet rich plasma (PRP) and platelet rich fibrin (PRF) together with DIS to support regeneration of the ACL and to quantify the biological response. Furthermore, a novel bioreactor has been designed and realized to culture full human ACL.

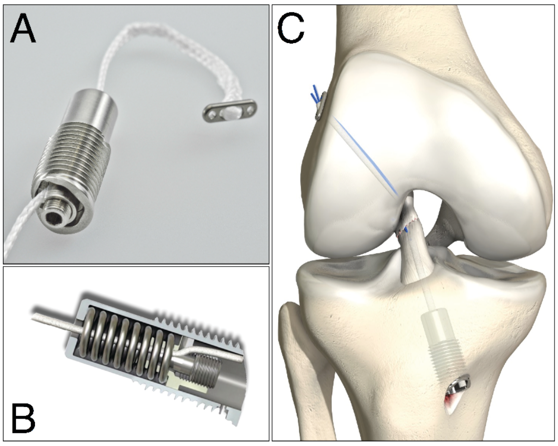

Fig. 2 Dynamic Intraligamentary Stabilization (DIS) screw called Ligamys© (Mathys, inc. Bettlach, Switzerland). A: Close-up of the outside of the screw made of titanium and illustrating with a mounted lace which mimics the polyethylene string that is mounted in the real surgery to stabilize the knee joint in case of an anterior cruciate ligament (ACL) rupture. B: Inside of the dynamic fixation screw with the spring that takes the dynamic load of the ACL and stabilizes the joint, C: Illustration of the exact position of the DIS *in situ* in the knee joint.

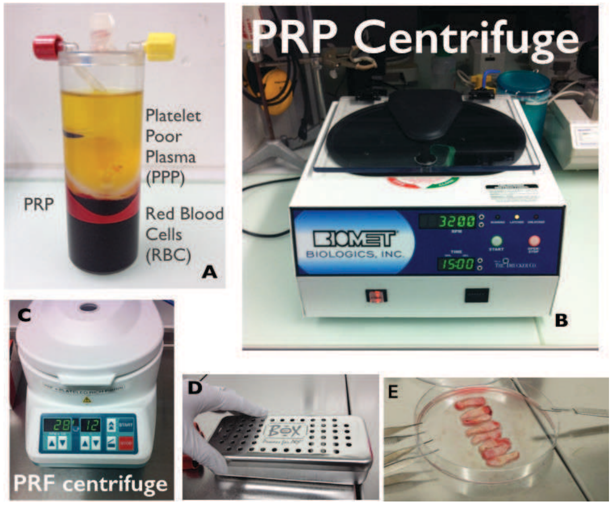

Fig. 3 Regenerative approaches for anterior cruciate ligament repair using patient's own blood. In order to accelerate ACL rupture healing, patient's autologous growth factors isolated and enriched from their blood are wrapped in a porcine-derived collagen 1/3 scaffold. Here is an overview of the preparation techniques. PRP isolation using commercial kit, B. PRP centrifuge, C. Specialized PRF centrifuge D. PRF box. E. PRF cut in pieces before application.

Exploring Ion Channel Communication under Microgravity[1]

Disuse or prolonged mechanical unloading of cartilage leads to enhanced degeneration. This is especially of concern for bed-ridden patients and astronauts while in space. Because cartilage has limited capacity for self-repair, restoration of damaged or degenerated cartilage remains a major clinical issue. Data from space experiments and experiments under simulated microgravity by using a so called Random Positioning Machine (RPM) suggest that mechanical unloading enhances the signs for degeneration and accelerates the phenotype dedifferentiation at the same time. Because the conversion of mechanical force into intracellular signal has not been fully elucidated yet, it is still not clear what mechanisms are responsible for the modifications of cartilage and chondrocytes to either real or simulated microgravity. Among other proteins, mechano-sensitive ion channels could play a crucial role in allowing the cell to detect external forces.

For future work a oocyte patch clamp device is further optimized to allow an electrophysiological examination of mechanosensitive ion channels, particularly under various gravitational loads as well as hypergravity. Furthermore the RPM shall be tested for its feasibility to modulate chondrocyte dedifferentiation. Thereby they also examine potential changes in the expression pattern of selected mechanosensitive ion channel genes that might occur under simulated microgravity conditions. This project is a collaboration with the CC Aerospace Biomedical Science & Technology, Space Biology Group, Lucerne, which also finances the PhD student.

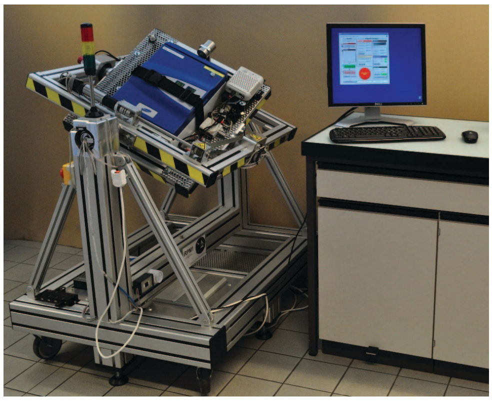
Fig. 4 Random Positioning Machine to simulate microgravity, which harbors an incubator for cell culture. (Picture courtesy of S. Wüest, CC Aerospace Biomedical Science and Technology, Space Biology Group, Lucerne University of Applied Sciences and Arts).

Selected Publications

1. Bertolo A., Gemperli A., Gruber M., Gantenbein B., Baur M., Pötzel T. and Stoyanov J., "*In Vitro* Cell Motility as a Potential Mesenchymal Stem Cell Marker for Multipotency", Stem Cells Transl Med. doi: 10.5966/sctm.2014-0156, 2014.
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[1]This project is an external collaboration and funded by the CC Aerospace Biomedical Science and Technology, Space Biology Group, Lucerne University of Applied Sciences and Arts.

Mechanical Design & Production

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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.

On the 1st of August 2014 Julien Meister became our new apprentice Polymechanic. He is currently completing his basic training for 6 month at the Astronomic Institute at the University of Bern, before continuing with us as part of the MDP group

Our apprentice Lukas Rufener completed his basic training exam at the end of the second year with good results and we congratulate him. In the coming two years his training will focus more on CAD-CAM technologies and manufacturing more ambitious parts.

In May Patrick Moser completed his apprenticeship exam successfully with a good result and we congratulate him. After completion of his training he was employed until the end of September in our machine shop as a Polymechanic.

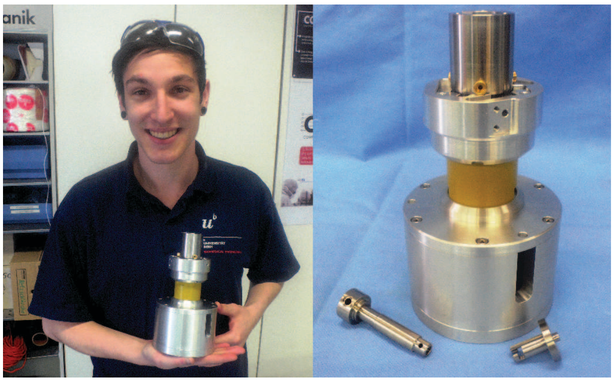
Since 1st of September we were able to employ Meret Ruch as a Polymechanic at a 60% rate, she decided to begin an extra-occupational bachelor's degree in micro-medical technology at the technical college.

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.

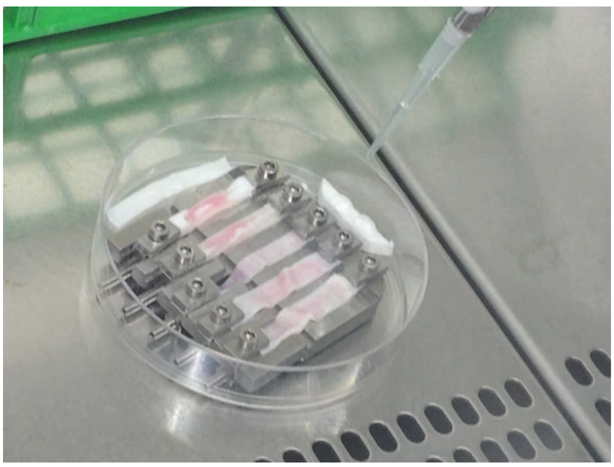
Project: ESRF Biaxial OB Group, Part of Patrick's Final Examination

The group of Uwe Wolfram was in need of a complex loading device to load bone specimens in tension, compression, and torsion in an in situ experiment on beamline ID 19 of the European Synchrotron Radiation Facility. Alexander Bürki designed the device. The complex parts were machined by Patrick Moser during his final practical exam.



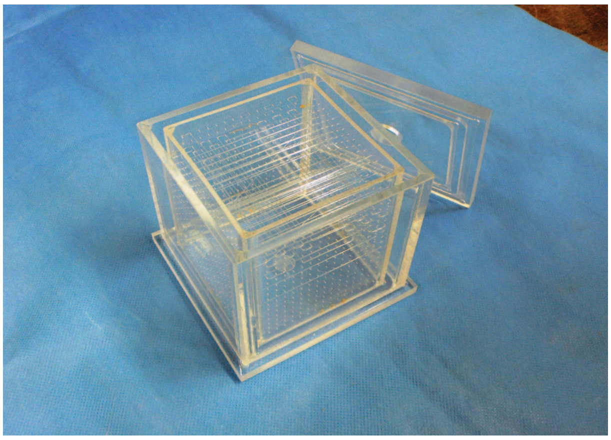
Project: Multi Collagen Stretch Device TOM Group

This compact clamping device for collagen coated strips was designed and machined by us. The device allows testing five collagen strips at a time in a small petri dish with five different tensile loading states under sterile conditions. This is a significant advantage over earlier solutions.



Project: Acrylic Phantom for Smart Sphincter Project CB Groupe

In collaboration with Tobia Brusa we developed and machined this acrylic glass phantom. Major challenges within the project were placement and manufacture of 1020 drill holes with diameter 0.5 mm. The device serves as a calibration unit for an ultra sound detector and to identify its resolution.



Research Equipment Design & Manufacturing ARTORG

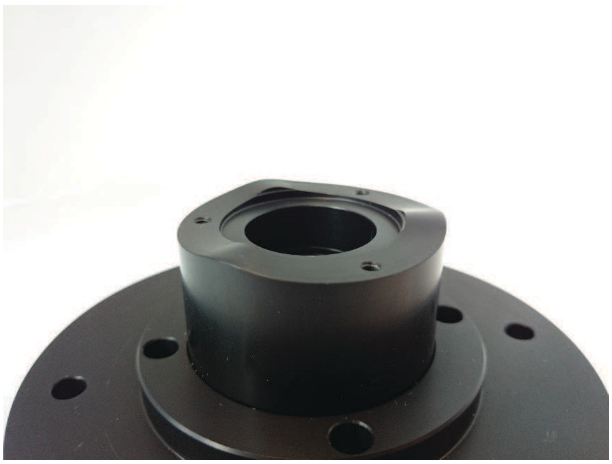
The workshop at the ARTORG Center is managed by Ronald Ramseier, he was the former Polymechanic in the ISTB MDP-group. This year the machine shop at the ARTORG Center manufactured a number of different projects, for the IGT and Computational Bioengineering Groups.

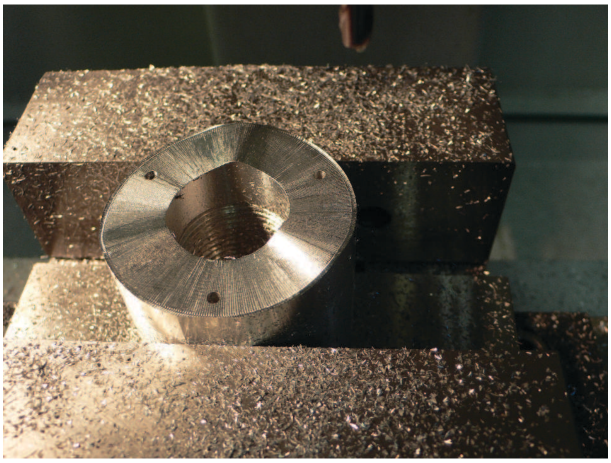
To support the Cardiovascular Engineering Group Danaël Gasser was integrated into the group as a Polymechanicer. His duties are to design parts of devices himself and to manufacture these parts afterwards in the machine shop.

As the ARTORG workshop pursues many of the same aims as the MDP group at the ISTB, and as much of the production equipment is located at the MDP. The partnership between the two groups this year was consolidated and is still growing. Some highlights of this year projects is shown in the following illustrations.

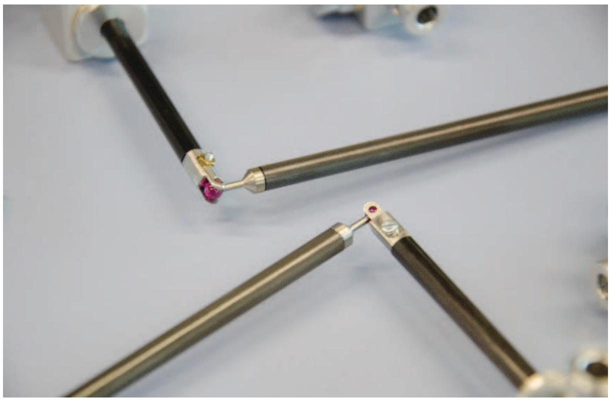
Cardiovascular Engineering/ ARTORG

This clamping device for artificial aortic valve closures is used in a tomo-PIV detector. The black anodized surface minimizes reflections and, thus minimizes measurement errors. The CNC-milled wave-form of the clamping is adapted to the form of the





artificial aortic valve closures to avoid unwanted deformations during clamping. The CNC-milling works were performed on the CNC-miller of the ISTB workshop.

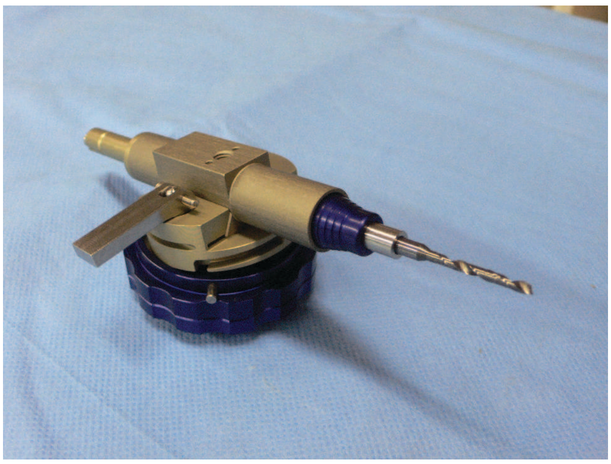


Light-Weight Robot Cardiovascular Engineering/ ARTORG

A light-weight robotic leg made of carbon fiber reinforced composite was developed in this study. The joints are equipped with sapphire spheres to minimize friction and allow for a low-wear operation. The rest of the parts are machined from light-metals or directly from carbon fiber reinforced profiles.

Cochlearobot Image Guided Therapy/ ARTORG

The connection between robot drive and spindle drive was over-worked and equipped with a new clamping system featuring inclined notches to increase the accuracy and the stiffness of the drill spindle. Position of the spindle-box is guaranteed by a dovetail guide that can be clamped.



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COMPLETED DISSERTATIONS

Johann Jakob Schwiedrzik

Experimental, theoretical and numerical investigaton of the nonlinear micromechanical properties of bone

Weiguo Xie

Development and Validation of Novel Image-free Navigation Techniques Based on Intraoperative Reference Plane (IRP)

AWARDS/PRIZES

Best Poster Award, 3rd Prize

Chengwen Chu, Cheng Chen, Lutz-P.Nolte, Guoyan Zheng
In the 28th International Congress on Computer Assisted Radiology and Surgery (CARS 2014)
Fukuoka, Japan

Best Paper Honorable Mention Award

Xiao Dong and Guoyan Zheng
In the 2nd MICCAI Workshop & Challenge on Computational Methods & Clinical Applications for Spinal Imaging
Boston, USA

MICCAI 2014 Student Travel Award Sponsored by MICCAI Committee

Li Liu
Computer Assisted Planning and Navigation of Periacetabular Osteotomy (PAO) with Range of Motion (ROM) Optimization
MIT, Boston, USA

MICCAI 2014 Brain Tumor Segmentation Challenge Sponsored by NIH

Raphael Meier
MICCAI conference 2014
MIT, Boston, USA

Best Master Thesis Nomination of the Swiss Society of Biomedical Engineering 2014

Raphael Meier
Decision Forest for Brain Tumor Segmentation
Zürich, Switzerland

AWARDS/PRIZES

Research Award of the Swiss Society of Biomedical Engineering 2014

Johann Jakob Schwiedrzik
Experimental, theoretical and numerical investigation of the nonlinear micromechanical properties of bone
Zürich, Switzerland

Shape Modelling Grand Challenge Award in Shape 2014

Guoyan Zheng and Cheng Chen
In 2014 Annual SICAS Conference on Statistical Shape Modeling
Delemont, Switzerland