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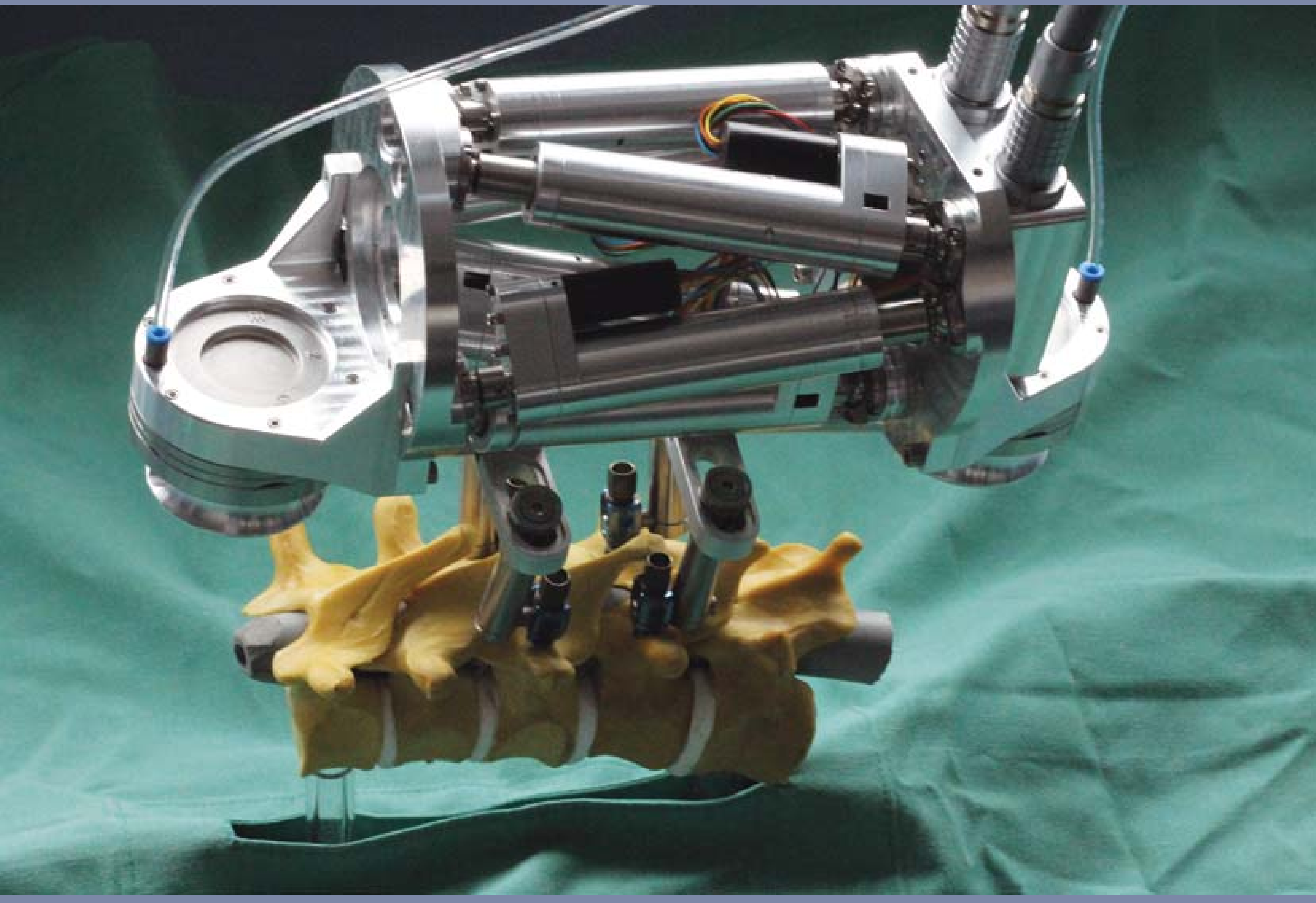
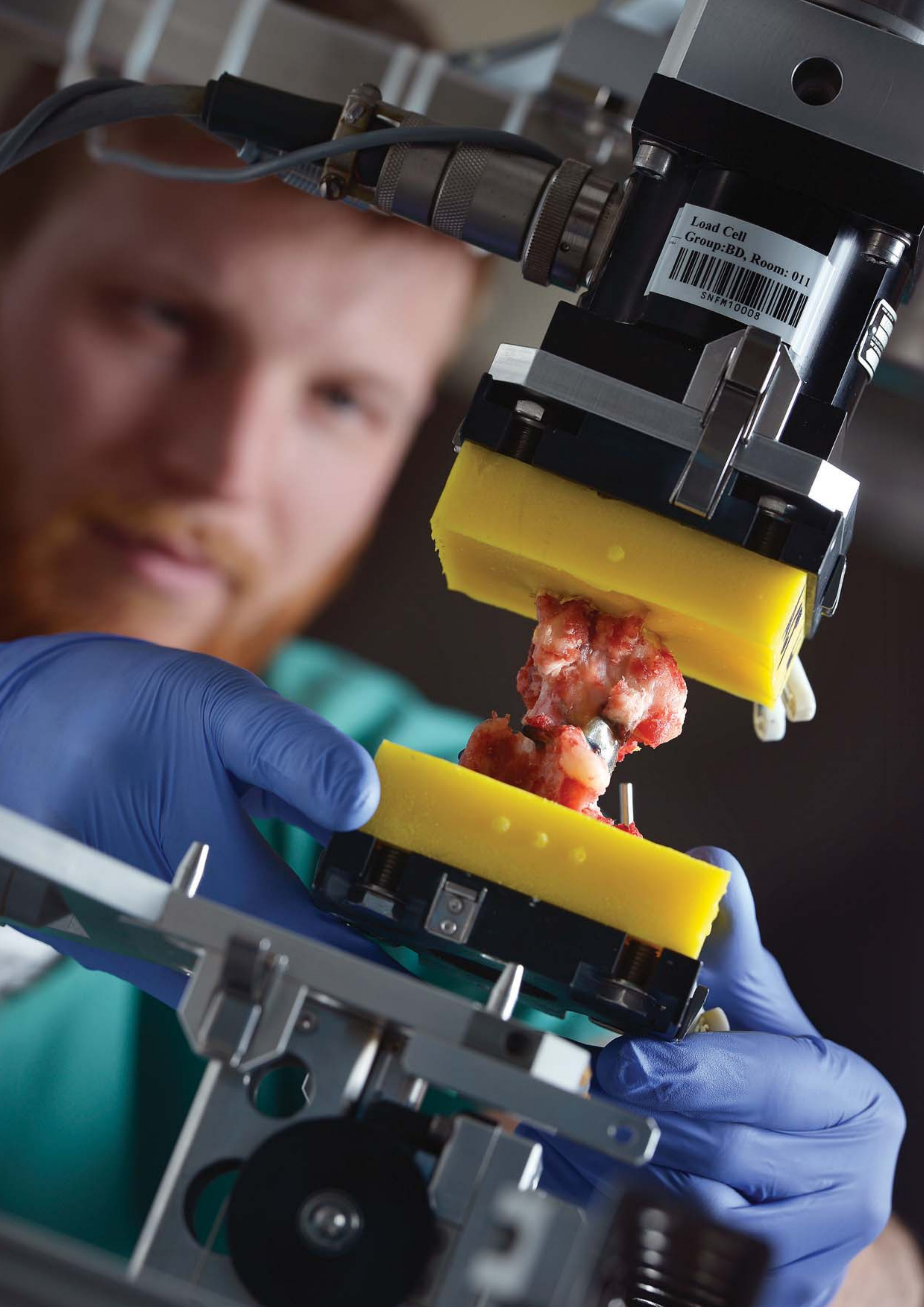
Institute for Surgical
Technology & Biomechanics

Annual Report 2013

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INSTITUTE FOR SURGICAL TECHNOLOGY AND BIOMECHANICS

The Institute for Surgical Technology and Biomechanics (ISTB) was established in 2003 as part of the former Maurice E. Müller Institute for Biomechanics. The institute stands in the tradition of Maurice E. Müller, the former chairman of the Department of Orthopedics at the University of Bern. As one of the pioneers of modern orthopedic surgery, Maurice Müller is known not only for his many innovations related to devices and instruments for joint replacement and fracture treatment, but also for his vision that only a close collaboration between surgeons, scientists, engineers, and industrialists will allow sustainable progress in the field.

To date the ISTB hosts five research groups in various fields of basic and applied research for the prevention, diagnosis and treatment of disease, working from the cell level to organ systems:

- Musculoskeletal Biomechanics
- Computational Bioengineering
- Tissue and Organ Mechanobiology
- Medical Image Analysis
- Information Processing in Medical Interventions

The mission of the multidisciplinary team of the ISTB is to advance human understanding, health, and quality of life. The focus is on developing solutions that address particular clinical problems or unmet clinical needs. It supports this effort through internationally recognized research, discovery, and invention in the area of biomedical engineering, translation of research results from the lab to the clinic to improve patient care, transfer of scientific discoveries and biomedical technology through national and international industrial collaborations and a world class post-graduate biomedical engineering education program.

Lutz P. Nolte
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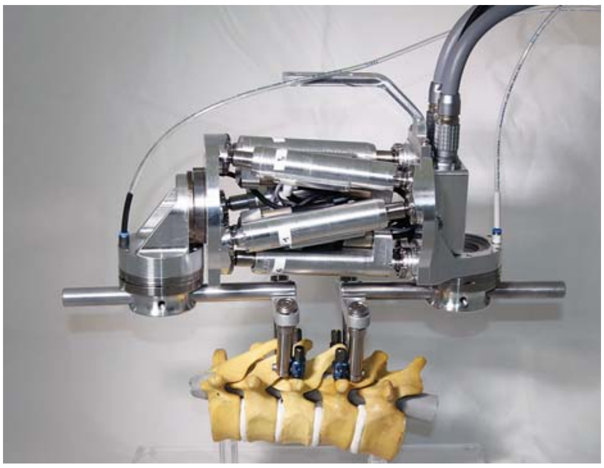
Research Profile

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 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 into the evaluation of bone biomechanics.

Biomechanics of the Scoliotic Spine

Non-fusion operative methods for the treatment of degenerative spinal diseases have tremendous potential to increase patient quality of life. In addition to the fact that motion is preserved or restored, a natural load transfer to the adjacent segments is sustained. This is important, as clinical experience shows that fusion of motion segments frequently entails adjacent level degeneration. However, non-fusion implants are challenging, particularly for the treatment of spinal deformities, in which several segments are commonly affected. A better understanding of the mechanical properties of healthy and pathological motion segments is essential.
A parallel kinematic robot – the SpineBot – has been developed to accurately measure the three-dimensional segmental stiffness of a patient's spine in-vivo. SpineBot transmits load to individual vertebra using pedicle screws implanted as part of the corrective procedure. The six DoFs of the robot allow an arbitrary motion to be applied to adjacent vertebrae and an integrated force-torque sensor measures the corresponding mechanical response. The small, compact, and lightweight parallel kinematic construction enables the device to apply moments of over 4 Nm to a FSU with a ±10° range of motion. The SpineBot will be used to quantify the stiffness at different levels of the spine of scoliosis patients as well as to compare stiffness of lumbar spinal stenosis patients before and after decompression surgery.
Numerical models of the scoliotic spine have also been developed for the design of motion preserving non-fusion treatment to correct spinal deformities. These models are unique because they consider patient-specific geometry and mechanical properties derived from intraoperative measurements. The finite element model has been used to design a new dynamic spinal anchoring system to complement a novel growing implant. In addition, these numerical simulation tools enable the optimization of the surgical procedure on a patient-specific basis



A robotic system was developed to measure the spinal mechanical properties intra-operatively.

Superficial Femoral Artery

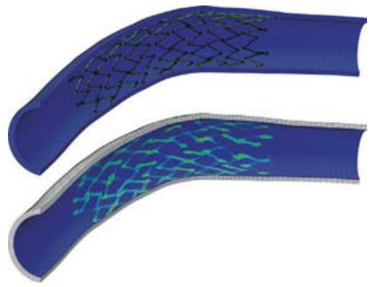
Endovascular therapy is currently considered the primary treatment modality for many patients with peripheral artery disease (PAD). Although the introduction of novel nitinol stents decreases restenosis rates compared to plain balloon angioplasty, restenosis still remains a significant problem in the peripheral arteries. In- stent restenosis, which occurs in up to 30% of the patients subsequent to bare nitinol stent placement, was reported to be associated with stent fractures and arterial wall damage. Stent failures are clearly related to the bending, torsion, and axial motion forces exerted on the femoropopliteal segment during hip and knee flexion.

To understand the causes of restenosis and to improve stent designs, an accurate characterization of this mechanical environment is necessary. Therefore, we quantified the in vivo deformations of the popliteal artery during leg flexion in subjects with clinically relevant peripheral artery disease. Rotational angiography has been used to acquire the three-dimensional arterial anatomy with the leg straight and with a flexion of 70°/20° in the knee/hip joints. Results showed that the popliteal artery of patients with symptomatic PAD is exposed to significant deformations during flexion of the knee joint. The severity of calcification directly affects arterial curvature, but not axial strain or twisting angles. These clinical observations are complemented with finite element simulations to evaluate stenting procedures.

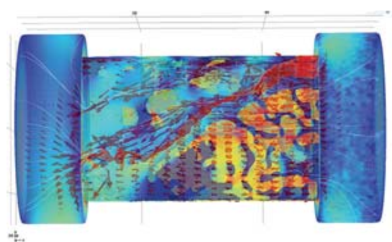
Bone Electric Conductivity

Minimally invasive cochlear implantation surgery has been proposed to replace conventional mastoidectomy for the placements of chochlear implant. To achieve this aim, a microsurgical robotic system is being developed by the group for image guided therapy of the ARTORG Centre. This system is designed to precisely drill a small tunnel through the temporal bone. However, due to the small distance between the tunnel and the facial nerve (FN) (0.3 – 0.5mm), an important challenge of this technique is the preservation of the facial nerve during the drilling procedure. Neuromonitoring is a technique widely used in surgery to locate and assess nerve function. An electrical stimulus is injected into the tissue surrounding the nerve, and electromyography is used to detect action potential elicited muscle responses. In the case of minimally invasive surgery, this technique can be used intra-operatively to monitor the distance between drill bit and the facial nerve. To detect critical distance to the FN, an electrical stimulation is sent through the drill. However, past experiments showed that it is difficult to give accurate distance predictions only based on the electric signal. For this reason, patient-specific parameters and modelling should be included to quantify the distance to the nerve. An experimental test bench has been produced to quantify the bone electric properties. The initial numerical simulations indicated that the porous network filled of marrow is mainly responsible for the flow of electric current in the tissue.

Patient-specific numerical models of the scoliotic spine have been used for the design of a motion preserving implant.



Finite element simulation of the deployment of a stent in the peripheral artery reconstructed from patients' images.



Flow of the electric current inside a bone sample.

Selected Publications

Studer HP, Riedwyl H, Amstutz CA, Hanson JVM, Büchler P (2013) Patient-specific finite-element simulation of the human cornea: A clinical validation study on cataract surgery. J Biomech 46(4):751–758

Elsheikh A, Whitford C, Hamarashid R, Kassem W, Joda A, Büchler P (2013) Stress free configuration of the human eye. Med Eng Phys 35(2):211–6

Bauer S, Lu H, May CP, Nolte L, Büchler P, Reyes M (2013) Integrated Segmentation of Brain Tumor Images For Radiotherapy and Neurosurgery. Int J Imaging Syst Technol 23(1):59–63

Gökgöl C, Diehm N, Kara L, Büchler P (2013) Quantification of Popliteal Artery Deformation During Leg Flexion in Subjects With Peripheral Artery Disease: A Pilot Study. J Endovasc Ther 20(6):828–835

Kistler M, Bonaretti S, Pfahrer M, Niklaus R, Büchler P (2013) The Virtual Skeleton Database: An Open Access Repository for Biomedical Research and Collaboration. J Med Internet Res 15(11):e245

Information Processing in Medical Interventions

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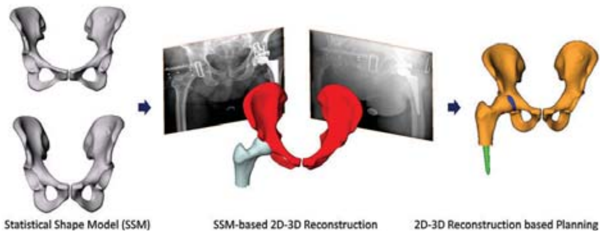
Research Profile

A large and growing family of medical interventions involve the processing of information in different stages of the intervention such as pre-operative planning, intra-operative treatment and post-operative control. Examples include the derivation of patient-specific anatomical models from pre-operative medical images, the calibration of intra-operative imaging devices and surgical instruments, the registration of medical images to patient physical space, and the measurement of treatment results from post-operative medical images. The Information Processing in Medical Interventions (IPMI) Group focuses on the development of smart information processing methods and enabling technologies to solve challenging problems in clinical routine medical interventions. In 2013 we continued our pursuit of novel information processing methodologies/systems for various applications. These include an X-ray radiography based true 3D planning and evaluation system called "iJoint" for total hip arthroplasty (THA), an X-ray radiography based true 3D planning and evaluation system called "iLeg" for lower extremity interventions, a fully automatic 2D and 3D segmentation method, and a comprehensive planning and navigation system for hip preservation surgeries.

iJoint: X-ray radiograph based true 3D planning and evaluation system for Total Hip Arthroplasty

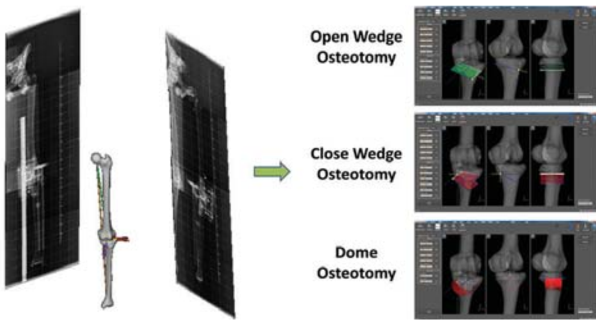
THA is considered a successful, safe and cost-effective medical intervention to restore functionality of the hip joint and to regain pain-free mobility in patients suffering from severe joint disease. Each year, about one million patients worldwide undergo THA surgery. Supported by the Commission for Technology and Innovation (CTI), we are aiming to develop an innovative framework for advancing modern total hip arthroplasty called "iJoint". Key techniques developed within this project include: a mobile and easy-to-use calibration phantom (European Patent Application No. EP2660776A1), a unique statistical shape model (SSM) based 2D-3D reconstruction method that can derive patient-specific 3D models of a hip joint from only 2D X-ray radiographs, a comprehensive planning module that supports both 2D and 3D THA planning, and a 2D-3D reconstruction based post-operative evaluation module.



2D/3D reconstruction based true 3D planning of THA surgery.

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

Supported by the Swiss National Science Foundation (SNSF), in this project we have developed a system called "iLeg" that allows the reconstruction of 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. Supported interventions include lower extremity osteotomy and total knee arthroplasty (TKA).



Patient-specific 3D model reconstruction and their application in planning different types of lower extremity osteotomies.

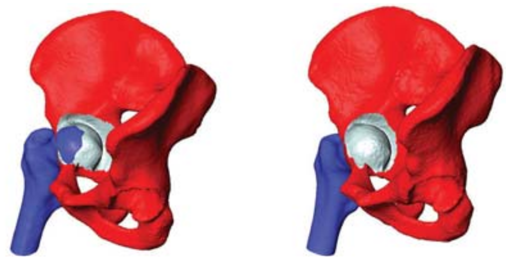
A landmark Detection Based, Fully Automatic 2D and 3D Segmentation Method

We have developed a novel method for fully-automatic landmark detection and shape segmentation in 2D X-ray and 3D CT images. To detect landmarks, we estimate the displacements from randomly sampled image patches to the (unknown) landmark positions, and then integrate these predictions via a voting scheme. Our key contribution is a new algorithm for estimating these displacements. Different from other methods in which each image patch independently predicts its displacement, we jointly estimate the displacements from all patches together in a data driven way, by considering not only the training data but also geometric constraints on the test image. Comprehensive experiments conducted on 2D X-ray images and 3D CT data demonstrated the efficacy of the developed method.

2D (top) and 3D (bottom) segmentation results obtained with our landmark detection based, fully automatic 2D and 3D segmentation method.

Articulated Statistical Shape Model-Based 2D-3D Reconstruction of a Hip Joint

Existing 2D-3D reconstruction techniques usually reconstruct a patient-specific model of a single anatomical structure without considering the relationship to its neighboring structures. Thus, when applied to the reconstruction of patient-specific hip joint models, the reconstructed models may penetrate each other and hence may not represent a true hip joint of the patient. To address this problem, we have developed a novel 2D-3D reconstruction framework using an articulated statistical shape model (aSSM). Our novel method has the advantage of preserving the hip joint structure and no model penetration can be found.



Comparison of the result obtained from an existing 2D-3D reconstruction method and that from our articulated statistical shape model-based 2D-3D reconstruction.

A Comprehensive Planning and Navigation Toolkit for Hip Preservation Surgeries

Hip preservation surgeries such as periacetabular osteotomy (PAO) and femoroacetabular impingement (FAI) treatment are efficient treatment options for younger patients with debilitating hip pain and dysfunction. However, these procedures are technically demanding and require detailed 3D information for diagnosis and intervention. To address this challenge, we have developed a comprehensive planning and navigation toolkit for hip preservation surgeries. Our comprehensive toolkit supports planning and navigation of both PAO and FAI treatment.

Selected Publications

Chen C, Xie W, Franke J, Grützner PA, Nolte LP, Zheng G (2013) Fully automatic X-ray image segmentation via joint estimation of image displacements. Med Image Comput Comput Assist Interv 2013, LNCS 8151:227 16(3):227-34

Chen C, Zheng G (2013) Fully Automatic Segmentation of AP Pelvis X-rays via Random Forest Regression and Hierarchical Sparse Shape Composition. Computer Analysis of Images and Patterns 2013 (Pt I), LNCS 8047:335–343

Murphy WS, Klingenstein G, Murphy SB, and Zheng G (2013) Pelvic tilt is minimally changed by total hip arthroplasty. Clin Orthop Relat Res 471(2):417–421

Schumann S, Nolte LP, Zheng G (2013) Comparison of partial least squares regression and principal component regression for pelvic shape prediction. J Biomech 46(1):197–199

Schumann S, Liu L, Tannast M, Bergmann M, Nolte LP, Zheng G, (2013) An integrated system for 3D hip joint reconstruction from 2D X-rays: a preliminary validation study. Ann Biomed Eng 41(10):2077-2087

Zheng G (2013) 3D volumetric intensity reconstruction from 2D x-ray images using partial least squares regression. Biomedical Imaging (ISBI), 2013 IEEE 10th International Symposium 1268-1271

Zheng G (2013) Expectation Conditional Maximization-Based Deformable Shape Registration. Computer Analysis of Images and Patterns, LNCS 8047:548–555

Edited Books

Liao H., Linte C.A., Masamune K., Peters T.A., Zheng G. (eds): Augmented reality environment for medical imaging and computer-assisted intervention - 6th International Workshop, MIAR 2013 and 8th International Workshop, AE-CAI 2013, held in conjunction with MICCAI 2013, Nagoya, Japan, Sep. 22, 2014. Proceedings, LNCS 8090, Springer 2013, ISBN 978-3-642-40842-7

Patents

Zheng G and Zhang X. Method and devices for computer assisted distal locking of intramedullary nails (a single image-based method). Patent No. US8444645

Zheng G and Schumann S. Image distortion correction and robust phantom detection. European Patent Application No. EP2660776A1

Medical Image Analysis

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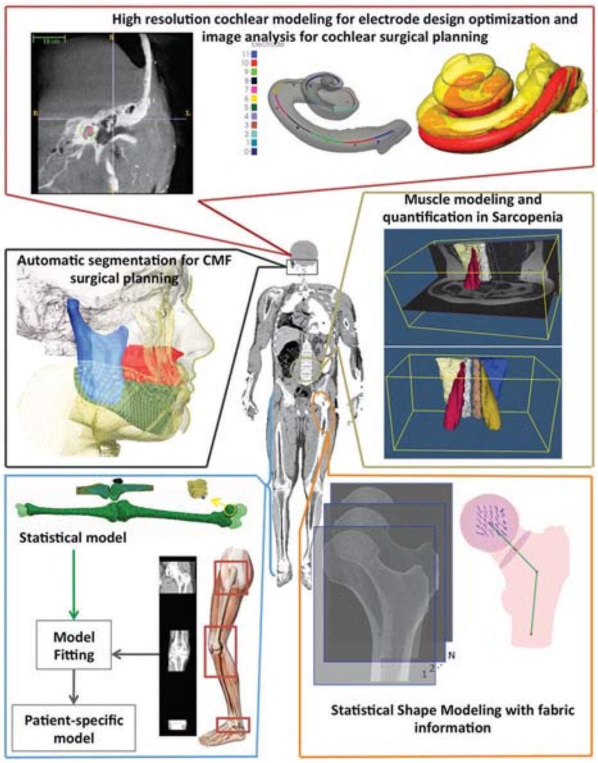
Research Profile

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 tumors?
- How to design planning and post-operative simulation algorithms and systems to assist plastic and cranio-maxillofacial surgeons?
- How to effectively encompass anatomical and physiological variability for the understanding of musculo-skeletal diseases, the design of orthopedic devices, and less invasive, yet more effective orthopedic surgical approaches?

Computational Anatomy for Orthopedic Research

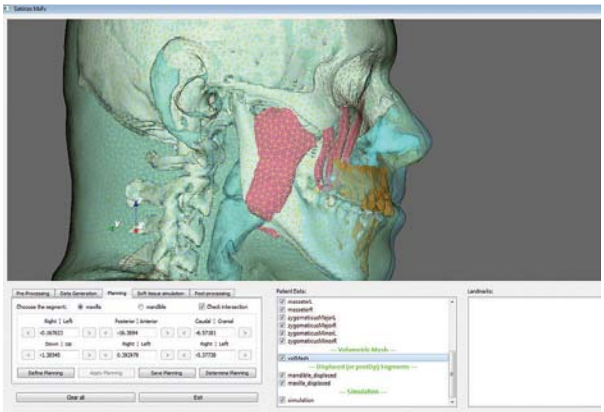
Computational anatomy enables analysis of biological variability throughout a population. Using statistical mathematical techniques, models can be built to represent the typical shape of an anatomical structure and its predominant patterns of variability across a given population. During 2013 we have used these techniques to propose population-based implant design for mandibular plates, where bone shape and bone mineral density are considered within an optimization process, as well for bone allograft selection from bone databanks. Similarly, through national and international projects we aim to use computational anatomy concepts to improve the design of cochlear electrodes, used to reestablish hearing on patients 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.



Modeling anatomical variability and its application to clinical applications such as cranio-maxillofacial surgery, cochlear surgery, bone fracture prediction and sarcopenia.

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 2013 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). The software is currently being evaluated in a multicenter study. On the basic research side, we have presented, along with our partners, an innovative approach termed inverse planning for CMF that allows the user to directly define the desired surgical facial outcome and obtain the corresponding surgical plan. In this way, trial and error planning can be avoided and the planning process made more effective. In addition, our developments jointly incorporate functional and anatomical considerations, such as dental occlusion and desired aesthetic outcome.



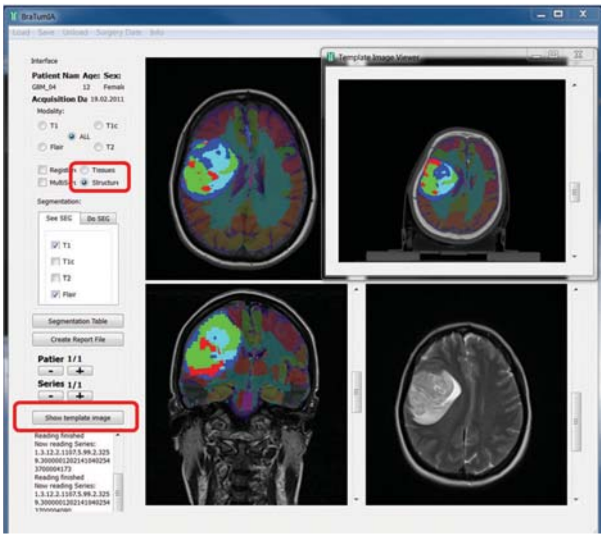
Sotirios MxFx Software: "Soft Tissue Reconstruction for IntraOperative Simulation - Maxilofacial". Sotirios enables a fast and accurate simulation of postoperative skin deformation for CMF surgery.

Brain Image Analysis

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

During 2013 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. The algorithms are based on supervised and unsupervised classification techniques tailored to the clinical scenario. Through this research, our group was awarded the 2nd prize in the international competition for brain tumor segmentation, held at Miccai 2013, Nagoya, France.

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). BraTumIA is currently being clinically evaluated and extended to consider other types of brain lesions.



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.

Selected Publications

Shahim K, Cattin P, Jürgens P, Nolte LP, Reyes M (2013) Prediction of Cranio-Maxilofacial Surgical Planning using an Inverse Soft Tissue Modelling Approach. Med Image Comput Comput Assist Interv 16(1):18-25

Bou-Sleiman H, Paul L, Nolte LP, Reyes M (2013) Comparative Evaluation of Pelvic Allograft Selection Methods. Ann Biomed Eng 41(5):931-938

Lu H, Beisteiner R, Nolte LP, Reyes M (2013) Hierarchical segmentation-assisted multimodal registration for MR brain images. Comput Med Imaging Graph 37(3):234-244

Bou-Sleiman H, Iizuka T, Nolte LP, Reyes M (2013) Population-Based Design of Mandibular Fixation Plates with Bone Quality and Morphology Considerations. Ann Biomed Eng 41(2):377-384

Bauer S, Wiest R, Nolte LP, Reyes M (2013) A survey of MRI-based medical image analysis for brain tumor studies. Phys Med Biol 58(13):97-129

Kim BR, Oh KM, Cevidanes LHS, Park JE, Sim HS, Seo SK, Reyes M, Kim YJ, Park YH (2013) Analysis of 3D Soft Tissue Changes After 1-and 2-Jaw Orthognathic Surgery in Mandibular Prognathism Patients. J Oral Maxillofac Surg 71(1):151-161

Musculoskeletal Biomechanics

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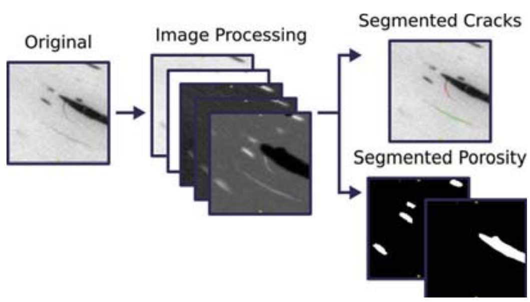
Research Profile

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 also provides 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 Damage

The risk of undergoing a bone fracture due to trauma may be increased by previous damage, i.e. micro-cracks initiated and accumulated under repeated physiological loading conditions. Accordingly, this research aims at exploring the loading mode dependent damage accumulation in bone tissue and its role in femoral fracture risk. The launched experimental program funded by the AO foundation was extended for image acquisition and image processing of cement lines, i.e. the interfaces where microcracks are most likely occurring. One sub-project focused on the development of cement line staining protocols and segmentation techniques, while another sub-project was devoted to the development of ITK-based segmentation algorithms. The latter were used to identify microcrack distributions from SRμCT datasets obtained at the European Synchrotron Radiation Facility. Besides the experimental efforts aiming at relating the occurrence of microcracks in cortical bone to the induced loads, the development of a constitutive model including plasticity and damage that accounts for these microcrack developments was initiated.



Automated segmentation algorithm to detect microcracks in a bone sample scanned with high resolution synchrotron radiation micro-computer tomography.

Indentation of Bone Extracellular Matrix

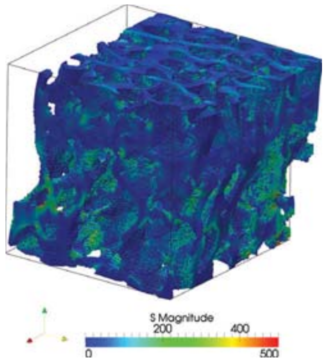
Quality of the bone extracellular matrix is a hidden variable in the diagnosis of metabolic diseases. Indentation at the micro- and nano- scale represents a powerful method to assess mechanical properties with a high spatial resolution. A protocol was developed that allows the sample to be kept in a physiological, hydrated state throughout the whole preparation process. Viscoelastic constitutive models for bone tissue were fitted to the experimental force-displacement data in order to identify the influence of hydration on the time-dependent response of the bone matrix. In a second step, the influence of the constitutive behavior of bone was assessed by means of a numerical study. An elastoplastic constitutive model was also developed and the influence of yield surface shape and maximum damage on indentation properties was explored. The ultimate goal of this research is to assess the role of tissue quality in bone fracture risk relative to aging and disease.

Finite Element Analysis of the Proximal Femur

Finite element analysis is becoming a new standard to predict bone stiffness and strength when QCT scans are available. Funded by the Swiss National Science Foundation, this research aims at establishing a novel standard QCT-based patient-specific finite element analysis of the proximal femur by including a distinct cortical bone phase and trabecular orientation into the current volumetric bone mineral density. In a first stage, linear homogenization analysis of femoral trabecular bone with mixed boundary conditions was realized in cooperation with Dieter Pahr at the Vienna University of Technology.

Clinical Applications of FEA – EuroGIOPS

Glucocorticoid-induced osteoporosis (GIO) causes rapid bone loss and impaired bone architecture leading to a reduction in bone strength, an essential determinant of vertebral fracture risk. The standard technique for diagnosis of GIO, dual energy X-ray absorptiometry, is not a satisfactory surrogate for bone strength as it accounts neither for geometry nor for spatial distribution of the bone tissue. Quantitative computed tomography (QCT) based



Shear loading on a femoral trabecular bone cube using mixed boundary conditions.

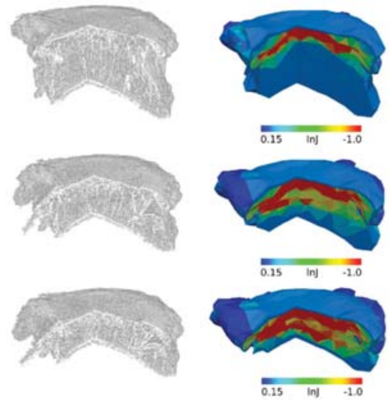
finite element analysis (FEA) can estimate patient-specific structural properties (stiffness, strength) of the vertebral body for various loading cases (e.g. compression, bending and torsion). The elastoplastic damage model developed to simulate the mechanical behavior of bone accounts for the stiffness reduction due to cracks accumulated during the post-yield loading history. Such models were used in the clinical trial EuroGIOPS to follow-up the status of patients with GIO, treated during 18 months with risedronate (antiresorptive) or teriparatide (anabolic drug).

Spine Research

In the frame of the Marie Curie Initial Training Network SpineFX supported by the EU, the aim of the spine research was to validate our recently developed constitutive model of trabecular bone for the prediction of strain localization and densification in human vertebral body subjected to large compressive deformation. Osteoporotic vertebral fractures can often only be diagnosed after a substantial deformation history of the vertebral body. Therefore, it remains a challenge for clinicians to distinguish between stable and progressive potentially harmful fractures. In order to analyze the collapse of the vertebral body under compression, a novel experimental setup based on stepwise loading of human vertebral bodies inside a high resolution peripheral quantitative computed tomography machine was designed and manufactured at the ISTB. On the one hand, the experiments helped us better understand the deformation and collapse of the vertebral body during compression. On the other hand, they served to validate our continuum finite element (FE) model of bone to simulate high compaction of trabecular bone with up to 65% strain. A fair qualitative correspondence of the strain localization zone between the experiment and finite element analysis was obtained. These encouraging preliminary results towards the prediction of extended vertebral collapse may help in assessing fracture stability in future clinical work.

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 clinical applications, the comparison of a novel technique versus established methods of olecranon osteotomies, devised by the department of Orthopaedics and Traumatology at the University Hospital Bern, was performed. In a further study, an investigations were performed on the primary stability of cervical canine spine implants designed by the VetSuisse faculty.



Collapse of a vertebral body: experiment and simulation.

Selected Publications

Kersh M, Zysset P, Pahr DH, Wolfram U, Larsson D, Pandy MG (2013) Measurement of structural anisotropy in bone using clinical-resolution CT images. J Biomech 46(15):2659-2666

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Tissue and Organ Mechanobiology

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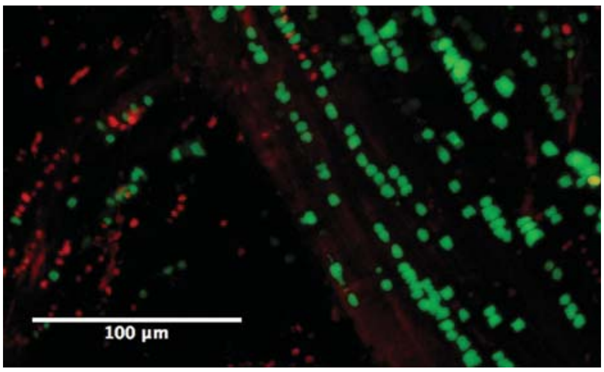
Research Profile

The Tissue and 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 to 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: investigation of the causes of lower back pain due to intervertebral disc (IVD) degeneration and identification of cell-based solutions for 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 closely match conditions within the human body and where regenerative therapy strategies, such as novel biomaterials and cells, can be tested in a realistic in vitro set-up.

Electro-spun silk fiber scaffold, spun at 30Hz on a rotating Mandrill. The alignment should be highly cyto-compatible for annulus fibrosus cells to grow.

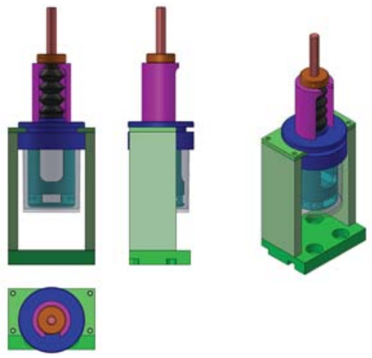
Intervertebral Disc Degeneration and Lower Back Pain

2013 has been a year of exploration of the new two degree of freedom bioreactor to test the importance of complex loading. The TOM group advanced further into the understanding the effects of complex forces such as compression and torsion on intervertebral disc (IVD) cells in situ in organ culture. Furthermore, the group explored non-viral gene therapy as an option for IVD regeneration using growth and differentiation factor 5 (GDF5) as a primary target for differentiating human mesenchymal stem cells towards IVD-like precursor cells. 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-clinically relevant enzymes such as papain or clinically relevant enzymes such as metallo-proteinases and high-temperature requirement A serine peptidase 1 (HTRA1). Furthermore, the group received an exchange fellow, Wai Hon Chooi from Barbara Chan's group at the University of Hong Kong to develop a novel collagen annulus fibrosus (AF) "plug" to repair the IVD. This exchange became possible through the achievement of a competitive AOSpine International Scientific Research Network grant. The project investigated the mechano-biological properties of the AF plug to seal the IVD. The AF is the outer fibrous part of an IVD which has very poor self-healing capacities if ruptured causing leakage of the inner more gel-like material, the nucleus pulposus (NP). This pathology is known as disc herniation. Thus, a "plug" consisting of photochemically crosslinked collagen to seal such a rupture has to fulfill a



Projection of ~200µm stack of confocal laser scanning microscope image. Live dead stain (green cells are alive and red cells are dead) of human Anterior Cruciate Ligament (ACL) cultured in standard culture medium supplemented with 10% fetal calf serum after 7 days.

demanding task list as well as withstanding the complex loading of the human spine. To test these properties and to monitor leakage of the plug the group applied fluorescent electromagnetic beads mimicking disc or stem cells and used magnet resonance imaging to monitor possible leakage prior to and after mechanical loading. Leakage and retention of beads was determined by measuring the total fluorescence and the number of beads in the culture medium and inside the IVD, respectively. The maximal force that the annulus plug could resist in the organ culture model was also investigated.
Silk is a very old and interesting biomaterial with high elastic properties and low allergenic potential if the amino acid sericin has been removed. Here, 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 and mesenchymal stem cells but also in our 3D organ culture model and the complex loading bioreactor.

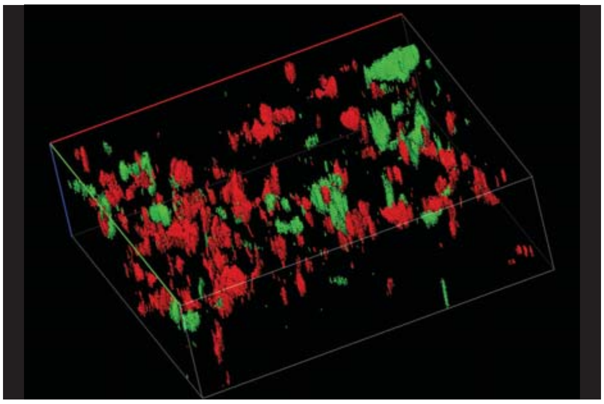


CAD Image of a new bioreactor device to culture ACL in 3D and to connect the ACL in the mechanical testing machine set-up for strain-controlled dynamic loading.

Application of Collagen Matrixes and Mesenchymal Stem Cells to accelerate Healing of the ruptured Anterior Cruciate Ligament

Anterior cruciate ligament (ACL) injuries are very common; in Switzerland the incidence of ACL rupture is estimated at 32 per 100,000 in the general population while this rate more than doubles in the sports community. The current gold standard for anterior cruciate ligament repair is reconstruction using an autograft. However, this approach has been shown to have a number of limitations. A new method has been heralded by the Knee Team at the Bern University Hospital 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 interest. The aim of this research is to investigate the use of collagen patches in combination with DIS to support regeneration of the ACL.

Scanning electron microscope image of two mesenchymal stem cells (MSC) grown on Novocart® collagen patches (B.Braun) for 7 days to test their cyto-compatibility for the application of repair of the anterior cruciate ligament of the knee joint.



3D reconstruction of a ~200µm stack based on a series of images taken with confocal laser scanning microscopy through a 1:1 cell mix of human mesenchymal stem cells (MSC, green labelled) and human tenocytes of the anterior cruciate ligament (ACL) taken at a 10x magnification. The cells were seeded on Novocart collagen matrix (B.Braun) for 24h.

Selected Publications

Bucher C, Gazdhar A, Benneker LM, Geiser T, Gantenbein-Ritter B (2013) Nonviral Gene Delivery of Growth and Differentiation Factor 5 to Human Mesenchymal Stem Cells Injected into a 3D Bovine Intervertebral Disc Organ Culture System. Stem Cells Int 2013:326828. doi:10.1155/2013/326828

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Mechanical Design and 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. 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 and Education

The MDP group has a secondary role in training. This training encompasses the skills required to safely and proficiently operate machine shop tooling and equipment, the knowledge required to achieve the best results with a variety of materials and the skills needed to efficiently manage the design and production workflow. Trial apprenticeships are used as a means to evaluate candidates for a full apprenticeship in the MDP group. This year, we performed one course and we selected Julien Meister as our next apprentice; he will begin his training in August of 2014 as a polymechanic apprentice.

Research Equipment Design and 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.

Extensometer Clamp and Indent Testing Device

The musculoskeletal biomechanics group required several different devices for a number of force and bone indent tests. The design and manufacture of these devices was supported by the MDP group. After manufacturing, the indent device was tested on the Synchrotron Radiation Micro-Computer Tomography machine in Grenoble. During experiments on the materials testing machine it can be difficult to accurately fix the measurement lever of the extensometer onto the thin bone samples. Subsequently, we have constructed a guide unit in collaboration with the musculoskeletal biomechanics group.

Custom extensometer clamp, constructed to ensure accurate fixation to thin bone samples.

Improved Acrylic Calibration Phantom

In previous years we have developed a large, universally applicable, calibration phantom for the IPMI group. Based on the measurement results with the large phantom we could now produce a phantom made of acrylic glass of a size which can be used directly on the patient.

Acrylic calibration phantom.

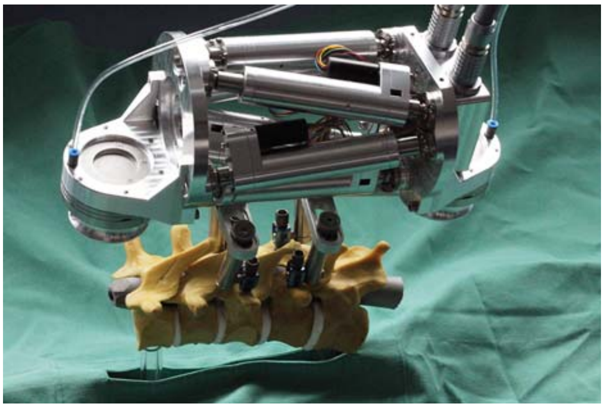
Periacetabular Osteotomy Chisel Calibration

In 2010 the MDP group developed a PAO chisel, capable of being navigated, for the Orthopedic Department at the Bern University Hospital. In a continuation of this project, we have designed an attachment for a new multi-calibration tool and constructed a prototype.

Navigated PAO chisel with calibration device.

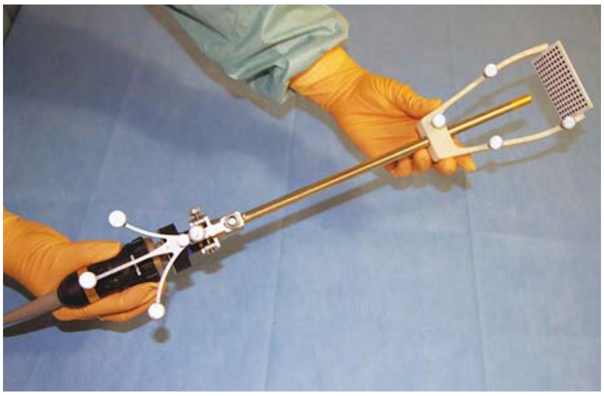
Research Equipment Design and Manufacturing (ARTORG)
The workshop at the ARTORG Center is managed by Ronald Ramseier, a former polymechanic in the ISTB MDP-group. This year the machine shop at the ARTORG Center supported a number of different projects for the IGT and Computational Bioengineering Groups, including design and manufacturing.
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 was further consolidated this year, and is still growing. Some highlights of this year's projects are shown below.

Spine Hexapod
The spine hexapod project of the Computational Bioengineering Group at the ISTB and the ARTORG Center was outfitted with new motors; this process required a number of adjustments and changes to the housing. In this embodiment, the gearbox is flange-mounted directly to the motor, leading to less power loss and vibration during operation than was observed in the initial version. Additionally, a new coupling and quick-release system was developed.



Hexapod robot for measurement of forces on the spine. A new prototype was developed with less power loss and vibration.

Endoscope Calibration Tool
With the integration of endoscopic imaging into the existing surgical navigation system of the ARTORG Center and CAScination AG, a simple and robust method of endoscope calibration was required. In order to achieve this aim, a calibration device, in the form of a stapes, was designed and manufactured.



An endoscope calibration device was developed for minimally invasive surgery.

Titanium High Accuracy Tracking Markers
The new patient and tool reference trackers for the high-precision robotic system of the IGT group were, for the first time, manufactured from medical grade titanium. This has a number of advantages; the new markers are light as aluminum but much more dimensionally stable. Surface treatment of the markers enhances the robustness and longevity of the tool while reducing the effects of reflections on measurement error. Increased viewing angle is enabled through the use of a countersunk illumination mask.

High accuracy tracking markers, constructed from titanium, allow measurement and control of a robotic system for minimally invasive cochlear implantation.

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