CONTENTS

1 BACKGROUND AND PERSPECTIVES

Background

The Maurice E. Müller Institute for Biomechanics (MIB) was established as a joint venture between the Maurice E. Müller Foundation and the Medical Faculty of the University of Bern when Prof. M.E. Müller retired, in 1981, as Chairman of the Department of Orthopaedic Surgery at the Inselspital. The Maurice E. Müller Institute for Biomechanics attained the legal status of a full University Institute on January 1, 1995, this decision having been reached by the Bernese Government on May 30, 1994 and approved by the State (Grosser Rat) on June 9, 1994. The objectives of the Institute are basic and applied biomechanical research of the locomotor system at the organism, tissue, cellular and molecular length scales. The Institute is supported by a basic operation grant from the Maurice E. Müller Foundation, by funds from the University of Bern, by a grant from the AO/ASIF Foundation, and by project grants from the Swiss National Science Foundation, as well as from various other foundations and industrial sources. The Maurice E. Müller Institute for Biomechanics is currently under the Directorship of Prof. Ernst B. Hunziker, who was elected to this position by the Bernese Government in autumn of 1989.

Objectives

The Institute's efforts are directed towards the development of an integrated understanding of the structure and function of the musculo-skeletal system at the organism, tissue, cellular and molecular length scales, and the development and optimization of information, materials, and techniques for clinical application in the detection and treatment of musculo-skeletal diseases. It is thus conceived as a link between academic research, surgical practice and industrial development. Collaborations with various Research Institutes of the University of Bern, a number of other University Institutes, the Department for Orthopaedic Surgery at the Inselspital and other clinical partners, industrial enterprises as well as with the AO/ASIF Foundation's Research Institute in Davos, are therefore embraced in its functions.

Previous and Current General Research Program

Since the time of its foundation in 1981 until 1988, the MIB was directed by Prof. Stephan S. Perren. The goals of the Institute during this period were to study the normal and disturbed loading patterns of the locomotor apparatus, to improve our understanding of this system, and to promote the knowledge thereby gained in relation to the principles, techniques, instrumentation, and implants applied in orthopaedic surgery. In 1989, Prof. Ernst B. Hunziker took over the Directorship, and he has then extended the Institute's research activities to include basic and applied biological aspects of skeletal tissue structure and function at the tissue, cellular and molecular levels, such as biochemistry, molecular biology, microstructural preservation, histological-morphometric analysis, compatibility of implant materials, interfacial (adhesion) biology, mechanical properties, and metabolic responses to mechanical stimuli. Research activities in the field of classical biomechanics are currently being continued by PD Dr. Lutz-P. Nolte, who broadened its scope to include computer-assisted

surgery. In 1993 Dr. Nolte was appointed Head of the Institute's Division of Orthopaedic Biomechanics. Prof. Hunziker is, in addition to being Director of the Müller-Institute for Biomechanics, also the Head of the Institute's Division of Biology, of which PD Dr. Beat Trueb is Associate Head.

With these new dimensions, the Institute aims at an integrated approach to questions raised in connection with the biomechanics of the musculo-skeletal system, prostheses, endoprostheses, fracture treatment and novel biological treatment strategies.

Organization

The Institute is comprised of a staff of about 55 people, including medical scientists, biologists, engineers, computer specialists, technicians and research fellows. It consists of two divisions, with a central unit for administration and maintenance. The research activities of one division relate to orthopaedic biomechanics and surgical techniques, while those of the other involve basic and applied research in the biology of the musculo-skeletal apparatus. The two divisions collaborate with one another and are supported by a basic technical staff furnishing histological-, computer-, mechanical- and electronic services. The Institute of Biomechanics can be reached through the World Wide Web (WWW) at http://www-mem.unibe.ch.

Significance of Research Program

The research activities conducted at the MIB contribute to our basic understanding of the structure and function of the musculo-skeletal system, and the control mechanisms operating at both the organ, tissue, cellular and molecular levels. The knowledge thereby gained will help us to further develop and optimize materials for clinical application, conceive novel biologically based treatment strategies and assist in a rational, scientific approach to the treatment of diseases of the musculo-skeletal system.

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2 RESEARCH ACTIVITIES

2.1. Division of Biology

2.1.1 Tissue Biomechanics and Structural Biology

The main activities in this research area are directed towards elucidating the structural characteristics of skeletal tissues, particularly of cartilage and bone, and their functional correlates, using both *in vitro* and *in vivo* systems. Current topics include analysis of the mechanical properties and structural composition/organisation of growth- and articular cartilages, as well as investigations relating to the basic physiological mechanisms underlying the differentiation and activity regulation in these tissues.

With respect to bone tissue, studies pertain to mechanisms of osseoinduction and tissue integration processes (particularly as regards to implant materials). These projects are being undertaken with a view to developing new strategies for the treatment of traumatized or diseased cartilage and bone tissue.

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Regulation of the Collagen XII Gene by Mechanical Strain
M. Chiquet, J. Trächslin, U. Mumenthaler, M. Matthisson and M. Koch

Collagen XII is a large multidomain protein associated with collagen I/III/V fibrils in tendons, ligaments, periosteum, and dermis (cf. Koch et al., J. Cell Biol. 130: 1005-1014, 1995). We are interested to know whether mechanical strain acting on these tissues can regulate the expession of the collagen XII gene. When chick embryo fibroblasts were cultured on strained collagen gels (ie. gels fixed to the culture dish), they were found to secrete at least five times more collagen XII than cells grown on relaxed (ie. freely floating) gels. By Northern blotting, similar differences were observed for the respective levels of collagen XII mRNA. To study regulation of expression at the transcriptional level, we isolated the promoter region of the chick collagen XII gene. So far, we have analyzed 2.6kB of 5'-flanking sequence, the first exon (containing 237bp of 5'-untranslated sequence), the first intron (2.3kB), and the second exon (108bp; coding for the signal peptide). The upstream promoter region is GC-rich and does not contain a classical TATA-box. We started to investigate the activity of various promoter-reporter constructs in transiently transfected fibroblasts. Previously, we have shown that tenascin-C has a similar pattern of expression as collagen XII, and that the tenascin-C gene promoter contains a putative "strain-responsive" element (Chiquet-Ehrismann et al., JCB 127:2093, 1994). We will test whether a similar cis-acting sequence is found in the collagen XII promoter.

Determination of the Interstitial Deformation of Articular Cartilage in Unconfined Compression and Indentation Geometry

P. Kolmonen, E.B. Hunziker, M.D. Buschmann and J.S. Jurvelin

During chemical fixation highly charged ruthenium hexaammine trichloride (RHT) precipitates proteoglycans within the cartilage matrix. The processing of RHT-fixed cartilage for autoradiography creates, in the absence of radio-activity, a chemographic signal (grains), which is proportional to local glycosaminoglycan (GAG) density of the tissue, as verified by dimethylmethylene blue dye-binding assay. Under compression, cartilage GAG density, and thereby RHT-grain density, increases. By mapping the local changes of grain densities in loaded articular cartilage we calculate interstitial tissue deformation under unconfined compression and indentation loading. Cylindrical cartilage disks (dia 3.5mm, thickness ~1 mm) were obtained from bovine humeral head. Matched samples were compressed statically by 0% (n=16) or 30% (n=16) in unconfined compression or under indentation (plane-ended indenter, dia 1mm) geometry. The samples were chemically fixed in the state of compression using 2%-glutaraldehyde (buffered) solution containing 0.7% RHT. Dehydration was performed in a graded series of ethanol, and embedding in Epon. Blocks were cut systematically through the disk centers, and sections of 1mm thickness were produced. Sections were covered with a thin layer of Kodak NTB-2 emulsion for exposure to the ruthenium salts and production of the chemographic signal. Following exposure of one week, the emulsions were developed.

The grains in sections were counted using a light microscope, a frame grabber and a computer. For samples under unconfined compression a column of adjacent images was captured at the center of section and the measurement area from articular surface to bone was divided vertically into 15 equal compartments. The relative grain number in each compartment was calculated. Based on the difference in the number of grains in compressed and uncompressed samples the axial strains in compartments were calculated. The effect of disk expansion under compression was corrected using the measured width of the section. In indentation, the analysis was analogous, but the grains were counted in half of the section from surface to bone and from center to edge. Subsequently, the measured area was divided into 20x20 matrix and the axial and radial displacements of each cell (node) were calculated.

Under 30% unconfined compression, the highest axial strain (45.9-61.9%) was found in the most superficial tissue layer. The strain decreased monotonically in the deeper layers, although showed high values in the tissue close to bone. A mesh, based on the calculated displacements demonstrated a complex state of strain under indentation load. High axial and radial strains were located close to the edges of the indenter.

In unconfined compression or indentation geometry the analyses demonstrate spatial differences in the local strains within the matrix. The low proteoglycan content of the superficial tissue renders it soft generating high strains in the superficial layer. Variations found in the interstitial strain pattern suggest that different structural characteristics may be responsible for load carrying under unconfined compression and indentation geometry. Our experimental technique may be used to verify results obtained from the theoretical simulations of cartilage mechanical behavior.

Extracellular Matrix Assembly and Deformation Around Individual Chondrocytes in Mechanically Compressed Cartilage Explants
T.M. Quinn, A.J. Grodzinsky, M.D. Buschmann, Y. Kim and E.B. Hunziker

The roles of mechanical forces and fluid flows as mediators of phenotypic expression and matrix metabolism in connective tissues are of significant interest for basic understanding of cell processes and in the engineering of functional tissue analogs. While many experiments have established relationships between mechanical stimuli and cell response over tissue-length scales (1 mm resolution), a complete understanding of these stimuli and their influences on individual cells requires the ability to make mechanical and biochemical measurements at cell-length scales (1 μm resolution). We have developed novel methods of quantitative autoradiography in order to examine relationships between mechanical loading, cell morphology, and extracellular matrix (ECM) deformation, synthesis, and turnover around individual chondrocytes in articular cartilage. These methods have been applied for the measurement, around individual cells, of (1) proteoglycan and collagen matrix turnover in the presence of cell-stimulatory substances such as interleukin-1-beta (IL-1β) and retinoic acid (RA), and in the presence of aggressive (injurious) mechanical compression, (2) proteoglycan synthesis and matrix assembly in the presence of static (inhibitory) and dynamic (stimulatory) mechanical compression, and (3) extracellular matrix deformation in cartilage under static compression. Data were acquired as a function of position within cylindrical cartilage explant disks for the correlation of cell-length scale mechanical/biochemical responses with well-characterized tissue-length scale mechanical stimuli. Results from turnover studies highlighted the presence of distinct pools of extracellular matrix (ECM) macromolecules which were incorporated and lost from the tissue at different rates as a function of distance from the cell membrane. Cell-stimulatory factors (eg. IL-1β, RA) and mechanical injury appeared to have significantly different effects on the turnover of different ECM macromolecules. Matrix synthesis and assembly were dramatically influenced by mechanical compression. These results suggest important roles for matrix mechanical deformations and fluid flows as mediators of ECM assembly processes and cell metabolism, and provide novel insights into the mechanical and biochemical microenvironments of single cells within their individual pericellular and intercellular matrices. These data may help to elucidate the role of mechanical forces and flows as mediators of chondrocyte activity in developing tissue analogs and in cartilage repair.

Ultrastructural Investigations on Extracellular Matrix: Evidence for a Distinct Water Rich Layer Surrounding Collagen Fibrils in Articular Cartilage Extracellular Matrix
D. Studer, M. Chiquet and E.B. Hunziker

Bovine articular cartilage was vitrified by high pressure freezing. On the one hand vitrified samples were cryosectioned and investigated by cryo-electron microscopy in an unstained frozen hydrated state. On the other hand, they were freeze-substituted in pure acetone, ethanol or methanol, respectively, and subsequently embedded in Epon. Ultrathin Epon-sections were poststained with uranyl acetate and lead citrate. The resulting ultrastructural representation was different for every protocol. The evaluation of the combined results provides evidence for a distinct water rich layer surrounding collagen fibrils in articular

cartilage extracellular matrix, which has not been recognised before. The possible composition and function of this layer is discussed.

Chondrocyte Biosynthesis Correlates with Local Tissue Strain in Statically Compressed Adult Articular Cartilage
M. Wong, P. Wuethrich, M.D. Buschmann, P. Eggli and E.B. Hunziker

The depth-dependent metabolic and structural response of adult articular cartilage to large strain, static, unconfined compression was investigated. Changes in cell biosynthetic activity and several morphometry-based structural parameters (cell density, cell volume fraction, cell surface area density, mean cell surface area, and mean cell volume) were measured at eight sites representing different depth-zones between the articular surface and the cartilage/bone border. In addition, local axial strain in the superficial, transitional, upper radial and lower radial zones was estimated based on the change in cell density values. Static compression of articular cartilage resulted in a highly heterogeneous deformation profile through the depth of the disk as well as zone-specific changes in biosynthetic activity, as reflected by 3H-proline incorporation. The axial strains in the top layers were greater than the applied surface-to-surface strain whereas axial strains adjacent to the cartilage/bone border were significantly less than the applied strain. Zonal changes in cell density and axial strain which occurred during static compression correlated well with alterations in metabolic activity. These coordinated changes between cell biosynthesis and cartilage structure suggest that zone-specific variation in mechanical stimuli could be responsible for spatially-varying patterns of cartilage metabolic activity under load.

Optical Measurement of Poisson Ratio in Mature and Immature Cartilage
M. Wong, M. Ponticiello, J. Jurvelin and E.B. Hunziker

In this study, we describe a new method to directly measure the instantaneous and equilibrium Poisson's ratio of cartilage tissue. Cartilage disks from adult, calf and fetal tissue were subjected to 5% unconfined compression and the time-dependent lateral expansion of the tissue was observed under the microscope. The Poisson ratio (υ) of the tissue was measured as the ratio of the average lateral strain to applied axial strain. Mature cartilage showed incompressible behavior (Poisson ratio ~ 0.5) immediately after compression while immature tissue had a lower instantaneous Poisson ratio (~0.4). The equilibrium Poisson ratio of mature articular cartilage varied with site and with age. Values for adult humeral head cartilage were significantly higher compared to cartilage from the opposing glenoid surface. Further, mature tissue had a higher equilibrium Poisson ratio than both calf and fetal epiphyseal cartilage. The Poisson ratio and the load relaxed at a similar time constant which was several times more rapid in the case of fetal tissue. These findings are consistent with the hypothesis that the interstitial fluid is the dominant load carrying mechanism in the *in situ* loading of cartilage.

2.1.2 Molecular and Cellular Biomechanics

The main activities encompassed within the scope of this research area are directed towards elucidating the composition and functional properties of skeletal tissue elements at the molecular and cellular levels. Experimental methodology involves principally in vitro systems, cartilage and connective tissues being the main tissues investigated. Current topics dealt with include the analysis of structural and functional properties of components contained in adult human articular cartilage, foetal cartilages and loose connective tissues. Newly-identified extracellular constituents are being cloned, sequenced and analyzed from a functional viewpoint.

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Construction of a Cartilage-Specific cDNA Library

D. Belluoccio and B. Trueb

Differentiated chondrocytes secrete an extracellular matrix composed of collagens (types II, IX, XI), proteoglycans (aggrecan) and noncollagenous proteins (CMP, COMP). In rheumatoid arthritis and osteoarthrosis, a dramatic loss of cartilage is observed. This loss is due to the degradation and altered expression of extracellular matrix molecules.
In order to identify novel cartilage-specific components we have constructed a subtracted cDNA library. Poly(A) RNA was isolated from chicken chondrocytes as well as from chicken fibroblasts and transcribed separately into double-stranded cDNA. The two cDNA preparations were subtracted from each other utilizing the biotin/streptavidin technique in combination with the polymerase chain reaction. Cartilage-specific cDNA molecules were finally ligated into the plasmid pUC19. The library prepared in this way contained many cDNA clones coding for known cartilage proteins, including collagen II, collagen IX, collagen XI and aggrecan. In addition, we found several cDNA clones which encoded novel molecules. These molecules seem to be composed of repeated motifs characteristic of extracellular matrix proteins such as the von Willebrand factor A domain, the EGF-repeat and the IgG module. Structure and function of the novel proteins will be investigated.

Native Chick Laminin-4 Containing the β2 Chain (s-Laminin) Promotes Motor Axon Growth

R. Brandenberger, R. A. Kammerer, J. Engel and M. Chiquet

Following denervation of muscle, motor axons reinnervate original synaptic sites. A recombinant fragment of the synapse specific laminin β2 chain (s-laminin) was reported to inhibit motor axon growth. Consequently, a specific sequence (leucine-arginine-glutamate, LRE) of the laminin β2 chain was proposed to act as a stop signal and to mediate specific reinnervation at the neuromuscular junction (Porter et al., Neuron 14: 549-559, 1995). By means of subunit-specific monoclonal antibodies, we were able to purify and separate laminin-2 and laminin-4, the two major isoforms found in muscle. We observed that native chick laminin-4, which contains a β2 chain and is present in the synaptic basement membrane, did not inhibit but rather promoted motor axon growth. Its activity was indistinguishable from that of laminin-2, which has a β1

chain and is found extrasynaptically. In native heterotrimeric laminin-4, the LRE sequence of the β2 chain is found in a triple coiled-coil region that is formed by all three subunits. We could demonstrate that the effect of LRE depends on the structural context. Whereas a recombinant randomly coil LRE peptide indeed inhibited outgrowth by chick motoneurons, a small recombinant triple coiled-coil protein containing this sequence did not. These findings cast doubt on the physiological significance of the LRE motif in native laminin-4 as a possible target for growing motor axons at muscle synapses.

DNA Methylation Accounts for The Inhibition of Collagen VI Expression in Transformed Fibroblasts
M. U. Kopp and B. Trueb

The expression of collagen VI, an adhesive glycoprotein of the extracellular matrix, is completely inhibited in virally transformed fibroblasts and in many cell lines derived from spontaneous mesenchymal tumours. We have obtained good evidence that DNA methylation accounts for this inhibition: 1) The mRNA level for DNA methyltransferase is highly increased in SV40 transformed fibroblasts compared to normal cells and this increase correlates with the decrease of the mRNA level for collagen VI. 2) Methylation of the α2(VI) collagen promoter in vitro abolishes the promoter activity in a transient transfection assay. 3) Genomic sequencing reveals extensive methylation of the promoter region in SV40 transformed cells, but virtually no methylation of the corresponding region in normal cells. Increased methylation is also observed in a rhabdomyosarcoma cell line. 4) Two of the cis-acting elements of the α2(VI) collagen promoter lose their affinity for transcription factor AP2 when methylated in vitro as demonstrated by gel retardation experiments. DNA methylation is therefore involved in the silencing of the α2(VI) collagen gene. It seems likely that the same mechanism is also responsible for the repression of other transformation-sensitive proteins.

A Novel Zyxin-Related Protein whose Synthesis is Reduced in Virally Transformed Fibroblasts
J. Zumbrunn and B. Trueb

We have cloned the gene for a novel LIM domain protein from human fibroblasts whose expression is substantially decreased in simian virus 40 (SV40) transformed cells. This protein has a calculated molecular mass of 61 kDa and comprises a proline-rich domain followed by three LIM motifs. It appears to be identical to the focal adhesion protein p83 that has recently been isolated and characterized from porcine and human platelets. Hybridization experiments demonstrate a very low degree of evolutionary conservation of its sequence between mammals and birds. It is therefore possible that the novel protein represents the human equivalent of the chicken protein zyxin as the two proteins display a very similar overall structure, although their amino acid sequences diverge markedly from each other. The repression of this zyxin-related protein in virally transformed fibroblasts may explain, at least in part, the dramatic morphological changes that occur at the cell surface and in the cytoskeleton of transformed cells.

Primary Structure of a Putative Serine Protease Specific for IGF-Binding Proteins

J. Zumbrunn and B. Trueb

From a subtracted cDNA library we have isolated a cDNA clone coding for a novel transformation-sensitive protein which is expressed by human fibroblasts, but not by their matched SV40 transformed counterparts. This protein has a molecular mass of 51 kDa and is highly related to the HtrA-family of serine proteases from bacteria. At the N-terminal end, it contains an IGF-binding domain which may modulate the activity of the associated serine protease. Our data are consistent with the assumption that the novel protein represents one of the proteases that regulate the availability of IGFs by cleaving IGF-binding proteins.

2.2 Divison of Orthopaedic Biomechanics

The activities of this Division are directed towards two major areas of research: basic and clinical orthopaedic biomechanics (BCB) and computer assisted surgery (CAS). Additionally, a Clinical Support Group (CSG) was established which consists of full-time orthopaedic surgeons (provided by the Department for Orthopaedic Surgery, Inselspital, Bern and the Semmelweis University of Medicine, Department of Orthopaedic Surgery, Budapest, Hungary) and medical students working on various projects.

In basic and clinical bimechanics, the major areas of focus are state of the art implant evaluations, musculoskeletal injury mechanisms and low back pain. Research methodologies in involve primarily *in vivo* and *in vitro* experimental work as well as mathematical (FE) models. The anatomic areas of interest are the spine, hip, and knee.

Research in the area of computer assisted surgery covers orthopaedic surgical procedures. Proposed and established CAS-systems allow advanced image data acquisition and processing, pre-operative surgical planning and simulation, and intra-operative real-time control and visualization of surgical tools.

The Orthopaedic Biomechanics Division can be reached through the World Wide Web (WWW) at http://cranium.unibe.ch/ or at http://www-mem.unibe.ch.

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2.2.1 Computer Assisted Surgery (CAS)

Restricted Surface Matching — A New Approach to Registration Combining Pair-Point and Surface Matching Techniques

J. Gong, R. Bächler, M. Sati and L.-P. Nolte

One of the key issues in CAS is to establish a relation between intraoperative data (collected e.g. with an optical position sensor) and preoperatively acquired image data of the patient. This process of computing a transformation from real world to image coordinates is referred to as registration. For operations like the periacetabular osteotomy (PAO) the classical pair-point matching that uses a 1-1 relation between real world and image points cannot be applied because it is intraoperatively not possible to identify the landmarks with the required precision. Restricted surface matching overcomes this difficulty by allowing the surgeon to define several coarse landmarks that can be captured with a deviation of up to 20mm from the precise location. These coarse landmarks are used to estimate an initial transformation from real world to image coordinates. The initial transformation is refined using additional points that are captured on the surface of bony structures. The registration algorithm minimizes the distance of these points to the surface of the object (extracted from the image data). The coarse landmarks are used to restrict the minimization to the desired area.
This registration technique has been used successfully in six PAO surgeries and current research tests the applicability of restricted surface matching to other areas such as the lumbar or cervical spine.

A C-Arm Based System for Distal Locking of Femoral Nails

R. Hofstetter, M. Slomczykowski, I. Bourquin and L.-P. Nolte

For distal locking of unreamed femoral nails, a C-arm based CAS system has been developed. It is capable of guiding the radiologist to align a C-arm for obtaining specific views of the femoral nail. In a second step it can visualize a surgical tool in C-arm images by simulation in real-time. The aim is to minimize the radiation exposure and to reduce the operation time for drilling the distal locking holes into the femur.
The system consists of a standard C-arm, a SUN-workstation, a stereotactic toolset, a specific patient application and an optoelectronic position sensor. This optoelectronic position sensor can determine the locations of the tools, the patient and the C-arm in the field of the operating table. In order to perform a simulation of the projection of the C-arm, its geometry has to be obtained by a preoperative calibration step. For this purpose an optoelectronically tracked calibration probe is imaged twice by the C-arm. All parameters describing the C-arm geometry are then calculated automatically using image analysis techniques and an error minimization method.
For positioning the C-arm, 3D-coordinates describing the distal locking holes in the femoral nail are digitized by a pointer before nail insertion. These points are passed through a projection algorithm which simulates the projection in the C-arm. The result is displayed graphically on the computer screen in real-time. This provides the surgeon with an abstract preview of the C-arm image.
Realtime tracking can be performed in single C-arm images obtained during operation. 3-D coordinates describing the drill axis are transformed into a coordinate system referring to the C-arm at the time of image acquisition. The resulting coordinates are passed through the projection simulation algorithm.

Then the drill is displayed as a colored bar superimposed on the planar C-arm image.
The system has been equipped with a practical user interface and has been evaluated in vitro.
The use of the C-arm based significantly navigation system may reducte the radiation exposure to patient and medical staff, shorten the surgical procedure and decrease rate of hole misplacement. Possible applications of the system can be extended to other surgical procedures requiring fluoroscopic images with and without preoperative CT and intraoperative matching routines.

Clinical Introduction of Image Guided Computer Assisted Hip Surgery
F. Langlotz, M. Stucki, R. Bächler, R. Ganz and L.-P. Nolte

A system for image guided computer assisted hip surgery has been developed and introduced clinically. It serves as a planning and navigation means during periacetabular osteotomy (PAO), a surgical intervention that attempts to correct dysplasia of the hip joint, particularly malposition of the acetabular roof. LED-equipped modified osteotomes are tracked optoelectronically with respect to a local frame of reference (FOR). This FOR is established by a so-called dynamic reference base that is mounted onto the patient's pelvic rim intraopertively. Spatial location and orientation of the osteotomes are presented in multiple static and dynamic CT images in real-time. To solve the difficult problem of matching between the medical image and the patient's anatomy, two different registration strategies have been evaluated. (a) For the combined fiducial and anatomic landmark based paired point matching three modified 3.5mm titanium cortical screws with spherical heads are inserted into the pelvic rim prior to CT acquisition. The delivery of these screws requires an additional operation and is performed under local anesthesia. These fiducial landmarks are combined with one anatomic feature point for use with a classical paired point matching algorithm. (b) To overcome the need for an additional surgical intervention, a restricted surface matching algorithm has been implemented. It uses only ten to twelve points arbitrarily digitized intraoperatively on the accessible bony surface. To keep the underlying iterative matching algorithm from running into local minima of the cost function, a set of three rough anatomic landmark pairs restricts it to a solution closed to the global minimum. So far, twelve patients have undergone the computer assisted approach of the Bernese PAO.

Computer Assisted Cruciate Ligament Placement
M. Sati, H.U. Stäubli, Y. Bourquin, S. Larouche and L.-P. Nolte

Rupture of the anterior cruciate ligament (ACL) and rupture of the posterior cruciate ligament (PCL) are pathologies that can destabilize the knee and lead to premature degenerative arthritis. Replacement of the ruptured natural ligament by an autogenous graft is currently the most popular option to stabilise the articulation. Proper surgical replacement of a ruptured ACL or PCL of the knee is however difficult. Knee stability and long-term success of the operation varies significantly with the surgical placement of the graft.
Optical fibre technology (arthroscopy) has been developed to help the surgeon see internal structures hidden deep within the joint. Even with this technology, it is difficult for the surgeon to know where and how to properly position the graft. This ongoing project involves the development of a computer assisted device to help the surgeon plan and guide the graft placement in situ.

Opto-electronic markers are used to track the relative movement of the femur and tibia in situ. The system is different from the present computer assisted systems since it allows the surgeon, through his endoscopic view, to define and label landmarks he is familiar with. We are currently developing a computer interface that represents these structures in such a way that they can help guide the surgeon towards the desired graft insertion sites.

Computer Guided Positioning of the Fluoroscopic based on Anatomical Landmark Measurements and Morphological Data of the Lumbar Spine
L.-P. Nolte, M. Slomczykowski, P. Shah, M. Strauss and Y. Bourquin

A computer guided system for the positioning of the fluoroscopy unit during lumbar spine surgery has been developed. The software uses a specified set of digitised anatomical points and a morphological database, and constructs a geometrical model of the lumbar spine. Using a C-arm unit with predetermined projection parameters this model is then projected onto an image plane generating a virtual Fluoroscopy. The spine can then be tracked by a digital camera and its representation can be seen in real-time. After positioning of the C-arm in relationship to the spine is satisfactory, the real fluoroscopy image of the lumbar spine is obtained. There are advantages of the new system such as reducing the total number of x-ray images necessary for the surgical intervention and more precise alignment of the C-arm, e.g. for pedicle screws insertion. The system is also beneficial since it is a passive system and need not be used if desired. There is no intervention by the system on the patient and the surgeon can determine whether he or she will accept the information given or reject it.

Image Guided Percutaneous Shanz Screw Insertion - A Novel Approach to Minimally Invasive Spine Surgery
M. Slomczykowski , P. Heini, R. Hofstetter and L.-P. Nolte

External fixation of the lumbar spine requires the precise percutaneous insertion of the Schanz screws into each pedicle. Traditionally, the surgical procedure requires the fluoroscopic guidance for recognition and targeting the pedicle. Our computerised fluoroscopy based navigation system allows the surgeon to insert the screws with only two C-arm expositions per vertebra. A dynamic reference base needs to be attached to the spinaous process of the vertebra. The fluoroscopic images of the lumbar spine are registered in the computer together with the information about the spatial position of the X-rayed part of the lumbar spine. The lateral view of the each vertebra as well as the oblique view along the pedicle are used. Using tools which can be tracked by the optoelectronic camera, the surgeon can percutaneously find the entry point for screw hole preparation and control the position of the screw in the real-time on the computer monitor. The computerised fluoroscopic navigation system allows to significantly minimise the total radiation time and to increase the precision of the surgical actions. The system's precision and reliability were checked in the laboratory on plastic spine models as well as on the human cadaveric material. The proposed clinical trail of the percutaneous screw insertion will be undertaken to prove the ultimate usefulness of the computerised fluoroscopy based navigator in the spine surgery, particularly its potential for minimally invasive approaches.

2.2.2 Basic and Clinical Biomechanics (BCB)

Pedicle Screw Insertion Torques are Greater In Vivo than In Vitro

D. Bühler, U. Berlemann, T. Lund, T. Oxland and L.-P. Nolte

The stability of transpedicular spinal instrumentation largely depends on the integrity of the implant-bone interface. It has been shown in vitro, that the measurement of screw insertion torque may serve as a predictor of screw pull-out forces and the number of cycles to ultimate interface failure. However, there are no comparable in vivo data on insertion torques. The purpose of the present study was to compare pedicle screw insertion torques in vivo and in vitro data and also correlate the values with vertebral bone density.

81 pedicle screws (USS instrumentation STRATEC Oberdorf, Switzerland, 6mm screws) were included in the study. 43 were intraoperative in vivo cases while 38 were in vitro lab specimens. DEXA bone mineral density data was available for 20 in vivo and 32 in vitro specimens. All screws were inserted after preparation of the pedicular canal using a blunt probe. A custom-made sterilizable six-axis loadcell was integrated into a torque wrench with a T-bar handle. Moments along the screw axes together with the orthogonal moments were measured and saved during the insertion. Minimum and maximum values of all moments were determined, and their mean values compared. Normal distribution of data allowed for statistical analysis using an unpaired t-test.

The difference between the in vivo and in vitro orthogonal moments (MX, MZ) was not significant ($p>.05$), however the insertion torque (MY) was highly statistically significant ($p<.001$). A linear correlation was found between insertion torque and BMD data, which was statistically significant for the in vitro data ($R=0.76$; $p<.001$) but not for the in vivo data ($R=0.23$; $p=.34$). However, no significant difference between in vivo and in vitro BMD data was detected ($p>0.1$).

The in vitro data determined in the present study is comparable to the results presented by others. The significantly larger in vivo torques were certainly of interest. Insertion torque largely depends on intrinsic bone properties. No differences between in vivo and in vitro BMD data was found. Therefore, we suppose that the detected difference between in vivo and in vitro insertion torques is caused by factors such as intraosseous pressure or microstability of the vertebral cancellous bone. Other moments (MX, MZ) do not seem to be influenced to the same extent by these factors. These detected differences question the general applicability of biomechanical in vitro data such as pullout or bending forces for spinal screws to the in vivo situation.

Three-Dimensional Motions of Femoral Prosthetic Stems: An In Vitro Evaluation of a Novel Measuring Concept
D.W. Bühler, D. Goertzen, M. Slomczykowski, T.R. Oxland and L.-P. Nolte

Primary stability of uncemented total hip replacements is regarded a major factor for the quality of bony ongrowth to the femoral stem and therefore for the long-term outcome. The objective of this study was to extend previous measurements made on two uncemented stem designs (CLS and Wagner Cone, Sulzer Orthopaedics) to additional designs.
The measuring technique is based on a sensor combining optoelectronic with precision mechanical components. The spherical measuring tip is placed on the prosthesis at predefined locations and precision ball bearing mechanics allows transition of the detected motion to a laser diode on the opposite end of the sensor. 3D motion analysis is made possible by considering output data of the PSD (x/y-axis) as well as the registered light intensity (z-axis). Static and dynamic validation indicated a maximal system error of ±4mm within a measuring range of ±750mm in each spatial orientation. Five paired fresh cadaveric femora were used for testing of two different types of uncemented femoral stems: CLW stem and BO Prosthesis. Following implantation of the prosthesis, the femora were subjected to sinusoidal cyclic loading in a two-axial materials testing machine at 1, 2, 3 and 4 times body-weight (BW).
The project remains in progress. Considerable differences in the "micro- and macro-stability" of the two prosthesis types could be detected. Analysis of different concepts of femoral stems with the presented standardized approach may further elucidate the role of primary stability for the long-term clinical outcome.

Influence of Surface Characteristics on the Interface Shear Strength Between Titanium Implants and Bone. A Biomechanical Study in the Maxilla of Miniature Pigs
D. Buser, T. Nydegger, T.R. Oxland, H.P. Hirt, D. Cochran and L.-P. Nolte

The purpose of the present study was to evaluate the influence of surface characterisitics on the interface shear strength of titanium implnats. Solid-screw titanium implants of identical macroscopical shape, but three different surfaces were inserted in edentulous areas of the anterior maxilla of 9 miniature pigs. The three tested titanium surfaces were a) a smoothly machined (SM), b) a titanium plasma-sprayed (TPS), and c) a sandblasted, acid-etched surface (SLA). After 4, 8, and 12 weeks of healing, mechanical removal torque testing was performed to evaluate shear strength of the bone-implant interface for each implant type at each healing period and each implant position. The test results demonstrated statistically significant differences between the smoothly machined surface (SM) and the two rough titanium surfaces (ANOVA, Scheffe's F-test, $p<0.00001$). The TPS and SLA surfaces, however, were not statistically differnt. SM implants demonstrated mean removal torques between 13 and 26 Ncm across the healing periods, whereas TPS and SLA implants showed mean removal torques ranging from 114 to 154 Ncm. There was no significant difference between the healing periods for any of the tested implants ($p=0.11$). The implant position, on the other hand, had a significant influence on the removal torques for each implant type ($p<0.0001$), since removal torques demonstrated a decrease the more posterior the implant was located. It can be concluded that the interface shear strength of titanium implants is significantly influenced by their surface characterisitics, since the smoothly machined

titanium surface demonstrated significantly reduced removal torques in maxillary bone when compared with the two tested rough surfaces. In addition, removal torques were also influenced by the implant position. To evaluate potential differences between the TPS and the SLA surfaces, a split-mouth designed study is necessary to exclude the influencing factor of the imppant position.

Vertebral Body Deformations Contrasted Under Compression and Shear Loading

H.P. Frei, T.R. Oxland, M. Slomczykowski and L.-P. Nolte

The human spine is subjected to a highly complex combination of compression, shear and bending loads during normal activity and particularly under injury-producing conditions. The behaviour of the spine has been studied extensively in compression and bending but there remains a lack of fundamental data under shear loading. Recent work has suggested that shear may be an important load in low back injury. Our overall goal is to determine the patterns of vertebral deformation under a wide variety of loading types and thereby better understand the mechanisms of spinal injury. The specific goal of this work was to contrast vertebral body strains under compression and shear loading in the thoracolumbar spine.

Five human cadaveric T12-L1 functional spine units (FSUs) were dissected of all non-ligamentous soft tissue. At four sites on each L1-vertebra, tri-axial strain gauges were applied: i) at the centre of the anterior surface near the superior rim, ii) at the left and iii) right side near the superior rim and, iv) on the inferior side of the end-plate through a 6 mm hole in the vertebral body. After gauge application, the upper and lower vertebrae were mounted in PMMA blocks. A pressure needle was inserted into the intervertebral disk to record the disk pressure during the tests. A series of compression and shear loads were applied to each FSU as follows. The compression series included a pure compression, flexion-comp., extension-comp., right lateral-comp. and left lateral-comp. load. The pure compression load was applied at the balance point of the specimen while the other loads were applied with 2 cm eccentricities to produce a combined bending-compression. The forces were applied to a 500 N maximum at a rate of 50 N/s. The shear loads include anterior-posterior shear, posterior-anterior shear, left-right shear and right-left shear. The shear forces were applied through the specimen centre of shear (i.e. approximately mid-disk plane) to a 500 N maximum at 50 N/s. Marker carriers with 4 LED's were placed on the upper and lower vertebral mounts such that intervertebral motions could be measured during all load applications with an optoelectronic camera system [Optotrak 3020, Northern Digital, Waterloo, Canada].

In the 5 specimens tested, there was wide variability in the measured strain values. Several general observations were made. Under the variously located compression forces, no significant differences in endplate strains were observed. In general the endplate strains were related to the disk pressure. The left, front and right vertebral body strains did vary with the type of applied load in that the axial strain was compressive when the load was close and tension when the load was far. Both A-P and P-A shear loads produced different strain patterns compared to compression loading. Overall, they resulted in lower end-plate strains and higher strains in the periphery. In A-P shear, higher strains were measured at the vertebral body front compared to P-A shear. Left-right and right-left shear produced different strain patterns in comparison to A-P and

P-A shear. The magnitude of strains in lateral shear lied between compression and P-A shear forces.
This study constitutes an intensive investigation into the mechanics of the FSU under different loading configurations. Several points are notable. The finding that different compression load positions did not affect the disk pressure or end-plate strains supports the hydrostatic behaviour of the intervertebral disk. It is expected that in advanced stages of degeneration, these results may change. There were significant differences in strain distribution between compression and shear forces. A much larger percentage of deformation occurred in the end-plate region under compressive loads. This is consistent with many observations that the end-plate is the first structure to fail in compression. In shear, the greatest deformations were in the periphery. This suggests that these regions may be susceptible to injury under shear loads. Further work will include destructive tests at high rates of loading to investigate the effect of bone quality and disc degeneration on strain and failure patterns.

Compressive Strength of Interbody Cages: The Effect of Cage Shape and Bone Density
B. Jost, P. Cripton, T. Lund, T. Oxland, K. Lippuner, Ph. Jaeger and L.-P. Nolte

Recently, many cages with different shapes were developed for lumbar interbody fusion. These implants are designed to stabilize the operated segment as well as restore and maintain the disc height. The purpose of this study was to investigate the influence of cage design, posterior instrumentation and bone mineral density on the compressive strength of lumbar spine segments.
Forty-eight human cadaveric lumbosacral functional spine units (FSU) from L2-S1 were used. DEXA scanning was performed on each specimen from a lateral and an anterior-posterior direction to obtain the bone mineral density (BMD) of the vertebral bodies. Twelve specimens were used for each of four different cage designs, six with and six without a standard pedicle instrumentation. An axial compressive displacement of 0.4mm/s was applied to the specimen until failure. The kinematics of adjacent vertebrae and each cage were measured using an optoelectronic measurement system.
There was a statistically significant relationship between all four bone densities and compressive strength. The lateral DEXA scan values (upper vert. R2= .53; lower vert. R2= .51) revealed a higher correlation than the A-P (upper vert. R2= .23; lower vert. R2= .09). Neither the implant design/ techniques nor the posterior instrumentation had a significant effect on the compressive strength (p=0.8). The average failure loads for all four cages were approximately 5000 N.
In this study, a direct relationship was observed between the failure load of the bone-implant interface and the vertebral bone density. The large range of observed failure loads overlaps the potential in vivo compressive loads, implying that failure of the bone-implant interface may occur clinically. Therefore, pre-operative measurement of BMD may be an effective tool in preventing settling around these implants.

The Effect of Interbody Cages with and without Posterior Instrumentation on the Three-Dimensional Stability of the Spine - a Biomechanical Evaluation

T. Lund, T. Oxland, B. Jost, P. Cripton, S. Grassman, C. Etter and L.-P. Nolte

In the past few years, several interbody cages of different designs have been developed to be used via an anterior or posterior approach. The goal of these implants is to stabilize the spine and ultimately achieve an interbody fusion. The goal of this study was to determine the effect of different interbody implant designs/surgical techniques and the effect of posterior instrumentation on the three dimensional stability of the lumbar spine.

Twenty-four human cadaveric lumbar functional spinal units (FSUs) were tested in four different conditions: i) intact, ii) posterior cage insertion, iii) cages with posterior instrumentation and iv) with additional cross bracing. Four different cage types were compared. Pure moments of flexion-extension, lateral bending and axial rotation were applied individually to the upper vertebra in four steps to a maximum of 10 Nm. Custom made markers with light emitting diodes were attached to each block and the movements of these markers were measured with an optoelectronic camera system. The rigid body motion in terms of the top vertebra with respect to the bottom was calculated using custom software.

In flexion-extension, the rectangular and cylindrical cages stabilized the spine to 50-60% of its intact motion but the difference between the four cages was not statistically significant. In axial rotation, the cylindrical cage reduced the motion to less than intact but due to variation, the difference between the cages was only marginally significant. In lateral bending, the rectangular cage was most stable but the difference between the cages was not statistically significant. Universally, the posterior instrumentation significantly reduced the motion in all directions and for all cage types. In flexion-extension and lateral bending, the posterior instrumentation reduced motions to between 10 and 20% of intact motion and to approximately 40% of intact motion in axial rotation. These changes with posterior instrumentation were statistically significant with no differences between the cages. Cross bracing further improved the stability in axial rotation, but the magnitudes were very small.

All cage types included in this study provided the greatest stabilization when used together with posterior instrumentation. The main question lies with what degree of primary stabilization is required to obtain a successful interbody fusion.

The Effect of the External Spinal Fixator on Anterior Column Motion: A Biomechanical Study

T. Lund, G. Rathonyi and T. Oxland

The external spinal fixator has been used by many groups to provide temporary fixation as a preoperative diagnostic tool for chronic LBP patients. Distraction and compression of the diseased segment by external fixation have been reported to provide pain relief. The purpose of this study was to investigate the effect of external fixation on anterior column motion, focussing on the effect of fixator distraction and compression.

Five lumbosacral (LIII-SI) human cadaveric spine segments were prepared with Schanz screws in LIV and SI. Each segment was tested in four different conditions: i) intact, ii) neutral external fixation, iii) distraction 12 mm, iv) compression 8-12 mm. Cyclic axial flexion-compressive loading in

physiological range of 60-600 N (0.5 Hz) was conducted for ten cycles in the four test conditions. The axial displacement at the load application point gave an indication of anterior column axial translation.
The average axial displacement range of the ninth load cycle for all specimens was 1.44mm (sd .16) for intact, 1.28mm (sd .13) for neutral external fixation, 2.55mm (sd .86) with fixator distraction and 1.12mm (sd .21) with fixator compression. The axial motion with distraction of the fixator was significantly greater than all other conditions, including intact. External fixation in unchanged (neutral) position did not significantly affect the overall axial translation ($p=0.06$, paired t-test).
The external fixator has been shown to decrease flexion-extension rotation. However, we have found that the fixator does not significantly reduce anterior column axial translation and, in distraction, this motion exceeds the intact specimen. Since pain relief is frequently observed during distraction with the external fixator, the mechanical basis for the pain relief is not well understood.

The Effect of Translaminar Screw Fixation on the Multidirectional Flexibility of Anterior Lumbar Interbody Fixation
G. Rathonyi, T.R. Oxland, U. Gerich, S. Grassmann and L.-P. Nolte

Several spinal implants for lumbar interbody fusion have been developed within the last five years, with encouraging clinical results. The devices are used with or without additional posterior fixation. Pedicle screw fixation in addition to the interbody implants provides a highly stable environment. However, posterior fixation techniques which are less invasive than pedicle screw insertion, such as translaminar screws, have not been evaluated biomechanically as an adjunct to interbody implants. The purpose of this study was to contrast the multidirectional biomechanical flexibility of interbody implant fixation, translaminar screw fixation, and the two methods combined.
Six human cadaveric lumbar spine FSUs were dissected of all non-ligamentous soft tissue and mounted in PMMA blocks such that the mid-disc plane was horizontal. Each segment was tested in four different conditions: i) intact, ii) translaminar screw fixation (TLS), iii) interbody implant fixation with the BAK interbody fusion system (BAK) [Spine-Tech Inc., Minneapolis USA], and iv) BAK and TLS combined. In each test condition, pure moments of flexion-extension, bilateral axial rotation and bilateral lateral bending were applied to the upper vertebra individually in 4 steps to a maximum of 10Nm for two cycles. At each load step, the specimen was allowed to creep for 30-45 seconds. The 3D rigid body motion of the upper vertebra with respect to the lower vertebra was measured using an optoelectronic camera system [Optotrak 3020, Northern Digital, Waterloo CAN] via marker carriers with 4 LEDs on each vertebral mount. For simplicity, the rotation in the direction of the applied moment was investigated. The Range of Motion (ROM) and Neutral Zone (NZ) were calculated in each direction and a repeated measures ANOVA with post-hoc Scheffé's F-test performed to determine statistical differences ($p<0.05$) between the specimen conditions.
The ROM data in flexion, extension, bilateral axial rotation, and lateral bending for each testing condition were determined. With fixation, the NZ data became very small and therefore, are not included.
Flexion: All specimen conditions had significantly less motion than intact. There were no differences between TLS, BAK or BAK w/TLS.

Extension: Conditions TLS and BAKw/TLS had significantly less motion than intact while the BAK had significantly more motion than intact.

Axial Rot.: Conditions TLS and BAKw/TLS had marginally less motion than intact (p=.067) while the BAK was not different from intact.

Lat. Bend.: All specimen conditions had significantly less motion than intact. There were no differences between TLS, BAK or BAK w/TLS.

This study was an in vitro evaluation of the multidirectional flexibility of various techniques for lumbar spine stabilization. Being an in vitro study, extrapolation to the in vivo situation must be done with caution. The study highlights the substantial stabilization provided by the relatively simple technique of translaminar screw fixation under pure moments. However, these results do not address the fact that these screws provide little anterior column support under axial compression which most likely has importance for discogenic pain sources. It is apparent that anterior interbody implant stabilization is effective in most directions, with extension and possibly axial rotation being problematic directions. This was a similar finding to that observed previously for posterior interbody techniques. Finally, for the greatest reductions of motion with anterior column support, the combination of anterior cage insertion and translaminar screws is advantageous.

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3.2 Division of Orthopaedic Biomechanics

Original Articles

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4 RESEARCH PROJECT GRANTS

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5 TEACHING ACTIVITIES

University of Basel:

- 4469 and 6485: New literature in extracellular matrix biology

University of Bern:

- 4011: Coordinated lecture series in physics, chemistry, embryology, ecology, genetics, molecular biology, anatomy and psychology at the University of Bern

- 4109: Ausgewählte Kapitel der Biochemie, Kolloquium für Fortgeschrittene am Institut für Biochemie und Molekularbiologie, Universität Bern

- 7202: Lecture at the Philosophisch-naturwissenschaftliche Fakultät der Universität Bern. Biochemische Methoden II.

- Angewandte Molekularbiologie, interfakultäre Vorlesung für Vorgerückte an der Universität Bern

University of Zürich:

- Vorlesung Nr. 538 ,705

Federal Institute of Technology, Zürich:

- 01-319: Kolloquium in Biochemie at the ETH Zürich

Teaching of regular students, PhD-students and MD-students in the lab

6 FELLOWSHIPS, DISSERTATIONS AND MASTER THESES

6.1 Fellowships

Quinn, Thomas M.: Doctoral Research Fellowship from Merck Co., U.S.A.

6.2 Dissertations Completed

Brandenberger Ralph, Ph.D. University of Basel
Laminin isoforms in nerve-muscle interactions: possible role of chick laminin-2 and laminin-4 and characterization of a novel, truncated variant

Kopp, Martin U. Ph.D. at the ETH Zürich
DNA Methylation of the α2(VI) Collagen Gene. Dissertation No. 11779 at the ETH Zürich

Quinn Thomas M., Ph.D. Massachusetts Institute of Technology
Articular Cartilage: Matrix Assembly, Mediation of Chondrocyte Metabolism, and Response to Compression

Wuethrich Patrick, M.D. Student, University of Bern
Differential Analysis of Chondrocyte Structure and Activity in Adult Bovine Articular Cartilage under Static Compression

6.3 Masters Theses Completed

Akbary T.: Design of a PC-based 8 channel telemetric system for biomechanical evaluations of implants (Dipl.-Ing. FH thesis), MIB, University of Bern, accepted at the FH Gießen-Friedberg, Giessen, Germany, 1997, Advisor.

Gleising V.: Design of a telemetric system with inductively powered transmitter (Dipl.-Ing. FH thesis), MIB, University of Bern, accepted at the FH Gießen-Friedberg, Giessen, Germany, 1996, Advisor.

Hofstetter R.: Integration of the fluoroscope into a generailized concept of computer assisted surgery, (Dipl.-Ing. Thesis, equivalent to M.Sc. thesis), MIB, University of Bern, accepted at the Department of Electrical Engineering, TU Berlin, Germany, 1996, Advisor.

Langlotz U.: Safety analysis of free-hand computer guided surgery using FMEA concepts, (Dipl.-Ing. thesis, equivalent to M.Sc. thesis), MIB, University of Bern, accepted at the Department of Mechanical Engineering, Ruhr-University Bochum, Bochum, Germany, 1996, Advisor.

7 HONORS AND AWARDS

L.-P. Nolte, was nominated Adjunct Associate Professor for Mechanical Engineering at the Faculty of Applied Science of Queen's University, Kingston, Ontario, Canada

T.R. Oxland, Honorary member of the Hungarian Spine Society, December 1996. Annual research award of the swiss scociety of biomedical engineering for his contribution to Computer Assisted Orthopaedic Surgery

B. Trueb, Fakultätsübergreifende Umhabilitation: Venia docendi für das Fach Biochemie, verliehen durch die Erziehungsdirektion des Kantons Bern am 25.11.1996

B. Trueb, Wahl ins Kuratorium für den Friedrich Miescher-Preis der Schweizerischen Gesellschaft für Biochemie

8 GUEST PRESENTATIONS

28.2. - Dr. Peter Paul Varga: Technical aspects of spinal tumour surgery. Division of Spinal Surgery and Rehabilitation, Semmelweis University of Medicine, Budapest, Hungary

8.3. - Prof. David L. Butler: The Effects of Altered Load on Tendon/Ligament Healing and Fibrocartilage Homeostasis. Noyes Giannestras Biomechanics Laboratories, College of Engineering, University of Cincinnati, Cincinnati, Ohio, USA

18.3. - Prof. Wilson C. Hayes: Biomechanics of Age-Related Fracture: Etiology and Prevention. Orthopaedic Biomechanics Laboratory, Beth Israel Hospital, Harvard Medical School, Boston, Massachusetts, USA

22.3. - Dr. David R. Haynes: Potential Non-Surgical Treatments of Wear Particle Induced Bone Loss. Department of Pathology, The University of Adelaide, Adelaide, Australia

23.7. - Dr. Thomas M. Quinn: Articular Cartilage: Matrix Assembly, Mediation of Chondrocyte Metabolism, and Response to Compression. Massachusetts Institute of Technology, Dept. of Electrical Engineering, Cambridge, Massachusetts, USA

31.10./1.11./4.11./7.11./8.11. - Prof. Alan Grodzinsky: Basic Course in Biomedical Engineering. Department of Electrical Engineering and Computer Science, Massachusetts Institute of Technology, Cambridge, Massachusetts, USA

9 PERSONNEL

9.1 Faculty

Hunziker Ernst B., M.D., Prof.	Director	11.89 -
	* * *	
Nolte Lutz-Peter, Ph.D.	Division Head	05.93 -
Trueb Beat, Ph.D., PD	Deputy Division Head	04.95 -
Chiquet Matthias, Ph.D. PD	Research Group Head (80%)	05.95 -
Häuselmann Hans Jörg, M.D.	Research Group Head (External Funding)	10.93 - 04.96
Oxland Thomas, Ph.D	BCB Group Head	08.95 -
Quinn Tom.M., Ph.D.	Research Group Head	07.96 -
Sati Marwan, Ph.D.	Research Group Head	07.96 -
Studer Daniel, Ph.D.	Research Group Head (40%)	03.92 -
Visarius Heiko, Ph.D.	CAS Group Head	02.94 - 04.96
Wong Marcy, Ph.D.	Research Group Head (70%)	02.92 -

9.2 Research Associates

Akbary Temor, cand. Ing.	Guest Student	10.95 - 05.96
Bächler Richard, dipl. Ing.	Ph.D.-Student	06.96 -
Belluoccio Daniele, dipl. Biol.	Ph.D.-Student	05.95 -
Bourquin Yvan, Dipl. Ing. HTL	Assistant	11.95 -
Brandenberger Ralph, dipl. Biol.	Ph.D.-Student	05.95 - 06.96
Brunner Peter, dipl.Ing. ETH	Assistant	06.91 - 08.96
Bühler Daniel, dipl.Ing. ETH	Ph.D.-Student	08.93 -
Cripton Peter, B.Sc., M.Sc.	Ph.D.-Student	11.93 -
Döppenschmitt Ingo, cand. Ing.	Guest Student	10.96 -
Driesang Iris, V.M.D.	Assistant	06.96 -
Frei Hanspeter, dipl. Ing.	Assistant	05.94 -
Geiss Jana, cand. med.	M.D.-Student	09.94 -
Goertzen Darrell, dipl. Ing.	Ph.D.-Student	10.96 -
Gong Jianxing, Ph.D.	Assistant	07.94 - 07.96
Grassmann Stephanie, M.Sc.	Exchange Student	09.95 - 08.96
Griessen Roland, dipl. Ing. HTL	Assistant	11.96 -
Hoffer Zoltan, Ph.D.	Assistant	10.96 -
Hofstetter Robert, cand. Ing.	Ph.D.-Student	06.96 -
Imhof Martin, dipl.phil.II	Ph.D.-Student	01.96 -
Jaquemar Daniel, dipl. Natw. ETH	Ph.D.-Student	08.95 -
Kamibayashi Lynne, Ph.D.	Postdoctoral Fellow	01.96 -
Kopp Martin, dipl. Natw. ETH	Ph.D.-Student	10.92 - 08.96
Langlotz Frank, dipl. Ing.	Ph.D.-Student	05.93 -
Langlotz Ulrich, cand. Ing.	Guest Student	07.96 -
Lund Teija, M.D.	Assistant	01.95 - 02.96
Nydegger Thomas, dipl. Ing. HTL	Assistant	05.96 -
Oetliker Martina, Dr. med. vet.	Ph.D.-Student	11.95 -
Ponticiello Michael, M.S.	Assistent	09.95 -
Portmann Daniel, cand. med.	M.D.-Student	10.96 -

Rathonyi Gabor, M.D.	Assistant	01.96 - 06.96
Rubino Raffaele, cand.med.	M.D.-Student	11.96 -
Scheer Carsten, dipl. Ing.	Assistant	07.94 -
Schmid Pirmin, cand.med.	M.D.-Student	09.96 -
Shah Parag, cand. Ing.	Guest Student	06.96 - 08.96
Slomczykowski Mike, M.D.	Assistent	04.96 -
Speirs Andrew, dipl. Ing.	Ph.D.-Student	11.96 -
Strauss J. Matthias, M.D.	Assistent	07.96 -
Stucki Manfred, cand. med.	M.D.-Student	03.95 -
Trächslin Jonas, dipl. phil II	Ph.D.-Student	06.96 -
Vanelli Jill, Ph.D.	Assistant	01.96 - 06.96
Wälti Heinz, dipl. Inf.	Assistent	12.96 -
Wentkowski Michael, cand. Ing.	Guest Student	07.96 - 12.96
Wüthrich Patrick, cand. med.	M.D.-Student	08.94 - 04.96
Zumbrunn Jürg, dipl. Biol.	Ph.D.-Student	04.95 -

9.3 Technical and Administrative Staff

Berger Elke	Res. Technologist (50%)	01.90 -
Fahnemann-Nolte Karin	Secretary (60%)	03.96 -
Fiechter Esther	Secretary (90%)	07.95 -
Gaschen Véronique	Chief Technician	09.95 -
Gnahoré Esther	Secretary (50%)	12.90 -
Hampton Ann, B.Sc.	Res. Technologist	11.96 - 12.96
Hutzli Walter	Aid Lab. Technician	11.89 -
Kapfinger Eva	Res. Technologist (75%)	11.89 -
Kaufmann Nicole	Res. Technologist	08.95 - 04.96
Künzli Silvia	Res. Technologist	08.95 - 10.96
Mühlheim Erland	Mechanicien (50%)	01.92 -
Mumenthaler Urs	Res. Technologist (80%)	06.95 -
Neseli Güler	Res. Technologist	08.96 -
Neuenschwander Annelies	Secretary (35%)	04.95 -
Perumbuli Prasanna	Res. Technologist	08.96 -
Rohrer Urs	Head Mech. Workshop	07.91 -
Schenker Thomas	Chief Technician	04.95 -
Walther Remo	Apprentice in Fine Mechanics	08.96 -

9.4 Scientific Consultant

Prof. Dr. Robert K. Schenk, Institute of Pathophysiology, University of Bern, Switzerland

9.5 Guest Scientists

Prof. Alan J. Grodzinsky, Massachusetts Institute of Technology, Dept. of Electrical Engineering and Computer Science, Cambridge, Massachusetts, USA

10 MISCELLANEOUS

In April 1996, Hans Jörg Häuselmann, External Research Group Head, moved with his research staff to the Rheumatology Clinic, University of Zürich, where he holds a clinical position as chief resident.

10.1 Conferences Organized

2nd CAOS-Symposium, Computer Assisted Orthopaedic Surgery, University of Bern, Bern, Switzerland, Nov 7-9, 1996

Biomechanics of Age-Related Fracture: Etiology and Prevention, University of Bern, Bern, Mach 18, 1996

Organization of the Annual Meeting of the Swiss Connective Tissue Society, University of Bern, Bern, May 31, 1996

Potential Non-Surgical Treatments of Wear Particle Induced Bone Loss, University of Bern, Bern, March 22, 1996

Satellite Workshop on 'Minimally invasive surgical approaches to the spine - State of the art and future innovations', Zürich, Switzerland, October 15, 1996

Special Workshop - Computer Assisted Orthopaedic Surgery (CAOS) at the CAR '96 - Computer Assisted Radiology - 10th International Symposium and Exhibition, Paris, June 29, 1996

The Effects of Altered Load on Tendon/Ligament Healing and Fibrocartilage Homeostasis, University of Bern, Bern, March 8, 1996

Tutorial C: Computer Assisted Orthopaedic Surgery, 4th International Conference on 'Visualization in Biomedical Computing', Hamburg, Germany, 1996

11 MEMBERS OF THE SCIENTIFIC ADVISORY BOARD (KURATORIUM)

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- Prof. Dr. R. Ganz, Department of Orthopaedic Surgery, University of Bern, Inselspital, Bern
- Mr. U.G. Jann, AO/ASIF-Foundation, Davos
- Prof. Dr. J. Reichen, Depts. for Clinical Research and Clinical Pharmacology, University of Bern, Bern
- Prof. Dr. H. Reuter, Dept. of Pharmacology, University of Bern, Bern
- Prof. Dr. E.R. Weibel (Secretary and Vice President), M.E. Müller Foundation, Bern
- Prof. Dr. M.E. Müller, Honorary Board Member, President of the M.E. Müller Foundation, Bern