RESEARCH

at the

DEPARTMENT OF ORTHOPEDICS

CLINICAL SCIENCES, LUND AND MALMÖ

LUND UNIVERSITY
SKÅNE UNIVERSITY HOSPITAL

2012
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The Department of Orthopedics at Skane University Hospital

The Department of Orthopedics at Skane University Hospital consists of two units, Lund and Malmö and an elective site in another hospital (Trelleborg). The unit in Malmö was founded in 1911 and in Lund in 1914. May 1, 2010 the two units were fused after a three year-period of increased collaboration.

In both Lund and Malmö, a complete orthopedic elective and emergency service is present. In Trelleborg elective orthopedic procedures, with special focus on hip and knee arthroplasties, shoulder surgery, foot- and ankle surgery and sports medicine are performed.

Both units have achieved a world reputation from its many years of research as well as continuous clinical experience, supported by being a World Health Organization Collaborating Centre for Evidence-Based Health Care in Musculoskeletal Disorders since 2007 and one of twelve members of the prestigious International Society of Orthopaedic Centres.

The Department of Orthopedics have access to 170 beds, 16 operating rooms, complete technology, 105 orthopedic surgeons (incl. 25 residents) and 500 other staff.

Annually we perform about 11 500 surgeries, 51 500 outpatient visits, 32 000 A/E visits, 34 500 other visits (nurse, physiotherapy). The total turnover is about 725 MSkr (80 M€).

Our physicians and other staff work in an integrated and cooperative group practice that strives to provide the highest-quality and cost-effective care for more than 50 000 patients annually.

For nearly a century, the Departments of Orthopedics in both Lund and Malmö has been involved in advances to alleviate suffering from musculoskeletal disorders. Problems identified in the clinic are taken to the laboratory bench for study, and the results are then translated back into clinical practice.

Currently, 250 investigators, including 10 professors (6 full professorships), 4 visiting professorships, 25 associate professors and 49 PhD students employed by the Department of Orthopedics or closely linked to it, with nearly 40 million SEK in annual funding, are doing research and performing clinical trials in virtually every aspect of musculoskeletal pathology. Since 2010, 11 doctoral dissertations were defended and over 300 peer reviewed scientific papers were published.
Lund University is Sweden’s strongest comprehensive research university and in recent years has been awarded more research funding than any other Swedish full-scale higher education institution. In an independent review “RQ-08” of the quality of all research at Lund University, the Department of Orthopedics in Lund was ranked as outstanding, and in Malmö as excellent.

Research as well as education of future doctors and other students within healthcare professions is a significant part of the activities. We are especially pleased to have an education unit, and our own training laboratory, which together with the new Skill Centre at the hospital, can provide practical treatment.

Magnus Eneroth
Clinical Head, Department of Orthopedics
Skane University Hospital
Descriptions of Research Activities and Strategic Research Aspects

DEPARTMENT OF ORTHOPEDICS
CLINICAL SCIENCES LUND AND MALMÖ

The major part of the health care consumption in musculoskeletal disorders is caused by fractures, joint diseases (osteoarthrosis and rheumatoid arthritis), back problems, injuries and tumors. This pattern is reflected in the research activities within the Academic Department in Lund and Malmö.

Research on joint disease and its consequences spans from basic genetic and biochemical investigations to applied projects which monitor nationwide the outcome of arthroplasty and includes the following aims:

• Develop methods for diagnosis and monitoring of early-stage osteoarthrosis through patient-administered outcome scores, radiography, arthroscopy, MRI and analysis of joint fluid and serum markers of cartilage turnover as well as investigate the disease mechanisms;
• Epidemiology and risk factors for osteoarthritis following joint injuries
• Improve diagnostic and reconstructive techniques after knee ligament injury;
• Improve and develop techniques for joint replacement in the rheumatoid joint;
• Study the process and causes of joint implant loosening in hip and knee;
• In a nationwide, population-based cohort study investigate patterns of knee joint implant failure related to time, implant type, infection, age, etc.

Research on osteoporosis, fragility fractures and its consequences spans from basic genetic and biochemical investigations to applied projects in large population based cohorts and in nationwide register monitor the development and outcome of fragility fractures and includes the following aims:

• Study the genetic background of reduced bone strength
• Study the pathophysiological process of reduced bone strength and in intervention studies evaluate if bone strength could be improved
• Epidemiology and risk factors for osteoporosis and fragility fractures
• Improve diagnostic procedures and prophylactic interventions for fragility fractures
• Improve and develop techniques for treatments of fragility fractures and study effects on femoral head vitality, fracture healing, and rehabilitation
• In regional registers in Skane investigate patterns of all fragility fractures and relate these to health care economics with calculations of future need of resources
• In nationwide, population-based cohort studies investigate the epidemiology and treatment of hip fractures and its effects on health care economics

Biomaterial, Bone and Matrix Biology Research includes:
• A study of the process of bone induction and its stimulation by human recombinant growth factors;
• Tendon and cartilage repair using cell culture techniques
• New synthetic bone substitutes and peptides for repair of fragility fractures

Research on lumbar back pain and sciatica aims to optimize patient information, surgical methods, postoperative treatment and utilization of hospital resources.

Research on different methods of treatment for gangrene of the lower extremity caused by diabetes is evaluated with regard to quality of life, cost, etc.

Research on orthopedic oncology evaluates diagnostic procedures, surgical techniques and prognostic classification of soft tissue tumors. Surgical treatment of skeletal metastases is studied concerning technique and outcome.

Research in hand surgery includes evaluation and treatment of ligament injuries in distal radius fractures in young patients.

Research in pediatric orthopedics targets gait and function analysis in children with cerebral palsy and pathophysiology in Perthes’ disease and outcome after treatment of congenital dislocation of the hip.

Laboratory facilities exist within the Department for the following areas: biomaterial, biomechanics, cartilage metabolism, bone metabolism, bone genetics, skeletal scanning in animal and humans, animal experiments, bone transplantation and radiostereometry.

In addition to some 30 M.D. clinical investigators, a total of 6 laboratory technicians, 4 engineers/engineering students, 6 statisticians and 8 secretaries are engaged in the research work.

Currently, a total of around 30 graduate students are working on their Ph.D. thesis within the Department. With the opening of the Biomedical Center (BMC) in Lund and Clinical Research Center (CRC) in Malmö, linked to the University Hospitals, the collaboration with preclinical research was enhanced.

In 2004 a National Competence Center for studies on musculoskeletal disorders giving statistical, epidemiological health economy advices to registers and researchers, funded by Federation of Swedish County Councils and National Board of Health and
Welfare, was opened and moved into new facilities in the hospital 2007. Today 25 national quality registers are served by Registercentrum Syd.
Website: web.rcsyd.se

The MORSE project, a longterm collaboration between the Southern Sweden regional health authority and the Swedish Social Insurance Agency, started September 1, 2006. MORSE focus on research and development on musculoskeletal health problems, sick leave, and health services utilization and also develops guidelines for the treatment and rehabilitation of musculoskeletal disorders and the effect of implementation of these guidelines.
Website: morse.nu.

The Medical Faculty decided in 2004 based on an external evaluation to fund a new program area – Tissues in motion, where the Department of Orthopedics is an active partner. The program was extended for another 3 year period 2008-2010
Website: www.med.lu.se/tissuesinmotion

In December 2007 the Department of Orthopedics in Lund has been designated as a World Health Organization Collaborating Centre for Evidence-Based Health Care in Musculoskeletal Disorders with Professor Lars Lidgren as director and Professor Kristina Åkesson as co-director.
Website: www.euro.who.int

The WHO European office in Copenhagen has started a Health Evidence Network (HEN) aiming at spreading information to decision-makers on well performed studies. The Department of Orthopedics is an active partner in HEN
Network: www.euro.who.int

A cooperation agreement has been signed with Spenshult Foundation in 2010.
Website: www.fou-spenshult.se.

University appointed professors during 2011 have been Anthony Woolf, Professor of Rheumatology, Truro, Elizabeth Tanner, Professor of Mechanics of Materials and Structures, Glasgow, and from 2011, Mathias Boström, Professor of Orthopedics, New York, Hanna Isaksson, Clinical Lecturer, Faculty of Engineering, Solid Mechanics, LTH, has been appointed part time researcher at our Biomechanical Unit.

The five new activities: RCSyd, MORSE, Tissues in Motion, Centre for Biomechanics (www.cbml.lu.se) and the WHO center, will all have a significant input on future research as well as the close research interaction between biomaterial, biomechanics,
cartilage metabolism, animal experiments, bone transplantation and radiostereometry. In the external evaluation of the whole University (RQ8), Orthopedics has been graded excellent and also top ranked in a national review concerning clinical research. This has now led the University to increase unrestricted departmental funding.

Three competitive research positions for 4 years have been granted from the Swedish Research Council to Eva Ageberg, Martin Enlund and Richard Frobell. The reviewed research grants from the Medical Faculty increased during 2010 as well as the total external funding, now reaching 3.5 million Euro.

A major 4-year EU grant of 2 million Euro on implementation research will be coordinated through Professor Anthony Woolf, at present Visiting Professor at our department, with our department as one of the major partners in the consortium.

WHO has for the first time decided to have a separate global group for musculoskeletal disorders in their revision to ICD 11. The work is chaired by Martin Sundberg assisted by Anette Dahl.

In 2009 it became clear that Lund and Malmö will form one clinical unit. As a result a musculoskeletal science institute (LUMSI) has been formed in 2010 with a broad representation from different fields including inflammatory diseases as well as basic research. Financial support of 0.3 million Euro for a start up period of 3 years has been given by the Region of Scania.

Website: www.lumsi.se

These research projects thus involve the whole staff at the Department of Orthopedics in Lund and Malmö. For a complete listing of participants in each project, please contact the primary investigator.

A list of publications printed in 2011 is enclosed. For further information you may also visit our websites at:

www.med.lu.se/klinvetlund/ortopedi
www.med.lu.se/klinvetmalmo/forskning#ortopedi

This report was edited by:

Professor
Lars Lidgren
Lund

Professor
Leif Dahlberg
Malmö
Published Scientific Paper

The two graphs below summarize some aspects of the academic activities of the Department during the last few years. Please note that Lund and Malmö for the first time in 2010 present together.
Awards and Prizes 2011

Marie Enekvist: Tutor of the year (the national prize)

Martin Englund: Clinical Research Award, Osteoarthritis Research Society International (OARSI)

Lars Lidgren: Honorary Member EFORT, Distinguished Member SICOT

F Strömqvist, B Jönsson, B Strömqvist: EUROSPINE Best Full Paper Award 2011

Maria Swanberg: President’s Poster Award from American Society of Bone and Mineral Research (ASBMR).

Max Tenne: Plenary Poster Award från American Society of Bone and Mineral Research (ASBMR)
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European Community
Faculty of Medicine, Lund University
Federation of Swedish County Councils
GlaxoSmith Kline
Greta and Johan Kock Foundations
Gunnar Nilssons Cancerstiftelse
Heraeus
Herman Järnhardts Foundation
Howmedica/Stryker
King Gustaf V 80-year Birthday Foundation
Landshövding Per Westlings Minnesfond
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National Board of Health and Welfare, Sweden
National Institute of Health NIH
Pfizer
Påhlsson Foundation
Region Skåne
Skåne University Hospital
SKL (Swedish Association of Local Authorities and Regions)
Sports Research Council
Stiftelsen för bistånd åt rörelsehindrade I Skåne
Stiftelsen Konsul Thure Carlssons Minne
Stiftelsen Skobranschens Utvecklingsfond
Swedish National Center for Research in Sports
Swedish Research Council
Swedish Rheumatism Association
Swedish Social Insurance Agency
Swedish Society of Medicine
The Swedish Children’s Cancer Foundation
Thelma Zoëga Foundation
Tore Nilsson’s Stiftelse för Medicinsk Forskning
Zimmer
Sensorimotor function in joint injury – mechanisms, training, outcomes and predictors

EVA AGEBERG

Musculoskeletal diseases and disorders are the leading cause of disability in the developed countries, involving 1/3 of the adult population. These conditions lead to functional limitations, decline in quality of life, and high costs for the society. Early and effective treatment is needed to reduce pain, improve function and quality of life, and to prevent or delay further joint problems.

Physical activity has beneficial effects on overall health, including the musculoskeletal system. General exercise, such as aerobic exercise and strength training, is generally recommended. However, training targeting the more specific needs related to the joint injury/disease may have an important role in the treatment. Sensorimotor function, such as muscle strength, may be of importance for the outcome after injury and in preventing future problems related to the injury. In this project, the injured knee is used as model, although the views expressed apply to also other joints.

A joint injury or joint disease leads to a disturbance in the sensory system, due to the loss of mechanoreceptors in the injured joint structures, causing effects on sensorimotor function. Sensorimotor function is the complex interaction between sensory and motor pathways, and the central nervous system (CNS) and is assessed by measures of sensory function (vibration and proprioception), and motor function (muscle strength and performance measures). Changes in central mechanisms and processing may also take place after joint injury, but this is sparsely studied.

In our studies, we: 1) elucidate the effects of joint injury on sensory function, motor function and cortical brain activation; 2) study the effects of different training methods with the aim of optimizing training as treatment; 3) develop and validate clinical methods of assessing sensorimotor function that can be used in large groups of patients, to identify those at risk of poor outcome; and 4) test the hypothesis that good sensorimotor function prevents or delays future problems related to the joint injury.

Given that we can optimize training as treatment and determine the role of sensorimotor function for joint health, this will have large impact on the disease burden for the individual, the health care system and society.

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Determining mechanisms of pathogenesis in joint cartilage disease to enable implementation of rational treatment

LEIF DAHLBERG

Background: OA is the most common cause of musculoskeletal disability in developed countries and is listed in the top 10 global disease burdens according to the World Health Organization. One in six people over 55 years old will consult their doctor about knee pain over the course of one year. OA susceptibility is related to an individual’s cartilage quality and to risk factors for developing the disease. Risk factors include meniscectomy, obesity, muscle weakness, major injuries and, in the hips, developmental joint anomalies.

Aim: Our research aims at getting the whole picture of osteoarthritis (OA); from comprehension at molecular and structural levels, to understanding which external factors that influence progression of the disease. This will enable improved disease definition, diagnosis and prognosis and facilitate implementation of preventive strategies.

Methods: We combine experimental in vitro state-of-the-art magnetic resonance imaging (MRI) technology with molecular analysis. Using this approach, we can identify metabolic events that will result in cartilage structural changes as well as relate MRI signal to molecular content. In vivo, we follow patient cohorts longitudinally with MRI and body fluid analysis which makes us able to correlate metabolic events and structural changes to OA diagnosis. The combination of advanced imaging with molecular indicators applied in parallel to in vitro models and patient cohorts provide unique understanding and novel means to detect the process leading to pathology. Moreover, we study effects of early intervention to improve treatment of OA patients.

Clinical Relevance: Knowledge gained in the proposed project will help us understand disease mechanisms on which primary prevention can be based. In the long run, implementing prevention programs and early treatment of chronic diseases, such as OA, rather than treating it once it has become established, simultaneously improves patient satisfaction and reduces costs.

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Musculoskeletal epidemiology with focus on osteoarthritis

MARTIN ENGLUND

Wp 1 – EPIMUSC: The prevalence of musculoskeletal conditions increases dramatically with age, and the numbers of elderly in European societies continue to increase rapidly. Musculoskeletal diseases and injuries are already among the leading causes of chronic individual suffering and incur major costs in the population.

Via linkage of Skåne County health care data to other registers, e.g., from Statistics Sweden and the Insurance Agency, using modern epidemiologic methods, I gain new insights on disease occurrence, risk factors, comorbidities, the burden of disease on society, and monitor societal effects of medical and surgical treatments in an entire population. I focus on common conditions such as low back and shoulder pain, fractures, rheumatic disease, and neck trauma.

Wp 2 – EPIOA: Osteoarthritis is the most common cause of musculoskeletal disability in developed countries, and is listed among the top 10 of the global disease burden according to the WHO. Traditionally, the focus in knee osteoarthritis research is on the loss of articular cartilage. My research recognizes another knee structure that has often been disregarded – the meniscus.

I study osteoarthritis, the meniscus, and analyses of bone as a biomarker in large prospective observational cohorts with repeat assessment using MRI and x-rays, e.g., the Osteoarthritis Initiative, the Multicenter Osteoarthritis Study, and data from Framingham, Massachusetts. The work has already resulted in multiple publications in the highest ranked journals in both orthopedics and rheumatology as well as articles general medical journals such as the New England Journal of Medicine and the Annals of Internal Medicine. I further study osteoarthritis using Swedish health care data and, for example, data from the Malmö Osteoarthritis Study Cohort with the goal of better understanding of burden of the disease.

The team: My research team is highly cross-disciplinary and consists of myself as epidemiologist, an orthopedic surgeon, a couple of physicians under specialty training or internship, physiotherapist, data managers, SAS analysts, a public health scientist, a political scientist, and a biostatistician. I am currently mentoring 5 PhD students, and further 2 students are pending their registration.

I am active in the Lund University Strategic Research Area “Epidemiology for Health (EpiHealth)” where I am part of the working group for the comprehensive
screening cohort, and in the newly created Lund University Osteoarthritis Network (LOAD). I have a comprehensive international network of active collaborators in the fields of clinical epidemiology, rheumatology, biomechanics, radiology, and MRI analysis methodology in USA, United Kingdom, Australia, Austria, Germany, and Norway.

In 2011, as the youngest recipient ever, I received the Clinical Investigator Award by the Osteoarthritis Research Society International (OARSI) and in 2012 I’ll receive the European League Against Rheumatism (EULAR) Young Investigator Award. I am currently undergoing a leadership program at Lund University, Scientific Leaders of Tomorrow, and I am supported by the Swedish Research Council, ALF, Kock Foundations, and Gustav V’s 80-Year Birthday Foundation.

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Figure 1: Hypothetical “meniscal pathway” to the pathogenesis of knee OA.

1. Risk factors: systemic, local & environmental (knee trauma, obesity, genes, malalignment)

2. Meniscal lesions or extrusion (loss of meniscal function)

3. Increased biomechanical stress

4. Cartilage loss
   Bone changes
   Bone marrow lesions
   Synovitis

OA

Pain
Joint Arthroplasty in the Hip and Knee  
– fixation, function and survival

GUNNAR FLIVIK, ULDIS KESTERIS, MARTIN SUNDBERG

Total joint arthroplasty in the hip and knee is successful operations with generally good results. Developments have been fast and indications for operation have gradually widened, with younger patients being considered for surgery as operation results have been improving.

However, late aseptic loosening as well as wear remains a problem, and sometimes early loosening occurs without an obvious reason. The consequence of component loosening and the ensuing bone loss is often a re-operation, which is a major, costly and for the patient trying operation.

We are studying different factors involved in the fixation and function of the prosthesis components, both initial and long-term variables. Our aim is to evaluate and improve the surgical technique and to analyze factors of importance for the implant survival and patient satisfaction, such as prosthesis design, material and positioning, but also pre- and postoperative levels of activity, exercise and pain level.

At present we have several patient studies in progress. In different studies we are evaluating surgically relevant factors such as types of bone cement, operative techniques, different bone preparation models and different component designs and the effect of periarticular analgesia during surgery.

We are exploring the importance of anatomic restoration in THA with the use of modular prosthesis and hip navigation evaluated with for example gait analysis. We are looking into the fixation of both uncemented and cemented components.

We are also carrying out studies on the relatively new concept of resurfacing hip replacements as well as the role of patella resurfacing in knee replacements. Furthermore we are investigating the effect of exercise pre- and postoperatively for total joint replacement patients with pain thresholds as an important factor, and with the aim of identifying non-responders to exercise and joint replacements.

Another area of ongoing study is the role for bisphosphonate in joint arthroplasty, both in revisions and primary prosthesis. In many of these studies we use RSA (RadioStereometric Analysis) which is a radiographical method by which the three-dimensional movements of the implant can be followed with a very high degree of accuracy.

This is the most exact method there is when it comes to measuring migration patterns of prosthesis components. With this technique, within two years and with a limited number of patients, differences can be demonstrated between various operation techniques, materials and prostheses. With conventional methods this

"
would take many years and call for a much larger number of patients at risk. Our groups of patients are also being followed up with strictly clinical and conventionally radiological examination methods as well as a comprehensive package of questionnaires, covering both general health and disease specific questions. Furthermore, we carry out complementary biomechanical laboratory studies, in which factors such as operation techniques, materials and surface finishes are being evaluated.

Concurrently with the continuous data we contribute to both the National Hip and Knee Registers we are also following up our own hospital’s material of primary as well as revision hip and knee prostheses.

The main goal of our studies is to contribute to even better joint function and life quality for patients with hip and knee prostheses and to decrease the need for re-operations.

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Knee injury & Osteoarthritis - outcomes, relation and treatment alternatives

RICHARD FROBELL

Knee injuries often occur in sports and are thus frequently seen among young active adults. The most severe knee injury is the anterior cruciate ligament (ACL) tear, resulting in instability and decreased activity level in the short term and increasing the risk knee osteoarthritis (OA) in the longer term.

Meniscus tear is another example of knee injury where an increased risk of subsequent OA have been determined but for other types of knee trauma diagnoses (such as patellar dislocations and contusions), a corresponding increased risk is still to be determined.

OA is the most common reason for musculoskeletal disability in the western world and accounts for a large proportion of the global disease burden.

Although OA is highly frequent, little is known about the pathogenesis and there is currently no disease modifying treatment available. OA often occur in the knee joint and previous knee trauma has been identified as a potent and independent risk factor for later OA development.

We focus our research on knee injuries and cover both short- and long term consequences using clinical outcomes, imaging modalities (i.e. MRI and radiographs) and biochemical analyses. The following cohorts are used:

1) The KANON-study, is a randomized controlled trial involving young active adults with an acute tear of the ACL of the knee. We compare two different treatment strategies: structured rehabilitation plus early ACL reconstructive surgery and structured rehabilitation with delayed ACL reconstruction offered to patients who continue to have symptomatic instability.

After 2 years, we did not find a difference in outcome and the five year outcome (including the frequency of radiographic OA) has been submitted for publication. This study is unique in its design and therefore we have several collaborations around the world where new and innovative methods are used, mainly in the imaging field.

2) The Acute Knee injury Project (AKP), is a prospective cohort study of more than 1300 patients with acute knee injury. All patients received treatment in the normal clinical setting and a 5-7 year follow up is planned.

The cohort includes approximately 600 ACL injuries, 200 patellar dislocations, 100 complete medial collateral ligament tears and 200 isolated meniscus injuries. Using this cohort, we first aim to describe the epidemiology of acute knee injury, and secondly to analyze the ‘diagnose-specific’ clinical and radiographic outcome.
3) The EDEMA-cohort, includes approximately 100 individuals with acute hemarthrosis where synovial fluid was aspirated within 25 days of injury and where MRI was performed within a week of aspiration.

4) The MOHAK-trial, is an ongoing trial currently recruiting patients with acute knee injury. Hemarthrosis is aspirated at the time of clinical assessment at the orthopedic ER at Helsingborg hospital and serum samples are collected at the same time for correlation analyses of biomarkers. MRI is routinely performed within 1 week of injury.

5) The Swedish national anterior cruciate ligament registry, is a national quality registry on ACL reconstructions performed from 2005 and ongoing. We plan to analyze per-operative factors influencing the 2 and 5 year outcome of ACL reconstruction.

We use biochemical analyses of joint fluid, serum and urine together with imaging data and clinical outcomes to shed light on the short and long term outcome after knee injury. Thus, we take an active part in sports medicine, orthopedics, radiology and osteoarthritis research.

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Prevention of hip dislocation and musculoskeletal deformities in children with cerebral palsy

GUNNAR HÄGGLUND, HENRIK LAUGE-PEDERSEN, MÅNS PERSSON BUNKE, ELISABET RODBY BOUSQUET

CPUP, a cerebral palsy register and a health care programme for children with CP, was established in Southern Sweden in 1994 as a joint project between the orthopedic departments and child rehabilitation units. The reason for this co-operation was that we saw that a number of children with CP had developed hip dislocation and severe contractures.

The purpose of CPUP is: 1) To prevent hip dislocation and severe contractures by continual and long-term examination of joint motion and if necessary, early preventive treatment. 2) To increase the knowledge of CP and the effects of different treatments. 3) To improve the co-operation between the different professionals involved in the care of children and young people with CP.

The basis of CPUP is to identify all children with CP and offer them participation in the programme. CPUP includes a standardized follow-up of each child in terms of an assessment form. The children are assessed 1-2 times a year. The form includes information on the child’s gross and fine motor function, passive range of motion, use of orthoses and treatment. The programme also includes a standardised radiographic follow-up of the children’s hips and spine. All reports are administered via Internet.

In 2005, we were able to present with a 10-year follow up, that hip dislocation is preventable and also that there was a decrease in the number of children that developed severe contractures in a total population. In 2005, CPUP received funding as a National Quality Register.

Since 2007 all counties in Sweden have joined CPUP. In 2009 CPUP became a National quality register in Norway, and in 2010 registration started in Denmark and Island. Scotland and parts of Australia plans for participation. At present about 3000 children with cerebral palsy are followed in CPUP. This total population followed prospectively is used for several research projects. Since 2011 also adults with CP are included in CPUP. Read more at: www.cpup.se

PhD student: Måns Persson Bunke, Elisabet Rodby Bousquet

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Risk Factors for Osteoporosis, Falls and Fractures with Special Reference to Physical Activity

MAGNUS KARLSSON

Background: Skeletal growth and age related bone loss influence who will develop osteoporosis. But also skeletal architecture influence bone strength. Furthermore, muscle strength and level of sarcopenia determine who will fall and sustain fractures. Thus, it is imperative to determine regulation and possibility to modify each trait and to identify high risk individuals for fractures. This is essential as the lifetime risk of fracture is 50% for women and 30% for men.

Objectives: To (i) study regulation and possibility to modify bone mass, skeletal architecture and soft tissues during growth and ageing, (ii) evaluate risk factors and prognostic factors for osteoporosis, fall and fractures, (iii) evaluate if benefits achieved by interventions in young years remains in old ages and, (iv) follow fracture epidemiology.

Methods: Secular changes in all types of fractures are followed in national registers. Gender specific evaluations are done in population-based cohorts of children, adolescents, adults and elderly who are followed by bone scanning (dual energy X ray absorbtiomtry (DXA), ultrasound (QUS), peripheral computed tomography (pQCT)), neuromuscular function (functional tests), anthropometry and quantitative muscle measurements (DXA and PQCT), muscle strength (Biodex), fall frequency (tri-annual post cards) and fractures (regional databases and radiographic archives).

Results: Hip fracture incidence has decreased. Other fragility fractures have increased and different types of fractures have been attributed do different secular changes. This has necessitated recalculations for future fracture burden. Daily physical training at growth enhances bone mass, bone size, reduces overweight, blood preassure, improve school performance. The benefits remains with an associated low fracture incidence in older ages. Impairment in functional tests identify fallers with fractures from fallers without and non-fallers and a Strength Index, taking both bone mass and bone architecture into account, predict fractures.

Clinical relevance: Out studies increase the understanding of the pathophysiology of osteoporosis and improve our ability to target risk individuals.

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Radiostereometric analysis of skeletal growth in children

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RSA (Radiostereometric analysis) as developed by Göran Selvik 1974 has been used extensively for orthopaedic and radiographic research. The radiostereometric technique can be used to determine the three-dimensional dynamics of one skeletal structure relative another and therefore we found it suitable for investigating physeal growth.

RSA permits accurate determination of longitudinal growth and rotational movements over short periods of time. This makes it possible to detect an incomplete physiodesis at a very early stage, and, if necessary, do a repeat operation before an angular deformity or inaccurate correction of LLD is of any clinical importance.

After establishing the accuracy of the method on the first 10 children and following another 30 children closely with this technique, we now perform RSA on all physiodesis as a routine follow-up postoperatively and at 12 and 15 weeks postoperatively.

Leg Length Discrepancy: Children with LLD are treated with percutaneous physiodesis and followed with RSA. The time perspective from physiodesis to physeal arrest is evaluated in relation to age and gender. A prospective study using eight plates instead of percutaneous physiodesis is carried out with the potential possibility of this method to be reversible and making correction of LLD a very accurate procedure.

Varus – valgus correction: The introduction of the eight plates has largely replaced the need for correction osteotomy in a number of paediatric diagnoses. Correction of varus- and valgus deformities can be followed clinically but with much more precision with RSA.

Extreme tall stature: Girls with predicted height > 187cm (+3sd) and boys >200cm were earlier on occasionally treated with hormones by the paediatricians to reduce height at skeletal maturity. This treatment includes very many complications and risks, and normally not very much correction.

In corporation with the paediatricians we now treat some of these children with knee physiodesis and follow them with RSA.
**Fractures:** Physeal fractures can result in partial or complete arrest of the physis leading to asymmetrical growth or growth arrest. Conventional radiographs are not able to predict whether the physis has been damaged or not but with RSA this can be revealed before any malalignment occurs.

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Optimized biomaterials for tissue reconstruction

LARS LIDGREN

The overall aim of the project is to develop improved biomaterials to obtain a better understanding of the biomaterial tissue interface, and to exchange knowledge between different disciplines.

The project consists of a basic/preclinical part and a clinical part. The basic/preclinical part will focus on (1) molecular and cellular binding patterns and mechanics of existing and new chemically and structurally tailored surfaces and materials. The biological function of calcium sulfates, phosphates and apatite as replacement for fracture healing as an antibiotic carrier are studied in animal models (2). A ceramic material has unique capacity in acting as an antibiotic carrier and at the same time giving bone induction.

Research on material degradation focus on polymers in bearing surfaces and around implants to study chemical, physical, mechanical, biological, rheology and tribology properties (3). Several imaging techniques are measuring implant motion and degradation. Multicenter survival studies including outcome measurements are used for the clinical biofunction evaluation (4).

Ad (1). Materials will be modified to achieve different tissue organization by functionalization of the surface by attachment of biologically active ligands primarily chosen from normally occurring matrix components.

Ad (2). Cell cultures and experimental models, which are closer to clinical applications, are used. The idea is to use synthetic bone or bone grafted knee prosthesis in rabbits, in which we will try to stimulate incorporation and remodelling of the grafts by, for example novel peptides. Chamber models are used for further characterization. New technique for tenocyte and chondrocyte cell cultures on a novel fleece are in clinical studies. Limited animal and clinical studies for an antibiotic carrying ceramic material show promising results. Pharmacokinetic studies and extended clinical studies need to be carried out.

Ad (3). The chemical, structural and rheological properties of the materials are characterized prior to and after wear testing by using spectroscopic and microscopic techniques. Analysis of components from retrieved clinical and donor implants constitutes a reference to the in vitro studies.

Ad (4). A national implant and biofunction register in Sweden is used for survival analysis. To reduce HDPE wear a radical scavenger, invented in Lund, has been added during the fusion process and are now in clinical testing.

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Osteoarthritis research
– a continuum from gene to patient

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**Background:** Osteoarthritis (OA) is on the top 10 list of the WHO Global Burden of Disease. OA represents a final common disease end stage with pain, stiffness and structural joint changes of cartilage, bone and other tissues. OA is caused by environmental factors such as joint injury and overload caused by e.g. obesity, interacting with a marked genetically determined risk for OA.

Our routine methods for diagnosis and assessment of progression are based on clinical and radiographic signs. With these methods the disease is diagnosed only in its final stages and progression is difficult to assess. There is no disease-modifying treatment that can stop or slow OA.

**Objectives:** 1) To identify risk factors and disease mechanisms for OA on the gene, molecule and patient level; 2) To develop methods for assessment and monitoring of patients with OA; 3) To develop and assess new (and old) treatments for OA.

**Results:**
1) We have in twin and family studies identified a marked familial risk for OA of both the hip and the knee, and identified chromosomal loci associated with OA. We have identified and mapped degradation mechanisms for key molecules in the cartilage matrix. In large population based studies we have quantified the greatly increased risk for severe OA of the hip and knee associated with overweight and obesity.

Joint injury is another important risk factor for OA. We use this disease model of OA to further explore interactions between genetic and environmental risk for OA. Specific molecular fragments released from the OA joint help us understand the dynamic changes of cartilage metabolism that occur after joint injury and which precede OA development.

We monitor the development of OA in long-term studies of groups of patients with injury to the menisci or ligaments of the knee to determine the influence of patient variables and current treatment on outcome.

2) We have developed patient administered questionnaires to monitor pain, function and quality of life in patients with OA. We identify and validate molecular fragments as biomarkers. Together, patient-administered, imaging and biomarker outcomes support our efforts to improve monitoring and treatment for OA.

3) We conduct internationally recognized studies on the natural history of injuries to the meniscus and cruciate ligament of the knee.
These studies are complemented by focused randomized controlled studies to assess and compare the efficacy of surgical and rehabilitation interventions for these injuries.

**Clinical Relevance:** OA is a major global disease burden. Our long-term studies of patients with meniscus injuries have led to a re-evaluation of the importance of these common injuries for the development of knee OA, and their optimal treatment. In a 2-year randomized trial comparing structured rehabilitation with or without reconstructive surgery after anterior cruciate ligament rupture of the knee, we showed that surgery did not provide any additional benefit. These results, published in New England Journal of Medicine, have received considerable international attention.

Our work is done in collaboration with groups in Iceland, England, Germany, USA, Canada, Australia and Japan.

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Foot & Ankle: Diagnostic and results of surgical treatment

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The Swedish Ankle Register. (www.swedankle.se) The register which is supported by the Swedish Association of Local Authorities and Regions contains all ankles replaced by uncemented total prosthesis since 1993 and in addition all revisions and reoperations. Since 2008 are also primary ankle fusions increasingly being reported.

Report forms and questionnaires -EQ-5D & SF-36 and a validated Self-reported Foot & Ankle Score (SEFAS) - can be downloaded from the abovementioned web-site. The intention is that the questionnaires are answered before and at regular intervals after surgery. Data are transferred and store din a central database at RC-Syd in Lund. The most recent results and what has been published can be found at the web-site. The register serves as a basis for clinical development and research.

Validation of the foot-specific SEFAS score (Self-reported Foot & Ankle Score). The score has been validated for ankle arthrodesis and ankle replacement and a manuscript will be published in Acta Orthopaedica 2012. The validity, reliability and responsiveness are excellent. Whether the same score, that is based on Oxford-12 for hips, is suited for evaluation of foot function before and after surgery of the fore- and hindfoot is presently investigated.

The Mobility ankle prosthesis has for more than 6 years been used in Malmö when the ankle is being replaced. All cases are followed at regular intervals with clinical and radiographic and C-T examinations. Function is then documented by established ankles scores and validated questionnaires covering both general health and foot- specific issues.

The prevalence of primary ankle osteoarthrosis. The prevalence is being estimated by a large number of phlebographies in which also the ankle joint can be scrutinized.

Radiographic diagnostic of ankle osteoarthrosis. The diagnosis ankle osteoarthrosis is often made in a specialised laboratory from pictures obtained in standing position. The optimal technique for evaluation of the ankle is now being evaluated in a control group and a group of patients with known osteoarthritis. The ankles in either group are radiographed unloaded, fully and half loaded.
**Balance and muscle strength.** Patients undergoing fusion or replacement of their ankles due to osteoarthritis have their balance tested in a standardised manner before and one year after surgery. At the same time isometric muscle strength is measured. A matched control group will undergo the same investigations.

**Self-reported function after fusion and replacement of the ankle.** Patient having answered the EQ-5D, SF-36 and SEFAS questionnaires before surgery are asked to answer the same questionnaires one and two years after surgery.

**Walking velocity and oxygen consumption:** Patients scheduled for fusion and replacement of the ankle due to osteoarthritis are equipped with an accelerometer, a small computer attached to a belt at the waist measuring physical activity 24 hours a day during a week. Thereafter walking speed and oxygen consumption are measured. All measurements are repeated one year after surgery.

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Shoes for people with diabetes: Impact of a rocker sole on balance

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Background: Footwear with rocker soles have long been used in patients with diabetes and plantar forefoot ulcers. Schaff and Cavanagh (ref. 1) have shown that peak pressures under the forefoot can be reduced by up to 30% through the use of rocker soles. 2009 Allet et al. (Ref. 2) wrote that patients with diabetes have difficulties on uneven surfaces even before the neuropathy has been established, and that this leads to increased risk of falling.

The use of rocker soles, despite being a common treatment, is poorly evaluated with respect to balance and fall risk. It is therefore the intention of this study to investigate whether a relationship exists.

Purpose: To explore the relationship between the use of shoes with rocker soles and balance. Poor balance is related to a higher risk of falling in people with diabetes.

Issue: Is balance affected and does this in turn increase the risk of falling when diabetic patients use shoes with rocker soles?

Method: Recruitment of volunteers will be done through the Endocrinology Clinic at Skåne University Hospital, Lund. All patients will be informed that participation is voluntary and that all data will be kept confidential.

Testing will take place at the gait laboratory in the orthopaedic department in Lund which is run by Scandinavian Orthopaedic Laboratory Ltd (SOL AB). The patients will first be fitted with two pairs of shoes before the testing begins. The shoes are identical except that one pair is constituted with a rocker sole. All tests will in turn be completed using shoes both with and without rocker soles.

A rocker sole is a sole construction with a rigid outer sole which is rounded in the forefoot. This reduces forefoot resistance and promotes a rolling motion in order to facilitate toe off.

We will measure sway, the movement of the center of gravity at standstill. The subject is instructed to stand quietly on a force plate when the measurement is recorded. The procedure is repeated for both types of shoes and with eyes open and closed. (Ref 3)

The test “Timed Up and Go” (TUG) is a simple test that measures the time it takes to get up from a chair and walk three meters, turn around and come back and sit down. The test is correlated to risk of falling (Ref 4, 5). We will also measure temporospatial parameters at normal walking speed. It is done by using reflective
markers on the test person’s shoes while the person is walking and infrared cameras record the gait.

**Significance of the project:** The use of rocker soles to minimize pressure under the forefoot is a common treatment for patients with diabetes and forefoot ulcers. We also know that generally people with diabetes have impaired balance. There is evidence that impaired balance may lead to falls which is a problem for the individual and costly for society.

**Schedule:** The project started in January 2012. Data collection will take place during autumn 2012. Analysis of the results and composition of an article will take place during 2013.

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Knee function and development of knee osteoarthritis in ACL injured patients

PAUL NEUMAN

Background: Anterior cruciate ligament (ACL) injuries are common among young athletes involved in sports with knee pivoting and cutting movements. ACL injuries are functionally disabling with knee joint instability predisposing the knee to subsequent injuries and in the long-term to the early onset of osteoarthritis (OA).

Risk factors for subsequent knee OA are clearly multifactorial. It has been estimated that OA develops in approximately 0-90% of patients with ACL tears 10-20 years after the injury (Öiestad et al., 2009) and so far there are no studies that prove that ACL reconstruction can minimize the future development of knee OA (Lohmander, 2007). (opposite: Daniel 1994, Fithian 2005, Keays 2007)

According to the literature meniscal injuries and meniscectomies are well documented risk factors for the development of knee OA after ACL injury (Neuman 2008, Öiestad 2009, Keays 2010). ACL reconstruction, cartilage lesions together with bone marrow lesions, obesity, knee joint laxity, loss of knee motion, decreased muscle strength and inferior neuromuscular function need further documentation.

Objectives: We study ACL injured cohorts both from Lund and Malmö in an ongoing effort to characterize patients with a good or an inferior outcome, and to find risk factors for development of knee OA.

We have evaluated the patients activity level, subjective knee function with self-administered questionnaires like the Knee Osteoarthritis Outcome Score (KOOS), knee function evaluated with manual examination, knee radiography, contrastenhanced MRI (dGEMRIC) and biomarkers from synovial fluid and serum after the acute injury and at follow-up during 16 years.

Results: We show that ACL injured patients treated with early neuromuscular knee rehabilitation and activity modification without primary ACL reconstruction have a low prevalence of radiographic knee OA. We also show that a concomitant meniscus injury treated with partial meniscectomy is the strongest risk factor for development of radiographic knee OA.

ACL injured patients, ACL reconstructed or not, have an inferior knee cartilage quality compared with controls according to indirect measurement of cartilage content of glycosaminoglycan (GAG) by dGEMRIC, both 3 weeks and 2 years after the injury.
The general decrease in cartilage quality in ACL-injured patients compared with references provide evidence for structural matrix GAG changes that seem more pronounced if a concomitant meniscal injury is present. The fact that post-traumatic OA commonly develops in ACL-injured patients, in particularly those with meniscectomy, suggests that decreased GAG content discerned by dGEMRIC may be an early biomarker for OA.

**Clinical Relevance:** Our results have direct clinical implications in counseling the ACL injured patient about different treatment options. If, the dGEMRIC method or different biomarkers of cartilage turn-over prove to serve as a structural or biochemical biomarker for early OA development, this would allow a faster and more rational assessment of new treatments for OA.

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Surgical treatment of skeletal metastases

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Paradoxically, with improved survival after treatment for cancer, the need for surgical treatment of skeletal metastases has increased. Until a decade ago, those with symptomatical skeletal metastases very seldom underwent surgery. A substantial development has taken place in other treatment modalities: e.g. radiation therapy, pain management, and in the field of prevention of symptoms from skeletal metastasis. Today, a growing body of evidence shows that some, but not all, patients with symptomatical skeletal metastases can gain from surgery. The main issue today is to be able to offer the patient the right combination of multi-modality treatment.

Our research is aimed towards identification of prognostic factors for long or short survival, which is of importance in deciding the right combination of treatment, and also in the development of surgical techniques for metastases in the spine and in the long bones.

Prospective registration of all patients undergoing surgery in the spine or in the long bones is done. The register is used for analyses of factors influencing the survival time. This is of importance, since patients must be able to gain from the often large operations. Furthermore, specific surgical techniques are analyzed with regard to symptom control and risk of complications.

Clinical relevance: Our results have immediate clinical relevance, foremost as regards who will, and who will not, gain from surgery, and also in refining surgical techniques and implants for maximum benefit of the surgery, while still minimizing the risks associated with surgery.

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Health services use and work disability in patients with musculoskeletal disorders

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Every third visit to a GP as well as one third of the disease burden in sick leave practice comes from musculoskeletal disorders which cause a high degree of functional impairment and decreased quality of life for people of all ages.

New strategies to improve health in patients with musculoskeletal disorders are monitored and further developed by using different types of registers and electronic patient record information sometimes linked to more specific patient reported outcomes (PROMs) for special patient cohorts. This can be used for structured and continuous follow-up, evaluation and bench marking.

In our research it is possible to achieve new ways for collaboration with research groups and decision makers within Sweden, Europe and other parts of the world. This also includes bench marking of Health Care Quality Indicators for RA and OA in European programs such as the EUMUSC.NET project (www.eumusc.net).

The Skåne population (about 1.3 million inhabitants) in south Sweden is the basis for studies on the Epi-center Skåne to gain more knowledge on the consequences for the individual and for the society. We have access to both sick leave data and health care utilization data for the whole population of the southern region of Sweden, Skåne. This covers both urban and rural areas as well as population with different educational, employment and immigration patterns. The Skåne population is 1/8 of the Swedish population with same distribution of age, sex, income and the proportion of individuals living in rural and urban areas.

For the research within musculoskeletal disorders we focus on

- Studies of the positive and negative predictive and prognostic factors of musculoskeletal disorders and their co-morbidities
- Studies of the impact on Functioning, Activity and Participation due to musculoskeletal disorders on a group level for different musculoskeletal disorders diagnoses
- In a prospective cohort of more than 3 000 individuals we study in more detail the impact of chronic inflammatory back pain (Spondylarthritis, SpA) on physical activity, function, health related quality of life, work ability, and the natural history of the SpA as well as the impact of Psoriasis (PSO) and Psoriatic arthritis (PsA) on health related quality of life, work ability and the costs for patients and the society
• Estimates of the impact of musculoskeletal disorders and other chronic conditions on the health care system and the national social insurance system
• Studies of the Burden of Disease and Cost of Illness due to musculoskeletal disorders on a group level for different musculoskeletal disorders diagnoses
• Studies of the effects and cost-effectiveness of the national rehabilitation program for neck-, shoulder and back pain with an assignment from the Swedish Government
• Development and implementation of guidelines for the treatment, rehabilitation and sick leave procedures for patients with musculoskeletal disorders
• Studies of the effect of knowledge transfer and implementation of guidelines on the health in the population

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RC Syd - National competence centre for quality registers

JONAS RANSTAM

Musculoskeletal research has become increasingly oriented towards collection and interpretation of large amounts of data. National knee and hip arthroplasty registries, and a national hip fracture registry, were established already about 25 years ago. New registries have evolved since and continue to evolve in more and more areas.

This development increases the demands on both the technical systems used for handling data and on the statistical methods for analysing them. The increasing complexity of the work implies that quality assurance is becoming an important part of the activities.

The national competence centre incorporates professional resources in data management, programming, biostatistics, epidemiology and health economics as well as medical expertise.

With these resources the competence centre constitutes a national education and consultation organization supporting both old and new registries. The competence centre has developed a general and dynamic database system for collection of data and establishment of registers. The system is based on modern relational database technology and includes secure patient data registration over the Internet.

The joint methodological know-how and development of a general database system reduce time and costs for initiation of registries for new purposes, for example evaluation of patient satisfaction and cost-benefit analyses, leaving more resources for assessments and improvement of data quality and for data analysis and reporting.

Record linkage with registers from the National Board of Health and Welfare (causes-of-death, cancer, diagnoses in in-patient care, etc.) and the databases of Statistics Sweden (population register and predictions) provides technical opportunities for developing new knowledge on etiology, treatment and prognosis of diseases and a for a better use of health resources.

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NEMEX-ATR; A randomised controlled trail of neuromuscular exercise after acute total Achilles tendon rupture

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At the Department of Orthopedics in Lund we treat Achilles tendon ruptures non-operative with an orthosis for 8 weeks. During this time, the patient bear weight within pain limits. The purpose of the project is to see if early training improves the functional outcome of the calf muscle in these patients thus leading to a more satisfactory result.


Current evidence indicates the use of early functional rehabilitation is safe regardless of surgery or non-surgery (Kearney 2012, Suchak 2005, 2008). Physiological studies in animals have shown that the tendons properties restoration enhances with early loading and that early loading is an important restorative factor during the healing process (Bring et al 2006, Enwekmeka 1989, Eliasson m.fl 2009)

In our present study NEMEX-ATR Achilles is constructed with five phases with an estimated guiding of timeframe. The phases will begin gradually and the treating physiotherapist surveys the quality of movement in each exercise to regulate and guide the participant to achieve adequate exertion and quality of movements.

The participant estimates the level of exertion by using a scale by Day et al (2004) and estimate pain on a visual analogue scale (VAS) (Price et al 1983). The ambition of NEMEX-ATR is to reach an exertion between 3-6 on the scale and a pain less than 5 on VAS. The exertion level of the exercise in the acute phase will be regulated by pain. The level of exertion will be a conducting parameter when absence of pain or discomfort is reached.

Purpose of the study: To evaluate the effect of early neuromuscular training on the function of the calf muscle in persons with total rupture of the Achilles tendon. Our hypothesis is that early neuromuscular training leads to a better functional outcome without an increase in complications.
Methodology and implementation: Prospective randomized study of all patients with Achilles tendon rupture in Lund. Two groups:

1. Patient in the early training group start within a week with gradually progressive training guided by a physiotherapist: earlier and more intense training according to a special protocol which includes early training with weight bearing in increasing portions.
2. Patients in the late training group start with gradually progressive training guided by a physiotherapist after 8 weeks, which implies the care as usual.

Our protocol includes weight bearing the first 8 weeks for both groups. The study is limited to otherwise healthy individuals with no other musculoskeletal complaints.

Outcome measures: The Achilles tendon total rupture score (ATRS) is used as the primary outcome and heel raise test as the secondary outcome.

Significance: If rehabilitation can be made more effective, persons with Achilles tendon ruptures can return to their previous level of activity and be able to exercise regularly instead of being forced to have a more sedentary life style.

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The training manual used in the study on Achilles tendon ruptures. Cover illustration by Karin Wermelin.
The number of knee replacement operations is continuously increasing. During 2010 12,920 primary arthroplasties and 820 revisions were performed in Sweden. 58% of the primary surgeries and 60% of the revisions are performed in women. Due to changes in the age-profile of the population in the coming years, demand is still expected to increase.

During the first ten years after surgery, five percent of the primary operations can be expected to be revised because of loosening, mechanical complications, infections, etc. The cost for revisions is substantially higher than that for primary operations, especially in infected cases.

The number of revisions is affected by many factors such as unsuccessful methods or implants, where the revision rate will be higher than the average. Therefore, it is of the highest importance that the use of such methods, implants and techniques can be limited to reduce the extra cost and suffering.

To maximize participation and facilitate complete reporting, the register has only gathered a minimal set of data for each primary operation containing information on identity, age, disease, treating hospital, what implant was inserted and the method of fixation. However, in 2009 the register added a number of questions to its form, which is to be filled in during or immediately after surgery.

The new question concern previous surgery on the affected knee, methods used (tourniquet, drainage, CAS, MIS), prophylaxis (infection, thrombosis) as well as timing. The completeness of the new forms has been better than expected and the new questions have already contributed to our knowledge of what methods are being used around the country. We hope that this new information in the short term will help improve quality and in the long term provide the basis for new scientific research.

After surgery, the patients are followed prospectively to identify failures, which are defined as re-operations if implant components are added, exchanged or removed.

Through statistical analyses it is then possible to estimate the risk of failures and to compare hospitals, implants, diagnoses, and eventually different types of surgical methods and prophylaxis.

As an additional measure of outcome, self-administrated questionnaires are sent to subsets of patients in order to evaluate patient-satisfaction and different health measures. Process measures such as volumes and need of surgery can be evaluated by comparing regions, studies of age-distribution, and the use of questionnaires.
All hospitals that perform knee arthroplasty surgery participate in the project. To estimate how many of the knee arthroplasties performed the Knee register captures, the Knee register was recently compared with the National Patient Register (an inpatient-care register of the health authorities, based on ICD coding) after which the percentage of captured cases was estimated to be 97% (SKAR annual report 2010).

The registry has in the past succeeded in giving early warning about inferior techniques and implants as well as stimulating hospitals and surgeons to improve their routines. It is therefore important to continue this work as new implants and operation techniques are continuously being introduced that needs monitoring.

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Optimizing treatment of hip fractures, focus on femoral neck fractures and implant research

CECILIA ROGMARK

Important improvements have been made during the last decade, with more efficient hospital care and particularly the use of arthroplasty instead of internal fixation for displaced femoral neck fractures (FNF). Still, research is needed to decide the best implant and surgical technique for different patient groups.

Even more worrying is that the overall result after a hip fracture, with permanent loss of function and health-related quality-of-life for many individuals, prevails despite these improvements. One can assume that the rehabilitation process during the first year after the hip fracture has to be more sustainable and accessible for all patients, regardless of their age, functional and mental status.

Our research is based on clinical studies at the Department of Orthopaedics, Skane University Hospital, Malmö and on register studies. The register studies are performed in cooperation with the Swedish Hip Arthroplasty Register (SHAR), Gothenburg, one of the oldest and most recognized national registers in Sweden. More complex analyses are undertaken by co-processing data from other national registers, both nationally and internationally.

Current studies comprises:

• Usefulness of movement restrictions after hemiarthoplasty – pseudo-randomized clinical study.
• Usefulness of medication reviews in hip fracture patients – clinical case-control study.
• Outcome after hip fracture, regarding complications and patient reported outcome – clinical cohort study.
• Risk factors for reoperations after hemiarthroplasty – national register study in SHAR.
• Patient reported outcome after various types of surgery due to FNF – national register study in SHAR and Rikshöft (national hip fracture register).
• Risk factors for dislocation after total hip arthroplasty due to FNF – national register study in SHAR and National Patient Register.
• Survey of complications after hemiarthroplasty for validation of data in SHAR and further risk factor analysis – national clinical site-visits and co-processing of SHAR and National Patient Register.
• Comparing clinical outcome in total hip arthroplasty and hemiarthroplasty for FNF – national register study in SHAR.
• Risks and benefits for the use of Dual-mobility cups in total hip arthroplasty – international register study in Nordic Arthroplasty Register Association database.

Dr Olof Leonardsson defends his thesis “Arthroplasty for Femoral Neck Fracture – Results of a nationwide implementation” in June 2012. Dr Ammar Al-Jobory is a newly recruited PhD-student. Physiotherapists and occupational therapists are engaged in the research group as well. Professor Kristina Åkesson acts as the senior advisor.

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Epidemiology of Fractures

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During the recent half-century an increase in fragility fracture incidence has been reported worldwide and has been predicted to continue. Some recent publications have however reported a stable or even a decreasing age-standardized hip fracture incidence which has been extrapolated to include a decrease also in other fragility fracture types.

With the anticipated changes in population size and age-structure even small changes in occurrence of disease can significantly alter the resource demands for society. Currently the lifetime risk of fragility fracture at age 50 years in Sweden is as high as 50% in women and 25% in men and more than 3 % of the Swedish national health care costs are the result of osteoporosis related diseases.

Even though effects of anti-osteoporotic treatment have been extensively examined in selected high fracture risk cohorts the current nationwide use mediates a poorly known risk modulation on a population level. Temporal trends in risk factors for fracture as for example bone mineral density or fall risk are largely unknown and it is presently uncertain if they apply equally for all fracture types, and in both urban and rural settings.

In spite of the major changes in society post World War II very few investigations have been undertaken to analyze how changes in fracture patterns are attributable to cohort and/or period effects. The multifaceted uncertainty on several levels makes adequate prediction of the future number of fractures most difficult.

Our earlier work infers that hip fracture incidence has levelled off also in Sweden and has since the mid 1990s been replaced by a decreasing age-standardized annual incidence. In women this appears to be the result of cohort+period effects, in that those born more recently had a lower cohort-specific incidence than those born earlier.

As no differences in BMD or prevalence of osteoporosis have been apparent in our examinations, the changes in hip fracture incidence seem attributable to other factors, probably linked to the major changes in society during the more than century-long lifespan (from year 1885 to 2011) of the examined individuals. In addition to our nationwide projects an in-depth examination of fracture disease in Region Skåne is ongoing in collaboration with Epi-centrum Skåne.
The overall aims of the project are to:

(A) Improve projections of the burden and costs of fractures in Sweden during the coming 3-5 decades, by defining gender specific changes in regional and nationwide fracture epidemiology during the recent 30 years including cohort+period effects (APC modelling) and effects of changes in medication, migration, and urbanisation.

(B) Produce algorithms to identify individuals at high risk of fracture in order to better target future fracture preventive strategies by investigating secular changes in known and novel risk factors. The algorithm will be tested in prospective cohorts of elderly men currently followed.

(C) Define time trends in fracture severity (classification) and treatment regime for common fracture types.

(D) Make adequate cost and resource descriptions and cost benefit-analyses (based on real and not modelled costs) for both pharmacological regimes and other interventions for osteoporosis and its consequences as well as other fractures types.

This project will increase the understanding of why we have seen an increasing incidence of fragility fractures during the recent century followed by a decrease not related to a change in prevalence of osteoporosis. The project enables more accurate prediction of the future fracture burden during the coming decades, imperative for society and politicians to know when planning the future resources for fracture care.

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Sarcoma Research

ANDERS RYDHOLM, FREDRIK VULT VON STEYERN

Soft tissue sarcoma is a heterogenous group of tumors with some 50 histopathologic types. Two thirds of the tumors are highly malignant and one third of the patients die because of metastatic disease. Novel prognostic tools, treatment-predictive markers and development of targeted therapies are needed for improved survival.

The management of soft tissue sarcoma patients in southern Sweden is since long centralized to the Sarcoma Group in Lund. A large data base on tumor characteristics, treatment and outcome and a tissue bank comprising close to 1000 patients have been created.

We apply a translational approach to study genetic and molecular profiles, validate gene/protein expression patterns in large clinical materials, link novel markers to prognosis, and apply the findings for refined diagnostics and prognostics.

The research group involves 7 senior researchers (Carneiro, Domanski, Engellau, Mertens, Nilbert, Rydholm and Vult von Steyern), one postdoctoral fellow (Jönsson) and 1 PhD student (Styring). The projects are carried out in collaboration between the Department of Orthopedics, Oncology, Pathology and Clinical Genetics. International collaborations include groups in Scandinavia within the Scandinavian Sarcoma Group, The Netherlands, and the USA.

We have recently:

- Demonstrated diagnostic and prognostic gene expression signatures across the soft tissue sarcoma subtypes
- Validated the prognostic importance of invasive growth pattern, which is now included in the high-risk criteria in the Scandinavian Sarcoma Group prognostic SING system
- Described the changing clinical presentation of angiosarcoma after breast cancer treatment, reported results indicating that surgical excision of all irradiated skin may improve prognosis in secondary angiosarcoma and identified differences in gene expression patterns between primary and secondary angiosarcomas
- Demonstrated that simple guidelines combined with an open access tumor clinic are efficient for referral and centralisation of soft tissue sarcomas

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Orthopaedic surgery on rheumatoid patients

URBAN RYDHOLM, ANNA STEFÁNSDÓTTIR

There is a long tradition of treating patients with rheumatic diseases at the orthopedic department in Lund and results from research in several fields have been published.

A pilot study on registration of rheumatoid surgery, with detailed patient reported outcome measures, has been conducted at the rheumatoid surgery unit in Lund and at Spenshult Rheumatism Hospital. The purpose of the study is to examine the effect of surgical interventions as measured by the patient-administered questionnaires EQ-5D, HAQ and SF-36.

Resurfacing arthroplasty of the hip joint was a decade ago considered to be a promising technique. A limited number of rheumatoid patients have received a surface replacement and these patients have been followed by clinical examination, radiography and radiostereometry (RSA) within a prospective study. During the last years it has become evident that the metal-on-metal concept is afflicted with potential serious complications and the patients are now being followed with magnetic resonance imaging and measurements of metal ions in serum.

A multi-center pilot study on a new ankle prosthesis is ongoing as well as follow-up of subtalar fusions with trabecular metal implants. Results of ankle fusions after prosthetic removal has recently been published and other techniques for this are under evaluation.

The long-term results of stabilizing and decompressive surgery of the cervical spine in patients with RA are investigated in co-operation with the Department of Neurosurgery.

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Hip and Knee Replacement: clinical, radiographic and radiostereometric analysis

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Aims
• To increase the knowledge of how the surface structure of the implants influences on their stability vis-à-vis underlying bone.
• To evaluate how the geometry of stem prostheses influences on the migration pattern.
• To investigate the relationship between bone quality and fixation of femoral stem prostheses.
• To find less trying methods for replacing the hip in patients that have fractured their femoral neck.
• To evaluate design details of knee prostheses that will imply optimal function, prosthetic survival an a low rate of complications.
• To find methods that more accurately can differentiate between mechanical and infectious complications.

The C-stem prosthesis. A prospective longitudinal radiostereometric study (RSA) in 33 patients. The 2-year results were published 2005. Thereafter the patients have been examined after 3, 5 and now 7 years. Data are now being processed for publication of the 7 year result.

Movement pattern of cemented prostheses at 10-15 years. Patients with a cemented Charnley Elite prosthesis and the patients from the above C-stem study are being evaluated with RSA, conventional x-ray and clinical follow up at regular intervals up to 15 years to evaluate movement pattern over time and to evaluate which early movement patterns predict latter failure.

The Corail prosthesis. The about 250 person who annually contract a dislocated femoral neck fracture were offered a hip replacement using an uncemented HA-coated total -or hemi-prosthesis. The former in patients aged 70-79 and the latter to patients above the age of 79.

The patients were examined clinically and by RSA at regular intervals up to 2 years. Dexa-measurements of the contra lateral hip are undertaken. We have found that the initial migration observed, stops after 3 months. In press.
**Bone cement.** A new type of bone cement (SmartSet, 97,5% Methyl metacrylate) which is claimed to make handling easier and safer and have been designed to increase “working time”. 40 patients will be included and followed by RSA as in a previously undertaken RSA study of the same prostheses.

**Infected prostheses.** Serologic methods for differentiation against mechanical complications will be tested. In acute haematogenous infections it will be evaluated whether irrigation -suction drainage combined with antibiotics is sufficient as treatment.

**Untreated CDH in adults.** Congenital hip dislocation that has not been treated in early childhood results in severe limp and pain usually when the patients reach the age of 30-40. Screening for CDH in newborn has made these cases rare and today mostly seen in persons born in other countries.

A number of cases have had their dislocated hips replaced in Malmö and the results have been published in 2003. The operative technique is demanding and specially designed implants are required. The patients are followed up at regular intervals.

**Relevance.** In the short run all prostheses have shown good or excellent results but for long run performance and patient satisfaction it is required that a selected patient material is followed up for many years. This is the only way to reveal whether a certain prosthesis or technique is related to a certain complication. In many instances the RSA-technique can shorten the time span.

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Deep infection after knee arthroplasty

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The incidence of deep infection after a primary knee arthroplasty is approximately 1.5%. As the number of operations performed steadily increases so does even the number of patients that are affected by this serious complication arise. Since 1975 the Swedish Knee Arthroplasty Register (www.knee.se) has registered information on knee arthroplasties performed in Sweden. This large nation-wide database provides unique possibilities to study a low-frequent complication like deep infection. Information on treatment modalities, results and microbiology for patients treated from 1975 to 2000 has been published. During the last decade it has become common to treat an infected knee arthroplasty with open debridement and exchange of the tibial insert, followed by antibiotic treatment. In the medical literature it is debated which patients should be treated in this manner. Special interest is on the time interval from the signs of symptoms until debridement, and on microbiology. Information on more than 150 cases of primary total knee arthroplasties having a first time revision due to infection with exchange of the tibial insert has been collected and is being analyzed.

Deep infections can be caused by bacteria that colonize the skin of the patient. 133 patients have had a culture taken from the nares and the groin prior to primary arthroplasty and the results reveal which bacteria colonize the patients, and the resistance pattern of the bacteria.

In Sweden, cloxacillin is the most common type of antibiotic used as systemic prophylaxis in conjunction with arthroplasty. The timing of the first dose of prophylactic antibiotic has been shown to be suboptimal. After various interventions the timing, which is continuously monitored on an individual basis in the Swedish knee arthroplasty register, has improved.

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From joint injury to osteoarthritis – molecular markers and structural changes

ANDRÉ STRUGLICS

Background: Osteoarthritis (OA) is the most frequent cause of musculoskeletal disability in the western world and it is on the top 10 list of the WHO global burden of disease. OA mainly affects the knee, hip and finger joints and is clinically manifested by pain, stiffness and decreased physical function. There is currently no disease modifying drug or reparative surgical intervention available and thus today’s treatments aim to reduce the symptoms of the disease.

A common belief is that OA affects only the elderly population, however, the number of younger and middle-aged people with symptomatic OA is increasing. One important factor for this increase is the strong linkage between joint injury and OA.

In healthy cartilage chondrocytes balance the turnover of extracellular matrix (ECM) proteins, where the fibrous collagen network interacts with the major glycosaminoglycan containing proteoglycan - aggrecan, providing the cartilage with the unique load-bearing and shock-absorbing quality. Aggrecan has also an important role in protecting type II collagen fibrils from proteolytic cleavage.

In OA cartilage, an overproduction and activation of proteolytic enzymes, mainly aggrecanases and matrix metalloproteinases (MMPs) disturbs the delicate balance between synthesis and degradation resulting in increasing amounts of proteolytic fragments of aggrecan and other ECM proteins in synovial fluid. Structurally this is seen as joint space narrowing, osteophyte formation, bone erosion, synovial inflammation and cartilage fibrillation.

Objective: (1) To investigate the biological response following joint injury and the processes leading to osteoarthritis; (2) To correlate molecular markers to imaging findings and to clinical outcomes in the acute and early phases of knee injury and in osteoarthritis; (3) To validate aggrecan protein fragments as biomarkers for joint injury and osteoarthritis.

Results: (1) We developed the first ELISA measuring synovial fluid aggrecanase generated aggrecan fragments starting with the N-terminal neoepitope sequence ARGS. Recently we converted this assay to a more sensitive method (electrochemiluminescence) for measurements also in serum.

(2) Analysis of bovine cartilage explant cultures showed that biomechanical injury of the cartilage does not alone increase the release of aggrecanase generated ARGS
and MMP generated FFGV aggrecan fragments. Co-culturing the cartilage with synovium (cytokine source) increases the release of ARGS fragments but not FFGV fragments. Both mechanical injury of the cartilage and co-incubation with the joint capsule increases ARGS and FFGV fragments. These data indicates differences in the mechanism of activating aggrecanases and MMPs.

(3) We confirm that aggrecanases are the dominant aggrecan proteases, but also show that MMPs contribute to aggrecan degradation, while calpains have a minor role in aggrecan turnover.

Our results also suggest that during the acute phase after knee injury there is an increased aggrecanase activity against both the inter globular domain (IGD) and the chondroitin sulphate (CS) region of aggrecan, seen as an increase of aggrecanolytic fragments in the synovial fluid – seen several years after. In contrast, analysis of the synovial fluid of juvenile idiopathic arthritis patients showed high aggrecanase activity in the CS region but very low activity in the IGD. These results indicate of differences in the aggrecan fragment pattern between patient groups.

(4) Using our meniscus injury cohort, we showed that synovial fluid ARGS-aggrecan levels 18 years after meniscectomy were no different from those of reference subjects and were not correlated to radiographic status. However, high levels of synovial fluid ARGS-aggrecan fragments were associated with a lower rate of joint cartilage loss, and decreasing levels of ARGS over time was associated with increasing risk of loss of joint space and pain worsening. These results provide new insight in how aggrecan degradation is related to radiographic and patient-related outcomes in OA.

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Lumbar pain and sciatica – diagnostics, RSA, treatment and long-term outcome

BJÖRN STRÖMQVIST

Surgical treatment of lumbar spine disorders is becoming more common. The main reason for this is the detailed information on anatomic structures obtained by modern radiological techniques such as MRI and CT, and also by diagnostic injections. The main aim of the surgical treatment is pain relief/pain reduction but retained or improved nerve and muscle function may also be achieved. To demonstrate the utility of new treatments, prospective long-term follow-up using multiple result parameters is required.

In prospective outcome studies of decompressive surgery and disc herniation operations and, subsequently, also fusion for degenerative disorders, tumors and fractures, the short- and long-term effect of these treatments has been documented. The aim is improved selection criteria for surgery in the individual and also to improve patient information.

Prospective long-term studies were initiated in 1986 and have resulted in a large database stepwise analyzed regarding short- and long-term outcomes, especially concerning diagnostic data and patient selection. Since 1993 a national register for lumbar spine surgery is run which covers 75-80 % of the degenerative lumbar spine surgery in Sweden providing an excellent source for indication and outcome analysis. Current analyses focus on gender differences, complications and regional variations. From 2006 the register covers all spinal disorders, more than 60 000 operations are included.

With the aid of precise radiographic measurement techniques [radiostereometry, (RSA), distortion compensated radiography], mobility patterns of the spine have been documented in healthy subjects and in defined disorders. This technique has also been used to evaluate the outcome after surgical interventions, especially fusions. An algorithm for evaluation of new implants has been presented. The importance of this is emphasized by the high number of new implants emerging on the market, such as disc prostheses, nucleus prostheses, and mobility retaining implants. A radiostereometric disc prosthesis study is running.

Biochemical studies of cartilage markers in disc herniation are performed in collaboration with the department of Cell and Molecular Biology. The aim is to enable monitoring of the disorder with a blood test from a prognostic and perhaps therapeutic point of view. This technique is also being applied to spinal trauma.

Bone inductive substances have been evaluated in conjunction with fusion. A study of non-invasive treatment of lumbar disc herniation using high intensity
focused ultrasound is running currently. If this proves successful, surgical treatment could be diminished. A pilot study of its safety in humans has been completed recently and a RCT is ongoing. The development of a non-heat curing bone substitute for expanding painful vertebrae with osteoporotic fractures or tumors, vertebroplasty, is being conducted.

Evaluation by functional and ADL parameters is studied in multidisciplinary projects before and after disc herniation surgery. The effect of surgical treatment, determined with health related quality of life protocols, is analyzed. Correlations between various outcome parameters are studied and patient selection for spinal surgery is gradually improved. Outcome predictors in lumbar spinal stenosis are currently the focus of evaluation.

**Clinical relevance:** All aspects of the research protocol are dedicated to clinically relevant questions for spine patients. Main benefits obtained will be improved patient information and patient selection for surgery, pinpointing the best surgical techniques and deleting non-efficient treatment modalities.

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Osteoporosis and fragility fractures, especially hip fractures

KARL-GÖRAN THORNGREN

Patients with hip fractures constitute one of the most resource consuming groups in health care. They consume 25 percent of all bed days in orthopedic departments in Sweden. We have pioneered a treatment program with fracture repair (osteosynthesis), immediate direct weight bearing, and continued walking rehabilitation in the patient’s own home.

During the last twenty years the risk of hip fracture has doubled in persons above 80 years of age and the total number of elderly in the population is increasing. We must therefore continue the improvement in operation techniques and rehabilitation of the hip fracture patients.

The research project contains epidemiological, prognostic, operative, and technical as well as rehabilitation and economical aspects on the hip fracture treatment. The project further contains optimized patient care including rapid handling to operation, prevention of infection and pressure ulcers, pain management and improved nutrition. It also includes a nationwide study of parameters for quality assurance (RIKSHÖFT, see www.rikshoft.se).

In a European Commission project called Standardized Audit of Hip Fractures in Europe (SAHFE), the Swedish national registration has spread internationally widely also outside Europe.

Projects:
• Fracture epidemiology, background factors, screening and prevention of osteoporosis and falls
• Comparison of operation methods
• Investigation of femoral head blood circulation and vitality after femoral neck fracture
• Hip joint tamponade after trauma, i.e. increased pressure within the hip joint capsule due to bleeding
• Acute fast track treatment from hip fracture to operation
• Nutrition, pain relief and prevention of pressure ulcers and cognitive impairment in hip fracture patients
• Bone transplantation
• Osteonecrosis (cell death and bone compression within the femoral head
• Nationwide, multicenter registration of quality in treatment of patients with hip fractures and international comparisons

**Techniques:** epidemiology, balance testing, patient inquiries, skeletal scintimetry, bone densitometry, histology, MRI, CT, X-ray, ultrasound, pressure measurement

The optimal treatment of this large and increasing group of patients has great importance both for the individual and the society with its limited resources for health care.

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Experimental orthopaedics and clinical studies to improve treatment of skeletal and joint diseases

MAGNUS TÄGIL

Our aim is to improve the treatment of fractures as well as control the consequences of joint diseases such as osteonecrosis, osteoarthritis and rheumatoid arthritis. We use experimental implants in animal models to test drugs or basic biologic parameters like mechanical load.

The research program starts with the single undifferentiated mesenchymal progenitor cell as it enters into the field of injury and how its fate is determined by the mechanical environment and by locally released differentiating proteins. In animal models we can alter the differentiation pathway for this cell to become cartilage by mechanical load. We describe the influence of different mechanical stimuli on the cell and determine the boundary conditions for tissue differentiation, when and how differentiating proteins are expressed during fracture healing, and finally match the mechanical and humoral stimuli in a computer finite element model.

Using pharmacological substances we are able to manipulate the anabolic and catabolic components of bone healing, separately or in combination, and inhibit bone resorption with bisphosphonates or increase the bone formation with morphogenic proteins (BMPs, PTH, sclerostin). In complex fractures with bone loss or infection, but also in cancer metastases, rheumatoid arthritis or aseptic loosening of a joint prosthesis, large bone volumes are lost and must be replaced by bone transplant or artificial bone substitute. We have shown that this loss can be decreased by bisphosphonates and that it is feasible to use bone substitute, maybe in combination with morphogenic proteins.

The aim of the experimental research is to implement the result in the clinical practise. Bisphosphonates are being tested regarding osteonecrosis of the knee (PhD-project Jan Jureus), fracture and nonunion healing (PhD-project Per Bosemark) and prosthetic fixation (PhD-project Ola Belfrage). With our research we aim to add a more biologic thinking into the classical orthopedics compared to a previously more mechanistic view.

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Treatment of distal radial fractures

MAGNUS TÄGIL

The distal radial fracture is the most common fracture in the emergency clinic. To determine the outcome and morbidity of the fracture in the population and validate the present treatment flow-chart, all distal radial fractures in Lund are followed prospectively.

Since 2002, for more than ten years, a subjective functional outcome score (DASH) is distributed to all patients, approximately 350 a year, at three and twelve months and the outcome is registered prospectively. The majority of the patients returns to an almost normal function but about 10-15% has substantial functional impairments at one year. The focus at present is to evaluate these patients and why the results are inferior and implement changes and improvements regarding the treatment. A similar register, with identical aims but regarding proximal humerus fractures has started in 2012 by Christian Anker Hansen as a PhD project.

Prospective studies and randomised series are added to the registration system comparing open versus closed treatment or various plates. Artificial bone substitutes have been tested in distal radial fractures and osteotomies as presented in a thesis by Antonio Abramo. The ten year register data is analyzed by orthopedic surgeon Marcus Landgren in a PhD project. A follow up of a cohort with wrist fracture patients from the 90s having concomitant ligament injuries is investigated by Ante Mrkonjic in a PhD project.

In some fractures, the joint surface is destroyed and artificial joint replacement necessary. Joint destruction is also found in diseases like rheumatoid arthritis and in joint infections. We have evaluated old and new prosthetic concepts in prospective and/or randomised studies in the thumb-CMC, finger-MCP and PIP-joints as well as in the wrist RC and DRU-joints.

A collaboration with the LTH is ongoing for mechanical testing, computer modelling of joints and prosthesis as well as in bioimaging (www.cbml.lu.se).

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We study prophylactic methods and risk factors with the aim to reduce the risk of complications during the treatment of tibial osteotomy by the hemicallotasis technique (HCO).

HCO is a method used to unload the damaged medial or lateral compartment of the knee joint by correction of the mechanical axis, in order to reduce pain and enhance function. HCO is used on 50-60 patients per year in Lund. 597 patients (654 knees) have been treated by the HCO since the modest start in 1993.

HCO is an alternative surgical treatment of younger and/or physically active patients with severe knee osteoarthritis (OA) and knee deformities. HCO is a callus distraction for correction of angular deviation, which utilizes the regenerative potential of the bone to achieve bone healing to the desired correction, and is based on an external fixation. A successful tibial osteotomy is dependent on a proper patient selection, achieved and maintained adequate correction and avoidance of complications.

Pin site infection is the most common complication of external fixation. By changing the pin site care step-by-step, from daily to weekly care, using Chlorhexidine instead of Sodium chloride solution and decreasing the prophylactic antibiotics from 14 days to no prophylaxis at all, we are able to reduce pin site infections and decrease the use of antibiotic during the time in external fixation from, on average, 47 to 11 days. Leaving the theatre dressing undisturbed during the first postoperative week resulted in less use of antibiotics compared with change of the theatre dressing during the first postoperative week.

Complications such as delayed bone healing and non-union generally imply longer time in external fixation and increased risk of further complications. We have shown that smoking is the single most important risk factor for complications. An extension of the study on smoking including patients using oral snuff – “snus” – indicates that the use of oral snuff does not have the negative effects, as delayed bone healing or increased risk for complications, as cigarette smoking.

We compare patient characteristics and patient-related outcomes with short- and long-term surgical and biological outcome of the HCO in collaboration with the Lund OA research group. In an evaluation of 500 patients, 92% of the patients...
were operated on for knee OA (82% for medial knee OA Ahlbäck grade I-III and 8% Ahlbäck grade IV-V). 13% of all patients were operated on for lateral deformity, showing similar improvements as patients operated on for medial deformities.

We have shown that the HCO improves self-rated pain, function and quality of life already during the treatment in external fixation and the improvements continue during a 2-year follow-up. Evaluation of mid-term results of HCO with special focus on clinically extended diagnosis criteria is ongoing.

**Clinical relevance:** Reduction of pin site infection decreases the risk of severe complications and the use of antibiotics. The pin site care developed from these studies is used in fracture healing and other corrections treated by an external fixation. The experience from the HCO cohort could be used in the selection of patients, to optimize the treatment as well as in the information to the patients.

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Biomaterials and Biomechanics Unit

JIANG-SHEN WANG, MAGNUS TÄGIL, GUNNAR FLIVIK, LIZ TANNER

Since May 1997, the biomechanics and biomaterials laboratory has provided an interface for researchers with engineering and medical backgrounds, bridging the biomechanical/biomaterial research with more biologically oriented animal models and clinical research.

The facilities within the unit are:
1. a mechanical testing laboratory with Instron/MTS machine;
2. computational facilities for mechanical analysis;
3. a RSA laboratory (RadioStereometric Analysis), utilizing a technique that with a very high degree of accuracy can measure the stability of artificial joints implanted into the body;
4. a biomaterials laboratory that enables production of ceramics for use as bone substitute materials;
5. animal model facilities for bone and bone substitutes in in vivo studies;
6. the laboratory is a part of a Centre for Biomechanics at Lund University.

The general aim of the biomechanics laboratory is to use the techniques of engineering, biomaterial and biomechanical sciences together with biological and animal models to improve the repair and regeneration of tissues in the skeletal system. A clear link to clinical use and clinical trials is prioritiesed.

Our Instron machine is used for mechanical testing of new materials or bone tissue. The RSA laboratory assesses the behavior of joint implants in the body. A large number of RSA-studies are ongoing evaluating factors such as cementing technique, bone preparation, prosthesis design and fixation methods, both cemented and uncemented. We are developing injectable bone substitute materials, that have a similar composition to bone, and which can integrate with normal tissue. We are studying how these materials can stimulate repair of tissue, through optimizing the chemical composition or the mechanical properties of the materials. We are also studying the effects of changing radio-opaque agents of bone cement on its mechanical and biological properties. Further information: www.med.lu.se/BBL/

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Molecular imaging of the hip - exploring the path from DDH to OA

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Background: In Malmö, a screening program for developmental dysplasia of the hip (DDH) has been in use since 1956. There is a general assumption that DDH in infancy is related to hip dysplasia in adulthood, but the link is far from understood.

Hip dysplasia, characterized by a steep acetabulum with undercoverage of the femoral head, is a major cause of osteoarthritis (OA). In order to detect early signs of OA, sensitive diagnostic tools are needed. Delayed Gadolinium-Enhanced MRI of Cartilage (dGEMRIC) is a non-invasive technique to study joint cartilage integrity, in particular the cartilage glycosaminoglycans (GAG) content. The method has been developed by our group since the late 1990’s.

In dGEMRIC, the negatively charged contrast medium (Gd-DTPA2-) is given intravenously and distributes in the cartilage in an inverse relationship to the amount of negatively charged GAGs, which are lost early in OA. Because Gd-DTPA2- shortens the longitudinal relaxation time (T1), T1 in the presence of Gd-DTPA2- (usually referred to as the dGEMRIC index) correlates to the cartilage GAG content.

![Acetabular index](image)

Figure 1: Hips with neonatal dislocation had a higher mean acetabular index than controls in spite of early treatment.
Objectives: The purpose of this project is a longitudinal follow-up of patients who were diagnosed with DDH in their infancy. The follow-up will include radiographic measures, dGEMRIC and clinical scores.

In a first radiographic evaluation of 332 children at age 1 year, the acetabular index (a measure of hip dysplasia) were significantly higher in patients who had a dislocatable hip at birth than in patients with unstable hips and in stable controls (see Figure 1). This indicates that a dislocatable hip does not normalize within one year, despite adequate diagnosis and treatment.

Future studies will include examination of adult patients who were dysplastic at the 1-year radiographic control to evaluate any persisting radiographic abnormalities and early degenerative cartilage changes, as evaluated with dGEMRIC.

Clinical relevance: OA is the most common joint disease with an economical burden for society that is second only to cardiovascular diseases. It is well known that hip dysplasia is a major cause of hip OA.

DDH is generally associated with hip dysplasia but very little is known about the longitudinal relationship. Our research group has a unique possibility to address this issue due to the DDH register since 1956, including radiographs, and a new sensitive method to detect early cartilage changes, dGEMRIC.

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Soft tissue pathophysiology in hip disease and arthroplasty

HANS WINGSTRAND

This project focuses on hip joint soft tissues. Sonography, intracapsular pressure measurements, MR and CT techniques were used in this clinical project to diagnose and follow hip synovitis in various disorders.

In one project, the soft tissue biomechanics of the hip joint capsule in and its influence on clinical symptoms, radiological findings and subsequent loosening in hip joint arthroplasties is studied. We use ultrasonography (US) as a method of examination THA hips for signs synovial edema/free fluid in the joint. Pain in OA hips might be of capsular/synovial origin due to its rich sensory innervation. We investigate the intracapsular pressure and the elasticity of the hip joint capsule in OA and correlated these parameters to pain and to the radiographic stage of OA. Joint dislocation remains one of the most disturbing complications after THA.

We investigate the soft tissue reaction in relation to soft tissue repair, component wear in relation to aseptic loosening of the prosthetic components.

In a second project concerning Legg-Calve-Perthes Disease of the child’s hip scintimetric and sonographic studies have indicated that increased intracapsular pressure, caused by synovitis with effusion is a factor in the disturbed blood supply to the epiphysis.

Synovitis causes cartilage oedema and ensuing cartilage hypertrophy with a risk of joint deformation, incongruency and poor containment. Serial MRI and plain radiography was used to follow the development of the femoral head. In cases of incongruency a proximal femoral varus, derotation and extension osteotomy reduced cartilage incongruency and an improved sphericity of the femoral head.

Six theses have to date been defended as results of these projects focused on the soft tissues around the hip, now continued in cooperation with Dept of Orthopedics, Kaunas Medical University, Lithuania, and Dept of Orthopedics, hip section, Liestal, Switzerland.

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Regulation of skeletal integrity:
Genetic variation, risk factors and fracture

KRISTINA ÅKESSON

Osteoporosis has become a major public health concern and is the result of low bone mass and micro-architectural deterioration of the bone structure leading to decreased bone strength. The clinical consequence is fracture, most commonly hip, forearm and vertebral fractures. Over 70,000 fragility fractures occur each year in Sweden, mainly in the increasing elderly population, inflicting enormous costs on the health care system as well as suffering on the individual.

The risk of osteoporosis and fracture increases with age. Already today, 1.3 million or 17% of the population is over the age of 65 years and a further increase to above 20% is expected within the next 15 years. The increase in life-expectancy in combination with a 50% lifetime risk of fracture in women after the age of 50 is a cause for concern. Therefore, it is imperative to identify risk factors for future fracture as well as to improve our ability to identify individuals at risk by increasing the knowledge of underlying biological mechanisms, including genetic factors and their interaction with the environment.

Within our project we connect basic science and clinical research by:
1. Using large, well-characterized population-based cohorts to define external and internal potentially modifiable risk factors for bone strength and fracture from young adults to the very elderly.
2. Identifying genes affecting attainment and maintenance of peak bone mass, as well as bone loss and fracture at different ages.
3. Investigating underlying mechanisms influencing bone cell activity in humans and animal models
4. Influencing clinical interventions based on evidence and evaluate outcome.

The continued focus of this project is on factors related to bone strength and bone fragility, delineating gene-environment interactions with an emphasis on interactions between bone and skeletal muscle, adipose tissue, glucose metabolism, and inflammation.

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Around 4% of the Swedish population has diabetes. A considerable proportion of these patients will at some point in their life have foot-related problems, the most severe being ulceration, infection and gangrene.

Almost half of all non-traumatic amputations in the industrialized world are performed on diabetic patients. In most studies the major (above the ankle) amputation rate only is reported. The principal aim of minor (below the ankle) amputations in these patients is to avoid major amputation in order to facilitate ambulation. Although minor amputations are performed in large numbers on diabetic patients, in most countries the incidence is unknown and little is known about the outcome.

We analyze factors leading to amputation and those that influence the outcome of such surgery. Can the outcome be predicted by using specific parameters? Which factors play a greater part in outcome after surgery? Trying to find the answers to these questions will hopefully lead to better treatment options for these patients.

Taking the patients’ aspect into account is also important. A large proportion of these patients are elderly and have to rely on family or social services in their everyday living. How amputation affects their quality of life is also subject to our studies.

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Scientific papers 2011

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This list includes original papers, review papers and book chapters (but not abstracts) authored by members of the staff and printed in 2011


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**DISSERTATIONS**

Susanna Stenevi Lundgren: Muscle function and physical activity in pre-pubertal school children, Department of Orthopedics, Clinical Sciences Malmö, Lund University, 2011

Max Tenne: On osteoporosis in elderly women. Bone traits, fracture and the PTH gene complex, Department of Orthopedics, Clinical Sciences Malmö, Lund University, 2011