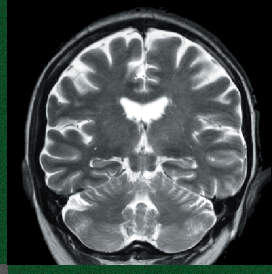
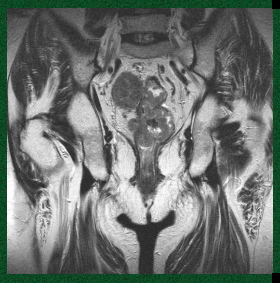
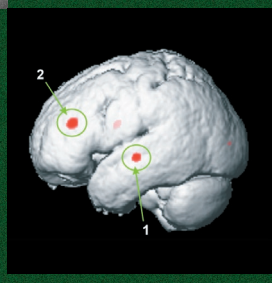
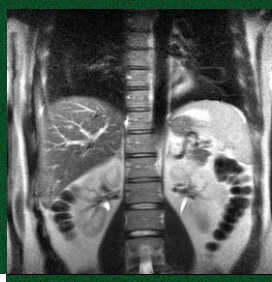






DRCMR

Annual Report 2002



Danish Research Centre for Magnetic Resonance

Introduction

The year 2002 became a milestone for the Danish Research Centre for Magnetic Resonance (DRCMR). A 3-Tesla Siemens Trio Scanner, kindly donated from the Simon Spies Foundation, was installed in July. This is the first clinical high field MR scanner installed in Denmark. The new scanner allows the centre to keep its frontline position in MR research. We expect the scanner to play a key role in the centre's research, especially brain research, in the coming years. Furthermore, the department is well-suited to apply the opportunities of high field MRI to clinical practise.

The installation of the new scanner required new facilities, and the centre was therefore expanded and a considerable part was restructured to accommodate this expansion. Although the reconstruction took several months, the patience of especially the clinical staff was rewarded with a more open and welcoming working environment.

During the year 2002, the centre strengthened the foundation for national and international collaboration in brain research in the coming years. Increased focus was thus put on the collaboration with our partners in the Copenhagen area with the establishment of the Copenhagen Brain Research Center in April. The new centre forms a platform for interdisciplinary collaboration in brain research with a high international impact.

Several PhD theses carried out at the DRCMR were defended during 2002. Some research projects were completed while others were commenced. Also the year 2002 witnessed initiatives to establish the DRCMR as a reading centre for MR scans in international projects and trials.

Finally, I would like to express our gratitude towards the foundations and institutions that have supported us financially over the years thus making it possible for the centre to achieve and maintain its frontline position within MR research.

Olaf B. Paulson
Head of the DRCMR

DRCMR Profile

The Danish Research Centre for Magnetic Resonance (DRCMR), also known as the Department of Magnetic Resonance, is located in the middle of Hvidovre Hospital, in section 340A and 340B. The centre has 3 Siemens whole-body scanners. The newest, a Magnetom Trio (3.0 Tesla) was installed in 2002 and the two others, a Magnetom Vision (1.5 Tesla) and a Magnetom Impact (1.0 Tesla), were installed in 1994. The two latter scanners have since been upgraded and continue to perform at a high level for the centre's clinical and research needs. All three scanners are located in 340A which also includes facilities for clinical work and a conference room. The centre's 1.5-Tesla Magnetom SP scanner from 1989 was shut down in 2002. Finally, the centre has an experimental scanner, a Sisco 4.7 Tesla scanner. This scanner is suitable for MR studies in small animals and was upgraded in 1998. The experimental scanner is located in area 340B which also holds facilities for data analyses and research.

Contents

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Layout
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Ian Rowland

Dansk Resumé

Året 2002 blev en milepæl for MR-afdelingen, Hvidovre Hospital, med installation af 3 tesla Siemens Trio skanneren, doneret af Simon Spies Fonden. Skanneren blev installeret i juli og er den første kliniske højfelts-MR-skanner installeret i Danmark. Den nye skanner giver den teknologiske basis for fortsat udvikling af forskningsaktiviteterne og tillader MR-centret af bevare en frontlinieposition i MR-forskning. Forskellige opgraderinger og installation af nye spoler vil blive udført i 2003 og skulle være tilendebragt ved slutningen af året. Dette vil yderligere øge centrets kapacitet, såvel klinisk som forskningsmæssigt. Det forventes, at mange nye forskningsprojekter vil finde sted på den nye 3 tesla højfeltsskanner, hvorved der vil blive mere tid til diagnostiske undersøgelser på afdelingens øvrige skannere.

Installationen af den nye skanner krævede en udviddelse af afdelingen. En stor del af afdelingen måtte igennem en ombygning for at gøre plads til udviddelsen. Ombygningen stod på i flere måneder, hvor især det kliniske personales tålmodighed blev sat på prøve, men belønningen er et mere åbent og venligt arbejdsmiljø på afdelingen.

I 2002 blev MR-afdelingens nationale og internationale samarbejde styrket. Øget fokus blev rettet mod samarbejde i København med etablering af Copenhagen Brain Research Center i april. Det nye center giver en styrket platform for interdisciplinært samarbejde og hjerneforskning på højt internationalt niveau.

Det er MR-afdelingens ønske fortsat at styrke brobygningen mellem MR-forskning og diagnostik. Med installationen af den nye 3 tesla skanner og med den hurtige og fortsatte udvikling i diagnostisk brug af MR kan denne udfordring få den største betydning. Sameksistens og samarbejde mellem klinisk arbejde og forskningsaktiviteter vil få høj prioritet, ikke blot på MR-afdelingen, men ved hele Københavns Universitetshospital.

Det forventes, at universitetet i 2003 vil etablere nye satsningsområder, herunder "Krop og bevidsthed". Disse satsningsområder skal dække aktiviteter, som spænder over flere af universitetets fakulteter. MR-afdelingen på Hvidovre Hospital forventer at have en nøglestilling indenfor dette satsningsområde og forventer at øge samarbejdet med bl.a. det Humanistiske Fakultet. Afdelingen har også etableret et øget internationalt samarbejde med etablering af et centralt evalueringscenter for MR-forskning i demens og for MR-evaluering af kliniske afprøvninger ved disemineret sclerose.

Slutteligt ønsker MR-afdelingen at bringe en varm tak til fonde og institutioner, som har understøttet afdelingens aktiviteter, hvorved det er blevet muligt at opretholde en frontlinieposition i international MR-forskning.

Organisation and Staff

The centre has both clinical and research responsibilities and is organized accordingly. The centre is chaired by Professor DMSc Olaf B. Paulson. The director of the clinical functions is Head Radiologist Margrethe Herning. The Head Physicist is PhD Lars Hanson and the Head Technologist is Sussi Larsen.

Staff

Senior Staff, Clinical
Margrethe Herning, 'Overlæge'
Sussi Larsen, Head Technologist
Anne-Mette Leffers, 'Overlæge'
Karin Markenroth, Clinical Physicist, PhD

Senior Staff, Research
William Baaré, Psychologist, PhD
Ellen Garde, MD, PhD
Lars G Hanson, Physicist, PhD
Maria Miranda, MD, PhD
Olaf B Paulson, Professor, DMSc
Poul Ring, Engineer
Egill Rostrup, MD & Human Biologist
Ian J Rowland, Chemist, PhD
Karam Sidaros, Engineer, PhD
Lise Vejby Søgaard, Physicist, PhD

Junior Staff, Clinical
Edith Grossman, MD
Annika Reynberg Langkilde, MD
Ali A. Muhamad, MD
Gulla Søby Rathje, MD
In addition residents from the Department of Radiology rotate through DRCMR for periods of 2 months.

Junior Staff, Research
PhD Students
Irene Klærke Andersen, Engineer
Daniela Balslev, MD
Elizbieta Kalowska, MD
Katja Krabbe, MD
Torben Ellegaard Lund, Engineer
Jacob Rørbech Marstrand, MD
Henrik Kahr Mathiesen, MD
Dorthe Pedersen, MD
Trine Stavngaard, MD
Susette Krohn Therkelsen, MD

Junior Researchers
Mikael Boesen, MD
Niels Broberg, Engineer
Minna Nørgaard, Human Biologist
Charlotte Ryberg, Biologist
Arnold Skimminge, Physicist
Stefan Wolff, Engineer

Research Assistants
Andreas Hansen, Medical Student

Technologists
Lill Andreasen, Laboratory Technician
Sascha Gude, Laboratory Technician
Nina Hansen, Laboratory Technician
Pia Olsen, Laboratory Technician
Hanne Schmidt, Laboratory Technician
Helle Juhl Simonsen, Laboratory Technician
Marlene Soelberg , Laboratory Technician

Secretarial Staff
Laila Andersen
Anne Cooper
Lotte Grønbech Hansen
Lisa Juhl Simonsen
Sussie K. Volkmann

Cleaning Assistants
Ruth Kielstrup
Elsebeth Nielsen

Visiting Staff

Senior Staff
Peter Born, MD, PhD
Mette Klarlund, MD, PhD
Jens Christian Nilsson, MD, PhD
Anders Stensgaard, Engineer
Lars Søndergaard, MD
Sverre Rosenbaum, MD, PhD
Mikkel Østergaard, MD, PhD, DMSc

Junior Staff
PhD Students
Bo Ejbjerg, MD
Elisabeth Hildebrandt-Eriksen, Human biologist
Bjørn Grønning, MD
Torben Mackeprang, MD
Gitte Nielsen, MD
Katrine Pagsberg, MD
Mustafa Taskiran, MD
Mikkel B. Stegmann, Engineer
Marcin Szkudlarek, MD

Junior Researchers
Helle Andersen, MD
Tim Dyrby, Engineer

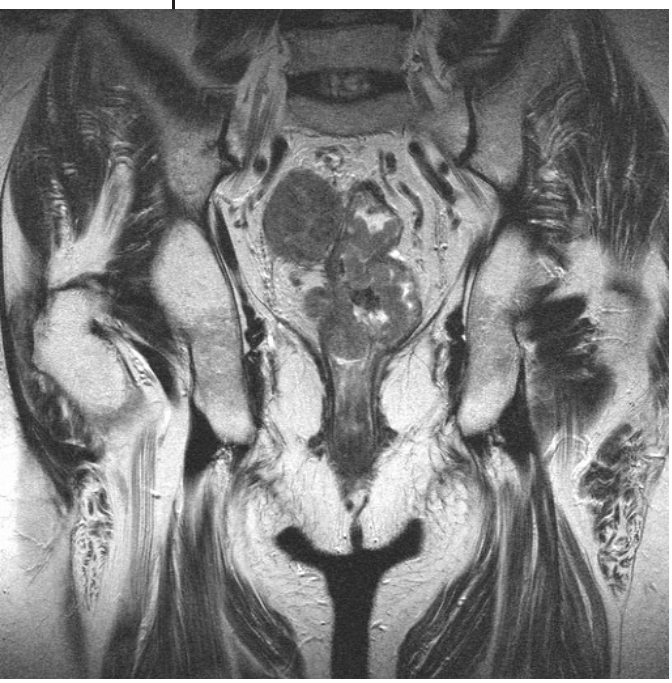
Clinical Imaging

In 2002, 5331 clinical investigations were performed, many of which were performed before and after administering intravenous contrast media. 4277 investigations were performed on patients referred from Hvidovre Hospital, 1054 investigations on patients referred from counties oustside Copenhagen. Investigations of neurological diseases, e.g. suspicion of stroke, multiple sclerosis, intracranial tumours, intracranial hemorrhagies and dementia have been an important part of the daily clinical, radiological work.

Many epileptic patients have been investigated concerning structural brain lesions causing seizures. Many of the epileptic patients were investigated before surgery with a special program including volumetric measurements of the hippocampus regions and T2-relaxation measurements.

MRI of patients with traumatic brain lesions has been a growing part of our MR-investigations. The prediction of the clinical outcome is very important in this type of patients.
Intracranial vascular diseases such as arteriovenous malformations and aneurysms were investigated with MR-imaging and MR-angiography. MR-imaging and MR-angiography are used as screening methods in patients with "warning leaks" from cerebral aneurysms, in patients with manifest subarachnoidal hemorrhage and patients with a family history of cerebral aneurysms. MR-angiography can be a valid supplementary investigation preoperatively.

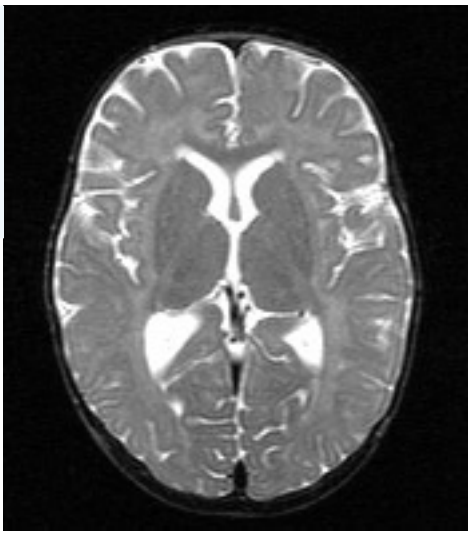
Tumours in the pituitary gland, acoustic neuromas, meningeomas and other intracranial tumors are best investigated with MRI. Traditional cerebral arteriographies are replaced by slow-flow MR-angiography in suspicion of sinus thrombosis or tumours near the venous sinuses.



Coronal T2W image in a patient with rectal cancer.

In pediatric radiology, MRI is used in neonates with hypoxic complications before, during or after delivery. Many children with seizures in the postnatal period were investigated. Congenital malformations and metabolic diseases are well described with MRI.

Patients with suspected cervical spinal stenoses or suspected cervical disc herniation are investigated with MRI. Suspicion of lumbar disc herniation is increasingly diagnosed with MR. In the case of post operative recurrent disc herniation, or in the case of infection, MRI is the preferred diagnostic method.



A 17-month-old child with 18q-syndrome. An axial T2W image shows delayed myelination/ hypomyelination/dysmyelination without hypointensity in the internal capsula.

In patients with metastatic spinal disease, MRI is the diagnostic method of choice.

Structural heart disease such as tumours, structural changes in connection with some kinds of arrhytmias and heart valve disease are best diagnosed with MRI.
In the near future it is likely that heart function will be described with MRI and MRA.

Musculoskeletal MRI is a growing clinical area. Diagnostic arthroscopy is more and more frequently replaced by MRI in the evaluation of meniscal lesions, lesions in the cruciate ligaments, collateral ligaments and damage to the cartilage. In the shoulder, MRI is used in diagnosing labral lesions, rupture of the rotator cuff and so forth. Preoperative investigation of musculoskeletal tumours can determine the extent of disease and help treatment planning and thereby limb-saving operations. Metastatic bone disease is well and best diagnosed with MRI.
In Sports Medicine the use of MRI will increase for visualising soft tissue regions, joints and bone structures.

In the abdominal area, MRCP is the investigation of choice concerning the bile ducts and pancreatic duct, when gall stones and obstruction are suspected. The alternative diagnostic ERCP is a method assosiated with morbidity and risk of some mortality. MRI of perineal fistulas and rectal tumours are well established methods. We hope to expand liver and pancreas investigations.

In the coming year, we expect our new 3T MR-scanner to bring new and better diagnostic imaging of all anatomical regions.

Collaborations

The DRCMR collaborates with many institutions both nationally and internationally. Primary collaborators in 2002, especially those with whom common funding was obtained and those who participated in supervision of PhD students, are listed below.

National Collaborations

Brain Research

Copenhagen University Hospitals
Division of Neurological Rehabilitation, Hvidovre
Department of Pedeatrics, Hvidovre
Department of Pathology, Hvidovre
Department of Microbiology, Hvidovre
Department of Gynecology and Obstetrics, Hvidovre
Department of Clinical Chemistry, Hvidovre
Department of Pedeatrics, Hvidovre
The Neonatal department, Rigshospitalet
Department of Neurology, Rigshospitalet
Sclerosis Research Unit, Rigshospitalet
Neurobiology Research Unit, Rigshospitalet
The Memory Disorders Research Unit, The Neuroscience Centre, Rigshospitalet
The Dementia Research Unit, The Neuroscience Centre, Rigshospitalet
Department of Neuropaediatrics, John F. Kennedy Institute, Glostrup
Department of Neurology, Glostrup
Department of Neurophysiology, Glostrup
Department of Neurology, Bispebjerg
Department of Psychiatry, Bispebjerg
Department of Oncology, Herlev

Department of Psychology, University of Copenhagen
Department of Medical Anatomy, University of Copenhagen
Department of Medical Biochemistry and Genetics, The Panum Institute, University of Copenhagen
Institute for Molecular Pathology, The Panum Institute, University of Copenhagen
Informatics and Mathematical Modelling, The Technical University of Denmark
Statens Serum Institut
Center of Functionally Integrative Neuroscience, Aarhus University

Heart Research

Department of Cardiology, Copenhagen University Hospital, Hvidovre
Department of Endocrinology, Copenhagen University Hospital, Hvidovre
Department of Cardiology and Endocrinology, Copenhagen University Hospital, Frederiksberg
Department of Paediatrics, Copenhagen University Hospital, Rigshospitalet
Department of Cardiology B, Copenhagen University Hospital, Rigshospitalet
Department of Nephrology, Copenhagen University Hospital, Rigshospitalet
Research Department of Human Nutrition, The Royal Veterinary and Agricultural University
Team Danmark Test Centre, Copenhagen University Hospital, Bispebjerg
Informatics and Mathematical Modelling, The Technical University of Denmark

Lung Research using Hyperpolarized Gasses

Department of Respiratory Medicine, Copenhagen University Hospital, Hvidovre Hospital
Department of Clinical Physiology, Copenhagen University Hospital, Rigshospitalet
Department of Respiratory Medicine, Copenhagen University Hospital, Gentofte

Rheumatology Research

Copenhagen University Hospitals
Department of Rheumatology, Hvidovre
Department of Radiology, Hvidovre
Department of Orthopaedic Surgery, Hvidovre
Department of Clinical Physiology, Hvidovre
Department of Pathology, Hvidovre
Department of Rheumatology, Rigshospitalet
Department of Radiology, Rigshospitalet

Department of Rheumatology, Herlev Hospital
Department of Radiology, Herlev Hospital
Department of Ultrasonography, Herlev Hospital
Department of Rheumatology, Gråsten Gigthospital
Department of Radiology, Gråsten Gigthospital
Department of Rheumatology Odense University Hospital
Department of Radiology, Odense University Hospital
Department of Rheumatology, Aarhus University Hospital, Århus Kommunehospital
Department of Radiology, Aarhus University Hospital, Århus Kommunehospital

International Collaborations

Brain Research

Centre for Magnetic Resonance, University Hospital, Trondheim, Norway
Massachusetts General Hospital, NMR-centre, Boston, USA
Center for fMRI, University of California, San Diego, USA
Brain Image Analysis Lab, University of California, San Diego, USA
Center of Cognitive Neuroscience, Nijmegen, The Netherlands.
Robert Steiner Magnetic Resonance Unit, Imaging Sciences Division, ICSM Hammersmith hospital, London, United Kingdom

Heart Research

The GUCH Unit, Middlesex Hospital, London, United Kingdom
Centre for Magnetic Resonance Imaging, University of Trondheim, Norway
Clinical Research Initiative in Heart Failure, Department of Cardiology, Western Infirmary, Glasgow, United Kingdom

Lung Research using Hyperpolarized Gasses

Klinik für Anesthesiologie, Radiologie, Johannes Gutenberg-University, Mainz, Germany
Section of Academic Radiology, University of Sheffield, United Kingdom

Rheumatology Research

Department of Radiology, University of California San Francisco, USA.
Departments of Rheumatology and Radiology, Leeds General Infirmary, United Kingdom.
Departments of Radiology and Rheumatology, St. George Hospital, Sydney, Australia.
Departments of Radiology and Rheumatology, University of Auckland, New Zealand.

International Multi-Centre Research Collaborations

The EU Polarized Helium to Image the Lungs (PHIL) project
Chaired by Prof. M. Leduc, PhD, Department de Physique Ecole Normale Superieure, Paris, France.

The EU project: Automated Removal of Partial Volume Effects (PVEOut)
Chaired by Prof. Bruno Alfano, Centro per la Medicina Nucleare, Naples, Italy.

The EU project: Leukoaraiosis and Disability in the elderly (LADIS)
Chaired by Prof. Domenico Inzitari, Department of Neurological and Psychiatric Sciences, University of Florence, Italy.

European Task Force on Age-Related White Matter Changes
Chaired by Prof. Philip Scheltens, PhD, Academisch Ziekenhuis Vrije Universiteit, Amsterdam, The Netherlands.

The EULAR and OMERACT collaborations concerning imaging in rheumatoid arthritis.

Copenhagen Brain Research Center

In April 2002, the Danish Research Centre for Magnetic Resonance entered a co-ordinated collaboration with other brain research institutions in the Copenhagen area, in the form of the Copenhagen Brain Research Center (CBRC). The centre consists of the following institutions:

- Department of Medical Chemistry, The Royal Danish School of Pharmacy
- H. Lundbeck A/S, Copenhagen
- Danish Research Centre for Magnetic Resonance, Copenhagen University Hospital, Hvidovre
- The PET and Cyclotron Unit, Copenhagen University Hospital, Rigshospitalet
- Informatics and Mathematical Modelling, Technical University of Denmark
- Neurobiology Research Unit, Copenhagen University Hospital, Rigshospitalet
- Department of Psychology, Faculty of Humanities, University of Copenhagen

Copenhagen Brain Research Center is established as a platform for interdisciplinary collaboration in brain research with a high international impact. In order to achieve this goal the partners of CBRC regularly meet, present, and discuss new projects. Numerous projects are carried out in collaboration between two or more of the partners, e.g. in form of combined supervision of PhD students in projects. Projects of interdisciplinary nature form the basis for joint grant applications.
(quoted from the CBRC website: www.cbrc.dk)

Research Projects

Multiple Sclerosis

Conventional MRI techniques have proven important in the diagnosis and the follow-up in clinical trials of patients with multiple sclerosis (MS). However, these techniques have low specificity for the pathological changes in the MS lesions, and the correlation between conventional MRI and disability is poor.
During the last decade new techniques with improved sensitivity and increased pathological specificity have been developed, such as magnetic resonance spectroscopy (MRS), diffusion weighted imaging, and functional magnetic resonance imaging (fMRI). MRS has demonstrated neuronal dysfunction or loss as well as pathological changes in normal appearing white matter (NAWM). Diffusion weighted imaging demonstrates demyelination and fibre architecture, and by using fMRI it is possible to detect which areas of the brain that are in response to a neuronal stimulus.
These new techniques are used in two PhD-projects along with conventional MRI techniques.

Research Group at DRCMR:
Annika R. Langkilde, Henrik Kahr Mathiesen, Egill Rostrup, Lars Hanson, Irene K. Andersen and Olaf B. Paulson.

A Longitudinal Study with Conventional and Non-conventional MRI Techniques in Patients with Optic Neuritis and RR-MS

20 patients with optic neuritis, 20 patients with relapsing-remitting MS and 20 healthy controls will be examined with conventional MRI as well as MR spectroscopy and diffusion weighted imaging serially over periods of 2 years. The patients are examined with EDSS and tests of cognitive functions, and we will measure cerebral atrophy, MS lesion volume, enhancing lesion volume and correlate these findings with measurements of ADC and NAA in MS lesions, NAWM and the whole brain.
The project is designed to answer the following questions: Can new MR techniques be used to monitor disease activity? Can they predict the development of MS from optic neuritis? Can they be used to predict the course of the disease? Will we get new pathophysiological knowledge?
Status: The inclusion will close spring 2003. The data from the first scans will be evaluated in the following months. The follow-up scans will continue in 2003 and 2004.
The first conventional MRI findings have been compared with PET, EDSS and tests of cognitive functions. No significant correlations were found.

Contact: Henrik Kahr Mathiesen.

A Longitudinal Study on the Effect of Interferon-beta Antibodies on the MRI Activity in RR-MS Patients

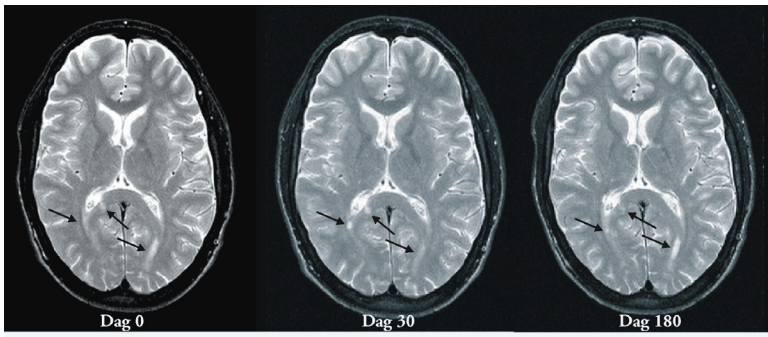
27 patients with relapsing-remitting MS treated with IFN-beta for at least 1 year were scanned 4 times with conventional MRI including gadolinium-DTPA in double dose (0.2 mmol/kg). Neutralizing anti-IFN-beta antibodies (NAB) were measured.
Status: High levels of NAB in MS patients hamper the biological response to IFN-beta, and consequently are related to high disease activity on MRI.
We plan a follow-up of 20 patients with high NAB levels. In 6 months they will be treated with steroids (methylprednisolone) and will not receive IFN-beta. We will investigate whether this will lead to decrease in NAB levels and a following response to interferon measured by a decrease in MRI activity?

Contact: Henrik Kahr Mathiesen.

Clinical and Immunological Effects of Treatment with IVIG in Patients with Optic Neuritis

In this randomised placebo-controlled study, the effect of treatment with intravenous immunoglobulin (IVIG) on the visual function in patients with acute optic neuritis is investigated. Testing of visual function, immunological effects and MRI are performed serially.
Status: 64 of 68 patients have been studied.

contact: Annika R. Langkilde

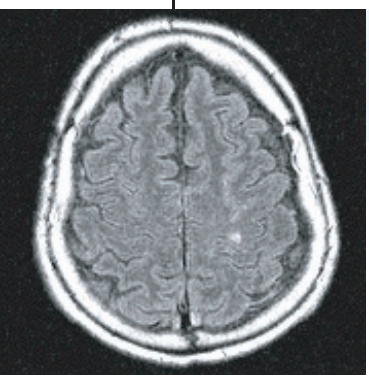


Three slices from T2 weighted MRI scans of a patient with acute Optic Neuritis obtained in the acute phase, after 30 and 180 days. Three lesions are seen (arrows), two lesions (one in the splenium of corpus callosum and one at the right occipital horn increase in size at day 30, but again decrease at day 180. The periventricular lesion at the left occipital horn, is seen to increase in size at day 180.

MECOMBIN Project

DRCMR is to be a reading centre for multi-centre multiple sclerosis and other studies. MR investigator sites around Europe are to send their MR images to DRCMR where the analysis and calculations will be performed. The first study is called MECOMBIN, initiated by Per Soelberg Sørensen and Mads Ravnborg at Rigshospitalet and performed in cooperation with Biogen. 350 patients are to be scanned twice: at inclusion and after three years. Half the patients will receive beta-Interferon and Methylprednisolone whilst the other half will receive beta-interferon only. DRCMR is responsible for developing MR protocols, associated documentation and databases. A set of programs for data evaluation has been made available and has been used on the first patient scanned. Patients from other Danish MR investigator sites will be included from January 2003.

contact: Irene K. Andersen



The FLAIR image was suggested for the Mecombin MR Protocol since it is highly sensitive to Multiple Sclerosis lesions in the upper part of the brain.

Functional Brain Imaging

Functional Magnetic Resonance Imaging (fMRI) is a method of acquiring MR images of brain activity. With proper design of MR-sequences, it is possible to acquire MR images weighted with, for example, perfusion, blood-oxygenation (BOLD) or several other physiological parameters. By acquiring thousands of such images during a cognitive task or sensory stimulation, it is possible to construct statistical maps locating, for example, regions of increased blood-flow during sensory stimulation or with increasing task difficulty. The fMRI-group at DRCMR has widespread activities ranging from investigations of the composition of the BOLD response to fMRI on patients suffering from sclerosis or schizophrenia.

Research Group at DRCMR:
Torben Lund, Daniela Balslev, Minna Nørgaard, Karam Sidaros and Egill Rostrup

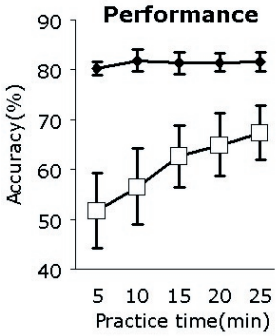
Representation of Tool Skills in the Brain

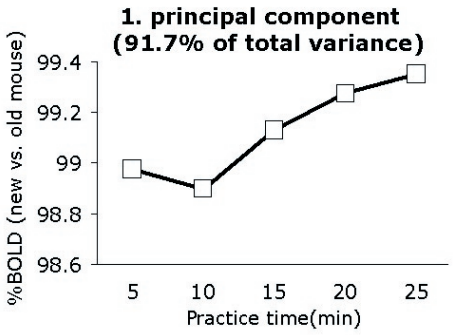
The aim of this project is to investigate how tool skills are represented in the brain using fMRI. To achieve this, two studies have been designed:

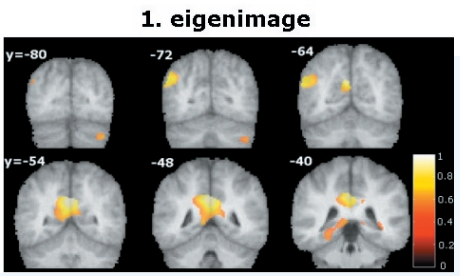
Study 1: In this fMRI study, participants held a manual device and saw a cursor move on a screen. The visual and proprioceptive feedback from movement was either congruent, producing the experience of using a tool - a computer mouse - or incongruent, disrupting such an experience. Compared with the incongruent condition, the congruent condition activated the left inferior parietal cortex. This brain site is often lesioned in apraxic patients and appears to recognise visuoproprioceptive congruence. Tool skills may be coded as a set of visuoproprioceptive patterns associated with tools.

Study 2: This fMRI study tested whether the region of interest identified in the previous study showed an increase of activity during tool skill acquisition. Using principal component analysis, we found that the representative time course of activity in the region of interest was indeed an increase in activity over practice time with the new tool - a mirror-reversed computer mouse. The easiest way to account for this finding is to assume that tool skills are represented as a set of visuoproprioceptive patterns that map the space around the tool on to the space around the effector.

contact: Daniela Balslev







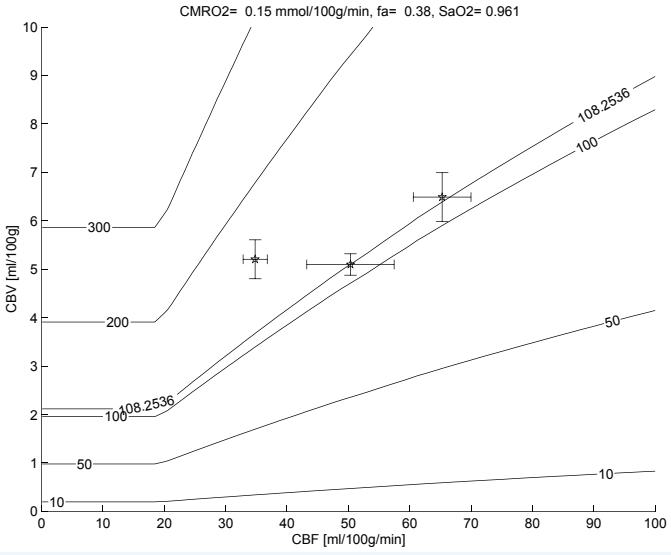
Following practice, performance with a new, mirror-reversed computer mouse (empty squares) improved towards the level of performance with the normal mouse (filled squares). Likewise, the brain activity increased over practice trials with the new mouse towards the level recorded during trials with the old mouse, as shown by the first principal component. Brain sites with high positive loading on this component were found in the left inferior parietal lobe and the posterior cingulate cortex. These areas respond to visuoproprioceptive congruence associated with tool use and show learning effects during tool skill acquisition. The easiest way to account for these findings is to assume that tool skills are represented as a set of visuoproprioceptive patterns that map the space around the tool on to the space around the effector.

Research Projects

Cerebral Oxygenation Dynamics: Investigations in the Basis of BOLD Imaging

The aim of this project is to obtain a quantitative understanding of cerebral oxygenation and the blood oxygenation level dependent (BOLD) effect, based on measurements of brain flow and oxygenation (using positron emission tomography (PET) and near infrared spectroscopy (NIRS)).
Description: The cerebral balance between oxygenated and deoxygenated hemoglobin is intimately linked to the balance between cerebral oxygen delivery and extraction. These two parameters are generally viewed as being tightly coupled, although the balance may change in situations such as neural activation or hypercapnia, where cerebral blood flow is increased. This so-called uncoupling effect is the basis for the frequently used BOLD technique for mapping cerebral activation using MR-scanning. NIRS is also sensitive to cerebral blood oxygenation, and can be used to detect neural activation. While the BOLD effect arises from changes in deoxyhemoglobin only, the NIRS technique is sensitive to both oxygenated and deoxygenated hemoglobin. We developed a mathematical model of brain oxy- and deoxyhemoglobin content and applied it to measurements of cerebral blood flow, blood volume and oxygenation obtained with simultaneous PET and NIRS. The measurements were performed in 5 normal subjects during varying conditions of hypo- and hypercapnia. Results: A simple hemodynamic model did not adequately predict the oxygenation changes observed in this and previous studies. It is concluded that other effects, such as hyperoxygenation and pH changes may be of importance.
Status: This project has been completed and the results published. Future applications of the model will be to data obtained during hypoxia.

contact: Egill Rostrup



Relation between cerebral blood flow, volume and oxygenation in steady state. Changes in cerebral hemodynamics that occur along each of the iso-deoxyhemoglobin line will be unaccompanied by changes in oxygenation. All other changes will induce oxygenation changes, and a potential BOLD effect. Each line is labelled with the corresponding deoxy-hemoglobin concentration (µmol/L, heme groups). Based on the measured CBF and CBV value (crossmarks) this simple model predicts only minor changes in deoxyhemoglobin during hypercapnia. This leads to the conclusion that flow effects alone cannot explain the BOLD response during hypercapnia.

Advanced Methods in Functional MRI

At the beginning of the year a PhD project was started on advanced methods in fMRI. The past year has been used to upgrade existing fMRI stimulation devices (the IFIS system) for use in the Trio scanner, and implementing simultaneous EEG/fMRI.
The existing stimulus system used an LCD screen in a hood, mounted on top of the head coil. As the hood did not fit on top of the headcoil of the Trio scanner, a new system had to be arranged. As the Trio was scheduled to come with three different headcoils (Standard, 8-channel and insert gradient head coil) a solution as general as possible was desired. The implemented solution consists of a waveguide behind the scanner bore and 3600 lumen video projector with a zoom lens placed outside the scanner room, projecting to a screen placed at the end of the scanner bore. The system is capable of presenting higher resolution, larger field of view, better contrast, than the previous one, and with its larger luminance it is capable of providing stronger flashes than the stroboscobic light used for visual stimulation during sleep. The remaining part of the IFIS system is still used for providing auditory stimulation and subject response.
The existing EEG-equipment was capable of monitoring EEG in the Vision scanner between image acquisitions. While this system was used in our recently published sleep study [Born et al. 2002] it is limiting for a range of possible EEG/fMRI experiments including localisation of epileptic spike generators, mapping of brain wave generators (alpha, beta, delta, theta etc.), and deeper understanding of the observed negative BOLD response during slow wave sleep. Therefore it was decided to implement true simultaneous EEG/fMRI on the Trio scanner. The goal was to be able to use optimal fMRI protocols and acquire EEG of good quality at the same time, preferable with near real-time filtering of pulse and imaging artifact. Even though we bought a commercial system designed for EEG/fMRI, implementing EEG/fMRI has been more troublesome than expected. Saturation problems of both the ECG and EEG were pronounced, and the hardware was returned to the manufacturer several times for modifications, before the saturation problems disappeared. Filtering software has been developed, but its testing has been prohibited due to the previously mentioned problems.

contact: Torben E. Lund

Stroke

Stroke is the third most common cause of death in western countries. The first-year mortality is about 25% and many survivors suffer major disability. In one third of the patients, stroke in progression is noted. These patients have an even worse prognosis with respect to mortality and clinical outcome. At present there is no effective treatment for patients with stroke in progression, probably reflecting limited knowledge of the underlying pathophysiological mechanisms.

Research Group at DRCMR:
Elizabeth Kalowska and Sverre Rosenbaum

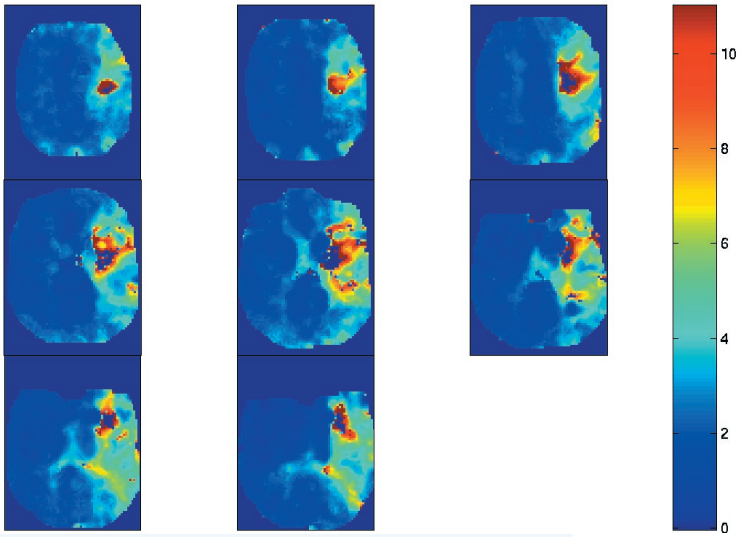
Stroke In Progression Study using MRI

The present prospective and consecutive study includes 41 patients with ischemic stroke within 24 hours of the initial symptoms. All patients are examined with a routine CT scan. After informed consent, the patients are scheduled for an MRI investigation within 24 hours after onset of symptoms. Another scan is scheduled after one week and finally the patients are investigated after 3 months. The MR investigation includes measurements of apparent diffusion coefficient, diffusion weighted imaging, cerebral blood flow and MR-angiography. In addition, echo planar imaging is performed aiming to study haemorrhagic transformation in the infarct. Finally, the measurements include spectroscopy to study the amount of metabolites in the brain, i.e. N-acetyl aspartate (NAA), choline, creatine and lactate. Patients with stroke in progression are compared to patients with completed stroke, investigating pathophysiological differences between patients in the initial phase and during follow-up. This study is designed to identify those patients at risk of progressive stroke. This may in the future enable the identification of a more efficient treatment of patients with acute stroke than that available today.
Status: 41 patients were included in june 2002.

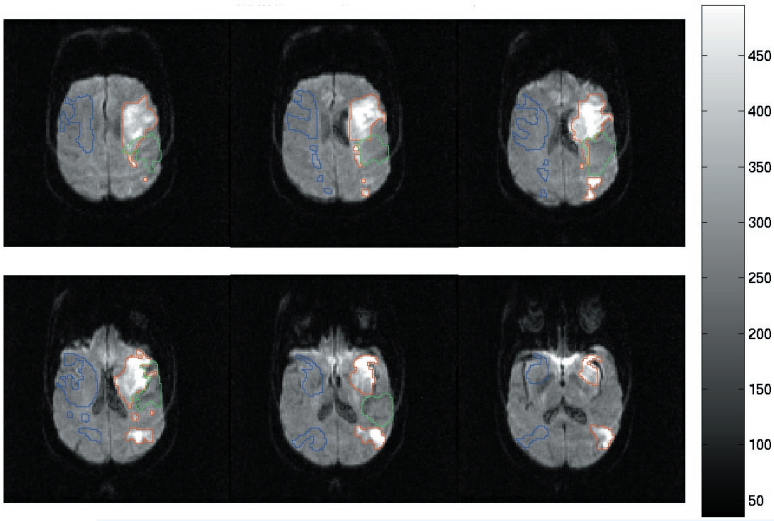
Blood-Brain Barrier

A number of pathological situations are associated with altered blood-brain barrier (BBB) function. In ischemic stroke, the cascade of reactions in the course of an ischemic lesion leads to a loss of blood-brain barrier integrity. The disturbance of the blood-brain barrier is also associated with an increased risk of secondary hemorrhages after recanalization (reperfusion).
An ongoing study focuses on a method to detect early BBB deficiencies in acute cerebral ischemia. We have developed quantitative measurements of BBB integrity based on changes in the longitudinal relaxation rate (ΔR1) after gadolinium DTPA administration.
Using quantitative R1 mapping in the hyperacute phase of cerebral ischemia, this approach seems to be sensitive in detecting early disturbance of the BBB. In our study, BBB deficiency was found in all cases of hemorrhagic transformation in the acute phase. This study could offer a substantial increase in the safety and success of advanced stroke therapies (thrombolysis).

contact: Elizabeth Kalowska



TTP (time to peak) images showing the transit delay (in seconds) needed for Gd-DTPA to reach the brain.



Detection of ischemic area (defined as hyperintense) by diffusion-weighted imaging (DWI).

Blood-Brain Barrier

The blood-brain barrier (BBB) protects the brain from fluctuations in the chemistry of the blood flowing through the cerebral blood vessels. The endothelial cells of the cerebral capillaries, which appear to be more tightly joined to one another than those of other capillaries, contribute to the slow diffusion into the brain. While the blood brain barrier is essential to the brain's survival and health, it can also prevent drugs and antibiotics from reaching lesions in the brain

Research Projects

Ageing and Dementia

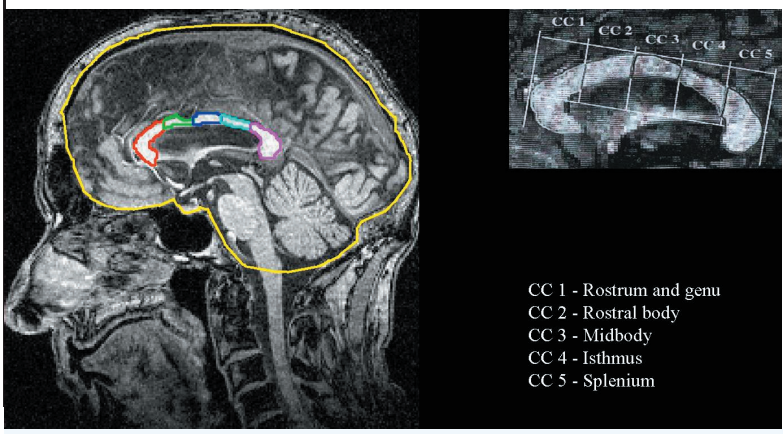
There is strong evidence of an overall age-related degeneration of structures in the white matter. In particular, focal white matter hyperintensities (WMH), or leukoariosis, is a noticeable radiological observation often seen in the elderly. There are indications that WMH may reflect a localised exacerbation of degenerating processes in the white matter, and that these alterations may be involved in the transition to disability.
MRI offers detailed topographic images due to unique contrast resolution. Particularly in the evaluation of cerebral white matter changes, the combined application of conventional imaging with newer MRI techniques makes it possible to visualise the structural changes and elucidate the pathophysiological mechanisms behind WMH. The overall aims of the projects described below are to provide valuable information on the dynamics of normal cerebral ageing as opposed to diseases such as dementia.

Research group at DRCMR:
Ellen Garde, Charlotte Ryberg, Jacob Rørbech Marstrand, Egill Rostrup, Lars Hanson and Olaf B Paulson.

Project A: Corpus Callosum (CC) Atrophy in Elderly Patients. An Indicator of Cognitive Performance

Aim: To investigate the relation between regional CC atrophy and changes in other brain structures, as well as changes in cognitive function in elderly patients
Description: Most population-based cross-sectional studies have shown associations between the presence and the severity of lesions in the white matter of the brain and cognitive function. But it is unclear why only some patients with white matter lesions have dementia. Neuropathological studies in Alzheimer's disease indicate specific loss of layer III and V large pyramidal neurons in association cortex. These neurons give rise to long cortico-cortical connections, projecting through the corpus callosum, in an anterior-posterior topology. One purpose of the study is to investigate the value of regional corpus callosum atrophy measurements as an indicator of cognitive impairment in groups of patients (LADIS- and AD2000) with an increased risk of developing Alzheimer's disease (AD).
Results: The brains of 57 (32 females and 25 males) subjects from the LADIS study were examined and found that the severity of dementia was significantly correlated with the size of the middle sections of the corpus callosum (rostral body $p=0.001$; midbody $p=0.032$; and Isthmus $p=0.046$).
Status: In addition to the LADIS patients the size of the CC have also been measured on 89 AD2000 subjects and are currently being compared to the neuropsychological tests.

contact: Charlotte Ryberg



To test whether or not the Danish LADIS group suffered from corpus callosum atrophy we choose to measure the cross-sectional area of the corpus callosum. The area is obtained from manual delineation of CC on the mid-saggital section of the MPRAGE data set. The CC cross-section is then subdivided into 5 smaller regions named CC1, corresponding to Rostrum and genu; CC 2, Rostral body; CC3, midbody; CC4, istmus and CC5 splenium. The total intracranial volume is obtained from an automatic segmentation of Flair and Turbo spin echo data. These results were used to correct the CC area for inter-individual variability in the head size.

Corpus Callosum

The corpus callosum is the main fibre tract connecting the two brain hemispheres, which consists of approximately 200-350 million fibres in man. Its purpose is to communicate perceptual, cognitive, mnemonic, learned and volitional information between the two brain hemispheres.
Given the corpus callosum's key role as the primary cortical projecting system, any focal or diffuse abnormalities of bilaterally connected cortical regions may be expected to have secondary effects on homotopically distributed fibres in the callosum. Effects on regional callosal structure have been reported in Alzheimer's disease (AD), where neuropathological studies indicate specific loss of layer III and V large pyramidal neurons in association cortex. These neurons give rise to long cortico-cortical connections, projecting through the corpus callosum.

Leukoaraiosis and Disability in the Elderly – LADIS

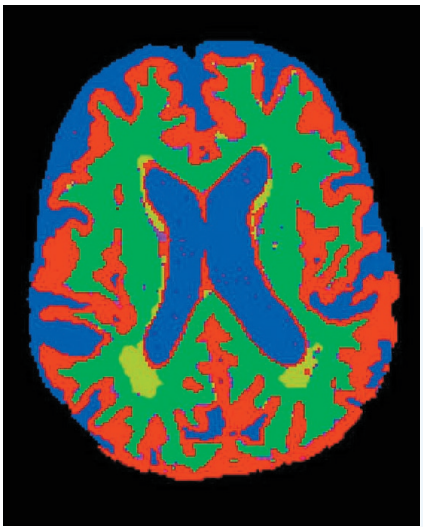
Aim: To investigate the relation between WML and cognitive changes in a group of LADIS subjects ranging in age from 65 to 84.
Description: Lesions in the white matter (WML) of the brain become more common with increasing age, but the pathological significance of these changes is unknown. A group of elderly subjects with normal or nearly normal daily function, but significant white matter changes, are recruited from the Memory disorders Research Unit at Rigshospitalet. All these LADIS subjects go through an extended neuropsychological evaluation. This clinical assessment is repeated after 14, 26 and 38 months (1, 2 and 3 year follow-up). At DRCMR structural and diffusion weighted scan are obtained just after recruitment and again after the 3-year follow-up clinical assessment. About 65 Danish subjects will be included in the project, which is part of a concerted action project under the 5th European framework programme. Together, it is hoped that the participating centres are to include a total of 700 LADIS subjects and at least three younger control persons per centre.
Visual rating or volumetric measurements are used to investigate if regional corpus callosum atrophy is related to white matter pathology (WML-load). The volumetric estimates of WML-load are obtained using a method for automatic segmentation of brain tissue. The segmentation method is based on an artificial neural network.
Results: The artificial neural network has been implemented and tested successfully. A visual rating on the extent of WML has been performed on 61 LADIS subjects. The results are presently being compared to the size of Corpus Callosum and the cognitive performance of the subjects.
Status: 61 LADIS subjects and 3 healthy controls have been scanned. Inclusion of subjects will be concluded in February 2003. Data transferral from other centres has commenced.

contact: Charlotte Ryberg

Risk Factors for WMH and Cognitive Decline Based on 30 Years Follow-up

Aims: With more than 30 years follow-up data, the Glostrup population study offers a unique opportunity to evaluate the association between changes in intelligence, risk factors and MR observable changes in the brain. This study aims to evaluate the impact of risk factors during a 30 year life period on:
1) Changes in intelligence from age 50 to 80, and
2) The extent of white matter hyperintensities (WMH) at 80 years of age.
Description: Potential risk factors are evaluated for coherence from the studies on the 50, 60, 70, and 80-year-old volunteers and correlated to the extent of WMH at age 80.
Results Sustained hypertension were significantly correlated to extent of WMH changes at old age. In this group of community-dwelling elderly, no correlation between cognitive decline and cholesterol levels was found.
Status: Data analysis continues.

contact: Ellen Garde



MR image of a 73-year old male with WML after automatic segmentation of the brain tissue. Gray matter is depicted in red, lesion is depicted in light green, white matter is depicted in green, CSF is depicted in blue and the area where the artificial neural network is uncertain is depicted in purple.

Progression of MRI White Matter Hyperintensities and Decline in Intelligence; a 5-year Follow-up Study

Aims: To determine the temporal relationship between changes in WMH and cognitive function
Description: Twenty-six non-demented subjects participated in the MRI study at age 80 and 85. Changes in WMH were evaluated by visual rating and compared to changes in cognitive function.
Results: Regional changes in WMH correlate with the decline in specific cognitive functions but not with MMSE (Mini-Mental State Examination) score at age 85. MMSE is a widely used screening test for mental status (dementia).
Status: Computer-based quantification of WMH volume at age 80 and 85 are currently being performed.

contact: Ellen Garde

Cerebral Atrophy and Intelligence

Aims: To test the hypothesis that individual variation in brain volume at old age reflects decline in cognitive function since middle-age.
Description: based on a 3D MR-images brain volume in 75 healthy 80-year-old subjects were quantified and compared to decline in intelligence from age 50 to 80.
Results: Although no significant correlation between brain volume and IQ score could be detected at age 80, brain volume did correlate with the decline in IQ subtests from age 50 to 80 in women and from 70 to 80 in men. In contrast to previous studies, no gender difference in brain volume was found in these octogenarians.
Status: Intracranial volume and brain volume at age 85 are currently being quantified.

contact: Ellen Garde

Research Projects

Vascular Load in Patients with a Clinical Diagnosis of Vascular Dementia

Aims: The aim of this study is to determine the diagnostic value of MR-parameters, and presence of cerebrovascular risk factors when differentiating between vascular dementia and Alzheimer's disease.
Description: Follow-up study of patients referred to a memory clinic and given a working diagnosis of vascular dementia (VaD) or Alzheimer's disease (AD). The predictive value of MR parameters such as rate of atrophy and indicators of cerebrovascular disease (WMH and infarcts) is evaluated for each patient group.
Status: Up to four repeated MR-scans have been performed on 20 patients with VaD and AD as well as on 20 controls. Data are currently being evaluated.

contact: Ellen Garde

AD2000

Aims: The aim of this longitudinal study is to determine the impact and prognostic value of MR parameters in patients referred to a memory clinic.
Description: Structural MR imaging and MR spectroscopy are performed on all patients in addition to extensive physical, neurological and neuropsychological examinations.
Results: In a cross-sectional study based on 94 consecutive patients a strong association between degree of WMH and performance score in all cognitive tests indicate that WMH do have an impact on mental abilities even in outpatients referred to a memory clinic.

contact: Ellen Garde

Other Degenerative Diseases in the Nervous System

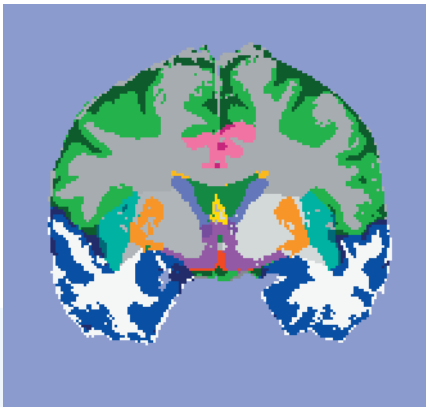
Parkinson's Disease
Parkinson's disease is a neurodegenerative disease characterized by tremor, rigidity and hypokinesia. Multiple System Atrophy (MSA) is a rare neurodegenerative disease with symptoms of Parkinsons disease along with cerebellar symptoms and signs of autonomic dysfunction. Clinically it can be difficult to distinguish between MSA and Parkinson's disease.

Research group at DRCMR:
Katja Krabbe, Egill Rostrup, Lars Hanson and Olaf B Paulson

MR Investigations in Parkinson's Disease

The aim of this study is to find out which of the new MR techniques are suitable to establish the diagnosis of MSA.
Previous pathology studies and studies with different MR techniques in these two patient groups have shown differences in brain structure between the two diseases
Patients and methods: 21 patients with Parkinsons disease, 11 patients with MSA and 18 normal age and sex-matched controls have been enrolled in the project.
All participants have been scanned with the following MR techniques: Conventional MRI, MR spectroscopy, MR diffusion weighted imaging and measurement of relaxation times.
Furthermore, patients and controls have undergone neuropsychological testing with a test battery specifically designed for patients with Parkinsons disease.
All patients have been examined clinically and disease state have been rated with Hoehn and Yahr scale and Unified Parkinsons Disease Rating Scale (UPDRS). MSA patients have been been tested for autonomic dysfunction.
Evaluation: Conventional MR images have been segmented into grey, white and CSF and regions have been outlined.
Spectroscopy and diffusion data will be evaluated in due course.

contact: Katja Krabbe



Segmented MR image with regions outlined

Psychiatry

Research in psychiatric disorders has to deal with diverse, complex and overlapping clinical symptomatologies. Over the last three decades in-vivo magnetic resonance imaging (MRI) studies have played an important role by advancing theories in psychiatry. Today it is generally accepted that psychiatric disorders such as schizophrenia, affective disorders, obsessive-compulsive disorder, have to be understood as brain diseases. MRI has been widely used to investigate macroscopic structural aspects of the brain (structural MRI). More recent applications include studying white matter microstructure (diffusion tensor imaging: DTI and magnetic transfer imaging: MTI), neuro-chemical features (magnetic resonance spectroscopy imaging: MRSI), and functional brain characteristics (blood oxygenation level dependent (BOLD) functional magnetic resonance imaging: fMRI and blood perfusion imaging). Together, these techniques allow for a comprehensive assessment of structural, functional and neurochemical changes throughout the brain. Significantly, each separate technique helps to guide as well as constrain the interpretation of research findings.

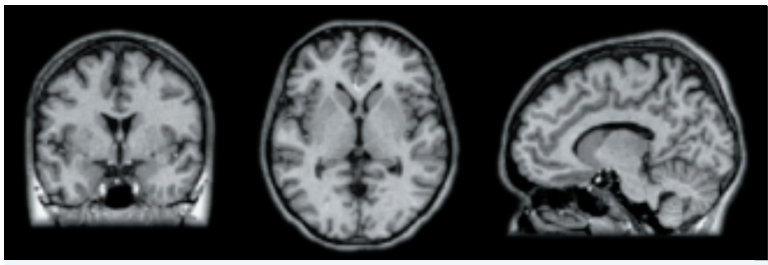
Research group at DRCMR:
Anne Katrine Pagsberg, Torben Mackeprang, William Baaré and Torben Lund

Functional and Structural Imaging Studies in First-episode Schizophrenic Children, Adolescents and Adults

Schizophrenia is a complex, chronic and invalidating disease in which different aspects of cognition and behaviour, including attention, perception, thought processes, emotion and volition are affected. The study of first-episode schizophrenia patients is of importance since the influence of factors such as hospitalization, neuroleptic treatment, and disease chronicity is minimised. Using structural and functional magnetic resonance imaging techniques, the project addresses the following questions: (a) what functional and structural abnormalities are present in (drug-naïve) first-episode schizophrenic patients? (b) How are these abnormalities and changes related to cognitive functions, behavioural symptoms, and social and medical history? (c) Which abnormalities emerge during the course of the illness? (d) Do these abnormalities deteriorate in the first years of the illness? Inclusion of subjects was concluded in the spring of 2002.

Functional MRI: The most frequently studied and reported functional abnormality, as measured with SPECT, PET and fMRI is the diminished ability of schizophrenia patients to activate the frontal lobes, particularly when they are engaged in tasks in which the frontal lobes are assumed to play an important role. Until now most studies investigated chronic schizophrenia patients.

In the present project, gradient-echo, echo planar imaging pulse sequences, sensitive to the BOLD signal, are employed. Subjects are scanned while performing a working memory task (the N-back task). This task reliably activates the frontal and parietal lobes, and the cingulate gyri in healthy controls.



Coronal, transverse (axial), and saggital MPRAGE images (left to right).

Preliminary results suggest that first-episode schizophrenia patients show an attenuated response, comparable to that reported in chronic patients, in frontal and parietal brain areas under conditions of increased working memory load. This suggests that the neural network underlying working memory is already compromised in an early stage of schizophrenia. Importantly, this diminished reactivity does not seem to be the result of differences in task performance.
Structural MRI: Structural brain abnormalities that are most consistently found in schizophrenia patients as compared to healthy controls in post-mortem studies and in-vivo imaging studies include enlarged ventricles, reduced grey matter volume, and smaller medial temporal lobe structures (i.e. amygdala- hippocampal complex, parahippocampal gyrus). Frontal, (superior) temporal, and thalamic abnormalities are also found. Grey matter seems to be more affected than white matter. The theoretical and clinical significance of these pathophysiological findings in schizophrenia is not clear. Disturbances in early (pre– and peri-natal) as well as late (adolescence) brain development have been implicated. Neurodegenerative processes might be involved after illness onset. Furthermore, the relationship between structural abnormalities, clinical variables (e.g. positive and negative symptoms, clinical outcome) and cognitive function is still poorly understood.
For structural analyses high-resolution 3D T1-weighted magnetization prepared rapid acquisition gradient echo (MPRAGE) scans of the whole head are acquired.

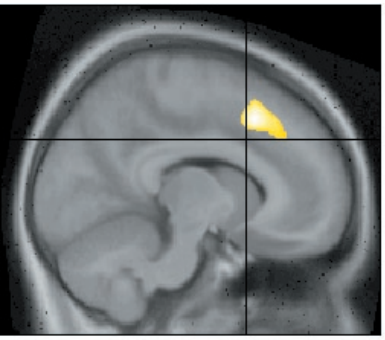
contact: William Baaré

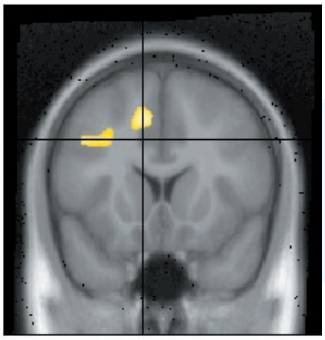
Structural Brain Abnormalities in First-episode Early Onset Psychosis

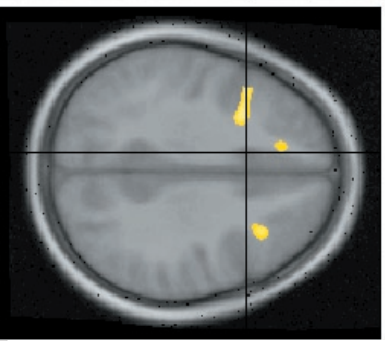
In the present study, it was investigated whether structural brain abnormalities are present in a very early stage of early onset psychosis. The subject group consisted of 29 children and adolescents (age younger than 18) experiencing their first episode of a non–organic psychosis and 29 healthy controls individually matched on age and gender. Patients were recruited from child- and adolescent departments from three hospitals (Copenhagen University Hospital, Bispebjerg,

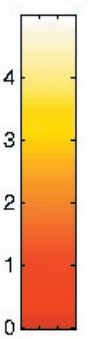
Research Projects

Glostrup County Hospital and Hillerød Hospital) in the Copenhagen and Northern Zealand areas, Denmark.
All subjects underwent a diagnostic and parent interview. The Scales for the Assessment of Positive and Negative (SANS) Symptoms were used to assess the severity of clinical symptoms in patients. Symptoms where grouped into three dimensions: reality distortion, disorganized behaviour and negative symptoms.
High resolution 3D T1 weighted MPRAGE images of the brain were obtained for all subjects. Optimized Voxel based morphometry (VBM) was used for structural analyses. A voxel by voxel statistical analysis allows for a comprehensive assessment of (regional) structural differences and structure/function relationships throughout the brain. Importantly, this method allows testing a priori hypotheses as well as more explorative analyses. Optimized VBM includes the creation of study specific templates in stereotaxic space, spatial normalization to these templates, tissue segmentation, brain extraction, correction for volume changes due to the spatial normalization (modulation) and smoothing.
Preliminary results show that in accord with expectations, patients had significant more CSF in the posterior part of the third ventricle and less white matter volume in specific left frontal brain regions as compared to healthy controls. In contrast, prior hypothesized grey matter reductions in volumes in amygdala, hippocampus, superior temporal gyrus, and frontal lobes were not observed. Finally, the severity of disorganized behaviour was significantly related to a reduced grey matter volume in the left anterior part of the posterior superior temporal gyrus. Moreover, left dorsolateral prefrontal GM loss may also be involved.
contact: William Baaré









The severity of disorganized behaviour in patients suffering from first-episode early onset psychosis was significantly related to a reduced grey matter volume in the left anterior part of the posterior superior temporal gyrus (left). Moreover, left dorsolateral prefrontal GM loss may also be involved (below).

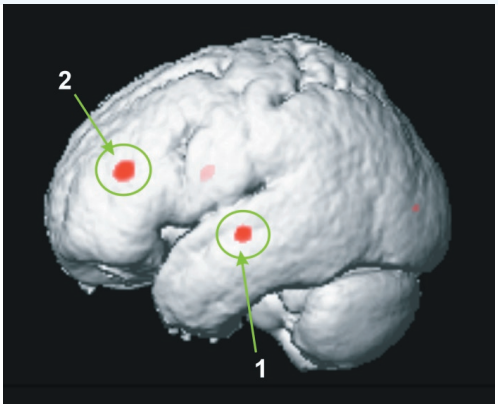


Image Segmentation and Visualization

MRI generates vast amounts of data, and methods for data reduction and visualization are therefore of great importance. Such methods include segmentation, where regions of interest are detected more or less automatically. The purpose of this may be to measure the volumes of white and grey matter in the brain, for example, thus deriving a few valuable numbers from full 3D data set. This task is inherently difficult due to noise, unwanted signal variation and limited spatial resolution.

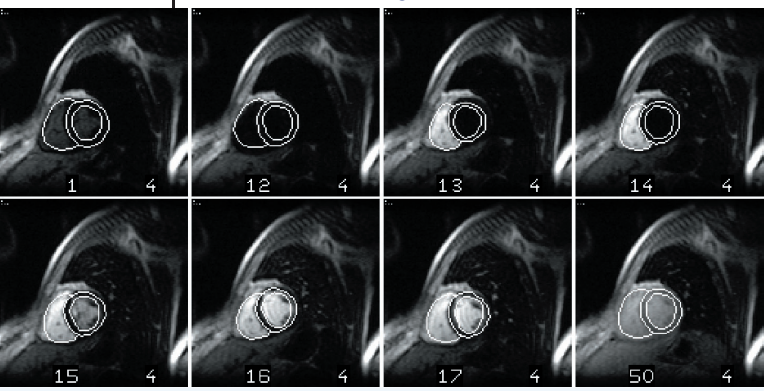
Research group at DRCMR:
Mikkel B. Stegmann, Henrik B.W. Larsson, Dorthe Pedersen, Egill Rostrup, Lars Hanson, Karin Markenroth and Olaf B. Paulson.

Automated Segmentation and Analysis of Cardiac MRI using Statistical Image Analysis

Aims & description: The purpose of this project is twofold;
i) To develop a fast and objective method for 3D segmentation of the left ventricle in short-axis cine MRI over the heart cycle in order to automatically obtain functional parameters of the human heart (e.g. ejection fraction).
ii) To develop a method for single-slice left ventricle segmentation in short-axis perfusion MRI during the bolus passage in order to obtain functional parameters of the human heart for tissue viability estimation et cetera.

Both parts aim at automating currently resource demanding routine post processing by employing and developing computerized segmentation methods using advanced statistical image analysis.
Results & status: In the year 2002, methods for wavelet compression and noise reduction of cardiac image data have been developed and presented. Further, a method for fast segmentation of cardiac perfusion MRI has been proposed and submitted for publication. Additional topics treated include methods for model truncation, model learning and exploitation of modern graphics processing units (in submission). All of the above work has been incorporated into one common framework for statistical segmentation.

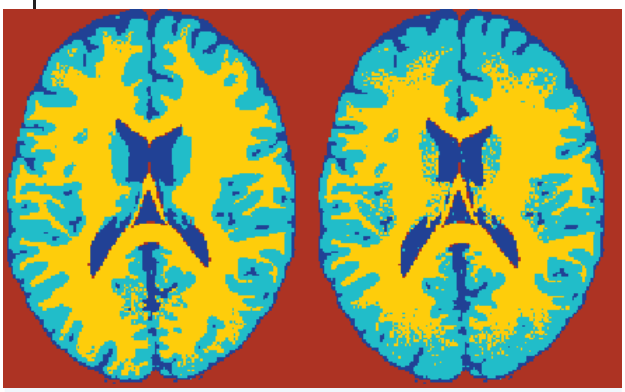
contact: Mikkel Stegmann



Automated segmentation of perfusion cardiac MRI - before, during and after the bolus passage - using a statistical texture ensemble (computation time < 34 ms/image).

Simultaneous Segmentation and Coil Inhomogeneity Correction

Radiowaves are transmitted and received using antennas (coils) during MR imaging. Differences in coil sensitivity cause unwanted intensity variation across the resulting images. This is a major problem for automatic detection of anatomical structures (segmentation). The variation differs between tissues and improved segmentation methods are expected as a result of the project.
Status: Tim Dyrby became Electrical Engineer from the Danish Technical University in 2002 based on work in this project.
Contact: Lars G. Hanson

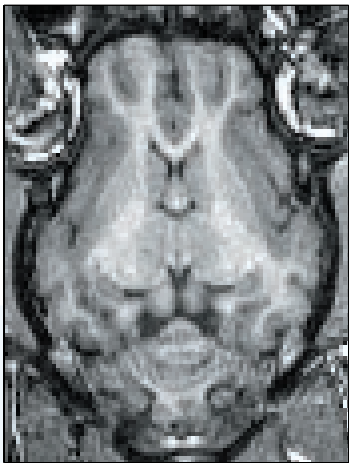


The images show segmentaion with (left) and without (right) simultaneous intensity correction. The developed intensity correction algorithm is seen to improve the classification significantly.

A Comparison of Brain Volumetry Based on MR Scans and Classical Histological Methods

Aims: To establish the accuracy and precision of MR volumetry and to identify the effect of limited resolution and other possible error sources in MR scanning.
Description: Structural MR scans are being used in several contexts to obtain information about the volumes of different brain structures. Typically, semi-quantitative information is obtained as a simple rating scale, but alternatively quantitative information may be obtained by manually drawing regions of interest. In classical anatomical research volumes are most often obtained using stereology. This is a quite different method, which has the virtues of being unbiased, and based on an underlying mathematical theory. However, there have been few direct comparisons of data obtained from scanning and by anatomical methods, as well as between different volumetric methods. In the present study we are investigating the pig brain in order to obtain the correspondance between in-vivo MR scans and post-mortem tissue samples. Results: A good contrast and resolution has been obtained after preliminary work to optimise scanning parameters on the departments new 3T scanner. The resolution has been significantly improved compared to 1.5T scanners.
Status: Four of a planned 12 scans have been obtained so far. Implementation of stereological methods is ongoing.

Contact: Egill Rostrup

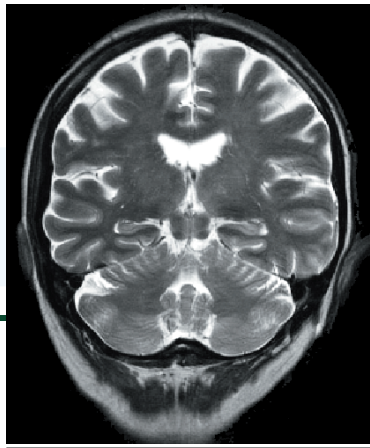


Structural image (T1 weighted, MPRAGE) of a pig brain, obtained at 3T. A good anatomical contrast is obtained in spite of the small voxel dimensions (0.7 mm isotropic resolution) .

Partial Volume Correction of Tc-SHMPAO SPECT Scans

Erroneous estimation of pixel intensities caused by too low image resolution is a serious problem for all scanning methods. This so-called partial volume effect is of particular concern for patients with brain atrophy, where the size of brain structures decrease. The MR department is collaborating with the Neurobiology Research Unit at Rigshospitalet in a project concerning partial volume correction. Reference material is collected using the new 3 tesla magnet for scanning a population of healthy volunteers aged 40 years or more. The image material will be used for several projects, including the EU PVEout project, aimed at development and validation of methods for partial volume correction.
Status: 20 volunteers have been scanned.

Contact: Lars G. Hanson



The very high resolution provided by the new scanner is of particular importance for imaging of small brain structures such as the hippocampi

Research Projects

Perfusion

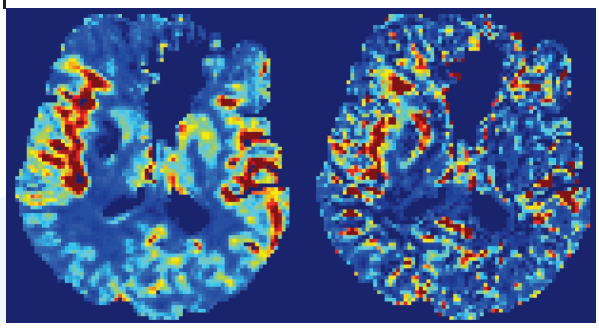
Perfusion weighted imaging is used in everyday clinical imaging, but inter-subject comparisons and patient follow-up require quantitative perfusion imaging methods. This group works with technical aspects of perfusion imaging to improve quantification. The research areas span from the development of scanner sequences and signal processing for improved perfusion measurements (with or without contrast agent infusion), over investigation of brain reactivity to Diamox, investigation of the perfusion/diffusion mismatch in rats and humans with stroke, to the latest evolving research of lung ventilation with hyperpolarized gases. Perfusion measurements are used in the department to investigate heart disease and multiple sclerosis.

Research-group at DRCMR:
Irene K. Andersen, Karam Sidaros, Jacob R. Marstrand, Sverre Rosenbaum, Ellen Garde, Lisa Hildebrandt-Eriksen, Lise Vejby Søgård, Egill Rostrup and Lars G. Hanson.

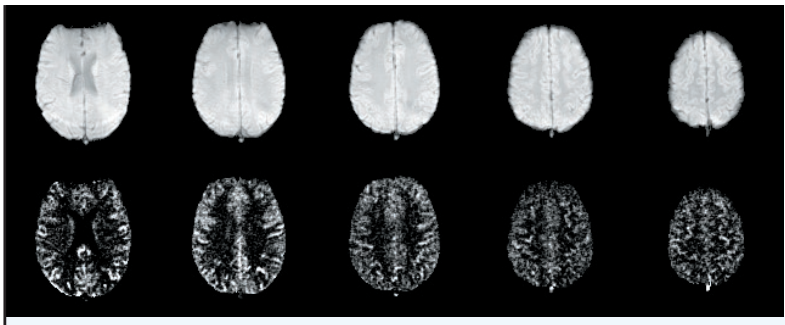
Brain Perfusion Quantification Based on T1-weighted Imaging

The existing methods for contrast enhanced perfusion quantification are based on T2-weighted imaging. The perfusion values obtained using these methods have some inherent uncertainties, since the perfusion estimates depends on the vascular geometry. T1 weigthed imaging methods are expected to provide more robust perfusion estimates. Initial experiments show that despite an expected poorer signal to noise ratio, the perfusion may be estimated using T1 weigthed methods. The initial results were presented at the ISMRM 02 conference. Improvements have been performed and a more thorough investigation is planned in 2003.

contact: Irene K. Andersen



The perfusion level of a stroke patient measured simultaneously with two different scanner sequences during passage of a bolus of contrast agent. The methods supply information about different parts of the vascular tree.



Upper row shows anatomical images of 5 axial slices in the brain, while the lower row shows the strongly perfusion-weighted images in the same slices, acquired using arterial spin labelling in 6 minutes without the use of any exogenous contrast agents.

Arterial Spin Labelling

Arterial spin labelling is a completely non-invasive method of measuring perfusion. It uses blood water as an endogenous natural tracer and relies on the difference between a perfusion-sensitive and a perfusion-insensitive image. The technique requires sequence optimisation and careful calibration to ensure correct perfusion quantification.
The project has resulted in a PhD thesis that was submitted in January and defended in June 2002. Ongoing work with the technique has been shifted to the new 3T scanner, which offers increased sensitivity and reduced imaging time. The initial results from the 3T scanner are very encouraging.

contact: Karam Sidaros

Perfusion Quantification using Gaussian Process Deconvolution

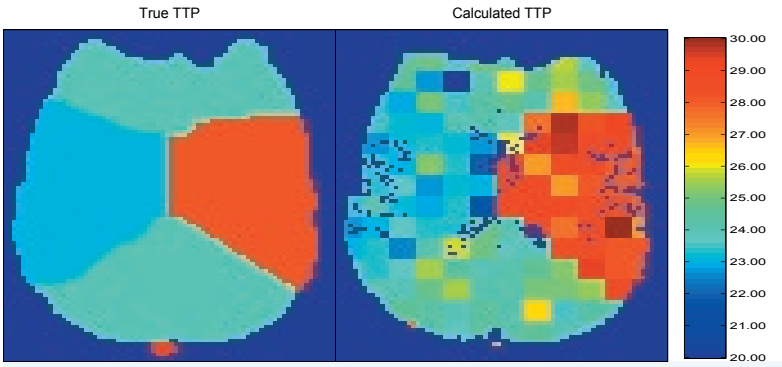
To quantify perfusion from bolus tracking experiments, the tissue concentration curves have to be corrected for the non-ideal shape of the arterial concentration curve that acts as input to the tissue. This is done through deconvolution, which is non-trivial due to the noise-level of the measurements. In this study, a new method for deconvolution for perfusion quantification was developed using artificially generated curves. The new method called Gaussian Processes for Deconvolution, GPD, is as good as existing methods in determining the perfusion value. Moreover, it is superior to existing methods in determining the entire tissue response to a bolus. The results were published in Magnetic Resonance in Medicine in August 2002 and is the key work in the PhD thesis of Irene K. Andersen.

contact: Irene K. Andersen

Blind Deconvolution in Brain Perfusion Imaging

Aim: To obtain a simultaneous estimation of the arterial blood supply to a region, as well as its perfusion and blood volume.
Description: Information about the mean transit time for a given tracer, and the blood flow and volume in a specific region can be obtained from its response to an infinitely short bolus of contrast agent. In practice, this information has to be derived by deconvolution from injections of considerable duration, and a prerequisite is that the shape and amplitude of the arterial input function can be correctly determined. Unfortunately, there are currently no ways to do that in a satisfactory manner. From a mathematical standpoint, however, it seems possible to calculate the shape of both the input and the impulse response function, due to the high number of (semi-) independent measurements available in a typical perfusion imaging experiment. We have developed an algorithm for stepwise optimization that uses a genetic search strategy to minimise the problems arising from multiple local minima.
Results: The algorithm has been shown to correctly separate the effects of the input and the response function on the measured tissue signal. As the genetic algorithm is especially time consuming, it has proven useful to combine it with a standard simplex search routine.
Status: Feasibility and robustness of the method have been ascertained using time series data with a simulated bolus passage. The final report on the method will include its application to real bolus injection data in a group of healthy subjects.

contact: Egill Rostrup

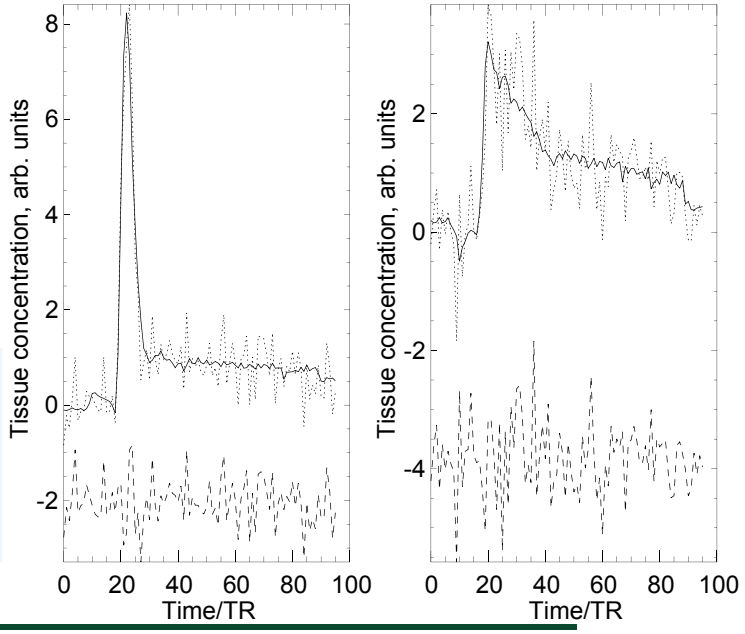


Blind deconvolution of brain perfusion data. The algorithm was tested using time series data from a volunteer under resting conditions. The data was modified to show a Gd-bolus passage with varying temporal characteristics in different brain regions. There is a good overall correspondence between the simulated values (time to peak arterial concentration, left panel) and the results from the deconvolution procedure (right panel).

Filtering of Perfusion Measurements using Training Data

Perfusion measurements are sensitive to system and physiological noise. A method was developed to reduce this problem. It detects time curve features that are reproducible across tissues and subjects. These trends derived from example data are used to separate signal from noise. The sensitivity to choice of training data has been explored.
Status: An abstract was presented at the ISMRM conference.

contact: Lars G. Hanson



The dotted lines show measured tissue concentrations after administration of an intravenous bolus of contrast agent for volume elements outside (left) and inside (right) the infarcted brain area in a stroke patient. It is seen how the contrast agent passes through the brain on two different timescales. The solid line shows filtered data. The noise is significantly reduced (dashed line) by the developed filtering method.

Perfusion

The term perfusion is attributed to the blood flow through the capillary network of a unit mass of tissue. Perfusion assures the delivery of oxygen and nutrients to the tissue and the removal of metabolic waste products from the tissue. Fresh oxygenated arterial blood is delivered to the capillary network, which is optimized for blood-tissue exchanges and deoxygenated blood is drained through the venous network. Although perfusion is closely related to other physiological parameters such as blood pressure, blood volume, blood velocity, capillary network density, it refers to the circulation of blood and is measured in units of ml of blood per 100g of tissue per minute.

Research Projects

Cardiology

The Cardiology Research Group at the DRCMR has a long tradition for broad involvement in cardiovascular MR research. MRI is extremely well suited for cardiac examinations allowing for detailed studies of chamber structure and function, as well as high-precision measurements of flow, perfusion and the new decipline of atherosclerotic plaque imaging. Within the past year, the group has been engaged with projects covering a variety of pathological conditions such as congenital heart disease, hypertensive heart disease, acute myocardial infarction, heart failure, atrial fibrillation, heart afflictions related to diabetes mellitus and obesity and finally the group have worked on setting up a new MR aproach for atherosclerotic plaque imaging insired by international experiences. Various aspects of these conditions have been investigated using a range of MRI techniques, among which some are well established, whereas others are more experimental. The specific projects are described in detail below.

Research group at DRCMR:
Helle Andersen, Mikael Boesen, Gitte Nielsen, Jens C. Nilsson, Dorthe Pedersen, Lars Søndergaard and Susette Krohn Therkelsen and Karam Sidaros.

Angiogenesis Stimulated by Granulocyte-colony-stimulating Factor in Patients with Ischaemic Heart Disease

During the past decades, the therapeutic repertoire against ischemic heart disease has been growing steadily. Nonetheless, ischemic heart disease remains a major cause of morbidity and mortality, which emphasizes the need for new treatment strategies. The purpose of the study was to evaluate potentials effects on different aspects of left ventricular (LV) physiology from angiogenesis stimulated by granulocyte-colony-stimulating factor (G-CSF) in patients with end-stage ischaemic heart disease. 11 patients have undergone cardiac MR examinations before and 2 months after treatment with G-CSF in order to measure LV systolic function and myocardial perfusion. The MR data are currently being analysed.

contact: Jens C. Nilsson

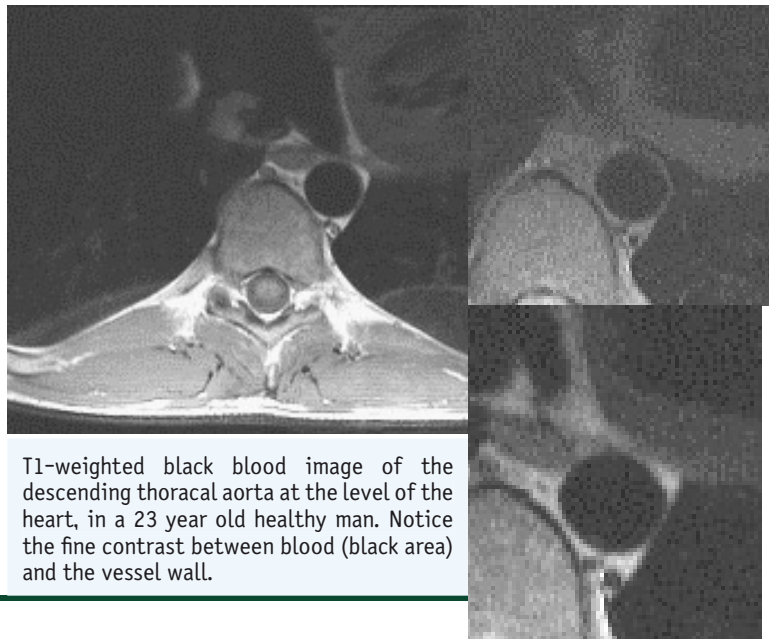
Evaluation of Left Ventricular Dimensions and Function in Hypertensive Patients during Treatment with Losartan or Atenolol (a Sub-study to the Losartan Intervention for Endpoint (LIFE) Reduction in Hypertension Study)

The purpose of the study is to evaluate potential effects on left ventricular (GPD) dimensions and function from treatment with Losartan or Atenolol in hypertensive patients with electrocardiographic signs of LV hypertrophy and correlate the changes to the blood plasma marker N-terminal pro Brain Natriuretic peptide (NT-pro-BNP). 41 patients randomised to either treatment in the LIFE-study have been submitted to cardiac MRI examinations before randomization and 21 patients completed the follow-up 5 years later in order to measure LV- volumes, myocardial mass and systolic function. The MR images and NT-pro-BNP data have been analysed, and the results will be submitted for publication in spring 2003. Our preliminary non-published data suggest that NT-pro-BNP is a potent marker for LV mass in patients with LV hypertrophy and preserved LV systolic function. The number of subjects examined was relatively small, and underlines the potential power in using MRI in assessing LV mass in coming study designs.

contact: Mikael Boesen

Atherosclerotic Plaque Imaging

Over the past decade, the western world has seen an increasing number of patients suffering and dying from cardiovascular diseases due to atherosclerosis, such as acute myocardial infarction, apoplexia etc. In the past year, inspired by work published in international papers, we have worked on setting up a method for atherosclerotic plaque imaging in the aorta with a conventional 1.5 Tesla clinical MR scanner. This MRI approach gives us the potential to view and in detail describe the plaque prevalence, plaque composition and plaque burden in the aorta of patients. As part of the contact person's PhD project, our goal is to use this method to describe the plaque burden and follow the plaque development over time, in a well-defined cohort of patients thus giving us an increasing understanding in-vivo of this growing and potentially harmful process.



T1-weighted black blood image of the descending thoracal aorta at the level of the heart, in a 23 year old healthy man. Notice the fine contrast between blood (black area) and the vessel wall.

The ultimate goal will be to use this method to screen, diagnose and treat patients with unstable atherosclerotic plaques before they give the patient symptoms. Our plan is to launch the project in spring 2003.

contact: Mikael Boesen

MRI of the Atria and the Left Ventricle in Middle-aged Normal Subjects, in Patients with Permanent Atrial Fibrillation and in Patients with Persistent Atrial Fibrillation Before and After Cardioversion

The purpose of the study is to measure right and left atrial and left ventricular dimensions together with systolic function using cardiac MRI in normal subjects, in patients with permanent atrial fibrillation (AF) and in patients with persistent AF before and after conversion to sinus rhythm. A range of neurohumoral substances will be measured along with atrial measures acquired with echocardiography and signal-averaged-p-wave duration (an estimate of the intra-atrial conduction time of the sinus node impulse). The normal subjects will serve as controls for the patients with AF and will also form the basis of a small introductory evaluation study to estimate the accuracy of the atrial measures. Whilst being primarily descriptive, the study aims to evaluate whether the cardiac measures or the plasma level of the neurohumorale substances possess any potential as prognostic markers for the risk of recurrent AF after successful cardioversion.
The 20 normal controls have all been examined and initial data evaluation has been performed. All 60 patients with persistent AF have been included and examined at baseline; six patients await the six-month follow-up. 11 out of 20 patients with permanent AF have been examined. Inclusion is expected to be completed in February 2003.
The project forms the basis for a Ph.D. thesis.

contact: Susette Krohn Therkelsen

Left Ventricular Dysfunction in Obese Subjects and Potential Antiremodelling Effects Following Weight Loss – an MRI Study (an Amendment to the Topiramat Study)

Objectives: To evaluate the degree of left ventricular dysfunction and left ventricular hypertrophy as well as potential cardiac effects from weight reduction in obese subjects. Furthermore, the study aims at investigating whether obese subjects have elevated plasma levels of neurohumoral substances (BNP, ANP, N-terminal pro BNP, endothelin, epinephrine, norepinephrine, renin, aldosterone, arginine-vasopressin), and whether there is a correlation with the cardiac findings before and after weight loss. Fifty-eight obese subjects with a BMI 33 kg/m2 and < 40 kg/m2 have been included and cardiac examinations and blood samples have been performed three times, before and after 8 weeks of diet and 8% weight loss and again after 10 months. The data is now being evaluated and twenty-four normal weight, control subjects are being scanned. The collected data will form the basis for a PhD thesis, which is expected to be submitted in the end of spring 2004.

contact: Dorthe Pedersen

Rheumatoid Arthritis

An increasingly aggressive therapeutic strategy, improved treatment options, and encouraging preliminary results have attracted growing attention to the potential of MRI in the diagnosis, prognostication and monitoring of rheumatoid arthritis (RA). MRI offers multiplanar imaging with unprecedented soft tissue contrast and high spatial resolution. Synovitis, the primary joint lesion in RA, can be detected and monitored, as can early bone destruction. In contrast, conventional radiography only shows the late signs of preceding synovitis.
Based on experiences from 2 PhD dissertations and a doctoral thesis, current main research efforts of the arthritis research group are divided on the 4 issues described below.

Research group at DRCMR:
Bo Ejbjerg, Marcin Szkudlarek, Mette Klarlund and Mikkel Østergaard

MRI of Small Extremity Joints in Rheumatoid Arthritis

This PhD study is designed to investigate the value of different MRI-methods in RA, particularly early RA. Specific aims, which are evaluated in a series of studies involving comparisons with clinical, radiographic and histopathologic parameters, include investigation of the following:
1) Which MRI sequences are the most sensitive for evaluating joint inflammation and destruction.
2) Whether qualitative or semi-quantitative methods can provide information similar to more time-consuming quantitative approaches?
3) Whether very detailed examination of a few joints is more sensitive to changes in rheumatoid inflammation and destruction than less detailed examination of many joints.
4) Whether a low-cost, dedicated extremity MRI system can provide similar information to that acquired using 'conventional', relatively expensive high-field MRI machines.
Status: Studies were initiated 1/1-2001. Preliminary results suggest comparable sensitivities of low-field and high-field units. Studies are still in progress.

contact: Bo Ejbjerg

Ultrasonography of Small Extremity Joints in Rheumatoid Arthritis

Ultrasonography (US) is more available and less expensive than MRI. Novel high-frequency transducers allow high-resolution assessment of the small joints of the hands and feet. The projects in the PhD study focus on ultrasonography, including the flow-sensitive Power Doppler technique, of the joints of the hands and feet in RA, including early RA. The projects include a number of methological studies, comparison with clinical, histopathologic, radiographic and MRI findings, as well as longitudinal studies to investigate the sensitivity to change.

Research Projects

Status: The PhD study was initiated 1/1-2000. Data acquisition in the cross-sectional studies is completed. Main results so far include a generally good inter-observer agreement on US-findings (in Press), a very high agreement between Power Doppler US and dynamic contrast-MRI (published 2001). This indicates that US is reliable for assessment of finger joint synovitis. Most data remain to be analysed.

contact: Marcin Szkudlarek

International Collaboration on MRI Definitions, Scoring Methods and Validation

As a consequence of the fact that MRI scoring methods of RA joints are insufficiently validated, an "OMERACT-MRI" study group with expertise in MRI in RA and in scoring methodology have since 1999 worked on developing definitions of RA changes and on developing and testing scoring methods. OMERACT is an international forum that performs validation studies and seeks consensus within Outcome MEasures in Rheumatoid Arthritis Clinical Trials.
Status: Based on biannual meetings and a number of validation exercises, MRI definitions of important RA joint pathologies and preliminary scoring methods have been suggested (published 2001). Further validation studies, particularly concerning longitudinal data, have been presented at the OMERACT meeting in Brisbane 2002 (In Press). The expected next step is development of an MRI in RA atlas for scoring of hand and wrist joint pathologies.

contact: Mikkel Østergaard

MRI of Wrist and Finger Joints as Outcome Measure and Prognostic Marker in Early Rheumatoid Arthritis - a Longitudinal Multicenter Study of 160 Early RA Patients.

Through sequential MRI of wrist and finger joints of patients included in a Danish multi-centre study of 160 early RA patients ("CIMESTRA"), the aim is to investigate the value of MRI as outcome measure and prognostic marker in early RA, compared with routine clinical, biochemical and radiographic parameters.
Status: All patients are included. 1-year follow-up studies will end in late 2003.

contact: Bo Ejbjerg

Respiratory Medicine

Conventional MR imaging does not provide functional lung information. Neither does it offer detailed structural information, as only the outline of the lungs can be visualized using conventional MRI. This is due to the enormous surface area, causing rapid signal loss. Instead, the clinicians rely on radionuclear techniques for imaging of lung diseases. Unfortunately, these give relatively poor spatial resolution even for high dose radiation. It has recently become possible to magnetize certain gasses using strong lasers and techniques relying on fundamental atomic physics. The magnetic gas can be inhaled by patients, and be used for forming detailed MR images of lung function and structure. The most promising gas for this purpose is an inert and non-radioactive helium isotope, 3He, which is completely harmless to the body. The gas can stay magnetised for days, when kept in special containers, and it can consequently be shipped over large distances. This is important, since it is immensely complicated to reach high levels of gas magnetisation, consequently helium imaging is only performed at a few institutions worldwide.

Research-group at DRCMR:
Trine Stavngaard, Lise Vejby Søgaard, Karin Markenroth, Lars G. Hanson and Olaf B. Paulson

Polarized Helium to Image the Lung (PHIL)

The DRCMR is one of three European clinical centres involved in the EU sponsored PHIL project . The aim of the project is to evaluate polarized helium imaging as a diagnostic and prognostic tool to study selected lung pathologies. The helium gas for imaging is polarized in Mainz, Germany, and is shipped by plane to Sheffield University and Hvidovre Hospital. Other centres in the PHIL project are working with animal models and improving the methods for polarizing and imaging the gas. Further information can be found on the PHIL project homepage: http://www.phil.ens.fr.
The patient population selected for the PHIL project suffers from COPD (chronic obstructive pulmonary disease). The cohort encompasses 120 patients, of which 30 will be examined at the DRCMR. The lung MR images will be compared to existing methods for diagnosis of COPD (conventional lung function test, CT and Kr scintigraphy).
Status: The project started December 2000. Unfortunately, the hardware upgrade to allow imaging of helium on a clinical scanner has been problematic, and all the necessary permissions were only received in November 2002. The first shipment of gas will arrive in January 2003 when the first volunteer scan will take place.

contact: Trine Stavngaard

Pre-Clinical Studies

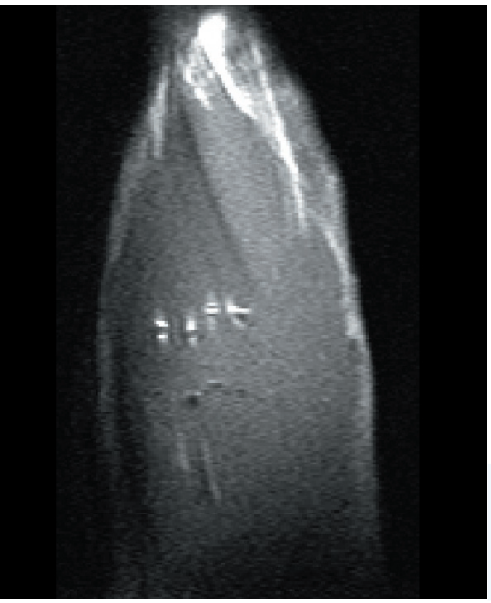
The pre-clinical studies performed at DRCMR are designed primarily to support the clinical work and research within Hvidovre Hospital. The pre-clinical studies aim to develop, evaluate, refine and implement new MR techniques in order to measure the biochemical (metabolic), physiological and morphological characteristics of disease states. The acquired parameters could then be used to monitor therapeutic interventions and facilitate the development of new therapeutic agents and strategies both in pre-clinical development and in clinical trials. Ultimately, developed techniques should be applied routinely in clinical diagnosis, prognosis and monitoring.

Research group at DRCMR:
Elisabeth Hildebrandt-Eriksen, Ian Rowland, Niels Broberg, Lise Vejby Søgaard and Helle Simonsen

Development of an Electroporation System for Use within an MR Scanner

In vivo electroporation is an established means of increasing cellular permeability to drugs and other agents (including DNA for gene therapy) by applying strong, pulsed electric fields to tissue to increase intracellular uptake. Successful clinical application of this approach requires identification of the tissue to be electroporated with subsequent monitoring of treatment efficacy. Consequently, an electrode system suitable for use within a MR scanner has been developed, assessed and applied successfully in vivo. Standard MR methods have been used to monitor the effects of high voltage pulses performed within the bore of a MR scanner. Results from this study indicate that MR methods could be applied to treatment planning, dosimetry and monitoring of electroporation based therapeutic strategies.

contact: Ian Rowland

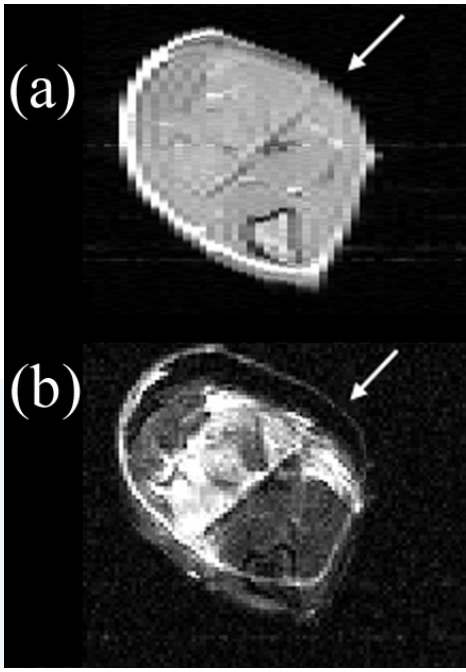


T1W spin echo image showing the release of iron from syringe needles. The four hyperintense regions are due to the release of paramagnetic iron species into the muscle from the four needle anodes.

Dynamic MRI Studies

The aim of this study is to develop methods of assessing early vascular changes following administration of a drug targeted to tumour vasculature. When used with a cytotoxic agent, the combined efficacy is likely to depend on the timing between agent administrations. A multi-dose dynamic contrast enhanced MRI study was performed and the whole enhancement profile for ROIs, including normal muscle and tumour following hydralazine administration, was used for segmentation of the tissues using k-cluster analysis. Such a method of monitoring early heterogeneous vascular changes could be used to optimize a specific combination therapy and would therefore be of clinical utility.

contact: Ian Rowland



T1W (a) and T2W (b) spin echo images acquired 80 minutes after electroporation. T1W images show little change whilst the T2W image reveals oedema formation between the electrodes. Note the dark areas (arrowed) revealing the location of the MR-compatible electrodes.

Silicone Vascular Casts

The aim of this study was to establish an ex vivo method of investigating tissue vasculature directly using MRI. Using standard corrosion casting methods, a variety of materials were assessed for their suitability for casting and MRI. The studied revealed that a silicone-based material exhibited properties suitable for both casting and obtaining 2D and 3D images. Furthermore, paramagnetic gadolinium containing complexes could be incorporated into the casts enabling the production of phantoms of differing magnetic susceptibilities suitable for assessing and validating direct and indirect imaging methods of obtaining vascular information.

contact: Ian Rowland

Research Projects

Spectroscopy

Magnetic Resonance Spectroscopy (MRS) is a widely used tool in various clinical and research projects, as is evident from this annual report. There is, however, still room for further development of the spectroscopic methods to overcome, for example, motion-induced artefacts.

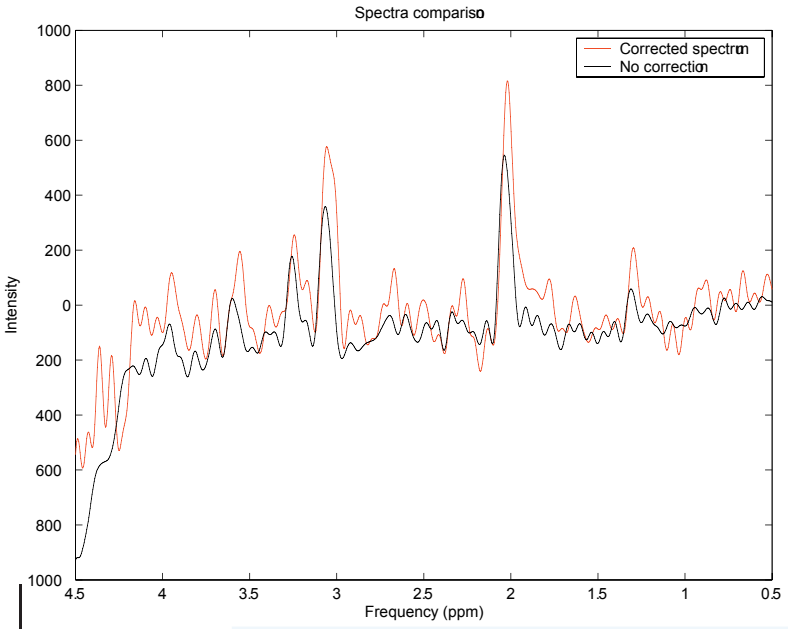
Research group at DRCMR:
Karin Markenroth, Arnold Skimminge, Maria Miranda and Lars G. Hanson

Improved Spectroscopy Using Cluster Analysis and Lipid Signals as Motion Indicators

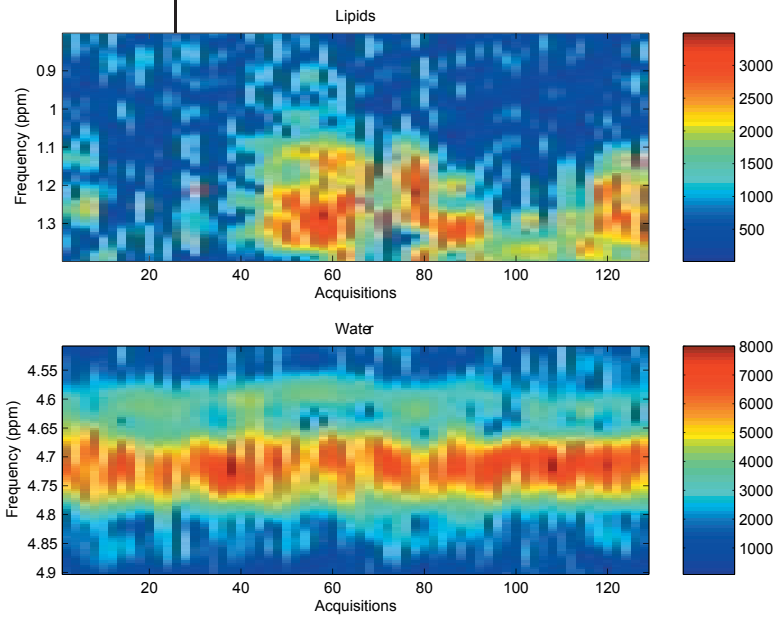
Incorporating MR spectroscopy into clinical routine demands robust sequences and post-processing methods. One obstacle that has to be overcome is patient movement. To obtain good quality spectra, several measurements are usually averaged. If the subject moves during or between those measurements, the result is shifted, or reduced, metabolite peaks and in the worst cases unusable data. Until now, 16 healthy volunteers were included in a newly developed analysis that reduces motion sensitivity. The aim is to refine the method and use it on data acquired for dementia patients, a patient group where motion distortions are often severe. The data in this project were not averaged as they were acquired, but the 128 measurements of the 8 ml voxels were saved individually to allow for offline motion correction. By evaluating the time evolution of these spectra, it was seen that small voxel displacements affected both the position and the shape of the lipid peak whereas water and metabolite signals were, comparatively, only slightly shifted. The reason for this difference is that the lipid signals are artefacts stemming from outer-voxel regions, and thus they are more affected by voxel displacements. To correct the motion-distorted spectra, the time evolution of the lipid peak position was analysed, and periods of motion were discarded. Consecutive scans without movement were rephased, and subsequently the clusters were averaged. This resulted in narrower metabolite peaks, compensating for the SNR loss that comes from discarding data.

Status: An abstract was sent to ISMRM 2003

contact: Arnold Skimminge



Comparison of the average of all acquisitions (black) and the average of the clustered acquisitions (red). The gain in signal and resolution is apparent.

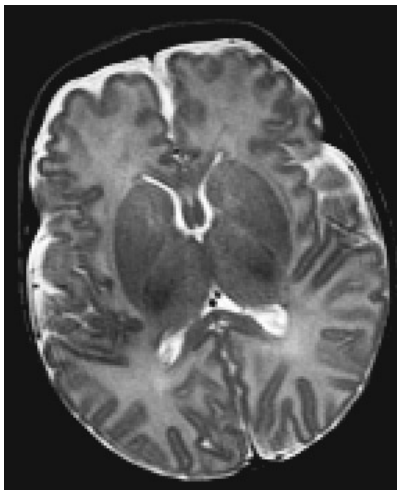


The norm of the lipid and water peaks as a function of acquisition number for one patient. Variations of the lipid peaks reveal subject motion.

Association between Infection in Pregnancy and Ischaemic Lesions in the Immature Brain

The aim of this study is to demonstrate an association between infection in pregnancy and WMD (white matter damage) in the immature brain at term-equivalent age.

Description: Premature infants are at risk of getting brain injury and neurodevelopmental deficits later in life. Pathogenesis of brain lesions is still controversial but apparently both infection in pregnancy and perinatal ischemia are implied in the development of WMD. Large epidemiological studies support the hypothesis that infection in pregnancy causes WMD in the immature brain. On the other hand, several studies support the ischemia hypothesis. As recent studies with single voxel spectroscopy (SVS) have demonstrated, lactate (as a sign of bad oxygen supply to the brain) is significantly higher in premature infants with WMD at term-equivalent age, as compared with premature infants at the same age with normal WM.



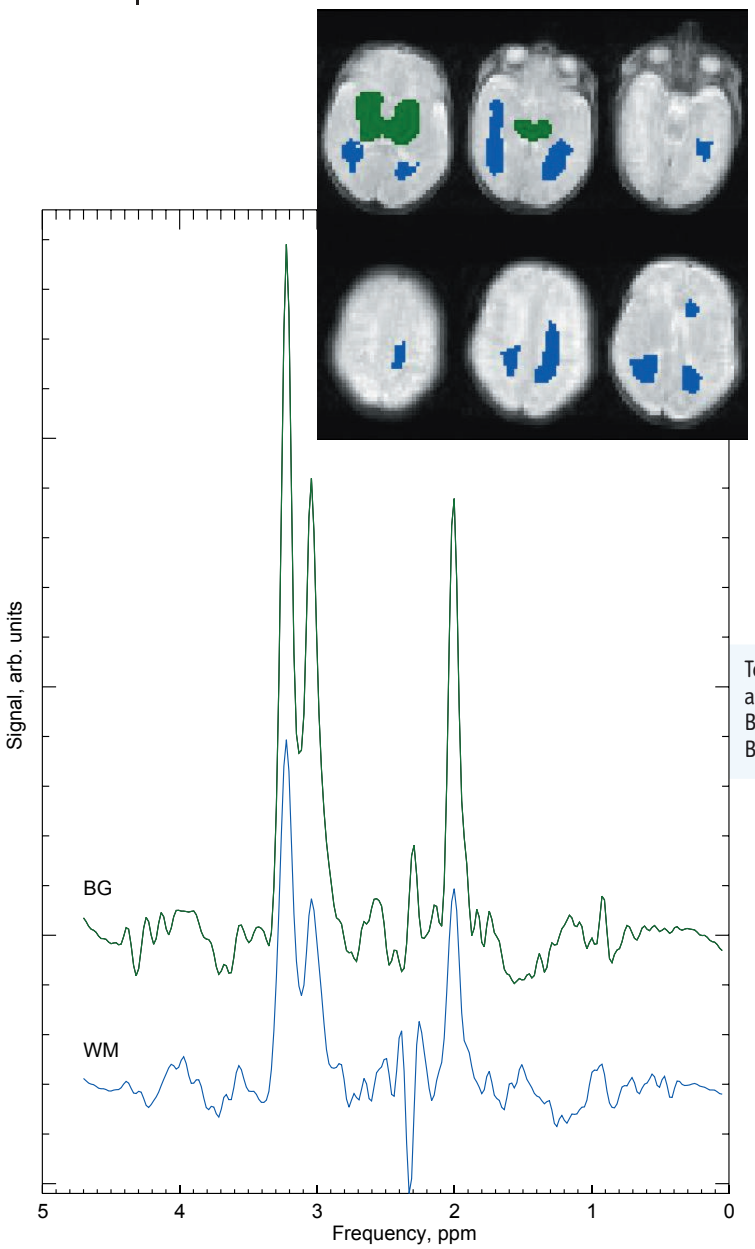
Turbo spin-echo T_2-weighted transverse brain image in a premature baby at term-equivalent age imaged at 3 Tesla.

Design: 200 premature infants (gestational age <33 weeks) born in Hvidovre hospital and Rigshospitalet will be included. Placenta will be examined by a pathologist (histology) and microbiologically. Umbilical cord blood will be examined for bacterial endotoxins and several inflammation cytokines. Infants will be cerebral MR-scanned at term equivalent-age searching for brain lesions and for lactate accumulation. MRI and SVS will be performed as MPRage and Diffusion Tensor sequences will be done.

The first 10 infants were examined at 1.5Tesla Vision scanner (EPSI) but the EPSI spectroscopic method was not reliable for lactate measurements on non-sedated babies. From November 2002 the 3-T Trio MR scanner has been used.

Status: 34 infants included from June- December 2002. The first 10 infants scanned on the 1.5T Vision scanner are summarised in an abstract to the ISMRM 2003-meeting.

contact: Maria J. Miranda



Top: White matter (WM) ROIs in blue and basal ganglia (BG) ROIs in green. Bottom: Spectra from the WM and BG ROIs.

3-Tesla Scanner

The year 2002 was a milestone for the Danish Research Centre for Magnetic Resonance since it witnessed the arrival of the centre's new 3-Tesla whole-body scanner, a Siemens Magnetom Trio. It is the first high-field human scanner in Denmark, and one of very few high-field scanners to be installed in a clinical setting in general.

The scanner was kindly donated by the Simon Spies Foundation, strengthening the bond between the foundation and the DRCMR. The Simon Spies Foundation has thus donated three MR scanners to the DRCMR over the past 18 years.

The Trio arrived on July 2nd, 2002, where the staff gathered to watch the 13-tonne magnet being lifted by the a huge crane and followed its journey to its position in the centre's new scanner room. The installation of the new scanner required new facilities within the centre, and the centre was therefore expanded and a considerable part of the centre was restructured to accommodate this expansion. Although the reconstruction took several months prior to the arrival of the scanner, the patience of especially the clinical staff was rewarded with a more open and welcoming working environment.


HVIDOVRE HOSPITAL
September 2002
PULSEN
Bolde i luften - temadag om uddannelse af læger Side 4
Nye sygeplejepapirer i journalen Side 6
Den ældre medicinske patient - temadag Side 8
13 tons MR-skanner løftes på plads
Den nye Spies-skanner fylder ikke mere end den første fra 1985, men dens indhold er af nyeste dato. Det er en højfeltsskanner, og MR-afdelingen er den første i Skandinavien, der kommer i besiddelse af det avancerede udstyr.
Læs mere side 2 og bagsiden

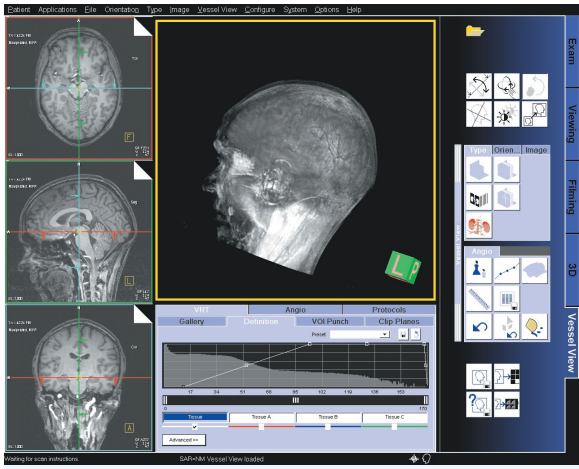
The arrival of the magnet makes it to the front page of the hospital magazine, Pulsen.

The Trio was finally inaugurated on September 2nd, 2002 at a reception attended by the board of the Simon Spies Foundation, the minister for interior and health, Lars Løkke Rasmussen, and other prominent persons from the Copenhagen Hospital Corporation and the University of Copenhagen. The inauguration was covered by the press and was broadcast on a local television channel.

Janni Kjær, the chairman of the Simon Spies Foundation, at the inauguration of the Trio scanner.

The new scanner will allow the centre to keep its frontline position in MR research. We expect the scanner to play a key role in the centre's research, especially brain research, in the coming years. The Trio scanner offers higher resolution, faster imaging and greater sensitivity than the centre's other scanners. Additionally the software provided with the scanner features many possibilities for online post-processing and 3D visualisation, features that were only possible offline with the older scanners.

The higher magnetic field in the new scanner has a positive effect on image quality in various imaging types, such as functional imaging, perfusion imaging and angiography. This will benefit many research areas that the centre is involved in.
Furthermore, the centre is well-suited to apply the opportunities of high-field MRI to clinical practise. Most high-field scanners are installed in research-only sites, which gives the DRCMR a unique position.



A screenshot from the Trio console showing online 3D visualisation of an anatomic scan.

The magnet in the air above the centre being lowered into position. The magnet weighs 13 tonnes.

PhD Theses

The DRCMR has over many years, provided facilities for PhD students in various research projects in the field of MR. In 2002, five PhD theses based on research carried out at DRCMR were defended succesfully.

Left Ventricular Remodelling in the First Year Following Acute Myocardial Infarction – Frequency, Extent and Prediction

Jens C. Nilsson, MD, PhD

Thesis defended April 8th, 2002

Remodelling of the left ventricle (LV) is a detrimental complication to acute myocardial infarction (MI) characterized by increased chamber volume, altered chamber geometry and progressive deterioration of ventricular function. LV remodelling is directly related to poor survival, and has been speculated to be one of the main reasons for the high and still increasing prevalence of heart failure in Western countries.

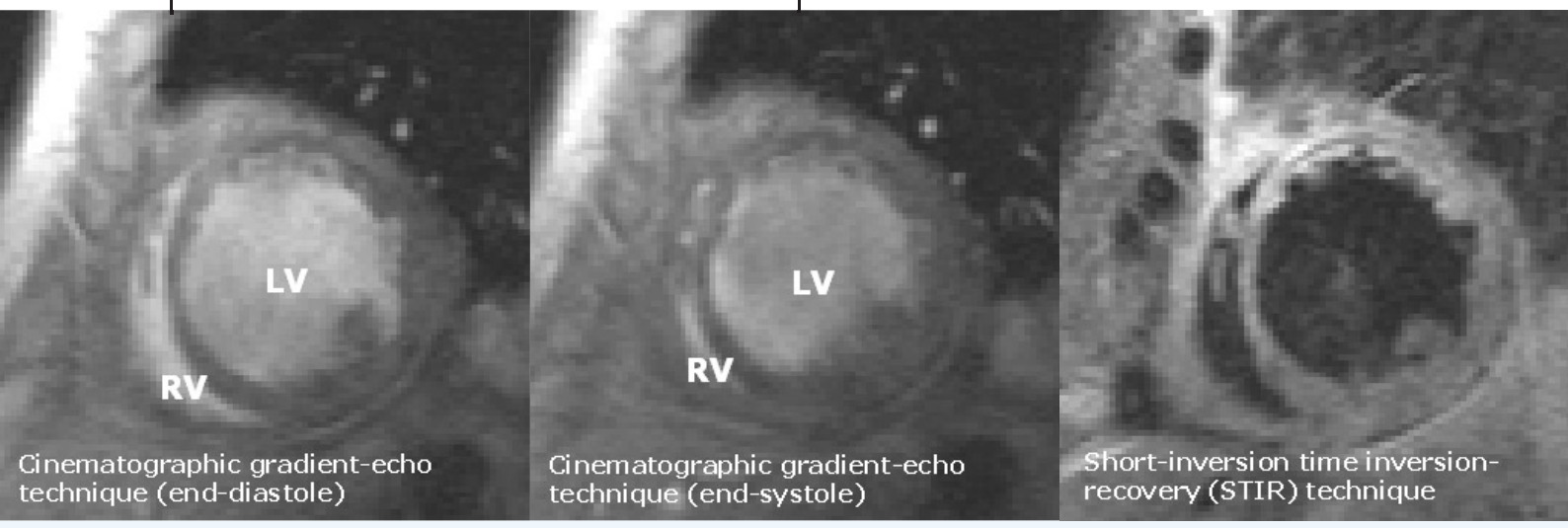
The purposes of the present thesis were to estimate the magnitude of postinfarction LV remodelling in an everyday clinical setting, and to explore the potential for its prediction. Furthermore, different aspects of postinfarction myocardial oedema were assessed.

A total of 42 patients with a first and transmural MI were examined after 1 week, 1 month, 3 months, 6 months and 1 year by blood samples and MRI. In 12 patients (29%), LV end-diastolic volume index (LVEDVI) and end-systolic volume index (LVESVI) increased by 24% and 22% ($p<0.0001$, $p=0.01$). In 12 patients (29%), LVEDVI and LVESVI decreased by 19% and 23% ($p<0.0001$, $p=0.0005$), whereas the remaining 18 patients (43%) were stable regarding these LV measures. LV ejection fraction at baseline was significantly reduced in all patient categories, but was unchanged over time.

Elevated NT-proBNP at baseline was identified as an independent predictor of increase in LVEDVI during follow-up ($p=0.007$). A baseline level of NT-proBNP > 115 pmol/l identified patients, who later developed LV dilatation with a sensitivity and specificity of 89% and 68% and positive and negative predictive values of 50% and 94%.

In 10 consecutive patients from the main study, postinfarction myocardial oedema was assessed by MRI. This substudy revealed that all patients displayed signs of myocardial oedema. The oedema was of largest extent at the initial examination 1 week after the infarction, and declined gradually during the following months. The median duration of oedema was 6 months. The extended duration of myocardial oedema could be important, as the oedema may compromise LV function and influence postinfarction LV remodelling.

In conclusion, the present thesis demonstrates that postinfarction LV remodelling remains a quantitatively significant problem, despite different lines of anti-remodelling therapy. One of many possible reasons seems to be that early identification and targeting of high-risk individuals solely on the basis of LV systolic dysfunction or symptoms of heart failure is insufficient, leaving many patients under-treated, and emphasizing the need for alternative high-risk measures. The current work suggests that plasma levels of NT-proBNP at discharge could be a valuable addition to conventional risk stratification.



67-year old female with an anteroseptal myocardial infarction (9th day). Corresponding short-axis images of the right and left ventricles acquired with two different MR techniques. Notice the obvious infarct expansion on all images, the compromised systolic wall thickening and the presence of myocardial high signal intensity (bright) areas signalling oedema in the STIR image. LV, left ventricle; RV, right ventricle.

Slice Profile Effects in MR Perfusion Imaging using Pulsed Arterial Spin Labelling

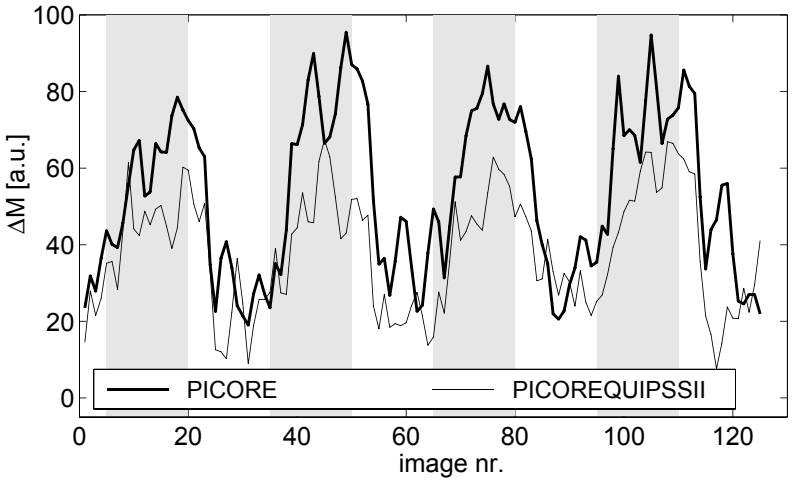
Karam Sidaros, PhD
Thesis defended June 20th, 2002

Arterial spin labelling (ASL) is becoming an established method for non-invasive measurements of perfusion using MRI. Although there exists a variety of different ASL methods, they are based on the same principle. Two images are acquired, one in which the arterial blood that perfuses the tissue has been magnetically labelled or tagged and one in which it hasn't. The difference between the two images can be used to determine perfusion.

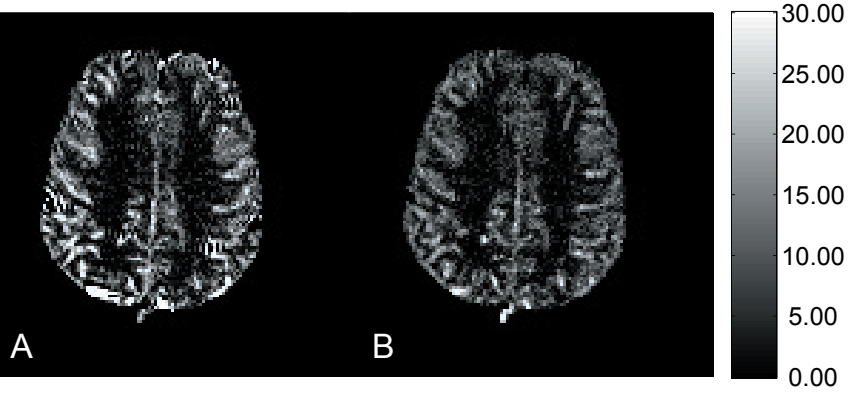
A general problem in perfusion quantification using ASL is ensuring that the signal from static tissue subtracts out completely in the difference images. In a category of ASL sequences known as pulsed ASL sequences, this is related to the slice profiles of the RF pulses used in the sequence. The common approach of ensuring complete static tissue subtraction involves the introduction of a finite gap between the region in which arterial blood is labelled and the region that is imaged. Unfortunately, this introduces transit delays for the tagged blood to reach the imaging region which in turn affect the quantification of perfusion.

The mechanisms by which the slice profiles affect the degree of static tissue subtraction are investigated in this study. It is shown how imperfect slice profiles may create an offset or bias in the magnetization difference signals. Using simulations and measurements, the dependence of this offset on the gap between the tagging and imaging regions is mapped for various pulsed ASL sequences. It is also demonstrated how the offset is affected by various factors such as B1 inhomogeneity and the use of presaturation pulses.
Although the offset can be calculated from the theoretical slice profiles of the RF pulses used, an entirely experimental method of estimating the offset on a pixel-by-pixel basis is introduced. The method uses the same ASL sequence used for perfusion measurements to measure the T1 relaxation curves of both the tag and control experiments. Based on non-linear fitting of a model for the magnetization to the measured curves, a number of parameters can be estimated which enables the calculation of the actual offset.

The proposed method for offset estimation is validated experimentally in both phantoms and in vivo studies. It is shown that by subtracting the estimated offset from the magnetization difference images, perfusion can be quantified correctly without the need of ensuring complete static tissue subtraction. The gap between the tagging and imaging regions and hence the transit delays can therefore be reduced while maintaining the correctness of perfusion quantification.
Finally, the proposed method of offset correction is applied in perfusion measurements during functional activation, where it is shown that using offset correction, perfusion changes can be quantified correctly even when static tissue subtraction is incomplete. Furthermore, it is shown that the inversion time in the ASL measurements can be reduced due to the reduced transit delay, thus increasing the activation detectability without sacrificing the quantitative nature of the perfusion measurements.



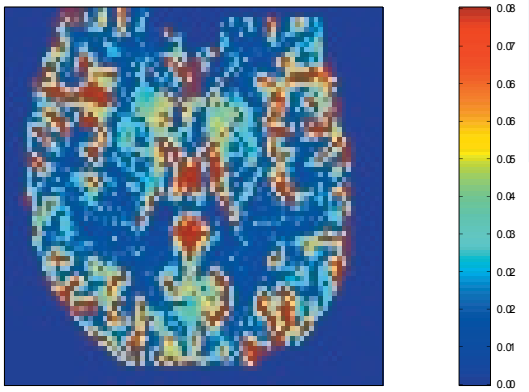
Perfusion timeseries in a functional run, with bilateral finger-tapping. The thin curve corresponds to quantitative ASL measurements while the thick curve is using non-quantitative ASL which has larger senstivity, but is also affected by changes in the transit delays of arterial blood. The shaded areas indicate periods of activation.



Difference between control and tag images [a.u.] in two ASL experiments. (A) The image is perfusion-weighted using non-quantitative ASL. (B) The image is proportional to perfusion using quantitative ASL.

Dynamic Contrast Enhanced Perfusion MRI for Perfusion Quantification

Irene Klærke Andersen, PhD
Thesis defended December 4th, 2002



A map of the calculated perfusion in each pixel. The perfusion is high in grey matter and lower in white matter. The perfusion values were calculated using Gaussian Processes for deconvolution.

Magnetic resonance imaging, during bolus passage of a paramagnetic contrast agent, is used world-wide to obtain parameters that reflect the pathological state of tissue. Abnormal perfusion occurs in tissues such as stokes or tumoure. Consequently, perfusion quantification could have significant clinical value both in diagnosis and treatment of such pathology.

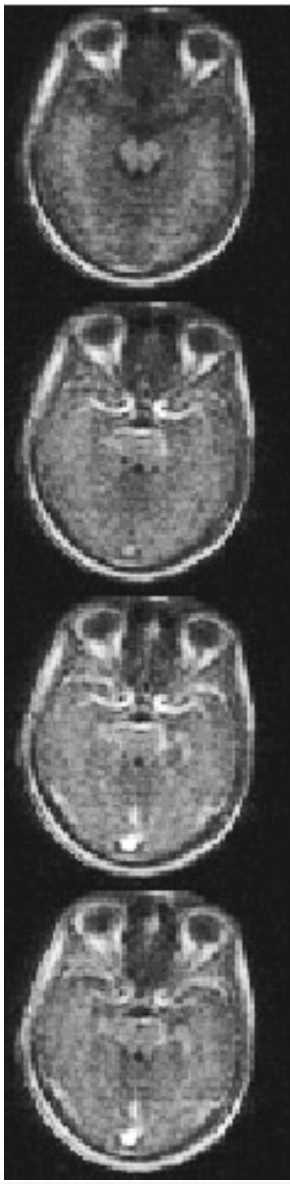
One approach for perfusion quantification involves using the contrast mechanism that affects the transverse relaxation rates of the magnetization, R_2 or R_2^*, since this provides the most pronounced effect. However, the linearity between the contrast-agent concentration, [Ca], and the changes in R_2 or R_2^* has been questioned.

In this thesis, an MRI scanner sequence for detection of the longitudinal relaxation rate, R_1 during bolus passage was modified for brain perfusion measurements, since the linearity between the changes in R_1 and [Ca] is expected to be more robust.

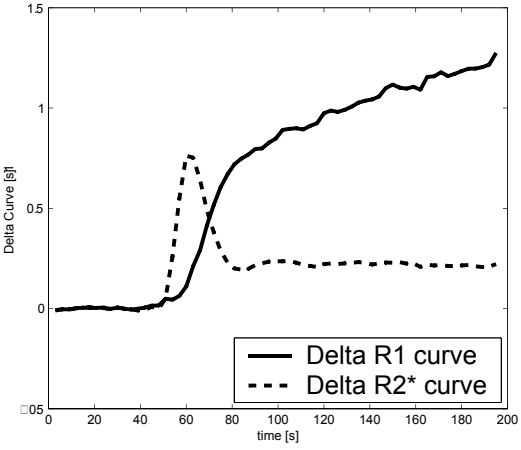
Successful brain perfusion quantification based on R_1 weighted signals has not previously been reported, due to the poor signal to noise ratio of the images. Initial experiments reported in the thesis show that improved sequence design may provide more accurate perfusion estimates in the brain.

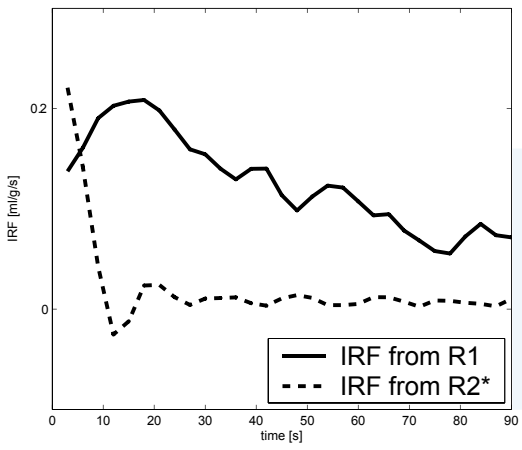
Images obtained during bolus passage are noisy, and the bolus is not an ideal impulse as it reaches the brain. The brain response to an ideal impulse is called the residual impulse response function, IRF. Thus, the measured tissue curves are expressed as the convolution of the input function with the tissue IRF. To obtain the IRF, the tissue curves and the input curves are deconvolved and perfusion is related to the peak of IRF.

In this thesis, a new method for deconvolution of perfusion data is introduced. It is the Gaussian process for deconvolution, GPD. The method is compared to singular value decomposition, SVD, which is the currently most frequently used method for deconvolution. It is shown that GPD has several important advantages over the optimized SVD as a method for deconvolution in perfusion imaging.



The bolus arrival in the brain appears bright on T1 weighted images. Note how the bolus first arrives in the arteries and later drains into the veins.





Left: The change in relaxation rates $R_1=1/T_1$ and $R_2^*=1/T_2^*$ in a region with a blood brain barrier breakdown (BBBB) in a stroke patient. As the bolus passes, R_1 detects the uptake of contrast agent in tissue, whereas R_2 is unaffected by the BBBB.
Right: The corresponding tissue impulse response. Perfusion is calculated as the peak of the curve and the volume of distribution is given as the area under the curve.

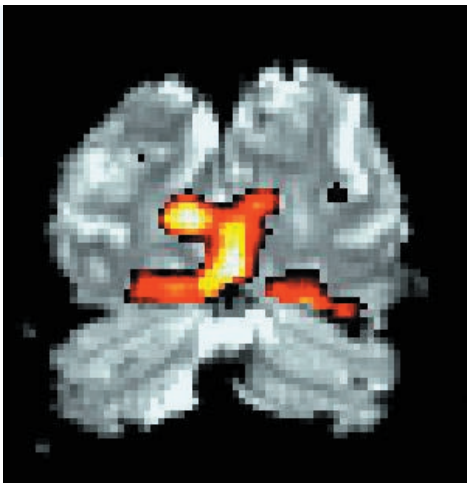
Functional MRI in Optic Neuritis

Annika Langkilde, MD, PhD

Thesis defended December 6th 2002

Multiple sclerosis (MS) is a chronic progressive demyelinating disorder, in which clinical dysfunction is induced by an altered condition through various fibre pathways in the central nervous system (CNS). Structural MRI has become the standard for MS diagnose, as it has a high sensitivity for detecting MS lesions. However, the correlation between the number of lesions and patient functional disability is limited. It has been suggested that adaptive mechanisms of cortical function take place in MS, and that this may affect patient disability. Using functional MRI (fMRI) the cortical function may be detected and quantified. Compared to other methods of detecting cortical activation, fMRI has advantages in being non-invasive, having a high spatial and temporal resolution, and not exposing the subject to ionized radiation.

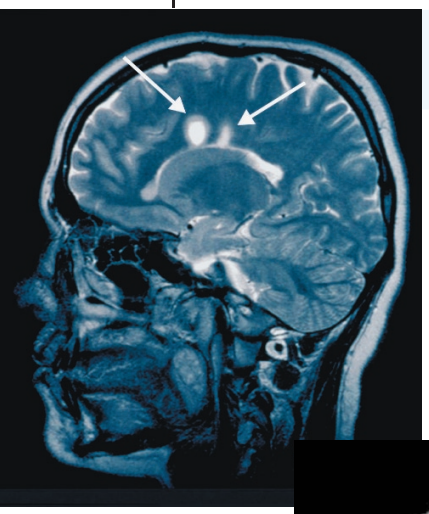
Optic neuritis (ON) is often the first manifestation of MS. In the present Ph.D study patients with previous ON and acute ON were investigated with fMRI, neuroophthalmologic testing and visual evoked potentials (VEP). The visual stimulus in the fMRI studies was a reversing checkerboard, both hemifields and full field, and the cortical activation in the visual cortex was detected. Also a group of healthy subjects were investigated with fMRI. The aim of the study of patients with previous ON was to compare fMRI results to the results neuroophthalmologic testings, and also to compare fMRI results of patients to fMRI results of healthy controls.



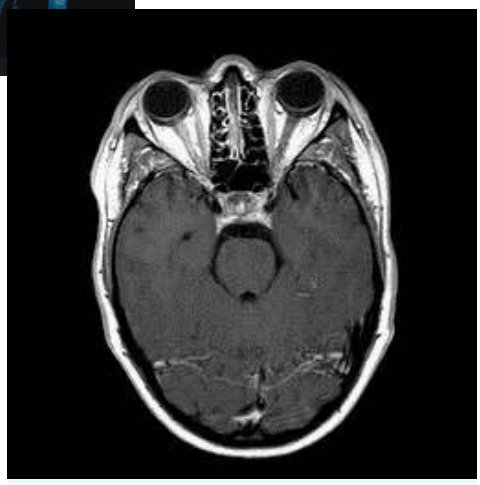
Cortical activation in the visual cortex when stimulating a healthy control using full field checkerboard.

The study of patients with acute ON was a serial study in which patients were studied on four occasions during one year. The aim was to investigate whether cortical functional changes took place during the recovery from ON.

The results from the two studies showed a significant correlation of fMRI results to Snellen visual acuity, contrast sensitivity and VEP amplitude when investigating the affected eye. Compared to healthy controls patients with previous and acute ON show a smaller cortical activated volume, both when stimulating the affected and the not affected eye. In patients with acute ON, however, a temporary significantly increased cortical volume was detected when stimulating binocularly at day mean 34 after symptom onset. The increased cortical activated volume indicate that dynamic adaptive cortical changes take place during the course of ON. If cortical adaptive changes take place and influence the clinical function, these may, at least partly, be responsible for the well known weak correlation between T2 lesions and disability in patients.

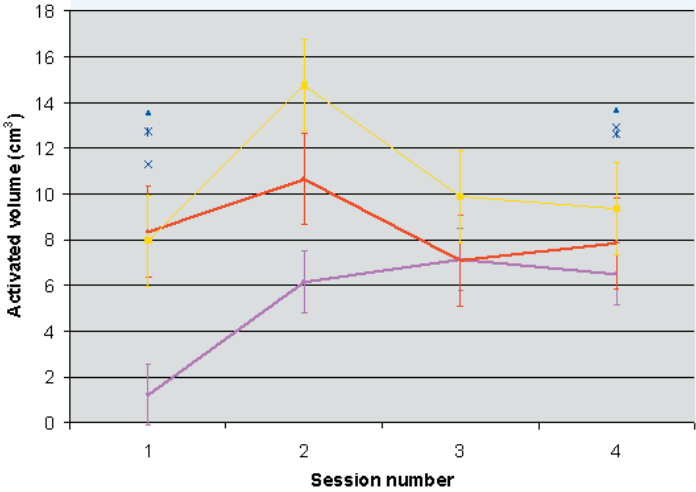


A saggital T2 weighted image of a patient with optic neuritis and two MS lesions (arrows)



T1 weighted MRI after contrast injection showing enhancement of the right optic nerve in a patient with optic neuritis.

The results of activated volumes in patients when stimulating binocularly (yellow), monocularly, affected eye (pink) and the not affected eye (red). The results for healthy controls are shown in blue. For all conditions a larger activated volume was revealed in controls compared to patients, except for binocular stimulation and monocular stimulation at day 34.



AMPA Receptor Antagonists in Mild Focal Cerebral Ischemia in the Rat. An Experimental Study with MRI and Histology

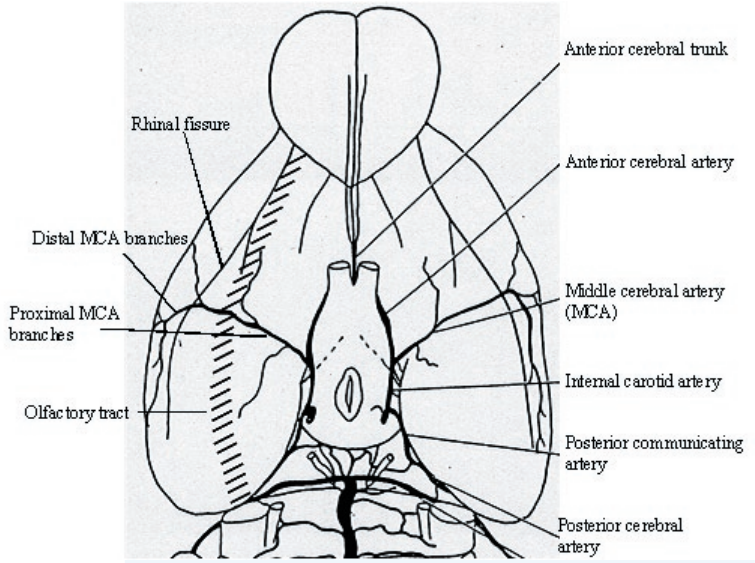
Elisabeth Hildebrandt-Eriksen, PhD

Thesis defended December 16th, 2002

The model of mild focal cerebral ischemia presented in the thesis was investigated with different MRI techniques and histological staining methods. It is based on a simultaneous occlusion of three arterial vessels, the distal part of the middle cerebral artery (MCA) and both carotid arteries, for 30 minutes. Complete control with physiological parameters during surgery was achieved. Temperature control at the site of the MCA turned out to be of paramount importance. The time course of infarct development was described with MRI and lesion development characterized with MR parameters ADC and T2. Perfusion-weighted MRI verified reperfusion of the previously occluded MCA territory. One principal finding was that infarcts could be produced in a consistent way and solely in cortical tissue. The infarct exposed characteristics of cell death by necrosis, with the main feature of a pan-necrotic lesion that did not expand beyond day 3 and had resolved by day 14. The infarct rim was marked by astrocytes expressing GFAP. This morphology is typical for ischemic lesions of short duration but intense ischemic depth, e.g. filament occlusion, and own findings agreed with others both based on the MRI parameters ADC, T2, and relative CBV[1], and histology. Very delayed neuronal death, a feature believed to be connected with this model by one group of investigators, was not observed, nor were signs of apoptotic cell death.

Another principal finding was that tests with the antagonists to the glutamate receptor of the AMPA subtype NBQX and SPD502 yielded positive results. Delayed post-ischemic treatment (by one and 2 hours, respectively) with both drugs resulted in infarct volume reductions of 35 and 40%, respectively against saline-treated controls. During the first 24 hours after reperfusion, the drugs reduced average body core temperature by approximately 1 and 0.6°C, respectively. This very mild hypothermia may have contributed to the neuroprotective effect observed, but is unlikely to explain a large fraction of it. The prevalent mechanism of the drugs is thus selective, competitive antagonism to the AMPA receptor. The nephrotoxicity observed with NBQX treatment correlated with pathology of acute renal failure, and dysfunction. It was ameliorated by infusion of saline for 48 hours.

Thus, this animal model for stroke in humans is well characterized, and suitable for in vivo testing of potentially neuroprotective substances.



Sketch of the ventral surface of a rat brain showing the arteries that supply the supratentorial regions. The carotid arteries enter the vascular tree in the center of the drawing, the distal part of the MCA is visible laterally.

Aligned diffusion-weighted (DW) MRI coronal sections through the brain of a representative saline-treated (top) and SPD-502-treated (bottom) rat, respectively, 24 hours after MCA occlusion. The lesion is characterized by the hyperintensity on DW MRI, which does not extend as far in the drug treated animal's cortex in neither the Superior-inferior nor the anterior-posterior direction as in the control animal (top).This illustrates the neuroprotective effect of SPD502, reducing infarct volume by ~40% on average.

[1] alpha-amino-3-hydroxy-5-methyl-4-isoxazole
[2] Magnetic Resonance Imaging
[3] Apparent Diffusion Coefficient
[4] Transverse Relaxation Time
[5] Glial Fibrillary Acidic Protein
[6] Cerebral Blood Volume
[7] 6-nitro-7-sulfamoyl-benzol(f)quinoxaline-2,3-dione
[8] (8-methyl-5-(4-(N,N-dimethylsulfamoyl)phenyl)-6,7,8,9,-tetrahydro-1H-pyrrolo[3,2-h]-isoquinoline-2,3-dione-3-O-(4-hydrobutyric acid-2-yl) oxime]

Other Activities

Congress and Workshop Participation

The staff of DRCMR have participated in the following international meetings and congresses related to their research fields.

- 10th scientific meeting of the International Society of Magnetic Resonance in Medicine, Honolulu, Hawaii, USA (13 delegates)
- fMRI Data Center's 2nd Annual Summer Workshop in fMRI Informatics, July 2002 (1 delegate)
- European Federation of Neurological Societies, 6th Congress, Vienna, Austria (1 delegate)
- Danish NMR meeting, Roskilde, Denmark (3 delegates).
- Danish Society for Neuroscience, Annual meeting, Sandbjerg, Denmark (7 delegates)
- Skandinavian MS/MR symposium, Stockholm, Sweden (2 delegates)
- 19th Annual meeting of the European Society for Magnetic Resonance in Medicine and Biology, Cannes, France (3 delegates)
- European Congress of Cardiology, Berlin, Germany (2 delegates)
- 11th European Stroke Conference, Geneva, Switzerland (1 delegate)
- 2nd Workshop on Diagnostic Criteria in Early Rheumatoid arthritis (DICERA), Vienna, Austria, (1 delegate)
- 6th International Consensus Conference on Outcome Measures in Rheumatology (OMERACT 5), Brisbane, Australia (2 delegates)
- 3rd Annual European Congress of Rheumatology (EULAR), Stockholm, Sweden (3 delegates)
- 14th Congress of European Federation of Societies for Ultrasound in Medicine and Biology (EUROSON), 2002, Warsaw, Poland (1 delegate)
- 29th Scandinavian Congress of Rheumatology (SCR), Tromsø, Norway (1 delegate)
- 4th Baltic Bone and Cartilage Conference, Binz, Germany (1 delegate)
- 9th Scientific Meeting of the European Society of Skeletal Radiology (ESSR), Valencia, Italy (1 delegate)
- 66th National Scientific Meeting of the American College of Rheumatology (ACR), New Orleans, USA (2 delegates)
- OMERACT (Outcome Measures in Rheumatology Clinical Trials) and OARSI (Osteoarthritis Research Society International) Workshop on Consensus in Osteoarthritis Imaging (1 delegate)
- European Conference on Computer Vision, ECCV 2002, Copenhagen, Denmark (1 delegate)
- Eleventh International Workshop on Matrices and Statistics, MATRIX02, (1 delegate)
- Medical Image Computing and Computer Assisted Intervention, MICCAI 2003, Tokyo Japan (1 delegate)
- American College of Cardiology 51st Annual Scientific Session, Atlanta, USA (1 delegate)
- The 6 th Dutch Endo-Neuro Meeting, Doorwerth, the Netherlands, (1 delegate)
- The biology of psychoses. European Congress of Biological Psychiatry, Copenhagen, Denmark: (1 delegate)
- 7th biennial meeting of the ESMRN (European Society of Magnetic Resonance in Neuropediatrics), London, United Kingdom (1 delegate)
- 32nd Annual Symposium of the Scandinavian Society for Laboratory Animal Science, Gardemoen, Norway (1 delegate)

Congress Organization

Olaf Paulson is a member of the local organizing committee for the European Society for Magnetic Resonance in Medicine and Biology 21st Meeting, Copenhagen 2004.

Teaching

- Staff from the DRCMR have participated in teaching and supervision in the following courses ans symposia
- Lægeforeningens kursus i sclerose "MRI billeddiagnostik ved MS"
- MR temaaften, Ungdommens Naturvidenskabelige Forening,
- PhD course, Neuropharmacology, Pharmaceutical University of Denmark
- Biophysics course, University of Copenhagen.
- Specialist courses in internal medicine and rheumatology
- "Digital billedanalyse og avancerede medicinske anvendelser" at Sygepleje- og Radiografskolen, Herlev
- clinical cardiology.
- Structural brain changes in schizophrenia; U-Course in Neuro-psychiatry
- Danish Radiological Society "Pædiatrisk og neonatal neuroradiologi i Ultralyd og MR i neonatal perioden"
- "Non-linear Signal Processing", the Technical University of Denmark
- "Advanced Digital Signal Processing", the Technical University of Denmark
- Supervision of diploma work at the Technical University of Denmark and University of Copenhagen.

National and International Committees

National Committees

- Chairman, Department of Clinical Neuroscience and Psychiatry, University of Copenhagen (Olaf B. Paulson)
- Secretary of the Danish Society for Neuroscience (Olaf B. Paulson)
- Board Member of the Danish Alzheimer Association (Olaf B. Paulson)
- Chairman of the Research Committe of the Danish Alzheimer Association and member of the Danish Alzheimer Research Foundation (Olaf B. Paulson)
- Member of the Neurology Committe of the Copenhagen Hospital Corporation (Olaf B. Paulson)

International Committees

- Past President of the International Society of Cerebral Blood Flow and Metabolism (Olaf B. Paulson)
- Member of the European Federation of Neurological Societies Working Group on Brain Imaging (Olaf B. Paulson)
- Country Coordinator for Denmark in the European Task Force on Age-related White Matter Changes (Ellen Garde)
- OMERACT-MRI study group (Mikkel Østergaard (co-chair) and Bo Ejbjerg)
- OMERACT subcommittee on healing of erosions (Mikkel Østergaard)
- EULAR-MRI study group (Mikkel Østergaard and Bo Ejbjerg))
- EULAR Working Party on Imaging in Rheumatology (Marcin Szkudlarek and Mikkel Østergaard)

Evaluation

- Member of the European Commission 6th Framework "Expression of Interest" expert panel 2002, Brussels (Olaf B. Paulson)
- DRCMR staff have been evaluators and external examinor at PhD theses and MSc theses at the Århus University, the Technical University of Denmark and University of Copenhagen.

Journal Review

DRCMR staff has particpated in the review of manuscripts for the following peer reviewed journals

- Stroke
- Neuroimage
- Scandinavian Journal of Rheumatology
- The Journal of Rheumatology
- Rheumatology
- Arthritis and Rheumatism
- Annals of the Rheumatic Diseases
- The Lancet
- IEEE Transactions on Medical Imaging, Special Issue on New Trends in 3D Cardiac Image Analysis

Awards

- EULAR/Abbott Abstract Award 2002 (Mikkel Østergaard)
- ESSR (European Society of Skeletal Radiology) 1st prize for best presentation (Mikkel Østergaard)
- William Nielsens Fonds Hæderspris 2002 for outstanding research (Olaf B. Paulson)

Outlook . . .

The installation of the new 3-Tesla scanner donated by the Simon Spies Foundation gives the technological basis for continuous evolution in the research activities. Different upgrades and new coils as part of the installation will take place in 2003 and should be completed at the end of the year. This will further increase the capacity of the centre for both clinical and research activities. It is expected that many research activities will take place on the new 3-Tesla scanner leaving more capacity on the other scanners for clinical diagnostic investigations.

It is the centre's wish to strengthen the bridge between MR research and diagnostic work. With installation of the new 3-Tesla scanner and with the rapid and continuous evolution of diagnostic possibilities using MR the department expects this to be a challenge of utmost importance. The coexistence and collaboration between clinical work and research activities will be given high priority at the Copenhagen University Hospital. It is anticipated that the centre will be able to obtain grant support for further improvement of the existing equipment and for the launch of new research projects.

It is expected that the University of Copenhagen in 2003 will launch new priority areas, one of which will be "body and mind" and which should involve activities covering several faculties of the university. The Danish Research Centre for Magnetic Resonance expects to have a key position in this priority area and to be able to incorporate an increased collaboration with e.g., the Faculty of Humanities. The department also expects to strengthen its collaboration nationally and internationally by establishing central facilities for evaluation of MR scans e.g., in the EU funded dementia projects and in trials in multiple sclerosis.

Publications

A large number of publications has resulted from the research carried out at DRCMR during 2002. The most important of these publications are listed here according to category.

PhD Theses

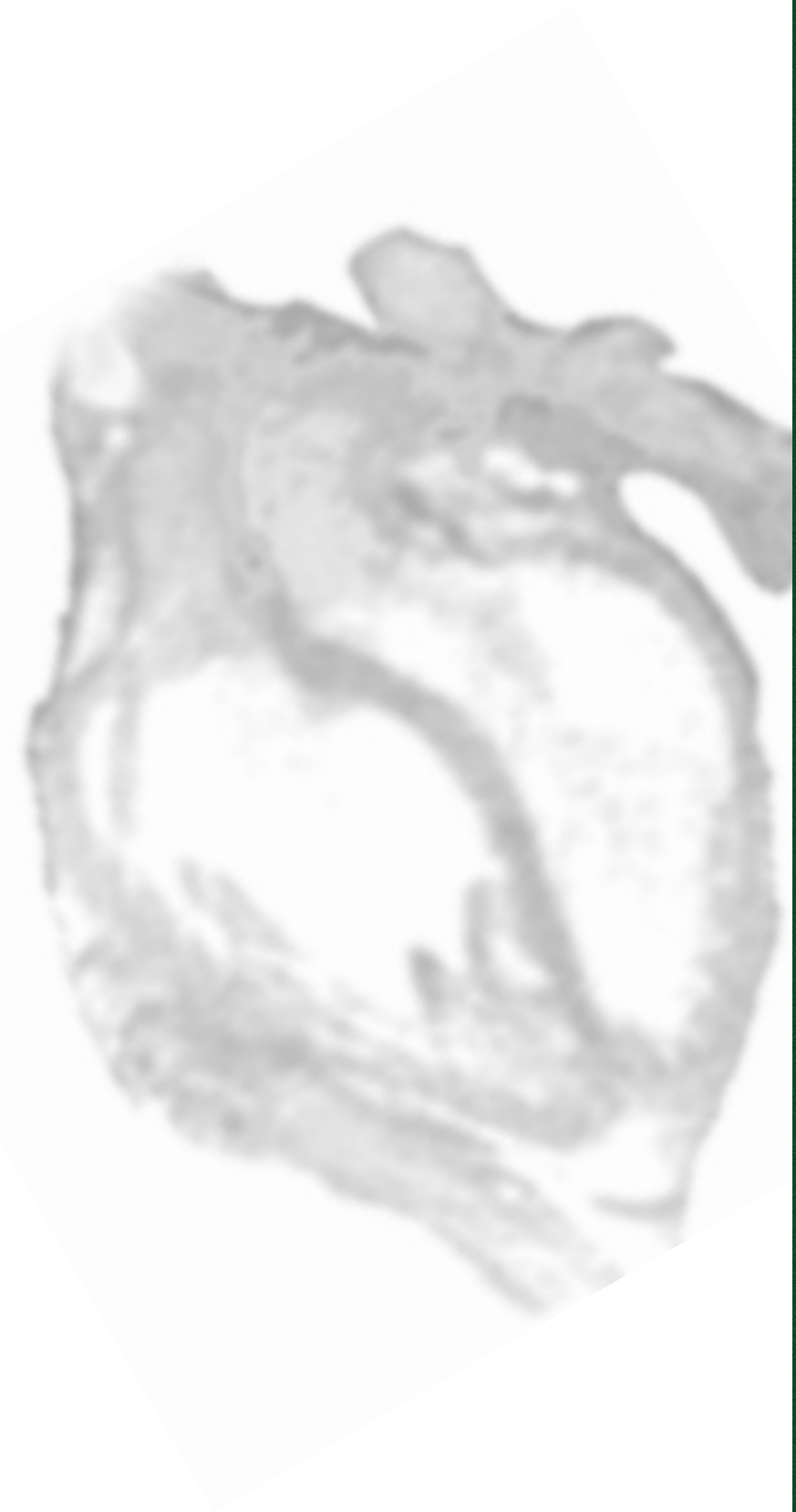
1. Irene K. Andersen. Dynamic Contrast Enhanced Perfusion MRI for Perfusion Quantification. Defended December 4th, 2002 at the Technical University of Denmark, Informatics and Mathematical Modelling.
2. Elisabeth Hildebrandt-Eriksen. AMPA receptor antagonists in mild focal cerebral ischemia in the rat. An experimental study with MRI and histology. Defended December 16th, 2002 at the University of Copenhagen, Faculty of Health Sciences.
3. Annika R. Langkilde. Functional MRI in optic neuritis . Defended December 6th, 2002 at the University of Copenhagen, Faculty of Health Sciences.
4. Jens C. Nilsson. Left Ventricular Remodelling in the First Year Following Acute Myocardial Infarction – Frequency, Extent and Prediction. Defended April 8th, 2002 at the University of Copenhagen, Faculty of Health Sciences.
5. Karam Sidaros. Slice Profile Effects in MR Perfusion Imaging using Pulsed Arterial Spin Labelling (phd-afhandling). Defended June 20th, 2002 at the Technical University of Denmark, Informatics and Mathematical Modelling.

Peer Reviewed Journal Articles

1. Andersen IK, Szymkowiak A, Rasmussen CE, Hanson LG, Marstrand JR, Larsson HB et al. Perfusion quantification using Gaussian process deconvolution. Magn Reson Med 2002; 48(2):351-361.
2. Balslev D, Nielsen FA, Frutiger SA, Sidtis JJ, Christiansen TB, Svarer C, Strother SC, Rottenberg DA, Hansen LK, Paulson OB, Law I. Cluster analysis of activity-time series in motor learning. Hum Brain Mapp 2002 Mar;15(3):135-45.
3. Born AP, Law I, Lund TE, Rostrup E, Hanson LG, Wildschiodtz G et al. Cortical deactivation induced by visual stimulation in human slow-wave sleep. Neuroimage 2002; 17(3):1325-1335.
4. Born AP, Rostrup E, Miranda MJ, Larsson HBW, Lou HC. Visual cortex reactivity in sedated children examined with perfusion MRI (FAIR). Magnetic Resonance Imaging 2002; 20(2):199-205.
5. d'Arcy JA, Collins DJ, Rowland IJ, Padhani AR, Leach MO. Applications of sliding window reconstruction with cartesian sampling for dynamic contrast enhanced MRI. NMR Biomed 2002,15,174-83.
6. Dzik-Jurasz ASK, Murphy PS, George M, Prock T, Collins DJ, Swift I, Leach MO, Rowland IJ. Human rectal adenocarcinoma: Demonstration of 1H-MR spectra in vivo at 1.5 T. Magn Reson Med 2002,47,809-811.
7. Groenning BA, Nilsson JC, Sondergaard L, Pedersen F, Trawinski J, Baumann M et al. Detection of left ventricular enlargement and impaired systolic function with plasma N-terminal pro brain natriuretic peptide concentrations. Am Heart J 2002; 143(5): 923-929.
8. Groenning BA, Nilsson JC, Hildebrandt PR, Kjaer A, Fritz-Hansen T, Larsson HB et al. Neurohumoral prediction of left-ventricular morphologic response to beta-blockade with metoprolol in chronic left-ventricular systolic heart failure. Eur J Heart Fail 2002; 4(5):635-646.
9. Hildebrandt-Eriksen ES, Christensen TC, Diemer NH. Mild focal cerebral ischemia in the rat. The effect of local temperature on infarct size. Neurological Research 2002, 24(8):781-788.
10. Hulshoff HE, Posthuma D, Baare WF, de Geus EJ, Schnack HG, van Haren NE et al. Twin-singleton differences in brain structure using structural equation modelling. Brain 2002; 125(2):384-390.
11. Hulshoff HE, Schnack HG, Bertens MG, van Haren NE, van der Tweel I, Staal WG et al. Volume changes in gray matter in patients with schizophrenia. Am J Psyciatry 2002; 159 (2):244-250.
12. Langkilde AR, Frederiksen JL, Rostrup E, Larsson HB. Functional MRI of the visual cortex and visual testing in patients with previous optic neuritis. Eur J Neurol 2002; 9(3):277-286.
13. Marstrand JR, Garde E, Rostrup E, Ring P, Rosenbaum S, Mortensen EL et al. Cerebral perfusion and cerebrovascular reactivity are reduced in white matter hyperintensities. Stroke 2002; 33(4):972-976.
14. Mathiesen HK, Langkilde AR, Larsson HB. Magnetic resonance and multiple sclerosis I. Conventional diagnostic techniques. Ugeskr Laeger 2002; 164(8):1026-1031.
15. Mathiesen HK, Langkilde AR, Larsson HB. Magnetic resonance and multiple sclerosis II. New diagnostic techniques. Ugeskr Laeger 2002; 164(8):1031-1036.
16. Murphy PS, Leach MO, Rowland IJ. The Effects of Paramagnetic Contrast Agents on Metabolite Protons in Aqueous Solution. Phys Med Biol 2002,47,N53-59.
17. Murphy PS, Dzik-Jurasz ASK, Leach MO, Rowland IJ. The Effect of Gd-DTPA on T1-Weighted Choline Signal In Human Brain Tumours. Magn Reson Imaging 2002,20,127130.
18. Nilsson JC, Groenning BA, Nielsen G, Fritz-Hansen T, Trawinski J, Hildebrandt PR et al. Left ventricular remodeling in the first year after acute myocardial infarction and the predictive value of Nterminal pro brain natriuretic peptide. Am Heart J 2002; 143(4): 696-702.
19. Paulson OB, Born AP, Bundesen C, Gade A, Gerlach C, Hansen LK et al. The working brain--how does it look like?. Ugeskr Laeger 2002; 164(17): 22672275.
20. Posthuma D, de Geus EJ, Baare WF, Hulshoff HE, Kahn RS, Boomsma DI. The association between brain volume and intelligence is of genetic origin. Nat Neurosci 2002; 5 (2):83-84.
21. Rostrup E, Law I, Pott F, Ide K, Knudsen GM. Cerebral hemodynamics measured with simultaneous PET and near-infrared spectroscopy in humans. Brain Res 2002; 954(2):183-193.

Conference Proceedings

- The 37th Annual General Meeting of the Association for European Paediatric Cardiology , Porto (1 poster).
- The 19th Annual Meeting of the European Society for Magnetic Resonance in Medicine and Biology, Cannes (2 posters).
- The 10th Annual Meeting of the International Society for Magnetic Resonance in Medicine, Honolulu (5 oral presentations, 10 posters).
- The 6th Dutch Endo-Neuro Meeting (1 oral presentation).
- The 3rd Annual European Congress of Rheumatology (EULAR), Stockholm (3 oral presentations, 4 posters).
- The European Society of Cardiology Congress, Berlin (4 oral presentations).
- Medicon Valley Bio Conference, Copenhagen (1 oral presentation).
- Medical Image Computing and Computer-Assisted Intervention 2002, 5th International Confernce, Tokyo (1 oral presentation).
- 18th Congress of the European Committee for the Treatment and Research in Multiple Sclerosis, Baltimore (3 posters).
- The 66th National Scientific Meeting of the American College of Rheumatology, New Orleans (1 oral presentation, 3 posters).
- The EURO CMR Meeting 2002, Basel (1 oral presentation).
- The 7th Biennial Meeting og the European Society for Magnetic Resonance in Neuropediatrics, London (1 oral presentation).
- IVth Baltic Bone and Cartilage Conference, Binz (2 oral presentations).
- The 29th Scandinavian Congress of Rheumatology, Tromsø (3 oral presentations).
- The 2nd Workshop in Diagnotisc Criteria in Early Rheumatoid Arthritis (DICERA), Vienna (1 oral presentation).
- Kommision Bildgebende Verfahren, Deutsche Gesellshaft für Rheumatologie, Düsseldorf (1 oral presentation).
- International Consensus Conference on Outcome Measures in Rheumatology (OMERACT 6), Brisbane (2 oral presentations).
- The 9th Scientific Meeting of European Society of Skeletal Radiology (ESSR), Valencia (3 oral presentations).
- Københavns Debatforum 2002, Copenhagen (1 oral presentation).
- European Congress of Biological Psychiatry, Copenhagen (1 poster).
- The 14th Congress and European Federation of Societies for Ultrasound in Medicine and Biology (EUROSON), Warsaw (1 oral presentation, 1 poster).
- Annual Meeting of Danish Rheumatologists (1 oral presentation).



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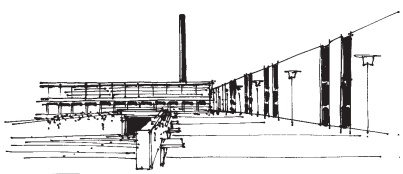

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