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1 BACKGROUND AND PERSPECTIVES

The Maurice E. Müller Institute for Biomechanics was founded in 1981 as a joint venture between the Maurice E. Müller Foundation and the University of Bern. It aims to continue and extend the work of Maurice E. Müller in biomechanical research and teaching as it relates to the locomotor system. The Maurice E. Müller Institute for Biomechanics is under the Directorship of Prof. Ernst B. Hunziker, who was elected to this position by the Bernese Government in autumn 1989.

The physiology and pathology of the musculo-skeletal apparatus, particularly as it relates to orthopaedic biomechanics, embraces a wide field of study. Macroscopically, this pertains, for example, to the physical properties of skeletal components, orthopaedic implantology, fracture fixation and physiology of the locomotor system. At the microscopic level, the mechanical properties and structural organization of skeletal tissues, such as bone, cartilage, tendon and ligaments, as well as the surface characteristics of implant-tissue interfaces and biodegradable matrices, are encompassed. At the cellular and molecular levels, biomechanics appertains to cell adhesion and cell-matrix integration processes, as well as to the identification and physical property analysis of biological macromolecules and their polymers in skeletal tissues. Research and teaching activities at the Maurice E. Müller Institute for Biomechanics fall naturally into these three disciplines, but each team of scientists, equipped with their own peculiar skills, is actively endeavoring by a concerted approach, to further our understanding of the musculo-skeletal system as a whole, and to develop improved strategies for the clinical treatment of traumas and diseases affecting this system.

We were sorry to lose Professor Mats Paulsson (Cellular and Molecular Biomechanics Division) at the end of the year, but wish him success in his new position as full-professor (ordinarius) of biochemistry and co-director of the Institute of Biochemistry at the University of Köln, Germany.

When the Maurice E. Müller Institute for Biomechanics was founded in 1981, it had an exclusively private status (Foundation), but it has always been the aim to intergrate it fully as an Institute in its own right within the medical faculty of the University, Bern.

On the basis of a decision by the Bernese Government 30th March, 1994, which was ratified by the State on 9th June, 1994, this goal has now been achieved, and the new status became operative on 1st Januar, 1995. The fixed financial contribution made by the Maurice E. Müller Fondation to the Institute has been defined by contract (Kooperationsvertrag) between this

body and the Ministry of Education, with the approval of the Advisory Board of the Maurice E. Müller Institute for Biomechanics.

Supervision of the Institute's scientific activities and apportionment of its financial resources will lie now with a newly-formed, Scientific Advisory Board (Kuratorium), which will be comprised of three representatives nominated by the Medical Faculty of the University of Bern and three nominated by the M. E. Müller Foundation. The president of the Board will be nominated by the Bernese Government, upon the recommendation of the Medical Faculty and the M. E. Müller Foundation.

2 RESEARCH ACTIVITIES

2.1 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 group termed Clinical Support Group (CSG) was established consisting of the permanent orthopaedic surgeon in our group (provided by the Department for Orthopaedic Surgery, Inselspital, Bern) and all medical students working in various projects.

Research methodologies in orthopaedic biomechanics involve mathematical (FE) models as well as *in vivo* and *in vitro* experimental settings and are applied to spine, hip, and knee problems. Current topics include the evaluation of prototype implants and implant components and the further enhancement of a comprehensive system to study metal-bone interface motion/micromotion.

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 following abstracts are derived from completed and published studies or reflect ongoing research activities.

In order to account for recent developments in network technologies, the Orthopaedic Biomechanics Division can be reached through the World Wide Web (WWW) at http://cranium.unibe.ch/.

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Computer Assisted Surgery (CAS) in Orthopaedics: General Concepts

L.-P. Nolte, H. Visarius, U. Berlemann, E. Arm, F. Langlotz, J. Gong, C. Scheer, O. Schwarzenbach and R. Ganz

Medical imaging (e.g. X-ray, CT, MRI etc.) provides an important basis for modern diagnosis as well as pre-operative planning of surgical procedures. However, information gained cannot be transferred directly into the OR

reality. Furthermore, it would be desirable to improve security and accuracy of the surgery by interactive navigation of the surgical instruments and body fragments.

This principles are now provided by the proposed system for Computer Assisted Surgery. The research group "Computer Assisted Surgery" transformed and extended concepts and procedures developed in the field of neurological surgery in order to also assist the orthopaedic surgeon by means of a system of tool visualization and guidance. Advanced computer technology is combined with precise navigation based on an optoelectronic motion analysis system and can be controlled by speech recognition or virtual keyboard.

As a first area of application the insertion of pedicle and sacral screws, which serve as an anchor for spinal implants, was selected. Image data from a pre-operative CT scan are reconstructed to form a three-dimensional image in the computer. After registration of the "real world" of the patient situs with the "virtual world" of the CT image it is possible to display the instruments in the CT image (e.g. the virtual bone) in realtime.

In the past months, 30 lumbar fusions (approx. 150 screws) were performed in collaboration with the Department of Orthopaedic Surgery at the Inselspital Bern. A special post-operative analysis has revealed that the screws were placed accurately and securely.

The first clinical experience confirms the good results obtained in *in vitro* studies and encourages us to extend the range of applications for the system to other anatomical areas, e.g. to assist in hip or knee surgery.

Critical Issues in Computer Assisted Surgery (CAS): Man-Machine Interface and Matching

H. Visarius, L.-P. Nolte, J. Gong, C. Scheer and H. Bunke

The clinical potential of Computer Assisted Surgery (CAS) is more and more acknowledged since CAS systems are introduced into the operating room (OR) theater. Especially, the improvements in safety and accuracy are remarkable and strengthened the ties between surgeons and engineers. Since the introduction of tumor stereotaxis to neurological surgery in the early 1980s, systems with and without robots are currently in use for specific medical indications. Lately, solutions for computer assisted orthopaedic surgery were developed and applied to various anatomical regions.

However, with the establishment of CAS *in vivo* a new problem complex, which was not present in the laboratory setups, was introduced - the man-machine interface. Currently, the complexity of available CAS systems requires the presence of at least one system engineer (often called "operator") in the OR. In turn, there is no possibility for direct communication between the surgeon and the machine or software.

Most of the program steps involved in CAS and choices to be made intra-operatively have to be transferred to the software by means of communication of the surgeon with the operator. Particularly, the establishment of a relation between the virtual object (i.e. a medical image) and the surgical object (i.e. the patient), often denoted as "matching" or "skeletal registration", requires intensive interaction of the surgeon with the computer.

A literature survey revealed that no CAS system worldwide exists without a system engineer or a comparable person and our clinical experience indicated that the matching process is a weak point in most systems. Since it appears to be contradictory to cost reduction efforts in health care to have a highly paid system engineer in the OR this research realizes strategies to facilitate the man-machine interface with the final goal to establish a direct control of the system by the surgeon or the medical personal traditionally present at surgeries. Options in different states of realizations include: (a) a CAS Control Panel as an extension of the existing optoelectronic system, (b) a touch-screen panel, and (c) introduction of a commercial speech recognition system. To facilitate the matching process, knowledge based techniques and the introduction of machine vision will be evaluated. In a second step, the implementation of the strategy of choice into the existing CAS setup at the Department of Orthopaedic Surgery at the Inselspital (University of Bern) is aspired.

Radiologic Aspects in Computer Assisted Surgery (CAS)

H. Visarius and C. Ozdoba

Our Orthopaedic Surgery and Planning System OSPS is one out of two orthopaedic CAS system for spine surgeries used in the OR on a routine basis. The successful introduction of the system to the OR theater has given the motivation to focus research efforts towards unresolved problems of CAS systems in general which are also inherent in our system. One of these problems is the multi-modality image acquisition and processing and its usability for the matching process, i.e. the establishment of a relation between the "real" surgical world and the "virtual" world of the image.

A crucial component of the combination of image guided stereotaxis and advanced opto-electronic position sensing devices is the image source. Three-dimensional reconstructions of anatomical structures from digitally acquired sectional cuts ("slices") require high in-plane resolution and minimal slice thickness in order to obtain maximal resolution with a minimum of spatial distortion. However, high doses of radiation are in conflict to efforts of reducing the radiation a patient is exposed to.

This research shall elucidates the possibilities for the use of patient-friendly imaging methods with low radiation exposures in orthopaedic CAS. The various parameters involved in the acquisition of a medical image as well as the introduction of different imaging techniques into CAS are studied.

Computer Assisted Spine Surgery

E. Arm, H. Visarius, L.-P. Nolte, U. Berlemann, F. Langlotz and D. Monin

In the past, *instrumented spinal fusion* has become a popular treatment for degenerative diseases of the lumber spine. Fixation devices are mainly anchored by transpedicular as well as sacral screws into the vertebra. Conventional surgical techniques, however, still bare a considerable risk of misplacement resulting not only in an improper bony interface thus qualitatively reducing the biomechanical properties of the fixation, but also in serious damage of nerve roots in the intervertebral foramen. Moreover, frequent intra-operative fluoroscopy as a guidance during the insertion process results in a heavy radiation load not only for the patient, but also for the OR-personnel. These were the main reasons to choose spinal surgery as the first goal towards the application of our system for Computer Assisted Surgery in Orthopaedics.

After successful introduction of the Orthopaedic Surgery and Planning System OSPS in the Department for Orthopaedic Surgery of the Inselspital Bern, 30 patients (approx. 150 screws) underwent lumbar surgery with this new method so far. As post-operative analysis showed accurate and secure placement of the screws, the system was further developed, tested and also successfully applied in the more critical thoracic spine, leaving only the cervical region to be introduced in early 1995.

Since the currently supported surgical techniques are all based on a standard, open posterior approach, current research deals with the development and implementation of new concepts for *minimal invasive surgery*. Not only new matching strategies, but also new concepts for instrumentation and clinical procedures have to be established to support the *percutaneous* insertion of

spinal implants. This will result in less hospitalization and recovery time for the patient.

Computer Assisted Complex Acetabular Osteotomy

F. Langlotz, U. Berlemann, R. Ganz, K. Klaue, H. Visarius and L.-P. Nolte

Residual dysplasia of the hip has been shown to be one of the major causes of osteoarthritis. Treatment of such a dysplasia or early degenerative changes in the younger adults usually requires some form of corrective surgical realignment of the hip joint components. In particular, acetabular osteotomies have gained more and more importance as they try to correct the basic underlying pathology.

Since 1984 a novel type of acetabular osteotomy has been performed at the Department of Orthopaedic Surgery in Bern in more than 400 cases. In addition an advanced image-based surgical planning module was developed at the same clinic to mathematically describe the required correction. However, the realization in the operating theatre is very demanding and requires imagination of the complex three-dimensional hip joint geometry without being accessible to the surgeon's eye. A surgical system allowing for advanced pre-operative planning, controlled separation of the acetabular joint component, and real-time control and visualization of surgical instruments as well as body fragments would assist in overcoming these limitations and improve accuracy and safety of the surgical procedure.

The purpose of this project is to establish a new surgical planning and guidance system combining complex surgical techniques, advanced three dimensional image reconstruction, principles of stereotaxis, and opto-electronic space digitization. Based on our established Neurological Surgery Planning System NSPS a novel approach towards flexible pre-operative planning and reliable intra-operative computer guidance during complex acetabular osteotomy will be developed. Infra-red light emitting diodes tracked by an opto-electronic space camera are used to instrument all parts involved in the surgical procedure including the bony fragments and to trace their rigid body motion. After the three dimensional reconstruction of a CT or an MRI image and an exact skeletal registration it is possible to display the actual location and orientation of surgical tools in the image on screen.

Thorough studies will be performed to analyze the complete cascade of intrinsic and extrinsic errors of the system for proper validation. An *in vitro* validation and first *in vivo* applications of the new technique are planned.

We believe that the development of the proposed method is an important step to establish a computer assisted technique for safe complex acetabular osteotomy and that it will open new frontiers towards further applications in hip surgery in particular and in orthopaedic surgery in general.

Development of an Opto-Electronic Positioning Device for Serial Direct Digital Images from Oral Structures

C. Scheer, U. Brägger, L.-P. Nolte, N.P. Lang and W. Bürgin

Since the introduction of dental radiographs in 1986 many efforts have been made to improve the quality of this technique. One of the latest developments is the so called Direct Digital Imaging (DDI). This method promises some important progresses in dental radiology as it improves inconveniences of conventional radiographs decreasing the radiation dose. avoiding film processing procedures and providing a flexible data storage. Subtraction radiography as another new digital imaging technique for the diagnosis of small changes in dental and bony tissues has been tested in various studies. However, this hybrid method relies on conventional film so far.

The major objective of the present series of studies is to find a way to combine the DDI with the subtraction radiography in vivo. In order to produce digital subtraction images from oral structures based on two direct digital images it is necessary to develop a system which provides repeated exact 3-D-positioning of the image receptor and the X-ray source relative to the area to be evaluated. In order to provide such a controlled and reproducible technique the planned research is subdivided into two specific projects with the following goals:

Project A: To generate the hard- and software for an opto-electronic positioning device for serial direct digital oral radiography.
Project B: To assess the methodical error when obtaining serial standardized direct digital images from oral structures.

The development of the positioning device is an important step to make direct digital imaging for the first time a diagnostic tool in clinical research. Further progress may even lead to applications in the dental office chair for monitoring special sites in patients.

Transpedicular Screw Placement - A Morphometric Study of the Lumbar Spine

D. Monin, U. Berlemann, E. Arm and L.-P. Nolte

The biomechanical integrity and safety of transpedicular spinal implants relies on the correct and secure placement of the pedicle screws. Various recommendations for a successful pedicle screws insertion based on anatomical findings and clinical experience have been reported previously. In order to enhance the precision of screw insertion a method utilizing computer aided visualization and guidance during pedicle hole preparation has been developed.

Tomographic images (CT scans) from lumbar spines are performed in 2mm slice distance in the Dept. for Neuroradiology (Inselspital, Bern). The CT data is forwarded via network and used for image reconstruction on a SUN workstation in the Institute.

The Trajectory Visualizer of the OSPS software package is used to define the optimal trajectory which is by our definition following a path as centered through the pedicle as possible. The three or four cross-sections showing the smallest pedicle diameter represent the major area of interest. However, the anterior cortex should additionally be approached as close as possible. 6mm screws are intended for use.

The length and the transverse and the sagittal angle of the optimal trajectory and therefore the pedicle orientation are calculated. The system allows also to calculate the minor diameters (cortex intern and cortex extern) of the pedicle.

After removal of soft tissue and disarticulation of the lumbar spine, the Pedicle Navigator (OSPS) is used to transfer the planning into the actual drilling of the pedicle hole. In each hole an aluminium rod is placed and all vertebrae are x-rayed. Following that, all pedicles are prepared and cut into 2mm histological sections which are also x-rayed. All x-ray films are digitized. This allows us to calculate orientation and length of the trajectories and diameters of the pedicles for verification.

The Effect of Cross-Bracing in Posterior Lumbar Spinal Fixation

P.A. Cripton, U. Berlemann and L.-P. Nolte

Cross bracing of Short segment posterior spinal fixators is thought to increase the stabilizing potential of the fixation construct, and may be indicated for extremely unstable spinal segments, e.g. resulting from burst fractures of a

vertebral body. The objective of this in vitro study was to quantify the additional stabilization achieved by cross-bracing fixators implanted in human lumbar spine segments.

Quasistatic lateral bending, flexion/extension and torsion moments of 10 Nm were applied to human L1-L3 specimens using a custom, pneumatic spine testing stand: moments were held steady for 30 sec after each step to minimize viscoelastic effects. Each specimen was initially tested in the "natural" configuration and then: in order, after fixator implantation and 1000 physiologic flexion/compression cycles, after cross-bracing, and after vertebrectomy of L2 with and without cross bracing. The resulting spinal kinematics were measured using a three-dimensional motion analysis system.

The fixator stabilized the intact specimen for every applied moment. The addition of the cross-brace, to the intact specimen had no significant effect on the measured kinematics. The vertebrectomy destabilized the specimens in all loading situations. The only statistically significant difference measured was in torsion: the average range of motion decreased 26 % from 23.6 to 17.4 deg. when the cross brace was attached.

Cross bracing may only be biomechanically beneficial for highly unstable spinal segments (e.g. burst fractures). However, clinically, additional anterior stabilizing procedures may be necessary in these cases.

New Means in Spinal Pedicle Hook Fixation - A Biomechanical Evaluation

U. Berlemann, P. Cripton, L.-P. Nolte, K. Lippuner and F. Schläpfer

Pedicle hooks which are used as an anchorage for posterior spinal instrumentation may be subjected to considerable three-dimensional forces. In order to achieve stronger attachment to the implantation site, hooks using screws for additional fixation have been developed. The failure loads and mechanisms of three such devices have been experimentally determined on human thoracic vertebrae: the Universal Spine System (USS) pedicle hook with screw, a prototype pedicle hook with two screws, and the CD pedicle hook with screw. The USS hooks use 3.2mm self-tapping fixation screws which pass into the pedicle, whereas the CD hook is stabilised with a 3mm set screw pressing against the superior part of the facet joint. A clinically established 5mm pedicle screw was tested for comparison. A matched pair experimental design was implemented to evaluate these implants in constrained (series I) and rotationally unconstrained (series II) posterior pull-out tests.

In the constrained tests the pedicle screw was the strongest implant with an average pull-out force of 1650 N (SD=658 N). The prototype hook was comparable with an average failure load of 1530 N (SD=414 N). The average pull-out force of the USS hook with one screw was 920 N (SD=279 N), not significantly different to the CD hook's average failure load of 740 N (SD=189 N).

The results of the unconstrained tests were similar with the prototype hook being the strongest device (average 1617 N, SD=652 N). However, in this series the difference in failure load between the USS hook with one screw and the CD hook was significant. Average failure loads of 792 N (SD=184 N) for the USS hook and 464 N (SD=279 N) for the CD hook were measured.

A pedicular fracture in the plane of the fixation screw was the most common failure mode for USS hooks. The hooks usually did not move from their site of implantation suggesting that they may be well-suited for the so-called segmental spinal correction technique as used in scoliosis surgery.

In contrast the CD hook disengaged by translating caudally from its site of implantation in all cases, suggesting a mechanical instability. The differences in observed hook failure modes may be a function of the type and number of additional fixation screws used.

These results suggest that additional screw fixation allows stable attachment of pedicle hooks to their implantation site. Hooks using additional fixation screws passing obliquely into the pedicle apparently provide the most rigid attachment. The second fixation screw of the prototype hook almost doubles the fixation strength. Thus, the prototype hook might be considered as an alternative to the pedicle screw, especially in the upper thoracic region.

Comparative in Vitro Testing of Fracture Treatment Concepts for Proximal Femur Fractures

P. Brunner, J. Bekic, A. Lustenberger and L.-P. Nolte

Due to increasing recognition of the role of interfragmentary motions in the understanding of fracture healing, measurement systems which allow the description of the six independent components of motion have been developed.

Based on the promising results of a static testing study of two AO implants for hip fracture fixation, the Dynamic Hip Screw (DHS) and a prototype

Spiral Blade System, a system to record the relative motion of fracture fragments and implant components has been developed. 25 cadaveric femora in which simulated fractures according to the AO-classification of fractures had been stabilized with the two different implant systems were subjected to cyclic long-term loading in a specially designed loading jig in a servohydraulic testing machine to mimic in vivo loading conditions.

Instrumentation of fracture fragments and device components, space digitization of anatomical and device landmarks allowed the definition of local coordinate systems lying on anatomical axis such as femoral shaft or neck axis and implant axis. Based on local rigid body concepts the evaluation of several clinical important parameters was possible: Varus angulation, rotational deformity in femoral shaft and neck axis, rotational instability of the implant in the proximal fragment, translational cutting out of the implant in the femoral head and proximal fragment impaction could be measured.

Biomechanical Evaluation of New Autogenous Cruciate Ligament Substitutes

L. Schatzmann, P. Brunner, L. Rincón, H.U. Stäubli and L.-P. Nolte

There is a need for an universally available autogenous cruciate ligament substitute of adequate mechanical strength in failed ACL reconstructions. The quadriceps tendon including a patellar bone block from the base of the patella was successfully used in the clinic but the structural and mechanical properties of the this tendon with respect to the patellar ligament have not been described. It was the aim of this study to investigate these properties in an advanced testing setup. The problem of soft tissue gripping in standard mechanical testing procedures was solved by use of a newly developed freezing technique. The new device allowed a secure fixation of the ends of the studied tendons and ligaments. Besides structural properties, such as ultimate load and deformation, the materials properties of the grafts were derived. A stereophotogrammetric technique to digitize and track surface markers on the specimens was developed for the measurement of strain and ultimate stress in different loading regimes.

A Newly Designed Clamp to Fasten Tendons in Tensile Tests

L. Schatzmann, P. Brunner, L. Rincón, H.U. Stäubli and L.-P. Nolte

Methodological difficulties presented in mechanical studies of isolated tendons are well known. Since the soft tissue is mainly composed of parallel-fibered collagen and water, it is not easy to fix this tissue to a loading device

without having slippage or failure at the jaw site when high clamping pressures are applied. However, a reliable technique made of two special-shaped aluminum jaws was developed. The two aluminum blocks which were cooled down by submerging them into liquid nitrogen, were fixed around the free end of the tendon, then water was poured in the space between the cryo-clamp and the tissue and an ice block that securely tightened the tendon was formed. This clamping method not only allowed a stable fixation without any slippage and rupture at the frozen end, but also prooved long term confidence and easy handling.

Three-Dimensional Motion of Femoral Prosthetic Stems: An in Vitro Evaluation of Novel Measuring Concept

D.W. Bühler, U. Berlemann and L.-P. Nolte

Primary stability of uncemented total hip replacements is regarded as a major factor necessary for good quality bony ongrowth to the prosthetic femoral stem and therefore for a successful long-term outcome. Micromovements as well as subsidence of the prosthesis should be considered under physiologic cyclic loading conditions. Most of the existing measurement techniques, e.g. based on micrometers, extensiometers, LVDTs, and/or strain gauges, provide information about only one component of the three-dimensional (3D) motion at the bone-implant interface. Furthermore, fixation of sensors away from the point of interface motion measurement, as seen in various studies, may result in the registration of motions due to elastic deformation of the femoral or prosthetic shaft in addition to the interface motion.

The objective of this study was to develop, validate, and apply a new technique which allows the precise measurement of the isolated 3D interface motion at three different points along the femoral shaft.

The measuring technique is based on a sensor combining optoelectronic with precision mechanical components. Spherical measuring tips of three sensors were placed on the prosthesis at predefined locations: the distal tip of the prosthesis and at the middle and proximal third of the femoral stem. The sensors are mounted on an adapter unit which is anchored in a transverse 9 mm hole drilled in the cortex. Precision, play-free, ball bearing mechanisms allowed transition of the detected motion to a laser diode on the opposite end of the sensor. Photons emitted by this LED were registered by a silicon position sensitive detector (PSD). 3D motion analysis was made possible by considering photon direction data of the PSD as well as the registered light intensity. Thermistors were also integrated to exclude thermodrifts during long-term testing. Custom software allowed for real-time, graphical display of

the applied forces and the detected movements. Static and dynamic validation indicated that the maximum system error was ±4 microns within a measuring range of ±0.75 mm in each spatial orientation.

Seven paired fresh cadaveric femora were used for testing two different types of uncemented femoral stems: CLS stem (Spotorno) and Cone prosthesis (Wagner; both Protek AG, Switzerland). Using a custom loading rig the femora were subjected to sinusoidal cyclic loading in a bi-axial materials testing machine. A cranio-caudal force Fcc was combined with an antero-posterior force Fap having a magnitude of 10% of Fcc. Loading steps of 1-, 2-, 3-times body weight (BW) were applied.

Considerable differences in the micro- and macro-stability of the two prosthesis types could be detected. The micromovemets of the Cone prosthesis in its distal portion showed a significantly smaller amplitude in all three spatial orientations indicating larger micro-stability compared to the CLS prosthesis. However, proximally the CLS prosthesis appeared more stable reflecting its concept of metaphyseal wedging. Both prostheses showed relative macro-stability under the 1- to 3-fold BW loading. However, the 4-fold BW caused a considerably increased subsidence. This was mainly detected for the Cone prosthesis indicating less macro-stability as the longitudinal ribs along the shaft cut into the inner femoral cortex.

Our novel technique provided repeatable and accurate data illustrating the 3D interface motion of uncemented femoral stems. The measured elastic deformation of the bone illustrates the fact that neither the bone nor prosthetic stem can be assumed perfectly rigid. Furthermore it is necessary to measure the stability of the prosthesis at several points in all three directions of the coordinate system to account for the 3D motion behavior of the implant with respect to the surrounding bone.

The two prostheses investigated in this study showed considerable differences in both their motion amplitude and total motion behavior. This reflects differences in their anchoring design.

Analysis of different concepts of femoral stem fixation with the presented standardized approach may further elucidate the role of primary stability in successful long-term clinical outcomes.

In-Vivo Measurement of Forces and Moments during the Periacetabular Osteotomy

D. Bühler and L.-P. Nolte

Periacetabular osteotomy is a method of acetabuloplasty in which complete cuts are made around the acetabulum and the entire isolated fragment is rotated to assure sufficient coverage of the femoral head. This extraarticular circumferential osteotomy of the acetabulum corrects the dysplastic acetabulum and displaced position of the femoral head at the same time with the expectation of a return to nearly normal hip alignment. There exist several operation reconstruction techniques which main differences are the location and number of cuts that are used to reorientate the acetabulum. A major question is if the forces and moment which are used to rotate the acetabulum are the same using different operation methods.

A special tool including a costume loadcell was designed to enable the in-vivo measurement of forces and moments during the osteotomy. The design of the costume 6-axial loadcell was based on a finite element study which allowed to detect forces and moments in all three spatial orientations at the same time. First test measurements on calibration stand showed good results, so that now in a second phase the tool can be use during the osteotomy.

Experimental and Mathematical Modeling of the Viscoelastic Behavior of the Human Spine under Shear Loading

H. Visarius and L.-P. Nolte

Besides a general lack of a proper definition of spinal instability a scarcity of data exists particularly for the shear loading of functional spinal units. The purpose of this research was to elucidate the response of the human lumbar spine to direct shear loading in a quasi-static, dynamic, and destructive loading scenario. The data obtained testing seventeen single-level human lumbar spines assisted in the determination of human tolerances towards shear loading and was compared with the response of the lumbar spine of the current standard anthropomorphic test device for automotive car crash research, the Hybrid III dummy.

Special attention was devoted to the loading rate sensitivity of the biomechanical response and the relation between failure modes and variations in the testing setup.

In order to both, complement and reinforce each other, the experimental results were used as a database for the derivation and validation of a general, closed-form solution of the hereditary integral in the quasi-linear viscoelastic theory. Using a logarithmic relaxation model and an arbitrary polynomial elastic response the nonlinear viscoelastic model was established. In order to

enhance the model, the effects of a finite loading ramp in the relaxation test and the influence of the relaxation on the elastic response test were corrected by an extrapolation deconvolution technique.

For the human functional spinal unit a higher shear stiffness in the anterior direction was found in the quasi-static tests as well as in the dynamic test series. This finding is assumingly related to increasing contact stresses in the facet joint interface in the anterior load direction. The specimens showed a dependency on the loading rate in the dynamic and the destructive tests. This resulted in increasing peak loads and energy dissipation for higher loading rates reflected by the hysteresis loop. The new analytical solution of the hereditary integral of the quasi-linear viscoelastic theory was applied to the data and succeeded in the prediction of high speed experiments.

Human tolerances towards shear as revealed by the destructive tests indicated a dependency of failure modes and the failure loads on the constraints imposed by the testing setup. The failure modes observed and the intradiscal pressures measured point to possible soft tissue injuries at human tolerance loading levels which might result into longterm instability even after hard tissue recovery.

2.2 Tissue Biomechanics and Structural Biology

The main research activities in this team are directed towards elucidating the structural and functional properties of skeletal tissues. Experimental methodology involves both in vitro and in vivo systems, cartilage and bone being the principal tissues being investigated. Current topics being dealt with include an analysis of the mechanical properties and structural composition/organization of growth- and articular cartilage, as well as investigations relating to the basic physiological mechanisms underlying differentiation and activity regulation processes. With respect to bone, studies pertain to mechanisms of induction and accompanying processes, such as angiogenesis and basement membrane formation. These projects are undertaken with a view to developing new strategies for the treatment of traumatized or diseased cartilage and bone. The following abstracts are derived from completed and published studies.

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(EBH: bitte eigene Abstracts noch einfügen)

Mechanical compression modulates matrix biosynthesis in chondrocyte/agarose culture

M.D. Buschmann, Y.A. Gluzband, A.J. Grodzinsky and E.B. Hunziker

This study focuses on the effect of static and dynamic mechanical compression on the biosynthetic activity of chondrocytes cultured within agarose gel. Chondrocytes/agarose disks (3 mm diameter) were placed between impermeable platens and subjected to uniaxial unconfined compression at various times in culture (2-43 days). [^{35}S]sulfate und [^{3}H]proline radiolabel incorporation were used as measures of proteoglycan and protein synthesis, respectively. Graded levels of static compression (up to 50%) produced little or no change in biosynthesis at very early times, but resulted in significant decreases in synthesis with increasing compression amplitude at later times in culture; the latter observation was qualitatively similar to that seen in intact cartilage explants. Dynamic compression of ~3% dynamic strain amplitude (•30 µm displacement amplitude) at 0.01-1.0 Hz, superimposed on a static offset compression, stimulated radiolabel incorporation by an amount that increased with time in culture prior to loading as more matrix was deposited around and near the cells. This stimulation was also similar to that observed in cartilage explants. The presence of greater matrix content at later times in culture also created differences in biosynthetic response at the center versus near the periphery of the 3mm chondrocyte/agarose disks. The fact that chondrocyte response to static compression was significantly affected by the presence or absence of matrix, as were the physical properties of the disks, suggested that cell-matrix interactions (e.g. mechanical and/or receptor mediated) and extracellular physicochemical effects (increased [Na^+], reduced pH) may be more important than matrix-independent cell deformation and transport limitations in determining the biosynthetic response to static compression. For dynamic compression, fluid flow, streaming potentials, and cell-matrix interactions appeared to be more significant as stimuli than the small increase in fluid pressure, altered molecular transport, and matrix-independent cell deformation. The qualitative similarity in the biosynthetic response to mechanical compression of chondrocytes cultured in agarose gel and chondrocytes in intact cartilage further indicates that gel culture preserves certain physiological features of chondrocyte behavior and can be used to investigate chondrocyte response to physical and chemical stimuli in a controlled manner.

Limits and Potential of High Pressure Freezing

D. Studer, M. Michel, E.B. Hunziker and M. Buschmann

High pressure freezing of biological material was first implemented about 25 years ago by Riehle and Moor and, to date, it is the only approach available to cryoimmobilise bulky tissue samples adequately. Vitrification represents the ideal solidification state of water in cryoimmobilised samples, since its liquid nature is retained and the distortive influences attributable to ice crystal formation and growth are avoided. Until recently, the practical means for confirming vitrification have not been available, and it was merely assumed to have occurred if no segregation patterns were observed in freeze-fractured or freeze-substituted samples. On the basis of these findings, it was claimed that a cooling rate of several hundred degrees K/sec was sufficient to completely vitrify a 600 µm thick biological specimen under high pressure conditions. That vitrification actually takes place under these conditions has never been verified. The technology for assessing vitrification in biological tissue is now available, and we have re-evaluated high pressure freezing from both a theoretical and practical standpoint. We calculated the freezing rate profiles through samples as a function of their thickness and superficial cooling rate. We also determined the depth to which bovine articular cartilage specimens could be vitrified using an improved high pressure freezing apparatus.

The theoretical freezing rate of an aqueous sample 600 µm thick is limited to about 500K/sec, irrespective of whether the cooling rate achieved at the surface is 5000K/sec or infinitely high; only the initial 90 µm-layer from each surface is influenced by the latter. Hence, no improvement in the efficiency of a high pressure freezing apparatus will be of avail in completely vitrifying a 600 µm-thick specimen. The situation changes dramatically when considering thinner aqueous layers. For a 200 µm-thick sample, a cooling rate of 5000K/sec at the surface (the maximum possible with a Balzers high pressure freezing machine) will yield one of 4000K/sec at the centre. With the Reichert HPF, a superficial cooling rate of 10000K/sec may be achieved, and this results in a cooling rate of 5000K/sec at the sample centre; an increase in superficial cooling rate above 10000K/sec would not improve cooling rate at the centre. Optimal cryoimmobilisation at the centre of a 100µm-thick specimen would require a superficial cooling rate of about 30-40000 K/sec.

Using the Reichert HPF, we were able to completely vitrify the lower radial zone of bovine articular cartilage throughout the entire thickness of a 150µm section on a reproducible basis, as assessed by electron diffraction analysis of frozen hydrated specimens. Analysis of the upper

radial zone, however, disclosed the presence of hexagonal ice crystals through a large portion of the sample thickness, although morphological inspection of freeze-substituted specimens revealed an apparently optimal situation. These differential results indicate that it is the intrinsic tissue properties which determine the cooling rate required for vitrification, and that efforts to further improve cooling rates and decrease specimen thickness will be of avail in future.

Vitrified Mature Bovine Articular Cartilage Extracellular Matrix Reveals a Dual, Fibrillar and Filamentous, Network in a Fine-Granular Proteoglycan-Rich Interfibrillar Substance

M. Michel, E.B. Hunziker, J. Wagner and D. Studer

Mature bovine articular cartilage tissue blocks were cryopreserved by a Leica EM HPF high pressure freezer. The freezing outcome was systematically evaluated by electron diffraction analysis of frozen-hydrated ultrathin cryosections, and the results obtained compared with those based upon morphological inspection of freeze-substituted, Epon embedded ultrathin sections. The freezing quality achieved varied as a function of the articular cartilage zones from the surface to the calcified cartilage layer. The lower -, and occasionally the upper radial zone, were optimally frozen (vitrified) within the entire 150 µm-thickness of the tissue discs. The transitional and superficial zones were, however, in most instances vitrified only along a surface layer ~ 5 - 50 µm in thickness. The different vitrification depths achievable in the various zones correlated proportionally with proteoglycan content, and inversely with water content.

The substantial improvement of the extracellular matrix preservation quality of vitrified articular cartilage allowed the identification of several novel ultrastructural features in comparison with previous results. The extracellular matrix proteoglycan organization within the vitrified layers appeared as a densely stained, fine granular matrix. This contained the well-known collagen fibrous network, consisting of thin (upper zones) and thick (lower zones) fibrils (~ 60 - 100 nm). A novel, extremely thin (~ 15 nm) filamentous network was additionally revealed in the lower radial zone. All types of fibrils exhibited a clear perifibrillar halo. In addition, contrary to the currently accepted concept of cartilage matrix compartment organization, a relative non-uniformity in structural appearance of the pericellular matrix compartment was observed. This was previously believed to be a fibrillar free

compartment. It exhibited in many instances cross-banded fibrils as well as fine filaments, hitherto not described in the literature.

Optical and Mechanical Determination of Poisson's Ratio of Adult Bovine Humeral Articular Cartilage

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

Equilibrium response of the articular cartilage to mechanical loading is controlled by the elastic properties of the tissue matrix. Unfortunately, the derivation of both (isotropic) Young's modulus, E_S, and Poisson's ratio, n_S, from a single mechanical test is complex or may be even impossible. Therefore, a novel optical (microscopic) method was developed for visualization of the behavior of the cylindrical bovine humeral cartilage disk (n=9) while immersed in physiological solution and compressed in unconfined geometry. The method allowed the *direct* calculation of Poisson's ratio of the tissue at equilibrium, but also made possible characterization of the shape changes of the sample during the nonequilibrium dynamic phase. In addition to optical analyses, equilibrium responses of unconfined and confined ramp-stress relaxation tests were measured and compared to obtain aggregate modulus, H_a, Young's modulus and, *indirectly*, Poisson's ratio for the bovine humeral cartilage matrix. The mean value for Poisson's ratio obtained from the optical analysis was 0.185$\pm$0.065. The values for elastic parameters obtained from the mechanical tests were 0.744$\pm$0.201 MPa, 0.673$\pm$0.224 MPa and 0.168$\pm$0.105 for H_a, E_S, and n_S, respectively. The similar n_S-values obtained with optical and mechanical techniques imply that, at equilibrium, for these two tests, the isotropic model is acceptable for mechanical analysis. However, the microscopic technique revealed that the lateral expansion, especially during the initial phase of relaxation, was inhomogeneous through the tissue depth. The superficial cartilage zone expanded less than the transitional, and particularly less than the radial zone. The zonal differences in the expansion pattern were attributed to the known zonal differences in the fibrillar collagen architecture.

Comparison of Optical, Needle Probe and Ultrasonic Methods for the Determination of Articular Cartilage Thickness

J. S. Jurvelin, T. Räsänen, P. Kolmonen and T. Lyyra

The accurate determination of tissue thickness is essential for the analysis of mechanical properties of articular cartilage. To evaluate the suitability of different methods for thickness measurements thickness of bovine and canine

knee articular cartilage (n=81) was determined with optical, needle probe and ultrasonic techniques. Using a commercial A-mode ultrasound device with a 10 MHz transducer, the time interval for the echoes arising from articular surface and tidemark was measured and used for calculation of thickness of uncalcified cartilage. After ultrasound measurement the specimen was positioned under a needle probe attached to a material testing device. The load cell of the device sensed the moments when the needle contacted surface and tidemark while penetrating the tissue, and made it possible to calculate the thickness from the displacement signal. Finally, thickness was measured with a stereomicroscope from the slice sawn across the test site. The results obtained with the stereomicroscope and the needle probe showed high, linear correlations ($r=0.97$, $n=81$). The thickness obtained optically (0.85 ± 0.34 mm, Mean$\pm$SD) was, however, significantly lower ($p<0.01$, paired t-test) than the thickness (0.89 ± 0.36 mm) obtained with the needle. The mean difference between optical and ultrasonic measurements was 0.032 ± 0.164 mm ($n=45$). The high scatter between optical and ultrasonic thickness, considered to be due to complex measurement geometry of canine knee articular cartilage, invalidated the use of our ultrasonic device for thickness measurements. It is concluded that the scatter in measured thickness values, which is transferred to calculations of mechanical parameters, is one of the important sources of variation in the measurement of mechanical properties of articular cartilage.

Indentation Instrument for the Measurement of Cartilage Stiffness under Arthroscopic Control

T. Lyyra, J. Jurvelin, P. Pitkänen, U. Väätäinen and I. Kiviranta

Changes in the biomechanical properties of articular cartilage are one of the first signs of tissue degeneration. Typical to the chondromalacia of the patella is tissue softening, which can later lead to fibrillation or even partial disappearance of the cartilage. During arthroscopy fibrillation of cartilage surface can be observed visually, but at the moment there is no objective measurement technique for determination of cartilage stiffness, except palpating cartilage surface with a blunt probe. We have developed an indentation instrument for the quantitation of cartilage stiffness under arthroscopic control. The instrument consists of a measurement rod joined to a handle. In the distal end of the rod there is an inclined flat surface with cylindrical, plane-ended indenter (dia. 1.3 mm, length 150 mm) in the center. During measurement the flat surface is pressed against cartilage surface, while the indenter imposes a constant deformation of the tissue. The indenter force, by which cartilage resists this deformation, is an indicator of the tissue stiffness. The instrument is washable, sterilizable and fulfills the IEC safety orders for medical instruments.The instrument has been tested in laboratory

conditions with elastomer and cadaver knee joint cartilage samples. A linear relationship (r=0.990, n=14) was found between the indenter force and elastomer stiffness given by the manufacturer. Cartilage stiffness of three human cadaver knee joints at several test sites (n=22) was measured under arthroscopic control. At 16 test sites measurements were repeated to evaluate the reproducibility of the measurements. A linear relationship (r=0.953) was found between the two measurements. After arthroscopic measurements osteochondral samples taken from the same test sites were measured with a material testing device to determine the shear modulus of articular cartilage. The correlation between arthroscopic indenter force and shear modulus obtained from reference measurements was linear (r=0.879, n=22). Quantitative detection of cartilage stiffness is possible with the instrument.

2.3 Cell- and Molecular Biomechanics

The main research activities of this team are directed towards elucidating the composition and functional properties of skeletal tissue elements on a cellular and molecular level. Experimental methodology involves principally in vitro systems, cartilage and connective tissues being the principle tissues investigated. Current topics dealt with include the analysis of structural and functional properties of elements of adult human articular cartilage as well as foetal cartilages and loose connective tissues. New extracellular molecular elements, involved mainly in mechanical and/or adhesional cell and tissue functions or differentiation and growth processes are identified, characterized and their functions investigated.

Characterization of COMP (Cartilage Oligomeric Matrix Protein) from Human Sources and Demonstration of its Presence in Tendon

P. DiCesare, N. Hauser and M. Paulsson

With the aim of exploring the potential of COMP release as a marker for cartilage degeneration we isolated the protein from human sources. This required a modified purification procedure but yielded a protein which is in all major features similar to COMP from bovine and rodent cartilage. An antiserum was raised against the human COMP which will now allow us to establish ELISA assays for COMP in synovial fluid and serum of patients with rheumatic disease. Immunohistochemical studies showed that while COMP is pericellular in young cartilage it is mainly present in the extraterritorial matrix in adults. More detailed studies of its distribution revealed it to be present in tendon in addition to in cartilage. Tendon fibroblasts may show a biosynthetic repertoire similar to that of chondrocytes

and this fact has to be considered when release of "cartilage-specific" proteins is used to study cartilage matrix metabolism.

Interactions of CMP (Cartilage Matrix Protein)

N. Hauser, M. Mörgelin and M. Paulsson

Our previous studies have led to a structural model for CMP. To understand its biological role we have attempted to identify interaction partners in cartilage matrix. Contrary to previous reports we were unable to demonstrate any CMP associated with cartilage collagen fibrils. On the other hand, abundant amounts of CMP were found associated with cartilage proteoglycans. The pool of proteoglycan-bound CMP increases with aging of the animal. The association is with the proteoglycan core protein and not with the glycosaminoglycan chains. While some of the CMP may be dissociated from the core protein by denaturing solvents, some resist dissociation even by reduction in the presence of denaturants. Further studies will be directed at the detailed characterization of the interaction and analysis of its consequences for the physical properties of the proteoglycan aggregate.

Interactions of Kidney Laminin with Cellular Receptors

G.O. Delwel, A. Sonnenberg, E. Forsberg, S. Johansson, R. Perris, A. Lindblom and M. Paulsson

The novel laminin isoform from kidney was assayed for biological activity in a number of different cellular systems. In all systems it was shown to mediate a stronger cell attachment than most laminins. This strong binding is in part due to that it interacts not only with integrin $\alpha 6\beta 1$, as most laminins, but also with integrin $\alpha 3\beta 1$. Studies with primary hepatocytes also indicated an interaction with a not yet identified integrin which is not of the $\beta 1$ class. The finding that laminin isoforms differ significantly in their affinity for different integrin receptors is a breakthrough in the understanding of the diversity of the laminin family. Expression of a given laminin variant in a certain tissue and time of development may be a specific cue for cellular behaviour.

Osteonectin is a Major Glutaminyl Substrate for Transglutaminase-catalyzed Cross-linking in Cartilage Matrix

D. Aeschlimann, O. Kaupp and M. Paulsson

the expression of tissue transglutaminase in skeletal tissues is strictly regulated and correlates with chondrocyte differentiation and cartilage calcification in endochondral bone formation and in maturation of tracheal cartilage. We now demonstrate the transglutaminase reaction product, the γ-glutamyl-ε-lysine cross-link, in the matrix of hypertrophic cartilage using a novel cross-link specific antibody. Incorporation of the synthetic transglutaminase substrate monodansylcadaverine (amine donor) in cultured tracheal explants reveals enzyme activity in the pericellular matrix of hypertrophic chondrocytes in the central, calcifying areas of the cartilage rings. One predominant glutaminyl substrate (amine acceptor) in the chondrocyte matrix is osteonectin as revealed by incorporation of the dansyl-label in culture. Indeed, non-reducible osteonectin-containing complexes of ~65 kDa, 90 kDa and 175 kDa can be extracted from mature tracheal cartilage. *In vitro* cross-linking of osteonectin by tissue transglutaminase gives similar products of ~90 kDa and 175 kDa, indicating that the complexes in cartilage represent osteonectin oligomers. The demonstration of extracellular transglutaminase activity in differentiating cartilage, i.e. cross-linking of osteonectin *in situ,* shows that tissue transglutaminase-catalyzed cross-linking is a physiological mechanism for cartilage matrix stabilization.

Nitric Oxide and Proteoglycan Biosynthesis by Human Articular Chondrocytes in Alginate Culture

H.J. Häuselmann, L. Oppliger, B.A. Michel, M. Stefanovic-Racic and C.H. Evans

Interleukin-1a and ß induced the production of large amounts of nitric oxide by normal, human articular chondrocytes in alginate culture; at the same time the biosynthesis of proteoglycan was strongly suppressed. In a dose-dependent manner, N^G-monomethyl-L-arginine both inhibited nitric oxide formation and relieved the suppression of proteoglycan synthesis. However concentrations of N^G-monomethyl-L-arginine which completely prevented nitric oxide production only partially restored proteoglycan biosynthesis, even at low doses of interleukin-1 where suppression of proteoglycan synthesis was modest. The organic donor of nitric oxide, S-nitrosyl-acetyl-D,L-penicillamine also inhibited proteoglycan biosynthesis, but not as extensively as interleukin-1. These data suggest that interleukin-1 suppresses synthesis of the cartilaginous matrix through more than one mechanism, at least one of which is dependent upon the production of nitric oxide.

New Evidence for Cytokine-Related Metabolic Differences in Human and Bovine Chondrocytes from Superficial and Deep Zones of Articular Cartilage

H.J. Häuselmann, J. Flechtenmacher, L. Michal, M. Shinmei, K.E. Kuettner and M.B. Aydelotte

Objective: To examine metabolic differences induced by interleukin-1 (IL-1), its different affinities and binding sites for IL-1 and its inhibitor interleukin-1 receptor antagonistic protein (IRAP) in various layers of normal human articular cartilage.

Methods: Superficial and deeper layers of articular cartilage from normal human knee joints were treated with hrIL-1 with or without IRAP. Proteoglycan synthesis and breakdown were measured using ^{35}S precursors, stromelysin and TIMP-1 were measured using commercially available ELISA kits. Binding studies with ^{125}I-IL-1 were performed on chondrocytes cultured in alginate, a novel three dimensional culture system.

Results: Chondrocytes of the most superficial zone showed greater responsiveness to IL-1 and a significantly lower ratio of TIMP-1/stromelysin compared with the deeper layers. IRAP was less effective in blocking responses to IL-1 and only partially restored the normal ratio between TIMP-1 and stromelysin in superficial while fully protecting the deep cartilage. Results of binding studies with ^{125}I-IL-1, revealed a double amount of high affinity binding sites for IL-1ß in superficial chondrocytes.

Conclusion: We demonstrate for the first time that human chondrocytes from the articular surface express more binding sites for IL-1 and are significantly more vulnerable to this cytokine than cells from the deeper layers. In addition the present study provides evdience of two classes of binding sites which differ 20-30 fold with regard to their affinity for IL-1ß in human articular chondrocytes from both superficial and deep zones.

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4 RESEARCH PROJECT GRANTS

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Jurvelin J., Hunziker E.B., and Aebi U.: The use of atomic force microscopy in the study of cartilage matrix mechanical properties. MIH-/MIB-Fellowship. M.E. Müller Foundation, Bern. 1.10.1993 - 30.9.1995

Paulsson M.: Structure and biological activity of extracellular matrix proteins. Swiss National Science Foundation, Bern. 1.10.1991 - 31.9.1994

Wong M.: Mechanical regulation of chondrocyte morphology. National Institutes of Health, Bethesda, Maryland, USA/Swiss National Science Foundation, Bern. 1.2.1993 - 31.1.1994

Wong M.: The Effect of Dynamic Mechanical Loading on Gene Expression and Biosynthesis in Adult Articular Cartilage. Swiss National Science Foundation, Bern. 1.10.1994 - 30.9.1996

5 TEACHING ACTIVITIES

(ALTE VERSION: EBH FRAGEN)

Lectures for students of human, dental and veterinary medicine of the University of Bern in the framework of the following coordinated lecture series:

- 4011: Coordinated lecture series in physics, chemistry, embryology, ecology, genetics, molecular biology, anatomy and psychology, as well as an introduction to the Swiss public health system
- 4021: Coordinated lecture series in biochemistry, morphology, physiology and psychology
- 4031: Clinical-theoretical course on the locomotor apparatus

Participation in practical exercises for students of human and dental medicine:

- 4013: Histology course
- Pathology: Block teaching for the fourth year medical students

Lecture series at the Biocenter in Basel, University of Basel:

- 2437: New literature in extracellular matrix biology
- 5392: Extracellular matrix molecules and their receptors.

Participation in hip courses for orthopaedic surgeons; seminars and colloquia within the postgraduate training program.

Doctoral students: E. Arm, J. Bekic, D. Bühler, P. Cripton, N. Hauser, F. Langlotz, and A.M. Maurer

6 DISSERTATIONS AND FELLOWSHIPS

Dateien noch ausstehend: EBH (Alte Version)

6.1 Dissertations Completed

Aeschlimann, D.: Tissue transglutaminase: A physiological role in cross-linking of extracellular matrix components (Faculty of Natural Sciences, University of Basel)

6.2 Fellowships

Buschmann M.D.: Postdoctoral fellowship of the Medical Research Council of Canada

Jurvelin J.: Postdoctoral fellowship of the M.E. Müller Foundation, Bern, Switzerland

Wong M.: Combined postdoctoral fellowship between the Swiss National Science Foundation, Bern and the National Institutes of Health, Washington

7 HONORS

PD Dr. Mats Paulsson was nominated Professor (nebenamtlicher Extraordinarius) for molecular biomechanics by the Bernese Government in March 1994.

8 GUEST PRESENTATIONS AT THE MIB

13.01. - Evans C.: Nitric Oxid and Cartilage Metabolism. University of Pittsburgh, Ferguson Laboratory for Orthopaedic Research, U.S.A.

04.02. - Archer C.W.: Development of Synovial Joints. Department of Anatomy, University of Wales College of Cardiff, Cardiff, U.K.

01.06. - Niederer P.F.: Forensische Biomechanik. ETH Zentrum, Institut für biomedizinische Technik.

08.07. - King A.I.: Research in Low Back Pain and Trauma Biomechanics. Bioengineering Center, Wayne State University, Detroit, U.S.A.

05.08. - Baumgart F.: Heat generation caused by instruments and implants in bone surgery. Davos.

05.08. - Baumgart F.: The Technical Commission of the AO. Davos.

18.08. - Farnum C.: Form, fate and function of the hypertrophic chondrocyte. College of Veterinary Medicine, Dept. of Anatomy, Cornell University, Ithaca, New York, U.S.A.

31.08. - Jacob H.: On the biomechanics of the forefoot. Balgrist Klinik, Zürich.

24.10. - Messner K.: The use of synthetic materials for repair of full-thickness cartilage defects in the rabbit knee joint. Dept. of Orthopaedic Surgery, University Hospital, Linköping, Sweden.

02.11. - Brinckmann P.: Shape of lumbar vertebrae and disks, A project to quantify overload damage in persons exposed to heavy physical exertions or whole-body vibration. Institut für Experimentelle Biomechanik, Westfälische Wilhelmsuniversität, Münster, BRD.

06.12. - Häuselmann H.J.: Progress Report. M.E. Müller-Institut für Biomechanik.

16.12. - Paulsson M.: Outlook. M.E. Müller-Institut für Biomechanik.

20.12. - Wallimann T.: Subcellular localization, structure and function of creatine kinase isoenzymes - the phosphocreatine shuttle concept. Institut für Zellbiologie, ETH, Zürich.

9 PERSONNEL

(Frau Gnahoré fragen)

9.1 Faculty

Hunziker Ernst B., M.D., Prof.	Director		11.89 -
	* * *		
Paulsson Mats E., M.D., PD	Deputy Division Head		10.90 -
Nolte Lutz-Peter, Ph.D.	Division Head		05.93 -
	* * *		
Studer Daniel, Ph.D.	Research Group Head		03.92 -
Häuselmann Hans Jörg., M.D.	Research Group Head (External Funding)		10.93 -
Visarius Heiko, Dr. Ing.	Research Group Head		02.94

9.2 Research Associates

Aeschlimann Daniel, Ph.D.	Ph.D.-Student / Assistant		10.90 - 08.94
Arm Erich, dipl.Ing. ETH	Ph.D.-Student		09.93 -
Berlemann Ulrich, M.D.	Assistant		07.93 - 12.94
Brunner Peter, dipl.Ing. ETH	Assistant		06.91 -
Bühler Daniel, dipl.Ing.	Ph.D.-Student		08.93 -
Buschmann Michael, Ph.D.	Fellow		05.93 - 05.94
Cripton Peter, B.Sc., M.Sc.	Ph.D.-Student		11.93 -
Frei Hanspeter, Dipl. Ing. HTL	Assistant		05.94 -
Gong Jianxing, Ph.D.	Assistant		07.94 -
Haralamb Sorin, Dipl. Ing. HTL	Assistant		10.94 -
Hauser Niklaus, dipl.Biol.	Ph.D.-Student		03.92 -
Jurvelin Jukka, Ph.D.	Fellow		09.93 -
Langlotz Frank, dipl.Ing.	Ph.D.-Student		05.93 -
Maurer Anne Marie, B.Sc., M.Sc.	Ph.D.-Student		05.93 -
Michel Martin, Ph.D.	Assistant	80 %	04.93 -
Noachas Gabriel, M.Sc.	Exchange Student		10.93 - 07.94
Rincon Liliana, Dipl. Ing.	Exchange Student		09.94 -
Scheer Carten, Dipl. Ing.	Assistant		09.94 -
Schmitz Andreas	Guest Student		09.93 - 02.94

Tobler Markus	Assistant	65 %	08.94 -
Wong Marcy, Ph.D.	Assistant	60 %	02.92 -

9.3 Technical and Administrative Staff

Berger Elke	Res. Technologist	50 %	01.90 -
Finsterwald Karin	Res. Technologist		09.93 -
Gnahoré Esther	Secretary	50 %	12.90 -
Hutzli Walter	Aid Lab. Technician		11.89 -
Kapfinger Eva	Res. Technologist	75 %	11.89 -
Kaupp Oliver	Res. Technologist		11.90 - 12.94
KauppTanja	Res. Technologist		11.89 -
Marsh Tracey	Res. Technologist		04.92 - 06.94
Mühlheim Erland	Mechanician	50 %	01.92 -
Oppliger Elisabeth	Res. Technologist		11.93 -
Rickli Verena	Secretary	90 %	03.90 -
Rohrer Urs	Head Mech. Workshop		07.91 -
Wagner Jeannine	Res. Technologist	80 %	11.89 -

9.4 Guest Scientists

- Dr. Zsuzsa Bösze, Institute for Animal Sciences, Agricultural Biotechnology Center, Gödöllö, Hungary
- Dr. Matthias Mörgelin, Department of Medical and Physiological Chemistry, University of Lund, Sweden
- Prof. Dr. Robert K. Schenk, Institute for Pathophysiology, University of Bern, Switzerland
- H. Frey, M. Meyer, C. Miescher and M. Schneider, Ingenieurschule Bern, Switzerland
- P. Zysset, Technical University of Lausanne, Switzerland

Neue Daten 1994:

- Dr. Cornelia E. Farnum, Deptartment of Anatomy, New York State College of Veterinary Medicine, Cornell University, New York, USA

10 MEMBERS OF THE MIB FOUNDATION BOARD

- Prof. M.E. Müller (President), M.E. Müller Foundation, Bern
- Prof. H. Fleisch, Institute of Pathophysiology, University of Bern, Bern
- Prof. R. Ganz, Department of Orthopaedic Surgery, University of Bern, Inselspital, Bern
- Mr. U.G. Jann, AO-/ASIF-Foundation, Davos

- Dr. M. Keller, Faulensee, Bern
- Prof. E.R. Weibel (Secretary and Vice President), M.E. Müller Foundation, Bern