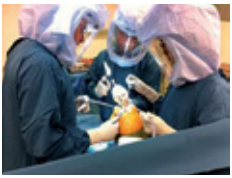
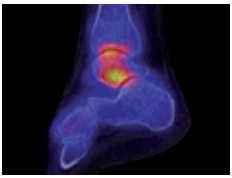
University Hospital Basel

# OSTEO ARTHRITIS RESEARCH CENTER BASEL

*– Innovation for you –*

University Hospital
University of Basel, Switzerland





# Contents

Prof. Dr. Dr. Victor Valderrabano

PD Dr. Dr. Thomas Hügle

**Dear Ladies and Gentlemen,**

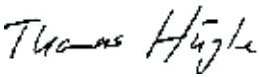
Osteoarthritis is the most common form of joint disease and leading cause of disability among people aged over 65. However, you can get this disease at any stage in your life, for instance after a serious sports or work injury. Regrettably, the disease is incurable and only symptoms can be treated. As a consequence, billions of Swiss francs are spent on management and care of osteoarthritis.

The Osteoarthritis Research Center at the University Hospital Basel was founded in 2005 by Prof. Victor Valderrabano, bringing together experts from different scientific and clinical disciplines to conduct high quality osteoarthritis research. Following our motto: "Innovation for you", we pursue translational research with the ultimate goal to significantly improve patient care.

Using state-of-the-art research facilities we focus on improving therapies, prevention, quality of life, diagnostics, long-term outcome, and also our understanding of the biomechanical and biomolecular mechanisms of osteoarthritis development and progression. Our professionals participate in patient education & counselling, academic teaching, scientific conferences and, most importantly, patient care from prevention to end-stage disease.

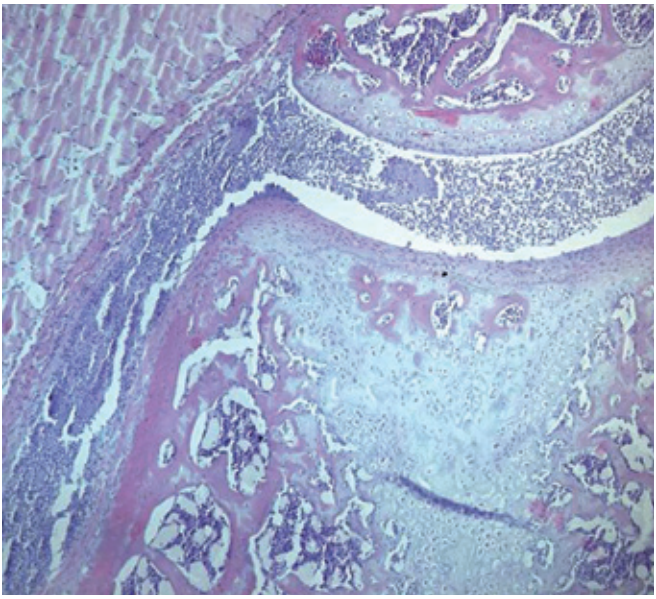
With this brochure, we would like to invite you on a short but exciting journey through the research activities at our center. Please share our enthusiasm on this fascinating topic!

Sincerely yours,



Prof. Dr. Dr. Victor Valderrabano
(Chairman)

PD Dr. Dr. Thomas Hügle
(Head of Research)



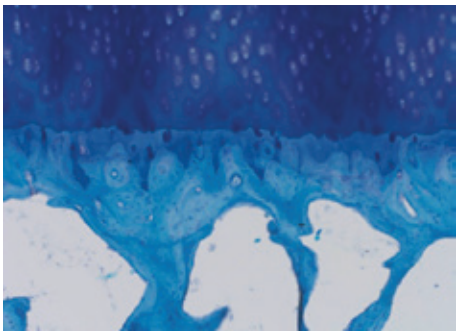
Inflammatory cell infiltrate in arthritis

# Osteoimmunology

**“When healing turns into hurting”**

Inflammation is our body´s protective response against tissue injury. A specialized set of immune cells enters the affected tissue and removes damaging organisms or molecules. Normally, inflammation resolves after the tissue is restored. Instead, if inflammation is sustained and becomes chronic, this ally turns into an enemy and promotes tissue destruction. Inflammation is a well-recognized, but incompletely understood phenomenon in osteoarthritis. Immune cells are frequently found in synovial and subchondral bone tissue, where they induce an inflammatory reaction in the tissue´s own cells.

At the biomolecular laboratory of the Osteoarthritis Research Center, we try to understand the interaction between immune cells and the cells that build bone, nerves and blood vessels. Our research combines clinically relevant specimens with innovative imaging and molecular biology approaches. The ultimate goal is to develop an urgently needed disease-modifying treatment for osteoarthritis based on a targeting with the ever-growing arsenal of anti-inflammatory compounds.



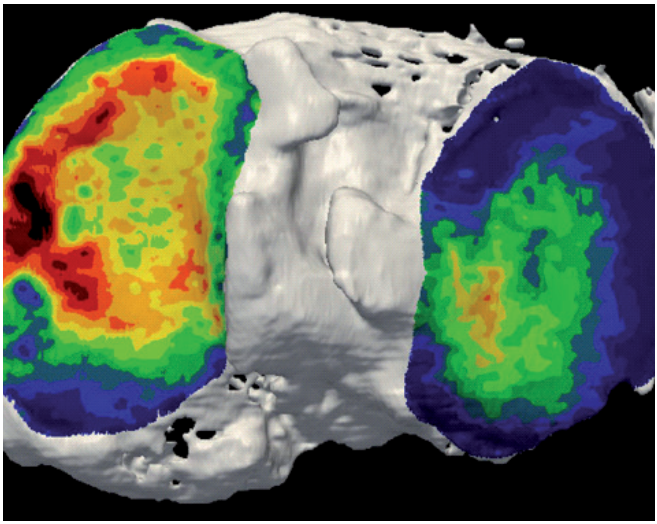
A potential target for gene therapy: the subchondral bone plate

# Gene Therapy

**“An InGENEious bone cast”**

The principle of gene therapy for osteoarthritis is to use the patient´s cells in the joint as a factory for therapeutic proteins. Gene therapy is well-suited for a long-term and local treatment of tissues in chronic diseases, such as osteoarthritis. Correct dosage of a therapeutic protein is essential for safety and efficiency of treatment. Conveniently, the gene therapy toolbox contains well-established options for matching the rate of protein production with the activity of disease. In other words, gene therapy acts as doctor within, who first diagnoses and then treats. Dr. Jeroen Geurts and his team in the Osteoarthritis Research Center operate at the forefront of gene therapy development. Research focuses on highly specific and safe targeting of cells in subchondral bone. From there, we try to combat pain, inflammation and mechanical overload.

The ultimate goal is to develop a long-term disease-modifying treatment for patients with progressive osteoarthritis based on local treatment of the joint with a gene therapeutic construct.



Computed tomography osteoabsorptiometry (CT-OAM) of the subchondral bone plate

# Cartilage and Bone Mechanobiology

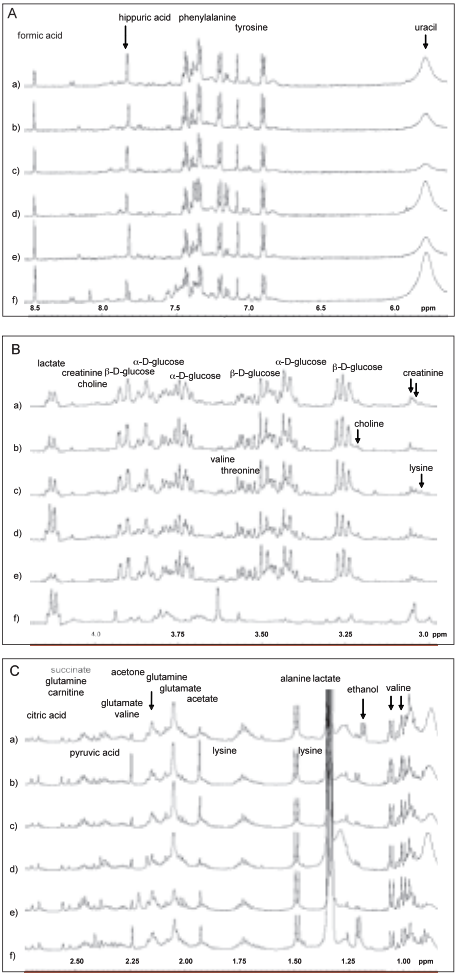
**“Shocking Research”**

During daily life our joints are exposed to forces up to four times our body weight. Without bone and cartilage, which act as shock absorbers, movement would be impossible. How do joint tissues sense, respond and adapt to mechanical loading ?

The joint is a living and dynamic tissue, in which forces are sensed by mechano-receptors on cells and translated into a biological response. This leads to a change in biomechanical properties, i.e. softening or stiffening of cartilage, which is crucial for efficiently absorbing a mechanic force.

At the Osteoarthritis Research Center, we study the effects of joint loading on cells of cartilage, tendons and subchondral bone. For this, we collaborate with Prof. Magdalena Müller-Gerbl from the Institute of Anatomy in Basel who is a pioneer of CT-Osteoabsorptiometry (CT-OAM) and combine imaging data with histological assessments.

These studies are of great importance for future development of tissue engineering approaches to repair or replace damaged cartilage in osteoarthritis patients. Ideally, these constructs mimic the dynamic behaviour of cartilage, rather than functioning as a static implant.




NMR metabolomics of OA

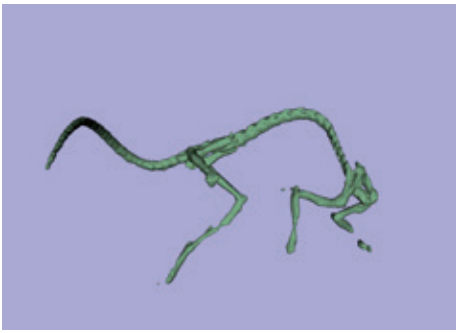
# Synovial Fluid Biomarker Analysis

**"Searching for the Needle in the Haystack"**

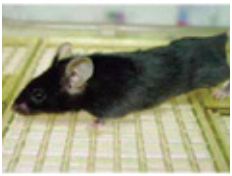
Synovial fluid is the lubricant of the joints and a source of nutrients for the cells that maintain the health of our cartilage. Also, this fluid acts as a trash bin that collects and disposes the metabolic products produced by cells in the joint tissues.

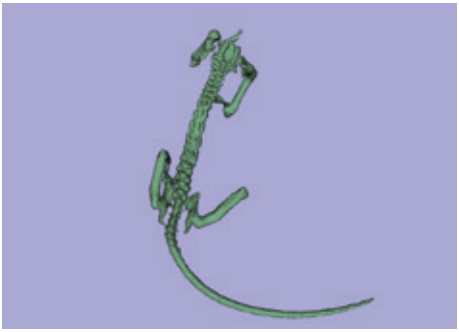
As a consequence of damage and inflammation, an osteoarthritic joint accumulates different and more waste products. Therefore, identifying and measuring the waste products in synovial fluid, can help to diagnose a patient with osteoarthritis. In order to efficiently treat disease, early detection is of vital importance.

Taking advantage of the extremely high sensitivity and feasibility of nuclear magnetic resonance (NMR) analyses, researchers at Osteoarthritis Research Center in collaboration are looking for waste products that are specific for different stages of osteoarthritis. First results indicate a similar metabolic environment in osteoarthritic and rheumatic joints, probably due to inflammatory and hypoxic processes. The ultimate goal is to develop a technique that assists clinicians in proper and early diagnosis of joint diseases.



Skeleton in a premature-aged mouse





Skeleton in a wildtype mouse

# Experimental Osteoarthritis

**“From Mice to Men”**

Aging, a phenomenon we all experience, is known as the biggest risk factor for developing osteoarthritis. But what happens to our joints at an older age that makes them sensitive to this disease?

To better understand the effects of aging, we need to study joints throughout their complete life cycle. It is obvious we cannot perform this research in humans. However, mice models of premature aging can greatly assist us in studying age-related changes of the joint in a short time frame.

In collaboration with renowned researchers from the Departments of Rheumatology and Anatomy here in Basel, we investigate the relation between structural alterations in bone and cartilage and molecular changes in cells and mitochondrial function in premature aging mice. This project is under the lead of Prof. Ulrich Walker who is a world expert on mitochondrial function and supported by Prof. Magdalena Müller-Gerbl who has an amazing expertise in bone and cartilage morphology.

The ultimate goal is to develop a treatment that is able to slow the progression of OA in older adults. This is extremely relevant, since our population as a whole ages.

Gait Analysis in patients with OA

# Gait Analysis and Muscle Function

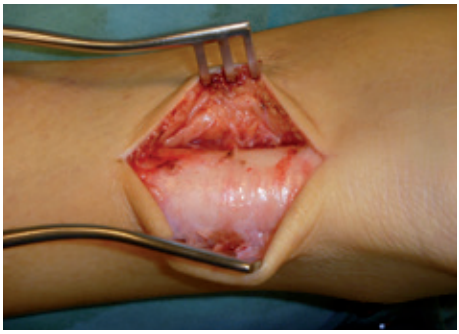
**“Standing still - is to fall behind”**

Osteoarthritis is a whole joint disease that affects not only cartilage, but also bone, ligaments, tendons, synovium and muscles, notably.

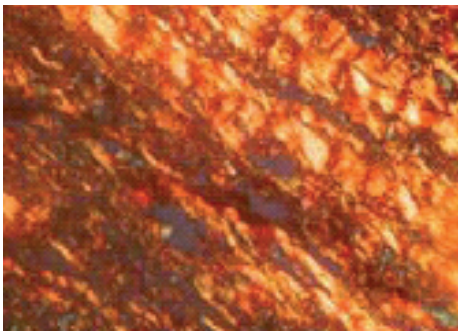
The coordinated interplay between muscles and the joint lies at the basis of movement. As a consequence, a change in one of these tissues in disease, will inevitably affect the other. Therefore, in order to better understand osteoarthritis, one has to study movement.

The Osteoarthritis Research Center houses an excellent biomechanics laboratory at which high quality movement studies are conducted, based on a combination of 3D gait analysis, MRI imaging and strength measurement. In collaboration with the expert Human Performance Laboratory (Calgary, Canada), we develop and apply new electro-myography technologies.

Our recent studies have revealed a crucial relation between osteoarthritis and chronic muscle atrophy. Proper treatment of atrophy before and after joint replacement has a substantial positive effect on patient care.



Inflammed achilles tendon



Improved tendon healing by gene therapy in the mouse model

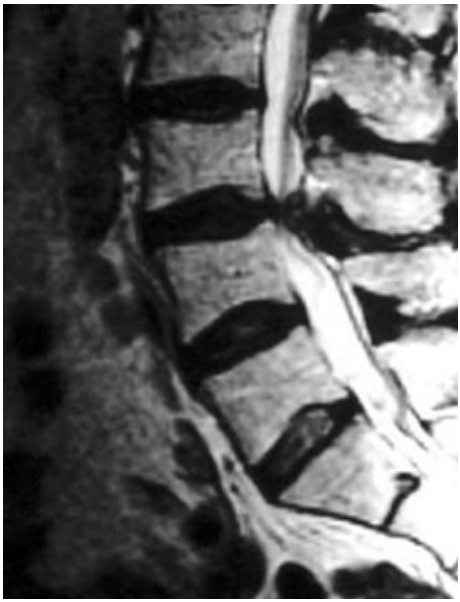
# Tendon Repair

**“Keeping Things Together”**

Tendon injuries are frequent in athletes and persons who lack daily physical activity. Tendinopathies differ from acute injuries, such as partial or complete rupture, in cause, symptoms and treatment. Pain and muscle atrophy are common consequences of tendon injury. The Achilles tendon, biceps and patellar tendon are most frequently effected.

Our aim is to improve the knowledge on the biomechanical role of tendons in specific pathologies, including osteoarthritis. In addition, we investigate the mechanisms of the tendon healing process.

Currently, we are conducting a multicenter study on Achilles tendon ruptures that evaluates open, percutaneous and conservative treatment approaches. Additional research efforts focus on innovative techniques for enhanced tendon healing after suturing, such as Platelet-Rich Plasma therapy and development of “tendon patches”.



Spinal stenosis (MRI)

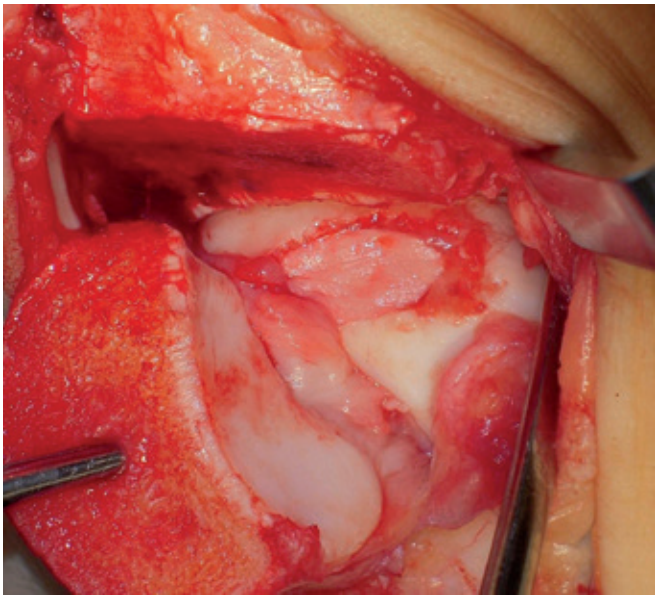
# Spinal Stenosis

**“Getting (the) Back On Track”**

Symptomatic lumbar spinal stenosis is a highly disabling condition. It is the most common reason for spinal surgery in patients over 65 years of age.

In the RESTORE study (Neuromuscular REhabilitation potential after Spinal STenosis OpeRation in the Elderly), we want to contribute to the understanding of this disease – and notably the surgical intervention by evaluating the pre- and postoperative muscular condition. Assessing the regeneration of muscle function will enable us to establish new objective outcome-parameters of postoperative results. We therefore hope to improve treatment strategies for patients with spinal stenosis by identifying patient subgroups with the greatest benefit from surgery. On the other hand, this study will help us to identify the right moment for the operation.

Another, probably even more important improvement could affect the conservative treatment in terms of developments of new concepts in prevention of deterioration or even occurrence of symptomatic degenerative lumbar spinal stenosis.



Autologous matrix induced chondrogenesis (AMIC), intraoperative view

# Osteochondral Lesions

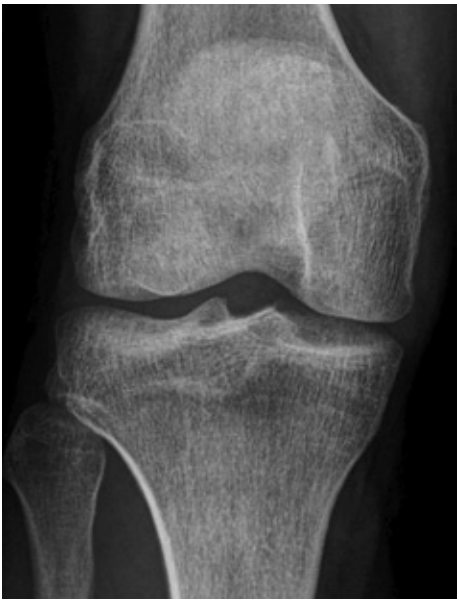
**“Mind the Gap”**

Focal damage to cartilage and underlying bone, so-called osteochondral lesions, are frequently found in knee and ankle joints – especially in young sports-active patients. When not properly treated, these injuries represent a major risk factor for developing osteoarthritis.

In order to prevent osteoarthritis development, accurate and early diagnosis of osteochondral lesions is of crucial importance. Thereafter, well-established and effective surgical techniques such as knee-to-ankle mosaicplasty and iliac crest plug transplantation are routinely applied for treatment.

In collaboration with the Department of Radiology, the Osteoarthritis Research Center pursues innovative non-invasive diagnostic imaging (MRI, SPECT-CT) of osteochondral lesions. Additionally, we investigate pathologic processes on a cellular and molecular level. Through prospective documentation of patients, we continuously evaluate and try to improve treatment methods.

Through a combination of high quality research, innovation and expertise, we strive for excellence in patient care.



Early osteoarthritis with preserved joint space and small osteophytes

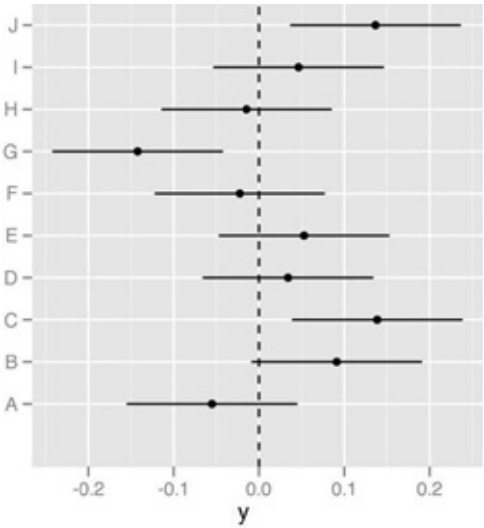
# Basel Study on Early Osteoarthritis (BaSE-OA)

**“Treat Before It´s Too Late”**

From a treatment perspective, the early phase of osteoarthritis is the most important one. Since only minor structural damage has occurred at this stage, this represents a window of opportunity for preventive treatment. For this, a thorough understanding of the pathological processes in early osteoarthritis is needed.

Prospective studies of patients with early osteoarthritis help to identify risk factors for disease progression. Recently, it has become clear that the prevalence of inflammation is increased in the early stage of disease. Characterizing inflammation in the different joint tissues is expected to contribute to a improved detection and treatment of osteoarthritis.

The Osteoarthritis Research Center premieres with the establishment of a specialized Early OA Clinic, as a joint effort of the Departments of Orthopaedics and Rheumatology. Through cellular, molecular and metabolomic analyses of synovial fluid and tissue we aim to decipher the risk factors for progression of osteoarthritis.



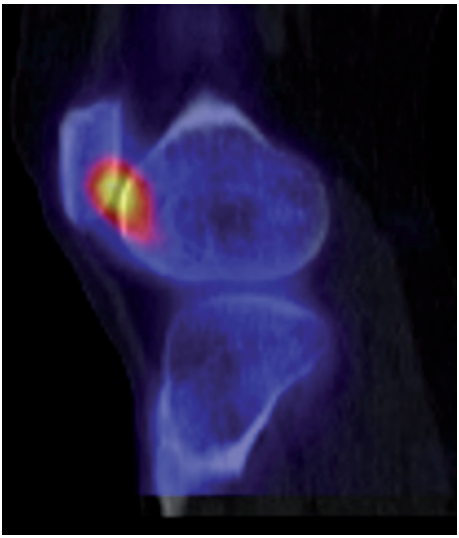

Forest plot as typical illustration for meta analyses

# Musculoskeletal Outcome Assessment Group

**"Let's Get Systematic"**

Musculoskeletal diseases are among the most important reasons for pain and impairment in present day, industrialized societies. As such the importance of treatment options for such diseases cannot be overestimated, and the availability of evidence based treatment algorithms and cost-effectiveness assessments is crucially important for physicians, economists, and health policy makers. Unfortunately, research on musculoskeletal diseases is highly heterogeneous in quality or simply nonexistent.

The objective of this group is to combine specialized knowledge from different field to establish evidence-based outcome assessments and cost-effectiveness assessment to guide clinical decision-making and health policy in Switzerland. The founding members of the musculoskeletal outcome assessment group under the lead of Dr. Patrick Vavken have postgraduate training and experience in orthopedic surgery, internal medicine, rheumatology, public health and epidemiology, biostatistics, basic science. We plan to join these skills to tackle pertinent questions in musculoskeletal health.



SPECT-CT analysis for morphology and biology of bone in OA

# Diagnostic Imaging

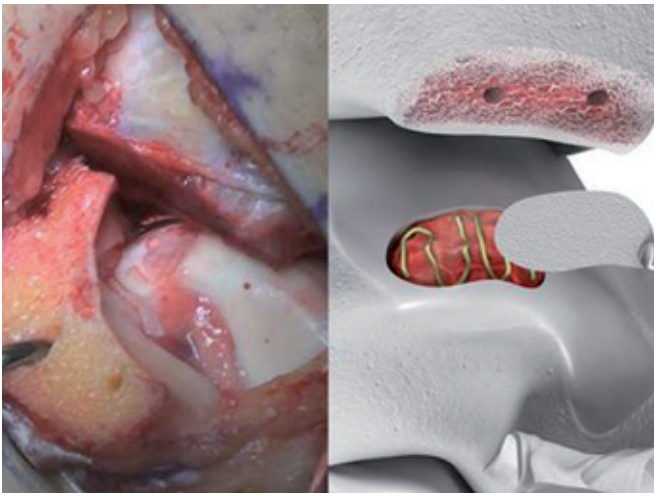
**"What You See Is What You Get"**

Computertomography (CT) enables excellent assessment of the complex and distorted bone morphology of an osteoarthritic joint. Apart from assessing morphological changes, monitoring pathological metabolic activity of bone is of great value for diagnosis. At the Osteoarthritis Research Center, we focus on the development, application an innovation of imaging techniques for joint diseases.

Scintigiraphic imaging of bone-specific radionuclides using single photon emission (SPECT) CT is routinely applied for identifying areas of bone remodeling, as a result of increased osteoblast activity. Cartilage thickness can also be assessed using CT, while magnetic resonance imaging (dGEMRIC) enables highly detailed analysis of cartilage structure and function. The latter is applied for monitoring cartilage after a repair treatment.

Currently, our innovative research focuses on novel contrast enhanced CT (CECT) imaging techniques. In vitro experiments showed CECT to be an excellent tool for quantification of proteoglycan content of cartilage.

Together, this well-filled toolbox of imaging technologies is essential to early and accurate diagnosis of - and measuring treatment effectiveness for osteoarthritis.



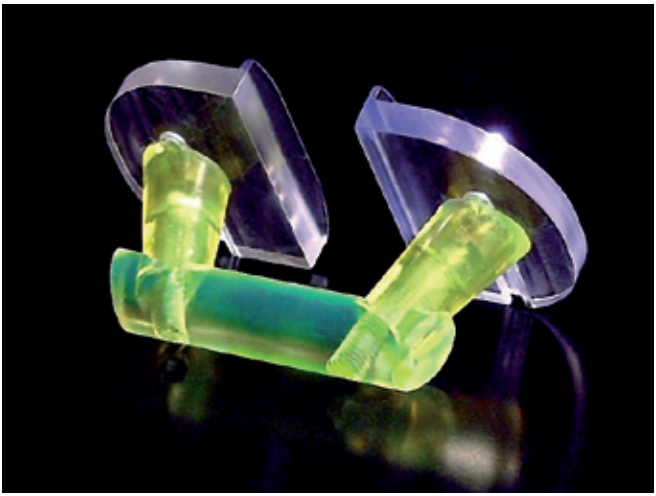
Surgical procedure for an osteochondral lesion of the talus

# New Therapies for Osteoarthritis

**"One Step Ahead"**

Treatment of osteoarthritis can be initiated on different levels. By preventing injuries and joint malfunction, such as tearing of the anterior cruciate ligament or chronic ankle instability, development and progression of osteoarthritis can be anticipated. In early and mid-term stages of disease, joint preserving therapies including osteotomy and cartilage reconstruction help to slow down disease progression. Improvements in total joint replacement can be achieved with new materials and new prosthesis designs.

The members of the Osteoarthritis Research Center focus on all aspects: For prevention, neuromuscular stability and patterns were measured in chronic ankle instability to understand differences in dynamic joint control. Patients suffering from malaligned ankle osteoarthritis may benefit from supramalleolar or calcaneal osteotomy. These patients are followed up closely by gait analysis and electromyography to reveal the rehabilitation potential. Furthermore, a new total knee joint prosthesis that allows ligament preservation and improves joint biomechanics, has been designed and evaluated. Robotic- and computed-assisted surgery is routinely applied to achieve the highest quality of surgery.



A new concept for a knee prosthesis by transversal support of the tibial plateau

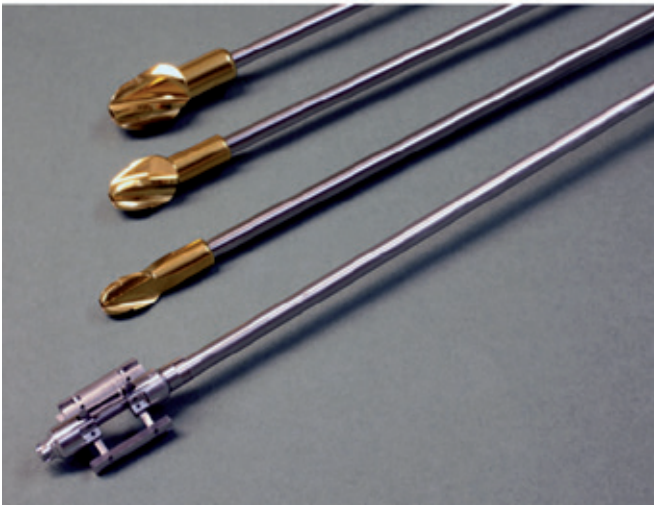
# Transversal Support Tibial Plateau

**"For Retaining Both Cruciate Ligaments"**

The important role of the anterior cruciate ligament with regard to knee stability, physiologic kinematics and proprioception are unquestioned.

Thus, various efforts have been made to retain the anterior cruciate ligament during total knee arthroplasty. Neither of the existing implantation techniques, such as bicruciate retaining prostheses and implantation of two unicondylar prostheses, have been successful because of concept-specific problems as well as general difficulties with implant fixation.

Dr. Andrej Nowakowski at the Osteoarthritis Research Center invented and generated a new transversal support tibial plateau concept. It is a prosthesis of two individual joint surfaces reinforced beneath the articular line by joint surface supports and buttressed by a single transversal support. This configuration, allowing retention of both cruciate ligaments, should provide good bony fixation and ensure long term alignment of the individual joint surfaces.



Universal Medullary Drill System for precise cement removal

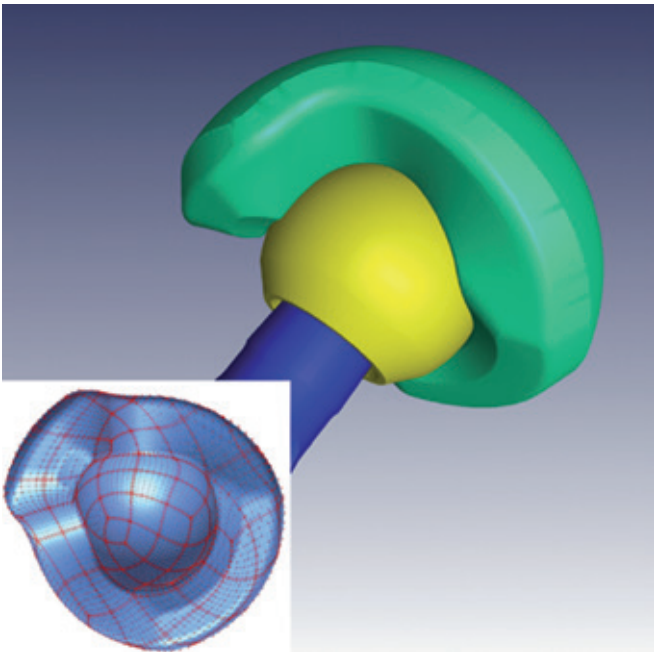
# Universal Medullary Drill System

**For cement removal in revision arthroplasty"**

In revision of cemented total arthroplasty, complete removal of the remaining intra-medullary cement mantle remains a challenging task, always fraught with the risk of extensive loss of substance as well as perforation or fracture of the remaining bone stock. By the use of the new Universal Medullary Drill System, invented by Dr. Andrej Nowakowski, safe and complete cement removal was performed successfully both in artificial bone and in real bone preparations under avoidance of perforation or fracture of the preparations.

The first adoption of the theoretical approach of guided drilling for intramedullar cement removal is promising. In order to be well achievable, further development should aim the following :

- efficient, safe and complete removal of the cement,
- preservation of bone stock,
- avoidance of perforation and fracture of the cortical bone,
- reduction of the operative radiation exposure,
- reduction of the operation time.



Bidirectional total hip prosthesis

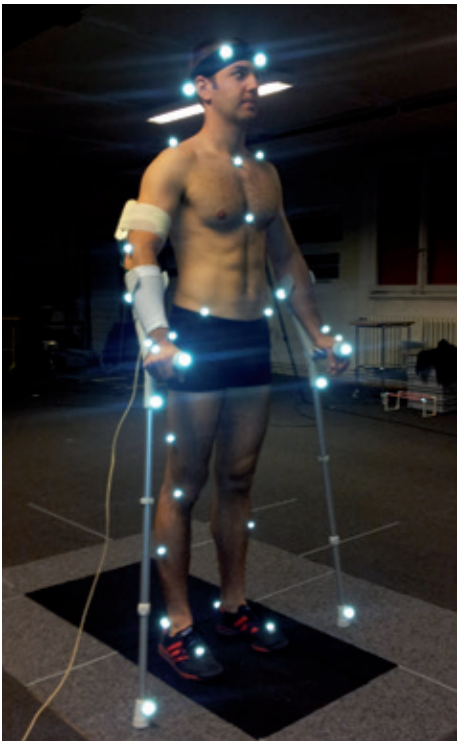
# Bidirectional Total Hip Prosthesis

**“Have It Both Ways”**

After total hip arthroplasty, dislocation is one of the most frequent serious early complications. This occurs in part due to impingement (catching and leverage of the neck-cup on the inlay/cup border). Impingement may also negatively impact long-term outcomes. Through isolation of the two main trajectories of motion, and modifications with corresponding gaps to the inlay/cup areas as well as oppositional banking in the abduction/adduction plane, the combination of a snap-fit acetabular cup with reduced cup profile was the result: the „bidirectional total hip prosthesis“, invented and engineered by Dr. Dr. Andrej Nowakowski at the Osteoarthritis Research Center.

Under standardized parameters, the ranges of impingement for typical implants are not directly opposite one another (at 180°), but are found instead at an angle of 108.3°.

Complications such as dislocation and impingement may possibly be avoided with the bidirectional total hip prosthesis. Typical implantation parameters yield an implant design with rotational asymmetry.



Development of new crutches in the gait laboratory

# Crutches for Long Term Usage

**“The Ulnar-Pro Technology”**

Demographic changes result in a higher prevalence of aged people. Therefore, degenerative musculoskeletal diseases such as osteoarthritis, rheumatic diseases or spine disorders are an increasing health burden. The number of individuals requiring permanent medical walking aids such as crutches will increase substantially in the near future.

Current available crutches are cheap and highly functional. The focus of conventional crutches purely is on function, they are not designed for long term use. Overuse is associated with skin bruises and pain. Subsequently, a decrease of mobility, a higher risk of falling and a reduced quality of life is reported by the patients.

We develop walking aids in our laboratory allowing long term use of crutches. The “Ulnar protection” technique preserves the ulnar bone, potentially leading to less bruises and less pain. Our prototypes are currently tested in a clinical trial.

University Hospital Basel

BETHESDA

Anatomisches Institut Basel

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BIOZENTRUM
Universität Basel
The Center for Molecular Life Sciences

n|w Fachhochschule Nordwestschweiz

UniversitätsSpital Zürich

# National and Local Collaborations

**"Networking is the Key to Success"**

Networking aims at creating a group of scientific and clinical professionals, through formal and informal connections, for mutual benefit. As the proverb says: "Two heads know better than one", combining different areas of expertise is pivotal to strengthening our scientific impact.

At the Osteoarthritis Research Center, we see Basel as a unique and fruitful "Think Tank" where expert knowledge, research facilities and clinical sample collection are shared. Successful and sustainable collaborations have been established between several medical centers and institutes of the University of Basel.

Following our motto "Innovation for You", our ultimate goal is to improve patient care. For this, we pursue true translational research through close collaboration between research scientist and clinicians. The key words to our approach are: unmet clinical needs, interdisclipinarity, open-minded two-way communication and professional excellence.


UNIVERSITY OF
CALGARY


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Newcastle
University


UNIVERSITY OF
TORONTO

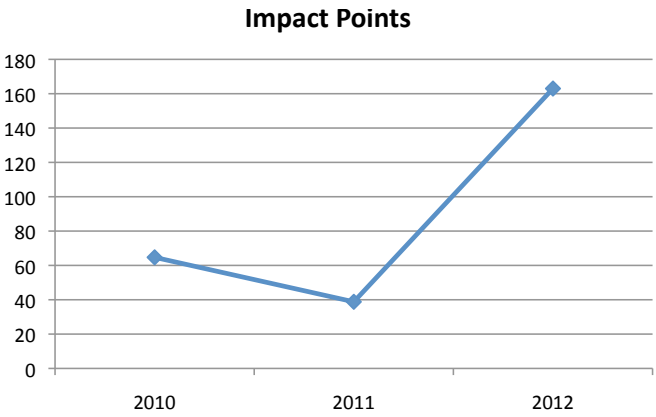
# International Collaborations

**"Who Travels Much, Knows Much"**

Each research center over the world has its own unique expertise and specialization. Exchange programs are optimally suited to benefit from each other's knowledge and skills in a sustainable fashion. Therefore, the Osteoarthritis Research Center regularly sends its clinicians and scientists to join laboratories of renowned and world wide experts in orthopaedics, biomechanics and immunology. Currently, fellows from Basel are performing research at a postdoctoral level at the top universities of Canada in Toronto and Calgary and at the prestigious Harvard School of Medicine in Boston, USA. During their fellowship abroad, our colleagues broaden their scientific horizon, acquire new technical skills and most importantly, create their own network, which fosters their academic carrier.

This is not a one-way street. At our research center and clinical department, we regularly welcome fellows from the whole world, in to participate in and acquire our expertise. Over the past years we have received scientist and clinicians from USA, Japan, China, Egypt and a variety of European countries.

Finally, by participating in numerous international congresses on a regular basis, our staff aims to foster existing – and establish novel collaborations.




General impact points 2010-12

2012

# Selected Publications

## 2012

**Improvement of tendon repair using muscle grafts transduced with TGF-β1 cDNA**. Majewski M, Porter RM, Betz OB, Betz VM, Clahsen H, Flückiger R, Evans CH. *Eur Cell Mater.* 2012;23:94-102

**Assessment of knee implant alignment using coordinate measurement on three-dimensional computed tomography reconstructions**. Nowakowski AM, Müller-Gerbl M, Valderrabano V. *Surg Innov.* 2012

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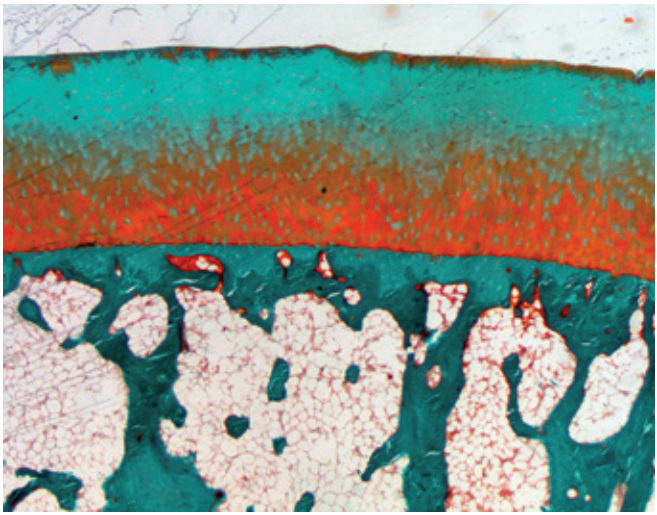

Histology of cartilage and subchondral bone

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## Membership

The Osteoarthritis Research Center  Basel is an open and interdisciplinary research environment and offers open membership to researchers working on different aspects of osteoarthritis. For membership application please contact Prof. Dr. Dr. Victor Valderrabano directly.

Microscopic examination of tissue samples

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