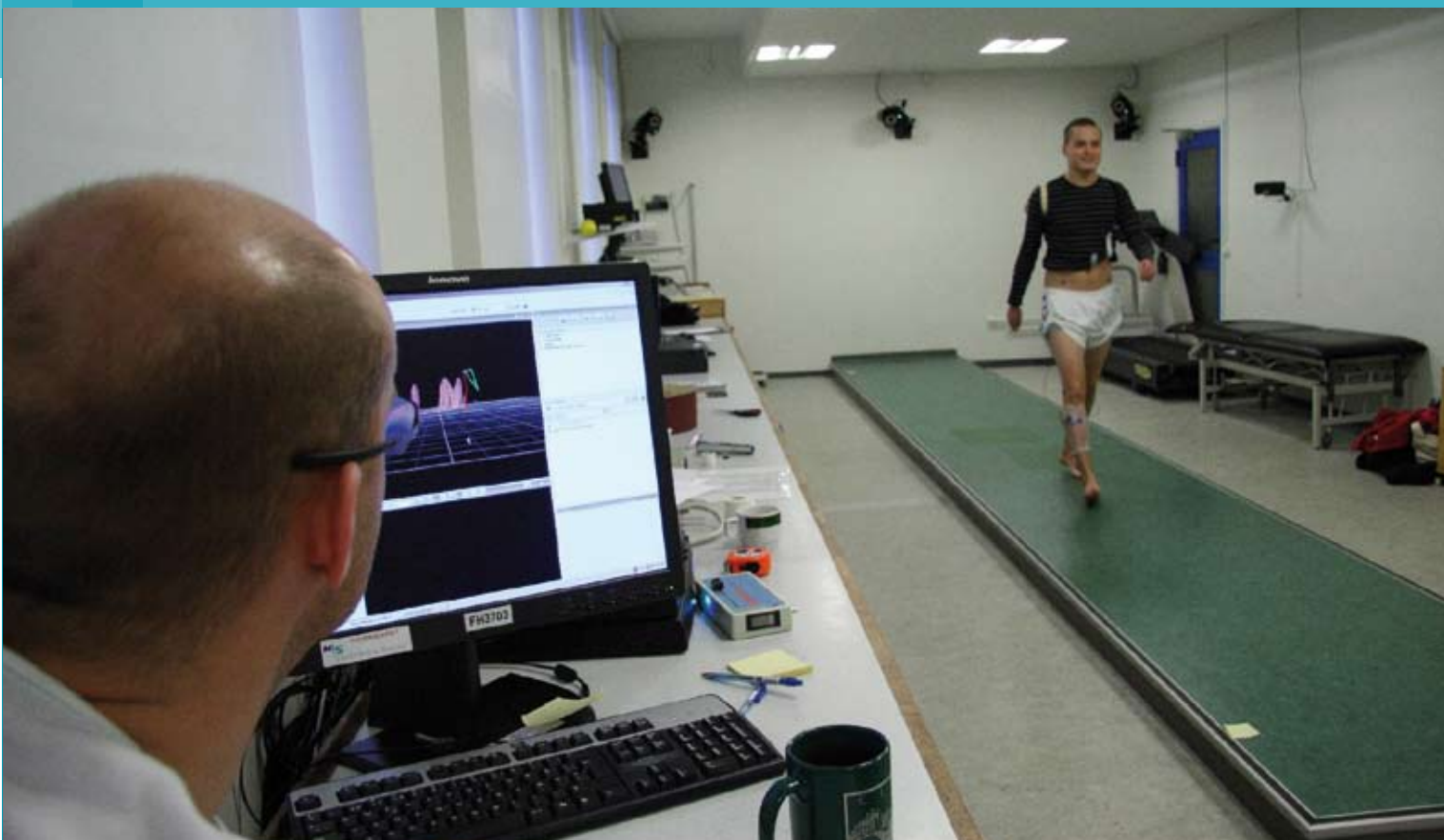


# THE PARKER INSTITUTE Annual Report 2007



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1. Head of research, Bente Danneskiold-Samsøe, Professor, MD, DMSc
2. Research professor Henning Bliddal, MD, DMSc
3. Consultant in rheumatological ultrasound, Søren Torp-Pedersen, MD
4. Head of the Gait Laboratory, Marius Henriksen, PT, PhD,
5. Head of the Biochemical Research Laboratory, Søren Ribel-Madsen, Pharmacist
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11. PhD Student, Rebekka Ryder, MSc
12. PhD Student, Robin Christensen, MSc
13. PhD Student, Anders Jespersen, MD
14. PhD Student, Karen Ellegaard, PT, MSc
15. PhD Student, Jens Aaboe, MSc
16. Physiotherapist, Sara Rosager Mortensen
17. Secretary, Mette Gad, MA
18. Secretary, Line Rustad
19. Research Manager, Claus Bomhoff, MA
20. Dietician, Pia Christensen, MSc

21. Research Laboratory Technician, Marianne Lipka Flensburg,
22. Research Laboratory Technician, Inger Wätjen
23. Research Nurse, Merete Wille, Nurse, Bcom

#### Not present in the picture

24. PhD Student, Birgit Falk Riecke, MD
25. PhD Student Mikael Boesen, MD
26. Physiotherapist, Elisabeth Bandak
27. Secretary, Helle Brandrup
28. Research Nurse, Chris Lang, Nurse
29. Research Laboratory Technician, Eva Jørgensen
30. Dietician, Elisabeth Grill
31. Database Consultant, Christian Cato Holm, MSc
32. Else Marie Bartels, Honorary Senior Research Fellow, PhD DSc, Senior Researcher at the Danish National Library of Science and Medicine.
33. Project participant, Pernelle K. Kristensen, BA
34. Josefine Eliassen, Student assistant
35. Julie Stage, Student assistant
36. Kasper Marstal, Student assistant
37. Mads Eliassen, Student assistant
38. Peter Severin Jensen, Student assistant
39. Kira Prahm, Student assistant

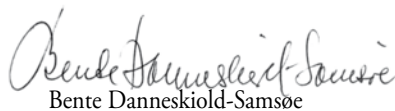
*Frontpage: With a runway more than 8 m long, 6 cameras and numerous electrodes the gait laboratory is heavy in both space and equipment*

## INTRODUCTION

2007 was a prosperous year for research at the Parker Institute. Two PhD students completed their work with interesting theses: “Ultrasound Doppler in Diagnosis and Treatment of Achilles Tendinopathy” by Morten Boesen, and “The significance of pain in knee joint loading during walking” by Marius Henriksen. We are grateful not only for these important contributions but also for other results produced by the keen and dedicated co-workers at the Institute. 2007 also saw a Parker Institute publication in the *Lancet* (Christensen R et al.); this gives some indication of the impact of the research carried out here.

Our collaboration with various institutions brought further inspiration to our research. These institutions included several foreign universities, where our research on imaging, in particular, gained acceptance and also led to publication (Kubassova O et al., Boesen M et al., Wakefield et al.). The Parker Institute is looking forward to participating in further developments on these fields of rheumatology with large potential for patient diagnosis and treatment. During 2007, a new structure was used for monitoring patients with widespread pain, and several hundred subjects were tested. The follow-up visits in the coming year will bring further knowledge of this painful disease and will lead to a better understanding of the treatment possibilities.

In 2007 we had the great pleasure of receiving representatives of the Copenhagen University, led by the Dean, Ulla Wewer, accompanied by professors Birgitte Nauntofte and Jes Bruun Lauritzen. We hope that this will initiate a closer collaboration with the University, which will prove mutually beneficial, leading to education and enrolment of students in research.



Bente Danneskiold-Samsøe

Professor, MD, DMSc

Director of the Parker Institute



*In October 2007 Bente Danneskiold-Samsøe was awarded the late Queen Ingrid's research prize. Seen from left: Prof. Bente Danneskiold-Samsøe, Mikael O. Olufsen; chairman of the board of the Danish Rheumatism Association, and Queen Margrethe II*

The Parker Institute received many grants during 2007. We are grateful for the continuing support from the Oak Foundation, which in 2007 was supplemented by many sponsors, all of whom we wish to thank for their contributions. A large grant from the Velux Foundation enabled us to launch the studies on osteoarthritis, especially the effects of weight loss on the knee joint. This complex of studies was further supported from the Cambridge Inc, supplying us with products and staff for the dietary intervention.

In addition, several foundations, among these Glunz and Jensen's Foundation and the Augustinus Foundation, supported the newly inaugurated movement-laboratory. This will allow further studies of joint loading during gait.

The director of the Parker Institute received the prominent grant of honour, Queen Ingrid's research prize, presented to Bente Danneskiold-Samsøe at the Royal Palace by the Queen; Søren Torp-Pedersen received the senior bursary of the Danish Rheumatism Association.



Henning Bliddal

Professor, MD, DMSc

The Parker Institute is Frederiksberg Hospital's rheumatological research unit. The Parker Institute was inaugurated in 1999 as a result of financial grants from the Oak Foundation, the Health Insurance Foundation (Helsefonden) and the Copenhagen Hospital Corporation (H:S). The aim of the Parker Institute is to conduct research into common locomotor diseases in order to create an improved platform for diagnosis, treatment and prevention of rheumatological diseases.

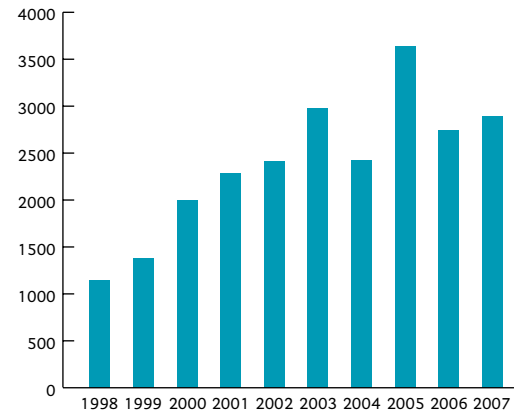
Research at the Parker Institute focuses on improving rheumatology patients' functionality and quality of life by contributing to and initiating clinical and scientific research studies relating to rheumatological diseases.

## ACTIVITY

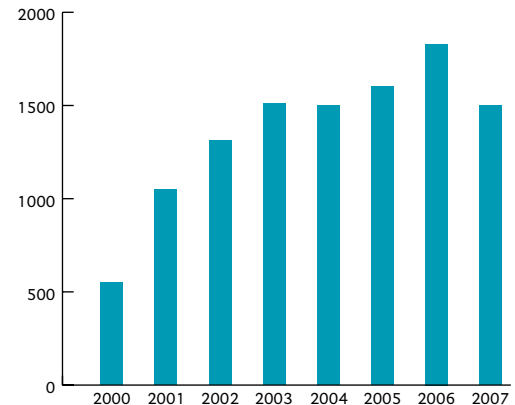
The rheumatology clinic provides medical check-ups for several thousand outpatients every year. The employees of the Parker Institute participate in the examinations and treatment of many of the more difficult cases or when patients are seen in connection with per-protocol therapy in projects. Patients referred to us re-present all forms of rheumatological diseases, but of special interest to the department is the diagnosis and treatment of rheumatoid arthritis and muscle diseases, including fibromyalgia, back complaints and degenerative arthritis. These areas are particularly therapy-demanding, since maintaining an acceptable quality of life, in which a patient can function independently, often involves continual treatment and physical training.

In 2007 physicians at the Parker Institute examined approx. 2800 patients, of these approx. 1150 were screening visits. These patients were either referred to the Parker Institute through the rheumatology clinic or enrolled in an appropriate project after routine treatments conducted by physicians from the Parker Institute in the clinic. In 2007 these activities involved about 2200 measurements of muscle strength, approx. 1500 ultrasound examinations – mostly with Doppler measurements – 200 Gait analyses, and finally some 700 blood tests on participants in research projects.

Patients examined by physicians from The Parker Institute in the clinic



Ultrasound Examinations



*Most patients cannot help competing with themselves when doing the 6-minute walk*

## OSTEOARTHRITIS

Osteoarthritis is the most common joint disease in the Western Hemisphere. It affects 50% of the Danish population over 50 years, and has severe disabling consequences for more than 10% of the population over 60 years. The cost of osteoarthritis (OA) is estimated to be somewhere between 1 and 2.5% of western countries' BNP. With this in mind, research into OA is a matter of high priority. The aetiology is mostly unknown and pathogenetic factors remain to be clarified.

For the individual, hip and knee OA means pain. It affects a person's ability to walk and other daily, essential functions, which leads to reduced life quality. The radiological changes, such as destruction of joint cartilage, osteophytes and joint space narrowing, are well described, but the correlation with clinical symptoms is weak. There is no curative treatment for osteoarthritis and most interventions concentrate on pain relief.

While many problems of this widespread disease remain to be solved, the Parker Institute has gained experience with weight loss as a highly effective therapy in the important subgroup of patients with combined obesity and knee OA. Some 50% of the patients above 60 years with painful knee OA are overweight and

have a BMI of at least 28. Research from the Parker Institute has previously demonstrated a large impact of a weight loss in obese patients with concurrent osteoarthritis of the knee. In fact, this may be the most significant treatment of such patients, with a potential for large-scale public intervention. Weight loss is relevant since it reduces the pressure on the affected joint, which is important since 50% of all OA patients are overweight. Loss of weight is shown to be the most efficient treatment when it comes to pain reduction. Weight loss will also help break the vicious circle of pain leading to less exercise leading to more overweight and so on.

### *Publications 2007*

*Several articles dealt with the aspects of weight loss in obese patients, of special interest for subjects with co-existing osteoarthritis of the knee. Other matters studied were test procedures, both clinical and laboratory measurements, in degenerative diseases. This included articles on imaging in both humans and animals.*



*Our newly established gait laboratory boasts state-of-the-art equipment for gait analysis*

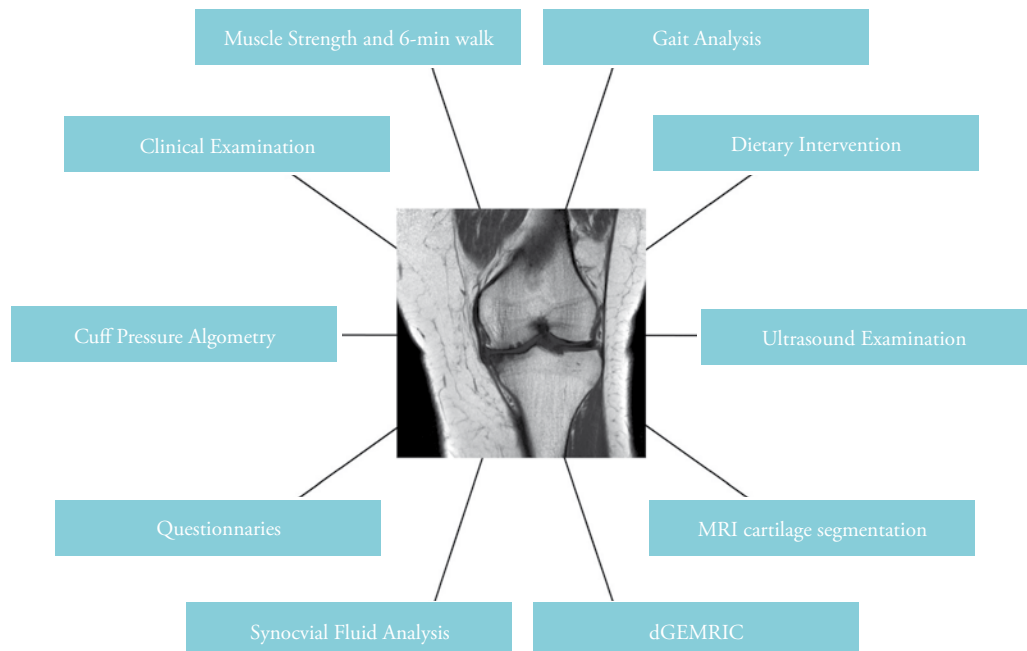
## OSTEOARTHRITIS

### PROJECTS

The weightloss projects conducted at the Parker Institute in the years 2002–2005 have shown that there is a significant effect of weight loss: in short, a 10% weight loss leads to a 30% decrease in pain, which again leads to increased physical activity. Based on current evidence in the literature, weight loss in obese individuals and exercise are the most efficient non-surgical therapies in knee OA, and exceed by far the effect of painkillers.

It is our hope to be able to give individual advice on non-surgical preventive measures to arrest or delay the deterioration of knee OA. This will include the Parker Institute's participation in the application of medication working directly on the cartilage and/or bone.

*Conglomerate of studies  
in the Carot trial*



*In our project on weight loss for  
patients with knee OA, participants  
are submitted to numerous tests*

## RHEUMATOID ARTHRITIS

Rheumatoid arthritis (RA) is a severely disabling disease, which may, at worst, cause invalidity of the patient. Much has been gained by more active therapeutic approaches with the best results obtained with a combination of a light chemotherapy (methotrexate) and biological medication against TNF- $\alpha$ , the primary proinflammatory cytokine in the joints. A certain percentage of the patients, however, do not benefit from these therapies and more refined diagnostic tools may have to be developed to single out high-risk patients for even more aggressive therapy.

The Parker Institute is involved in projects with the aim of refining diagnosis and treatment of RA. The response to therapy is traditionally measured by a combination of clinical examinations of the joint, blood tests and the patient's self-reported evaluation. We wish to do supplementary imaging analysis in all patients with active disease with both MRI and ultrasonography. Much effort is put into standardizing these imaging procedures in order to reduce the variation from scan to scan.

Objective function tests of muscle strength and performance across joints are performed in all patients to demonstrate the effects of therapy.

The biochemical laboratory of the Parker Institute measures the changes in arthritis activity in blood tests. In the patients with more localized changes, material is obtained from the site in question, e.g. a joint or tendon sheath, for biochemical analysis. Leucocytes of various kinds play a key role in the arthritic process and correlations between local and generalized activity in leucocytes are studied to gain further knowledge of the pathogenesis of arthritis.

### *Publications 2007*

*Infections with Helicobacter Pylori have been implicated in various diseases; in two articles the subject of the possible influence of Helicobacter Pylori on rheumatoid arthritis is raised. The focus is increasingly on evaluation of the arthritis by imaging and several articles have dealt with this aspect. Both ultrasonography and MRI may be used, and a significant effort has been made towards standardization and automatization of the examinations.*



*The ultrasound group has standardized the wrist scan for patients with RA*

## RHEUMATOID ARTHRITIS

### PROJECTS

Inflammation markers and growth factors in synovial material

The aim of the study is to gather information on cellular and biochemical key factors in the pathogenesis of both rheumatoid arthritis and osteoarthritis in order to improve the molecular understanding of these diseases. Anti-TNF treatments (biologics) work on only some RA patients and prognostic factors for this are of major interest. At the Parker Institute a cohort of about 150 patients is followed longitudinally during anti-TNF therapy with biochemical and imaging data. With analysis of these results, we hope to be able to distinguish subgroups of RA according to their predicted responsiveness.

Lymphocytes in blood and synovial fluid

Inflammatory markers and cells from RA patients are obtained from joint fluid aspirated before injection therapy. The lymphocytes isolated from the joint fluid have characteristics that may be distinguished from lymphocytes in blood circulation, which opens for analysis of upregulated genes in the arthritis. More than 50 samples of joint fluid and parallel blood samples

have been collected and are currently under investigation in collaboration with the Tissue Typing Laboratory at the Copenhagen University Hospital.

Imaging: Ultrasound

The ultrasound specialists at the Parker Institute have developed a standardized protocol for examination of the wrist and finger joints. In collaboration with 10 departments of rheumatology throughout Denmark, this protocol is now being validated in a cohort study with a one-year follow-up of RA patients entering treatment with the biological medication Etanercept.

Imaging: MRI

The Parker Institute is participating in a European collaborative effort to standardize a computer-based algorithm for measurement of synovial activity in RA. In a cohort study, patients are scanned prospectively with low-field MRI to validate this patient-friendly version of MRI. The data for the study are collected at the Parker Institute and Genova University and data processing is performed at the University of Leeds.



*PhD student Rebekka Ryder analyzes cytokine data from a patient with RA*

## CHRONIC WIDESPREAD PAIN AND FIBROMYALGIA

Chronic pain is very common in all European countries with a predominance of musculoskeletal problems. The syndrome, fibromyalgia (FMS), has a prevalence of about 1% in the adult population with predominantly females affected. Characteristically, multiple tender points are present and the patient has back or neck pain, and a number of associated problems from other organs including a high frequency of fatigue. Some patients develop extensive pain in musculoskeletal tissues, which in many respects are normal, except for the weakness from lack of exercise.

The typical patient has a history of hypermobility and long-lasting regional pain, which at some time becomes generalized. While the pain may originally have been initiated in the peripheral tissue, a malfunctioning central nervous system must be involved in the process of chronification. Both afferent and efferent dysfunctions are suspected as well as changes in the central processing of stimuli. Evidence points to central sensitization as an important neurophysiological aberration in the development of FMS. These neurological changes may result from inadequately treated chronic focal pain problems such as osteoarthritis or myofascial pain.

It is of importance for health professionals to be aware of this syndrome and to diagnose the patients to avoid a steady increase in diagnostic tests. On the other hand, patients with chronic widespread pain have an increased risk of developing malignancies, and new or changed symptoms should be diagnosed, even

in FMS. In rheumatology practice it is especially important to be aware of the existence of FMS in association with immune inflammatory diseases, most commonly in lupus and rheumatoid arthritis. Differential diagnoses are other causes of chronic pain, e.g. thyroid disease.

The costs of this syndrome are substantial due to loss of working capability and expenditure on medication and health system usage. Fibromyalgia patients need recognition of their pain syndrome if they are to comply with treatment. Lack of empathy and understanding from health care professionals often leads to patient frustration and inappropriate illness behaviour, possibly associated with some exaggeration of symptoms in an effort to gain some legitimacy for the problem.

FMS is multifaceted and treatment consists of both medical interventions, with emphasis on agents acting on the central nervous system, and physical exercises.

### *Publications 2007*

*Several articles have concentrated on the evaluation and therapy of torture victims. Treating the survivors after torture matters, and documentation of the sequels draws attention to the violations against humanity in some countries. The risk of co-morbidity associated with chronic widespread pain is another matter of concern as demonstrated by a study using our database of fibromyalgia. Additionally, the diagnostic examination of the patients is also of interest, as shown by articles on both pain evaluation and urinary excretion of collagen metabolites.*



*A practical tenderpoint examination is part of the fibromyalgia research program*

## CHRONIC WIDESPREAD PAIN AND FIBROMYALGIA

### PROJECTS

Fibromyalgia database and the Frederiksberg prospective cohort  
The Fibromyalgia database of the Parker Institute is of pivotal importance for the studies. This database gathers all information on the cohort of patients diagnosed at Frederiksberg Hospital with fibromyalgia. The database is active from 1990 onwards and has been compared to the Danish National Registry of Cancer for detection of possible cancer risks in patients with generalized pain (Dreyer et al 2007). The same database has information on a number of function characteristics of the fibromyalgia patients and further data processing will be preformed in the coming period. Points of interest are isokinetic muscle strength, myalgic score and the self-reported function and symptom scale (FIQ) of the patients, who are all registered in a prospective study of a cohort of fibromyalgia patients. The patients of this cohort are consecutively enrolled in an extensive programme with both measurements and a group-based course in coping strategies for living with chronic pain.

Objective measurement of function in relation to other signs and symptoms in fibromyalgia

A crucial question in the therapy of fibromyalgia is the objective evaluation of the impact of the disease in everyday life. In an ongoing study, measures of ability to perform activities of daily living (ADL) by subjects with fibromyalgia are compared with self-reported ADL ability as well as other indicators of disease. The instrument used is the Assessment of Motor and Process Skills (AMPS), and in this study the AMPS is also tested in subjects with other rheumatic diseases.

Computerized algometry

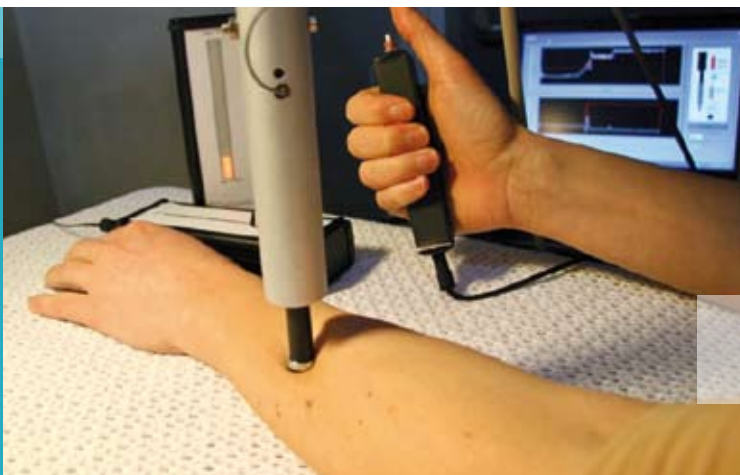
Reproducible methods for pain measurement have been developed and are currently being assessed in patients with regional and generalized pain syndromes. Computerized Pneumatic Cuff Pressure Algometry (CPA) is being used for the measurement of deep muscular pain (Jespersen et al. 2007). The method was developed to avoid some of the sources of error seen when using hand-held algometers. Also, the method allows an estimate of signs of central sensitization, which may be of importance for the prognosis of fibromyalgia as well as other painful soft-tissue diseases in rheumatology.

Distribution of tender points

In collaboration with SMI, Aalborg, the distribution and function of tender points in muscles are studied. The experimental part of the study has been finalized, and the next part will be a practical test on patients with trapezius myalgia.

Biochemical mediators of pain

Abnormal functioning of the skin nerves has been suggested as part of the generalized pain in fibromyalgia and axonal flow of pain mediators from skin nerves may be studied by the suction blister method. In this study blister fluid is collected and compared to saliva, and in some cases cerebrospinal fluid in 16 fibromyalgia patients and 15 healthy control persons.

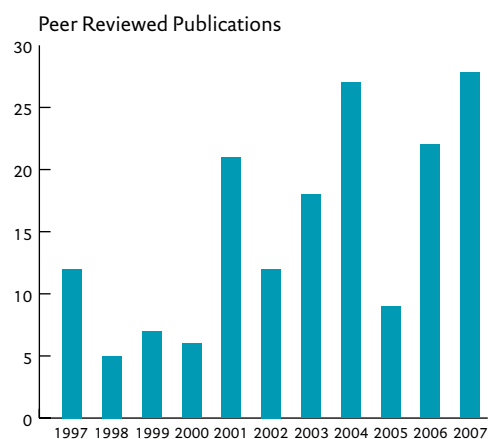


*This device has been invented for the study of tender points in muscles*

## SUMMARY

### OF SCIENTIFIC PRODUCTION BY RESEARCHERS AT THE PARKER INSTITUTE IN 2007

Two PhD theses were completed this year, “Ultrasound Doppler in Diagnosis and Treatment of Achilles Tendinopathy” by Morten Boesen, and “The significance of pain in knee joint loading during walking” by Marius Henriksen. In addition to these important contributions, the Institute had 28 articles in peer-reviewed publications and many are currently in the printing process. Parker Institute staff participated actively in several congresses with 18 posters and abstracts as well as many other publications of public interest. Parker researchers gave a large number of lectures, and senior researchers from the Parker Institute arranged and conducted 4 courses. In all matters we are grateful for the important participation of numerous patients, who readily dedicated their time, often at unconventional hours, to our research and teachings.



*PhD student, Jens Aaboe, at his desk*

## ARTICLES

### PUBLISHED IN JOURNALS WITH PEER REVIEW

1. Amris K, Danneskiold-Samsøe S, Torp-Pedersen S, Genefke I, Danneskiold-Samsøe B. Producing medico-legal evidence: Documentation of torture versus the Saudi Arabian State of Denial. *Torture* 2007;17(3):181-95.
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## FINANCIAL SUPPORT

The Parker Institute is grateful to the following foundations, institutions and companies for the assistance and financial support received in 2007

- Abbott Laboratoriums A/S
- Augustinus Fonden
- B-K Medical ApS (DUDS)
- Beckett-fonden
- C. C. Klestrups og hustru Henriette Klestrups Mindelegat
- Cambridge Manufacturing Compagny Ltd.
- Civilingeniør Frode V. Nyegaard og Hustrus Fond
- Copenhagen University
- Danske Fysioterapeuters Forskningsfond
- Danske Fysioterapeuters Jubilæumslegat
- Det Obelske Familiefond
- Direktør Einar og Vera Hansens Fond
- Direktør Ib Henriksens Fond
- Elisabeth Margrethe Schlingsogs Fond
- Enid Ingemanns Fond
- Frederik og Emma Kraghs Mindefond
- Frimodt-Heineke Fonden
- Gigtforeningen The Danish Rheumatism Association
- Glunz og Jensen Fonden
- Grosserer L. F. Foghts Fond
- Hans Henrik Holm Foundation
- Health Insurance Foundation
- Institut de Recherche Pierre Fabre
- Minister Erna Hamiltons Legat for Kunst og Videnskab
- Nordic Phytopharma A/S
- Pfizer
- Praksisfonden
- Roche
- Støtteforeningen for Gigtbehandling og Forskning ved Frederiksberg Hospital
- The A.P. Møller Foundation for the Advancement of Medical Science
- The Capitol Region of Copenhagen
- The Oak Foundation
- Velux Fonden
- Wyeth Lederle A/S
- Aase og Ejnar Danielsens Fond

### The Advisory Board

We wish to extend our thanks to the Board of The Parker Institute for their considerable effort and for their instructive comments on our work, be them critical or laudatory.

Robert Bennett, MD, FRCP, Professor, Oregon Health and Science University, USA, Board Chairman of the International MYOPAIN Society

Hans Hultborn, MD, DMSc., Professor of Neurophysiology, Former Dean of Medical Faculty, Copenhagen University

Lars Lidgren, MD, DMSc, Professor, Department of Orthopaedics, Lund University Hospital, Sweden

Bent Sørensen, MD, DMSc (chairman of the board), Professor of Surgery, Former Dean of the Medical Faculty, Copenhagen University



*The members of the Parker Institute's advisory board*

## COLLABORATION PARTNERS

In 2007 the Parker Institute benefited from its close liaison with other researchers and research groups. We worked with clinical and academic institutions, particularly those in Greater Copenhagen.

### Osteoarthritis and Degenerative Diseases Research

- Dept. of Human Nutrition, Faculty of Life Sciences, University of Copenhagen
- Dept. of Natural Sciences: Statistics section, Faculty of Life Sciences, University of Copenhagen
- Informatics and Mathematical Modelling, Technical University of Denmark
- Nordic Bioscience A/S, DK
- Dept. of Physiology, National Institute of Occupational Health, NO
- Department of Radiology, Rigshospitalet, DK
- Dept. of Orthopaedic Surgery, University of Lund, SE
- Department of Radiology, University Hospital of Vienna, AU

### Rheumatoid Arthritis Research

- Centre of Experimental Rheumatology, University of Zürich, CH
- Division of Arthritis Surgery, John Hopkins University School of Medicine, Baltimore, Maryland, USA
- The Faculty of Pharmaceutical Sciences, KU, DK
- Dept. of Physiotherapy, University of Jyväskylä, SU
- Dept. of Physiotherapy, University of Lund, SE
- Dept. of Rheumatology, University of Lund, SE
- The Dept. of Autoimmunity, The National Serum Institute, DK
- School of Computer Science, University of Leeds, UK
- EURA Study Group

### Pain and Muscle Function

- Department of Radiology, Rigshospitalet.
- Laboratory of Gait Analysis, Hvidovre Hospital, DK
- The Institute of Medical Anatomy, KU, DK
- Institute of Biotechnology, DTU, DK

- Department of Biostatistics, KU, DK
- Center for Sensory-Motor Interaction (SMI), University of Aalborg, DK
- International Rehabilitation Centre against Torture (IRCT), DK
- Dept. of Neuromuscular and Locomotion INR, Health Sciences University of Linköping, SE
- Dept. of Community Medicine and Rehabilitation, Umeå University, SE
- Copenhagen University Library, DK
- Division of Clinical Rheumatology and Immunology, University of Alabama, Birmingham, USA
- The Rheumatology Department, Oregon Health and Science University, USA
- Department of Basic Animal and Veterinary Sciences, Faculty of Life Sciences, KU, DK
- Sub-Department of Clinical Health Psychology, University College London, UK

### Organisations

- International Myopain Society (IMS)
- International Association for the Study of Pain (IASP)
- EULAR's (European League Against Rheumatic Diseases) Working group on fibromyalgia
- EULAR's (European League Against Rheumatic Diseases) Ultrasound Standardization Group
- The Danish Fibromyalgia Association
- The Danish Rheumatism Association
- Cancer epidemiology section, The Danish Cancer Society

Further information

[www.parkerinst.dk](http://www.parkerinst.dk)

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