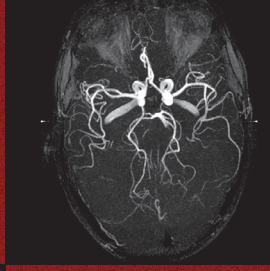
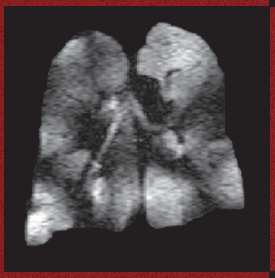
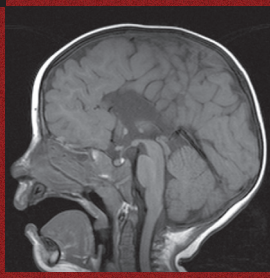
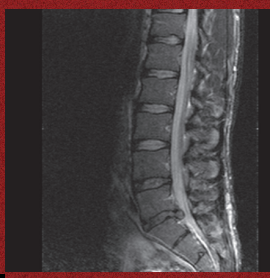


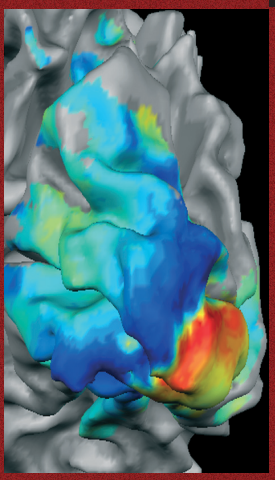




DRCMR

Annual Report 2003





Danish Research Centre for Magnetic Resonance

Introduction

This report summarizes the aims and organization of the Danish Research Centre for Magnetic Resonance (DRCMR), also known as the Department of Magnetic Resonance, at Hvidovre Hospital and describes the accomplishments of the DRCMR Staff during 2003.

The principal aim guiding the activities at the DRCMR is to advance the use of magnetic resonance as a clinical and investigative tool in the biomedical arena. In the service of this aim, DRCMR Staff employ state-of-the art instrumentation and bioinformatics tools for the diagnosis and management of medical patients and for a range of biomedical investigations. The clinicians and investigators of the DRCMR are active participants at national and international level in the community of biomedical scientists. In the last year, the Centre has experienced significant growth. This growth, and the anticipation of continued expansion of our scientific activities, has prompted substantial reorganization designed to facilitate both focused and integrative activities within the Centre. We are proud to present here our new organization and recent accomplishments.

Finally, I would like to express our gratitude towards the foundations and institutions that have supported us financially over the years and whose support has enabled the Centre to achieve and maintain its frontline position in 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 sections 340A and 340B. The centre has 3 Siemens whole-body scanners. The newest, a Magnetom Trio (3.0 tesla) was installed in 2002 following a generous donation by the Simon Spies Foundation. Two other systems, 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. To complement the clinical research, the centre also has an experimental imaging and spectroscopy system, a Sisco 4.7 Tesla scanner. This scanner is suitable for MR studies in small animals and will be upgraded in 2004. The experimental scanner is located in section 340B which also holds facilities for data analyses and research.

Contents

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Layout
Karam Sidaros
Ian Rowland

Dansk Resumé

En lang række skanningsmetoder baseret på magnetisk resonans (MR) er udviklet gennem en årrække. Den enorme effekt som MR-teknikkerne har haft på den kliniske diagnostik og forskning blev senest markeret med tildelingen af Nobelprisen i Medicin 2003 til amerikaneren Paul Lauterbur og englænderen Peter Mansfield for udviklingen af billeddannende MR-metoder. Det er ikke den første Nobelpris, og næppe heller den sidste, der tildeles indenfor MR-området, som stadig er i rivende udvikling.

På MR-afdelingen, Hvidovre Hospital foregår omfattende patientdiagnostik og forskning. Centret blev grundlagt efter en stor donation fra Simon Spies i 1984 og allerede fra starten var der lagt lige vægt på såvel forskning som kliniske anvendelser. I 2002 sikrede Simon Spies Fonden med donationen af landets første højfeltsskanner, at afdelingen er forblevet i front. Denne position har sikret international anerkendelse i form af blandt andet projektstøtte fra EU, samarbejde med udenlandske forskningsinstitutioner, omfattende publikationsaktivitet i internationale tidsskrifter og udvælgelsen af afdelingen til MR-evalueringscenter ved internationale medicinafprøvninger.

Det glæder os overordentligt at denne indsats også er blevet bemærket i Danmark, hvilket blandt andet i 2003 har givet anledning til at centrets chef, professor Olaf B. Paulson, er blevet tildelt en af landets fornemste priser, Lundbecks Nordiske Forskerpris, for sin mangeårige indsats indenfor neurovidenskab.

Året 2003 bød på markante udviddelser og deraf følgende omlægninger af aktiviteterne. Samarbejdet med blandt andet Danmarks Tekniske Universitet og Københavns Universitet blev udviddet som en direkte følge af forbedrede muligheder for forskning i hjernens virkemåde. Det lykkedes også at tiltrække en topforsker, professor i psykiatri og radiologi, Terry Jernigan, fra en stilling som centerleder i San Diego. Grundet disse udviddelelser blev det nødvendigt med en stærkere koordinering af forskningen, der nu er organiseret i tre store grupper. 2003 blev også et år med udviddelse af det kliniske virke, herunder i antallet af skanninger, samtidig med at afdelingen stadig tilbyder visse undersøgelser, der er unikke i landet.

Overview of 2003

A unique strength of the Danish Research Centre for Magnetic Resonance (DRCMR) is the multi-disciplinary nature of its activities. The Centre is home to an active clinical department providing a full range of diagnostic MRI services. Patient referrals come from a broad range of referral sources, including other hospitals in Copenhagen and throughout the eastern parts of Denmark in addition to Hvidovre Hospital. The clinical services of the department are performed alongside the investigative imaging, providing valuable integration between primary clinicians and clinical researchers.

Distinguishing the DRCMR from other academic radiology settings in Denmark is the juxtaposition within the Centre of a vigorous basic research program with the patient-oriented activities of the department. This ensures the highest level of scientific support for the Centre's biomedical mission, and places it at the forefront of MR method development. Through interaction with partners in the Copenhagen Brain Research Center, the DRCMR also participates in groundbreaking research in neuroinformatics, neuropharmacology, and cognitive science.

Imaging facilities

The Centre has 3 Siemens whole-body clinical scanners. The newest, a Magnetom Trio (3.0 tesla), was installed in 2002 after a generous donation from the Simon Spies Foundation. This new equipment is state-of-the-art, and further enhancements have continued to arrive in 2003 as they were released from Siemens' development laboratories. These enhancements included a body coil – i.e., an "antenna" necessary for applications outside the head region. With additional 8-channel head and body coils offering the highest of sensitivities, "parallel imaging" also became possible. This exciting new technique is particularly useful at high field and is used to speed up measurements considerably. Rather than measuring the radio waves emitted from the body with one large antenna, several small highly sensitive antennae are used. The two other clinical scanners, a Magnetom Vision (1.5 tesla) and a Magnetom Impact (1.0 tesla), were installed in 1994. These scanners have since been upgraded and continue to perform at a high level in support of the Centre's clinical and research needs. All three clinical scanners are located in area 340A of the hospital, where there are also facilities for clinical work and conferences.

In addition, the Centre has an experimental Sisco 4.7 tesla scanner. This scanner is suitable for MR studies in small animals and was last upgraded in 1998. The experimental scanner is located in area 340B where there are also facilities for data analysis and other research activities. In 2003 an almost complete upgrade of the experimental animal scanner was put out to tender. This 4.7 tesla system used for preclinical research has lacked the fast imaging capabilities necessary for special studies such as functional imaging. Funding contributions from several sources, including Hvidovre Hospital, have made the planned upgrade possible. Only the magnet and gradient coil will remain from the old instrument, so in effect the result will be a new scanner with state-of-the art hardware and software. The scientific group working mostly in preclinical research (including two senior researchers and two technicians) are anticipating installation of the upgrade in 2004 and expectations are high.

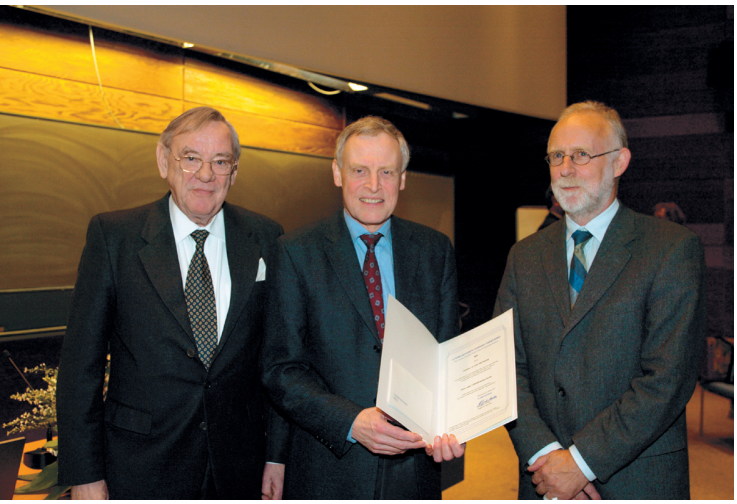
Departmental organisation

With new and upgraded MR systems and increasing numbers of staff, the department has undergone a restructuring and a new organisational arrangement implemented. Three (overlapping) groups of investigators have begun to meet regularly to exchange information and review the progress of their projects: a group of investigators focused on method development (Methods Group), a group of investigators conducting preclinical research in the animal facility (Preclinical Group), and a group conducting human brain research (Brain Research Group). Each group has a group leader charged with organizing the agenda and chairing the sessions, and this individual represents the group of investigators on the Research Coordinating Committee (RCC). The RCC is comprised of the leaders of the DRCMR, and the com-

mittee meets weekly to review the progress of the research, and to discuss issues of general interest, regarding both scientific and administrative matters.

Clinically orientated activities

Compared with 2002, this last year has seen a 12% increase in the numbers of patients investigated. This significant increase includes a 25% increase in the number of patients referred from counties outside of Copenhagen and illustrates the Centre's position as a provider for local and national radiological services. The department's radiological expertise is also in demand as the Centre becomes more established as a reading and MR-coordination site for several large clinical trials. An essential component of these trials is data analysis and the Centre has made considerable effort and progress in establishing a "configurable" analysis pipeline. MR images acquired using sequences designed to obtain differing morphological, physiological or functional information can be entered into the 'pipeline' and automatically analysed using a wide range of methods including alignment, intensity correction and segmentation. There is little doubt that this will be of major benefit to most patient studies in the future. Consequently the Centre has appointed new staff to ensure that it can expand the increasing role of MR informatics into everyday investigations.



Presentation of the Lundbeck Foundation Nordic Research Award to Olaf B. Paulson. From left to right: Sven Dyrløv Madsen, President of the Lundbeck Foundation, Olaf B. Paulson, and Mikael Rørth, Member of the Lundbeck Foundation Council.

2003 and the future

The Danish Research Centre for Magnetic Resonance is led by Prof. Olaf Paulson, a scientist whose contributions to neuroscience have been recognised this year by the 2002 Lundbeck Foundations' Nordic Award for Outstanding Research. The Centre would like to take this opportunity to congratulate him on this prestigious award.

The new 3 tesla whole body system has provided a demanding new environment where researchers have invested significant effort becoming familiar with their new powerful imaging and spectroscopy equipment. As the year progressed, additional coils were acquired for the 3 tesla whole body system. The high quality of morphological and functional images obtained at 3 tesla ensures that the system will have an important future in the department's research activities.

The accomplishments of the year, described within this report, illustrate the depth and breadth of expertise within the department. This has been expanded further this year as Prof. Terry Jernigan joined the department as a visiting professor. Her experience as a clinical neuropsychologist and as co-director of the Laboratory of Cognitive Imaging will be an invaluable asset to the Centre. The Centre, therefore, continues to attract scientists from abroad to make the DRCMR a truly international environment in which to work. The interaction between radiologists, clinicians, psychologists, physicists and engineers together with other scientists from different disciplines both within the department and collaborating centres continues to create a rich multi-disciplinary environment to pursue MR research and apply it to clinical problems.

With the anticipated expansion of the facilities and staff numbers over the next year, the department is confident that it will continue to make significant scientific contributions and remain at the forefront of MR research at an international level.

Organisation and Staff

Department Chair

Olaf B. Paulson, D.MSc., Professor

Senior staff, Clinical

Margrethe Herning, M.D., Senior Physician and Clinical Chief
Anne-Mette Leffers, M.D., Senior Physician

Senior Staff, Research

Irene K. Andersen, Ph.D., Clinical Physicist
William Baaré, Ph.D., Psychologist
Ellen Garde, M.D., Ph.D.
Lars G. Hanson, Ph.D., Chief Physicist
Karin Markenroth, Ph.D., Clinical Physicist
Maria J. Miranda, M.D., Ph.D.
Poul Ring, Engineer
Egill Rostrup, M.D. & Human Biologist
Ian J. Rowland, Ph.D., Chemist
Karam Sidaros, Ph.D., Engineer
Lise Vejby Søgaard, Ph.D., Physicist

Junior Staff, Clinical

Edith Grossmann, M.D.
Annika Reynberg Langkilde, M.D., Ph.D.
Camilla Gøbel Larsen, M.D.
Henrik Meelby, M.D.
In addition residents from the Department of Radiology rotate through DRCMR for periods of 2 months.

Junior Staff, Research

PhD students
Elizbieta Kalowska, M.D.
Annette Skræp Nielsen, M.D.
Katja Krabbe, M.D.
Torben Ellegaard Lund, Engineer
Henrik Kahr Mathiesen, M.D.
Dorthe Pedersen, M.D.
Kirsten Nielsen, M.D.
Trine Stavngaard, M.D.
Thomas Z. Ramsøy, Psychologist

Junior Researchers
Niels Broberg, Engineer
Tim Dyrby, Engineer
Matthew Liptrot, Engineer
Arnold Skimminge, Physicist
Robin de Nijs, Hospital Physicist
Charlotte Ryberg, Biologist
Mark Schram Christensen, Student in Engineering
Kristoffer Madsen, Student in Engineering
Jon Wegener, Student in Life Sciences and Chemistry

Research Assistants
Andreas Hansen, Medical Student

Technologists

Nina Hansen, Laboratory Technician
Pia Olsen, Radiographer
Sascha Gude, Laboratory Technician
Sussi Larsen, Head Technologist
Helle Juhl Simonsen, Research Technician
Hanne Schmidt, Radiographer
Rune Mau, Computer Technician

Secretarial Staff

Lotte Hansen
Laila Andersen
Lisa Juhl Simonsen
Sussie K. Volkmann

Cleaning Assistants

Ruth Kielstrup
Elsebeth Nielsen

Visiting and Associated Staff

Senior Staff

Terry L. Jernigan, Ph.D., Psychologist and Visiting Professor
Peter Born, M.D., Ph.D.
Jens Christian Nilsson, M.D., Ph.D.
Anders Steensgaard, Engineer
Lars Søndergaard, M.D.
Sverre Rosenbaum, M.D., Ph.D.
Mikkel Østergaard, D.MSc., Ph.D.
Katrine Pagsberg, M.D., Ph.D.

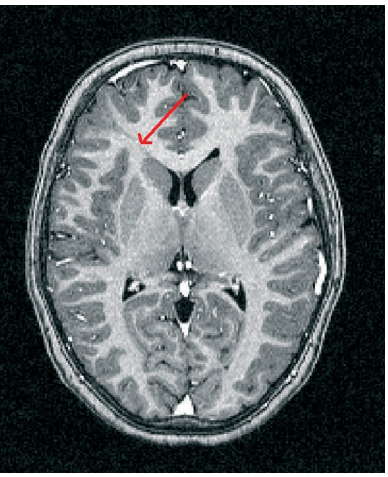
Junior Staff

Susette Krohn Therkelsen, M.D.
Daniella Balslev, M.D.
Bo Ejbjerg, M.D.
Mikkel B. Stegmann, Engineer
Marcin Szkudlarek, M.D.

Clinical Imaging

In 2003, 6502 clinical investigations were performed; many investigations were performed before and after intravenous contrast media. 3649 investigations were carried out on patients referred from Hvidovre Hospital, 2853 investigations on patients referred from other counties outside Copenhagen. Investigations of neurological diseases, e.g. suspicion of stroke, multiple sclerosis, intracranial tumours, intracranial haemorrhage, dementia and epilepsy are an important part of daily clinical radiology.

The Centre is a member of the 'EPI-KIR' group, a national organisation responsible for national epilepsy patient management that selects patients suitable for surgical intervention and is responsible for post-operative patient management. Consequently, many patients with epilepsy have been imaged for the presence of structural brain lesions causing seizures. Many of the patients with epilepsy were investigated with a specific protocol including volumetric measurements of the hippocampus regions, T2-relaxation measurements and, where appropriate, proton spectroscopy.



MRI of a 7 year old boy with severe epilepsy resistant to medication. The arrow indicates a fine linear heterotopia in the right frontal lobe.

MRI of patients with traumatic brain injury has been a growing part of our MR investigations. MRI applied in the sub-acute or early chronic phase, following severe head trauma, is a promising prognostic tool in this type of patient for whom long-term clinical outcome is very difficult to predict.

Patients with suspected intracranial vascular diseases such as arteriovenous malformations and aneurysms are regularly referred to the department for investigation with MRI and MR angiography. MR imaging and angiography are also used as screening methods in patients with "warning leaks" from cerebral aneurysms, in patients with manifest subarachnoidal haemorrhage and patients with a family history of cerebral aneurysms. MR angiography can be a valid supplementary investigation preoperatively. Tumours in the pituitary gland, vestibular schwannomas, meningiomas and other intracranial tumours are best investigated with MRI. Clinically suspected sinus thrombosis or tumours near the venous sinuses are now investigated using slow-flow MR-angiography as interventional x-ray based cerebral angiography is replaced as the modality of choice.

45 year old woman with a benign intradural tumour

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

Patients with suspected cervical spinal stenoses or suspected cervical disc herniation are also preferentially investigated with MRI. Suspicion of lumbar disc herniation, post-operative recurrent disc herniation, or infection, MRI is the preferred diagnostic method. Also, intradural pathology such as tumours of the spinal cord, intradural meningiomas and neurinomas are well characterised by MRI.

Musculoskeletal MRI is an important clinical area and is rapidly replacing diagnostic arthroscopy 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 potentially resulting in limb-saving operations. Metastatic bone disease is also best diagnosed with MRI.

Increasing numbers of scans are being performed at the DRCMR on the abdomen. MRCP is the investigation of choice concerning the bile ducts and pancreatic duct when gallstones and obstruction are suspected. The alternative diagnostic ERCP is an invasive method associated with risk of morbidity and mortality.

MRI of perineal fistulas and rectal cancer are well established and the department has become a regional centre for rectal cancer MRI. It is the diagnostic method of choice for focal tumour staging thereby facilitating patient management.

In the coming year, we expect the 3T MR scanner to bring new and better diagnostic imaging especially in the head and abdomen.

Collaborations

The DRCMR collaborates and works closely with many institutions both nationally and internationally. Primary collaborators in 2003, 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 Hospital (CUH)
Department of Neurorehabilitation, CUH Hvidovre
Department of Pediatrics, CUH Hvidovre
Department of Clinical Chemistry, CUH Hvidovre
Department of Clinical Phsyiology, CUH Frederiksberg
Center of Functionally Integrative Neuroscience, Aarhus University
Department of Neuropaediatrics, John F. Kennedy Institute, CUH Glostrup
Department of Neurology, CUH Glostrup
Department of Neurophysiology, CUH Glostrup
Department of Neurology, CUH Bispebjerg
Department of Physics, The Technical University of Denmark
Department of Psychiatry, CUH Bispebjerg
Department of Psychiatry, CUH Rigshospitalet
Department of Psychology, University of Copenhagen
Department of Medical Anatomy, University of Copenhagen
Department of Medical Biochemistry and Genetics, Panum Institute, University of Copenhagen
Department of Medical Physiology, Panum Institute, University of Copenhagen
Institute for Molecular Pathology, University of Copenhagen
Informatics and Mathematical Modelling, The Technical University of Denmark
The Memory Disorders Research Unit, The Neuroscience Centre, CUH Rigshospitalet
The Neonatal Department, CUH Rigshospitalet
Neurobiology Research Unit, CUH Rigshospitalet
Sclerosis Research Unit, CUH Rigshospitalet
State Serum Institute

Heart Research

Department of Cardiology, CUH Hvidovre
Department of Clinical Nutrition, CUH Hvidovre
Department of Clinical Physiology, CUH Rigshospitalet
Department of Nephrology, CUH Rigshospitalet
Research Department of Human Nutrition, The Royal Veterinary and Agricultural University
Informatics and Mathematical Modelling, The Technical University of Denmark

Lung Research using Hyperpolarized Gases

Department of Respiratory Medicine, CUH Hvidovre
Department of Clinical Physiology, CUH Rigshospitalet
Department of Respiratory Medicine, CUH Gentofte

Rheumatology Research

Department of Rheumatology, CUH Hvidovre
Department of Radiology, CUH Hvidovre
Department of Orthopaedic Surgery, CUH Hvidovre
Department of Clinical Physiology, CUH Hvidovre
Department of Pathology, CUH Hvidovre
Department of Rheumatology, CUH Rigshospitalet
Department of Radiology, CUH Rigshospitalet
Department of Rheumatology, CUH Herlev
Department of Radiology, CUH Herlev
Department of Ultrasonography, CUH Herlev
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,
Department of Radiology, Aarhus University Hospital

International Collaborations

Brain Research

The Brain Imaging Centre at the Montreal Neurological Institute, Montreal, Canada
Center of Cognitive Neuroscience, Nijmegen, The Netherlands
Center for fMRI, University of California, San Diego, USA
Centre for Magnetic Resonance, University Hospital, Trondheim, Norway

Department of Clinical and Experimental Epilepsy, Institute of Neurology, London, United Kingdom
Laboratory of Cognitive Imaging, University of California, San Diego, USA
The NMR-Centre, Massachusetts General Hospital, Boston, USA
Robert Steiner Magnetic Resonance Unit, ICSM Hammersmith Hospital, London, United Kingdom
University Laboratory of Physiology, Oxford University, Oxford, UK
Wellcome Department of Imaging Neuroscience, London, United Kingdom

Heart Research

Institute of Clinical Radiology, Munich, Germany

Lung Research using Hyperpolarized Gases

Clinic for Anesthesiology, Radiology, Johannes Gutenberg-University, Mainz, Germany
Institute of Physics, Johannes Gutenberg-University, Mainz, Germany
Section of Academic Radiology, University of Sheffield, 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 project: Polarized Helium to Image the Lungs (PHIL). 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.
(from the CBRC website: www.cbrc.dk)

Basic Research

Methodological innovations arise naturally in an environment where cutting-edge techniques are used to address problems in medicine, psychology and biology. However, technical research projects also serve two specific purposes at the DRCMR. Firstly, new advanced techniques are necessary to remain competitive, i.e. to provide first class research for the benefit of patients and society. Secondly, the methodological research, which is funded mostly from external sources, provides part of the Centre's basic infrastructure for the benefit of both the individual projects and the DRCMR.

To people who are new to medical imaging research, the level of technical complexity and necessary workload associated with MRI-based clinical research is normally quite surprising. Although understanding the measurement techniques behind MRI relies on basic physics and highly advanced technology, there is much more to it than meets the eye.

As an example, consider functional MRI, where a series of brain images are acquired while the subject performs some task. Planning of the optimal task or paradigm requires understanding of the cognitive processes required to solve the given task as well as understanding how the actual neural activation is reflected in the measured signals. Once the paradigm that will be presented to the subject during the scan has been designed, it must be programmed on the computer that controls the stimulus presentation. Furthermore, optimising the image acquisition requires understanding the physical principles governing the image attributes. Once the data have been collected, a major part of the work still remains, namely post-processing of the thousands of images acquired during the scan. This is performed on a separate computer system and is typically comprised of several steps, such as realignment of the measured images to compensate for subject motion during the scan, registration of the 3D images of different subjects to a common coordinate space, so that the measurements can be compared, and automatic grey and white matter segmentation of the brain performed. Finally, statistical analysis of the millions of pixel time series is needed to locate areas activated by performing the presented task.

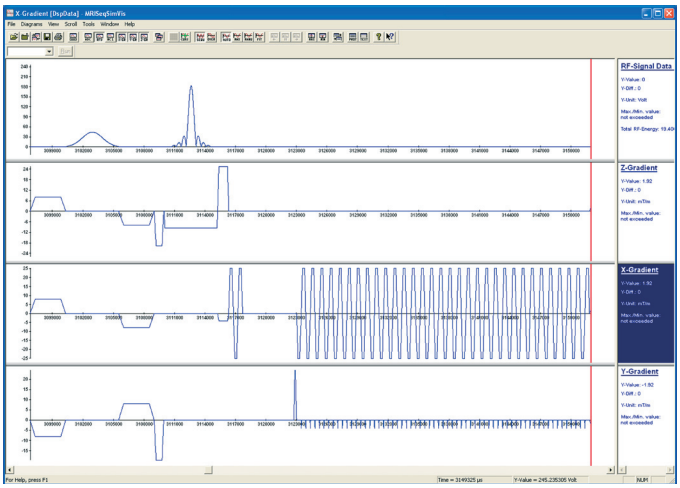
This significant data analysis requirement was for the example of functional scanning only. Other MR techniques require similar levels of technical investment on a per-project basis. This requires highly skilled and specialised personnel with expertise in engineering, physics and programming. Over the past few years, the DRCMR has therefore witnessed a shift in the composition of researchers where the number of researchers with a background in the basic sciences has increased compared to the number of researchers with a medical background. This composition is naturally reflected in the ongoing research and is essential in making the most of the huge potential of MRI as a research tool.

The basic research at the centre can be divided into four categories: development and optimisation of new MR sequences (MR physics) and development of novel post-processing strategies and experimental design (MR informatics). The activities of the centre within each of these categories are described in the following.

MR Physics

Although numerous clinical MR sequences are provided with the MR scanners by the scanner manufacturer (Siemens), there are a variety of research projects at the centre that rely on sequences that are either written in-house or that are modified in some way from the clinical sequences. The Centre therefore has a research agreement with Siemens that gives researchers at the centre access to the source code of sequences provided by Siemens. This eases the process of modifying and optimising MR pulse sequences.

A main area of sequence programming at the DRCMR is magnetic resonance spectroscopy. Fast multi-slice

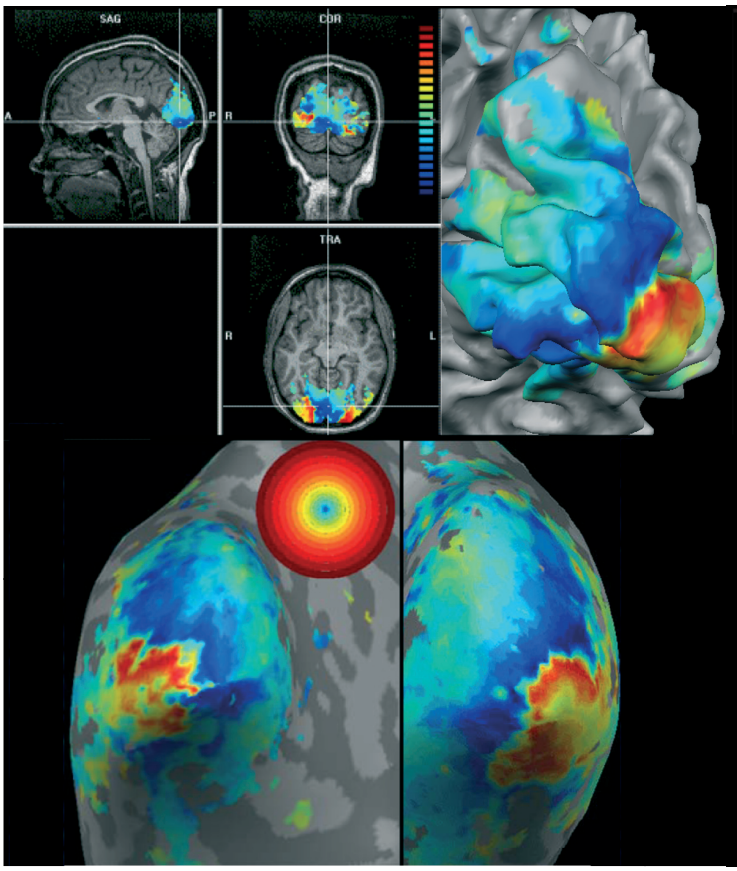


MR sequence programming requires controlling the timing of events on the scanner on a microsecond scale. The image shows a screenshot of the simulation tools available to sequence programmers on the 3T scanner. The example shown here is an echo-planar imaging sequence.

spectroscopic imaging (MRSI) was implemented on the 1.5T Vision system by Lars Hanson several years ago. The analysis and visualisation software has continuously been extended, recently for cortex spectroscopy that is a hot topic in multiple sclerosis research. At the end of the year, funding was provided for a PhD student, Robin de Nijs, who will be developing fast MRSI for the 3T system using parallel imaging techniques. The high field offers high sensitivity but the methodological challenges are numerous.

Another main area of sequence development at the centre has been in the development of arterial spin labelling (ASL) sequences. ASL is the only completely non-invasive method of measuring regional blood flow in vivo. Karam Sidaros has been working with methodological development of ASL at the DRCMR since 1997 and has recently ported the centre's ASL sequences to the 3T Trio scanner. A lot of effort has been put into implementing a highly flexible version of the sequence that incorporates several ASL techniques with online post-processing on the scanner. The flexibility of the sequence makes it suitable for both exploratory investigations of ASL techniques as well as incorporating ASL perfusion measurements in clinical research protocols. ASL has already been incorporated in neonatal imaging and studies of visual awareness at the DRCMR.

There has been an increase in the number of research projects that incorporate functional MRI (fMRI) whereby blood flow changes related to neural activation can be detected. The 3T scanner at the centre is especially suited for fMRI, and has yielded impressive results compared to the older 1.5T scanner. This has been mainly due the increased sensitivity at higher field, but also in part due to the faster imaging gradients available on the 3T scanner. One disadvantage, though, of fMRI at high field is that there are increased image distortions in areas of the brain that are close to tissue-air boundaries. These distortions are related to inhomogeneities in the magnetic field caused by magnetic susceptibility differences between air and tissue. These image distortions pose a problem for functional studies where such areas are activated. One such area is the orbitofrontal cortex (OFC) and a special version of the fMRI sequence that is optimized for the OFC was therefore implemented in a project looking at the neural basis of social behaviour where activation is expected in the OFC. The project is headed by Jon Wegener and the optimized sequence was found to recover a considerable amount of the signal lost due to the magnetic field inhomogeneities.

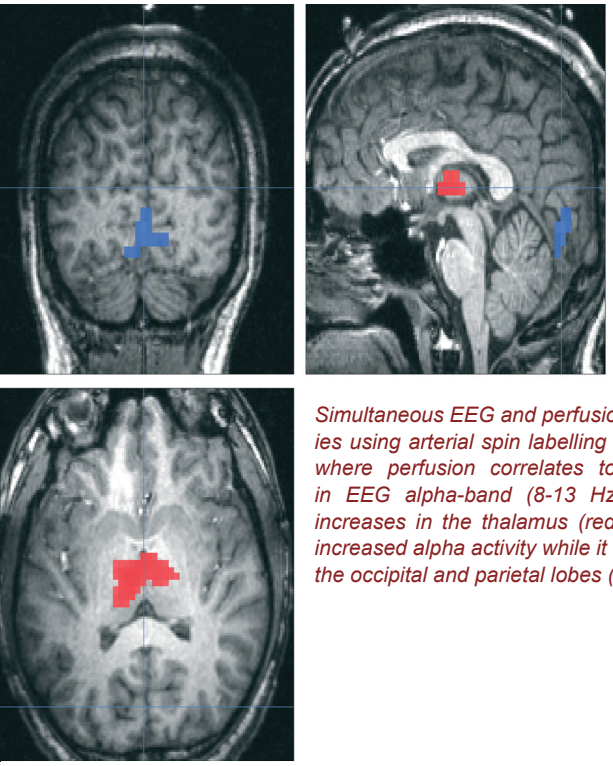


The figure shows results from an eccentricity mapping of the human visual cortex. The right hemisphere is shown in the folded representation (top right) whereas both hemispheres have been inflated to show details more accurately (bottom). The colour coding shows how different eccentricities are represented in the cortex going from blue (center of visual field) to red (periphery) as shown in the centre.

Furthermore, Torben Lund at the DRCMR has found that the analysis of functional studies is more robust and consistent when information about respiration and blood circulation is included in the analysis. Specific features were therefore added to the fMRI pulse sequences to enable the recording of respiration and pulse time series during the scan.

Another area that has seen substantial progress in 2003 is the simultaneous acquisition of functional images and electro-encephalogram (EEG) recordings. This is a highly difficult task due to the interference between the two recordings. The acquisition of MR images causes an artefact signal in the EEG recordings that is about 3 orders of magnitude higher than the actual EEG signal. This sets very high demands of both the hardware used to record the EEG signals and the software used in their analysis. Torben Lund has been the main driving force behind this work at DRCMR and the work has already lead to several

Basic Research



Simultaneous EEG and perfusion fMRI studies using arterial spin labelling reveal areas where perfusion correlates to the power in EEG alpha-band (8-13 Hz). Perfusion increases in the thalamus (red areas) with increased alpha activity while it decreases in the occipital and parietal lobes (blue areas).

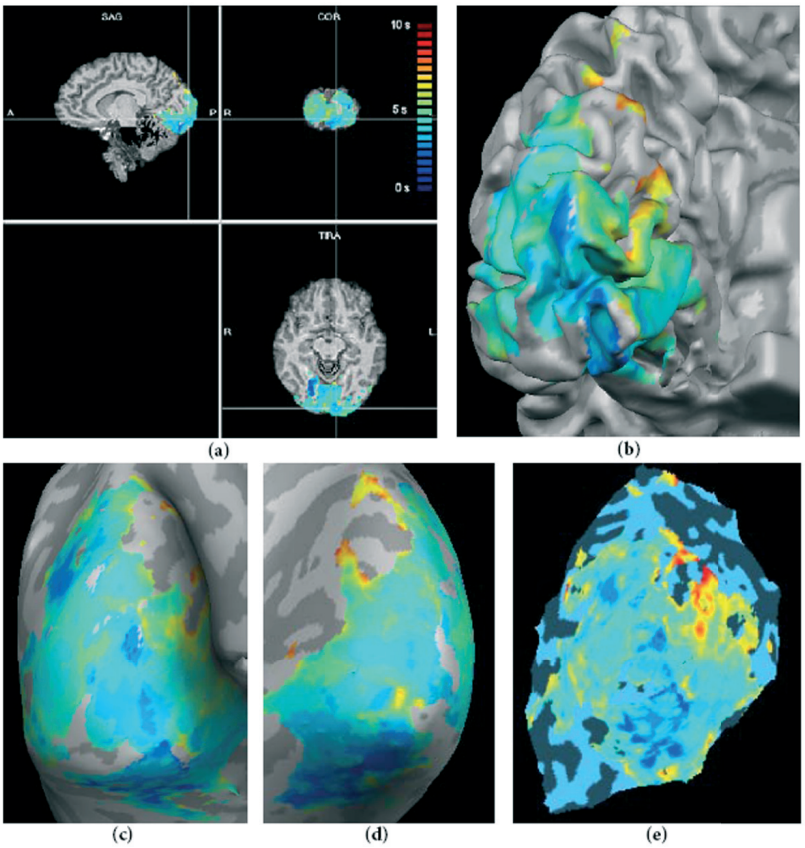
abstracts to be presented at international meetings in 2004. Based on the experience with EEG and fMRI acquisition, Lars Hanson has headed a group looking at a novel method for recording the two simultaneously. As a result a patent for this method is being sought by the Hospital.

Working with contrast-based perfusion measurements, Irene K. Andersen has been working on the implementation and optimization of perfusion quantification using T1-weighted dynamic measurements. Contrast-based perfusion measurements usually rely on T2*-weighted imaging to monitor the susceptibility effects of the paramagnetic contrast agents used. However, T1-weighted imaging, albeit less sensitive, offers a number of other advantages over T2*-weighted imaging, especially when quantifying perfusion. Irene has been working on the 1.5T Vision scanner on implementing fast T1-weighted sequences for implementing this technique.

Also on the Vision scanner, Mikael Boesen and Karam Sidaros have been optimizing sequences used to collect pilot data on atherosclerotic plaque imaging. The technique relies on acquiring T1-, T2- and proton-weighted high-resolution images of the arterial walls. Based on the mutual information obtained with the three modalities, plaques can be characterized according their stage, composition and stability. This is a new promising new field with a huge potential since atherosclerotic plaque formation is one of the leading death causes in the Western Hemisphere.

MR Informatics

For each patient, MRI provides several sets of images with different contrasts. These are aligned and analysed together by a set of available methods, appropriate for the project at hand. In order to do this efficiently and reproducibly, a configurable analysis "pipeline" has been established, that will be of major benefit to most patient studies in the future. MR-images are fed into the pipeline and are automatically analysed using a selection of the available methods, such as alignment, intensity correction and segmentation. Establishing a



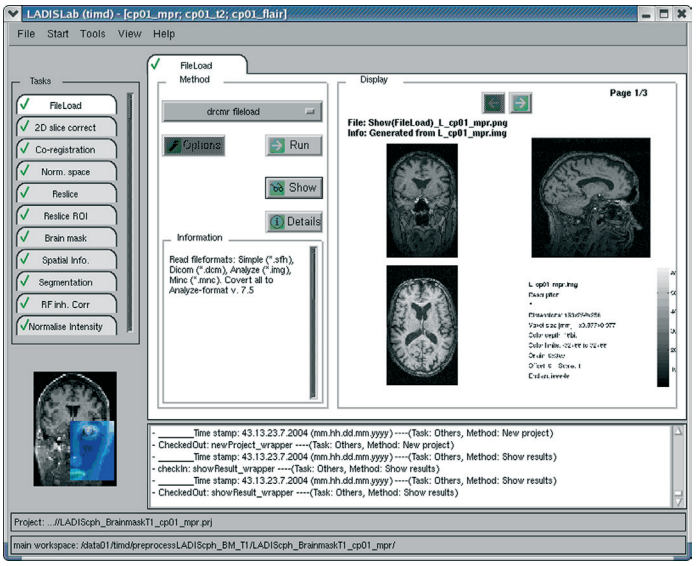
Spatial distribution of hemodynamic lag (time to peak). The activation overlaid onto the structural scan is shown in (a) whilst (b) shows the lag overlaid on a folded representation of the cortical surface of the left hemisphere (dilated and smoothed grey matter/white matter surface). Inflated versions of left (c) and right (d) hemispheres with overlaid hemodynamic lag are also shown. The view shown in (e) is an unfolded view of the right hemisphere, only the occipital cortex has been unfolded allowing the unfolding to be performed without defining cuts. This method requires manual definition of the region of interest and unfolding vectors and is thus very time consuming. All hemodynamic lags are in the same colour scale from 0 – 5 s (as shown in (a)). The GLM was fitted using 5 harmonics.

pipeline is a major task and many contributed: Arnold Skimminge, Tim Dyrby, William Baaré, Egill Rostrup, Poul Ring, and Irene K. Andersen. The functionality of the pipeline will steadily increase as new methods are added.

MRI can be used to measure the regional blood supply (the perfusion) by several methods, that each have their problems and advantages. By analysis of a rapid succession of images (a film) acquired after injection of contrast media, the perfusion can be calculated. The quality of the result, however, relies on the arterial input function, that is inherently difficult to measure using this method. Egill Rostrup has pioneered a fundamentally sound, so-called blind deconvolution method using methods known from astronomy. The arterial input function and the impulse response function are estimated simultaneously and on equal footing. Using a different approach, Thomas Stoltz has studied the application of independent component analysis in determining the arterial input function in his Master's thesis which concluded his studies at the Technical University of Denmark (DTU). This was carried out under the supervision of Irene K. Andersen and Lars Kai Hansen.

Vision is studied intensively with fMRI because knowledge of the levels of visual processing gives general insight into the organisation of the brain and the process of perception. For each location in the visual field, there is a dedicated part of the brain that performs basic analysis and relays the visual inputs to other parts of the brain. In both research and clinical diagnosis it is highly relevant to map this so-called retinotopic organisation. A technique for this was implemented by Kristoffer Madsen as part of his study of depth-perception. This "Master's project" concludes Kristoffer's graduate study of applied physics at DTU, supervised by Torben Lund, Per Skafte Hansen and Lars Kai Hansen.

Another DTU student, Mark Schram Christensen, also performed ground breaking research as part of his final work for the degree of applied physics. Based on a hypothesis on the nature of consciousness by Rodney Cotterill, Mark studied the mechanisms involved in visual perception and cognition using fMRI, in a study supervised by Torben Lund, Karam Sidaros and Rodney Cotterill.



The graphical user interface (GUI) of the Pipeline Program has been specially designed for use by non-technical users. From here the user can obtain a quick overview of the status and current results of a processed dataset. Behind the GUI exists an advanced and flexible database that controls the order and execution of image processing programs developed using different programs on different computer platforms. The Pipeline Program is designed to handle the increasing demands of image processing at DRCMR due to both local and international multi-centre projects and is able to fulfil the requirement of the analysis of many thousands of MR brain scans each year.

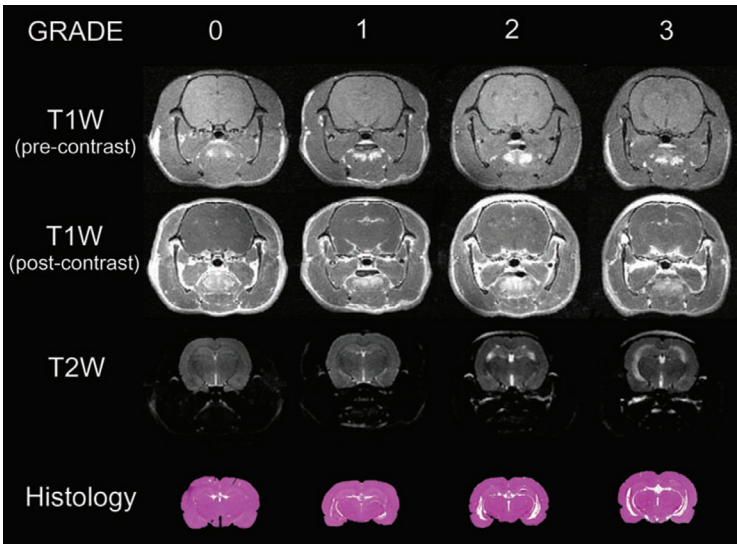
Classification of tissue types and anatomical structures based on MRI images are tasks often performed with little conscious effort by trained radiologists. Automating the process, however, is highly challenging, but is needed to get quantitative results without the exceptionally labour demanding job of manually classifying tissue types on the hundreds of images resulting from modern MRI exams. Important progress was made within the area of brain and heart segmentation by Mikkel Stegmann. In collaboration with Charlotte Ryberg and Egill Rostrup, Mikkel used active appearance modelling for automatic delineation of corpus callosum in MRI data as part of his PhD study at DTU. Also, Tim Dyrby made important improvements in automated brain tissue classification for the case where white matter lesions are present.

Preclinical Research

The preclinical research group primarily utilizes a 4.7T SISCO scanner designed for small animal imaging and spectroscopy research. The system will be upgraded in 2004 to provide a modern 4.7T system for the departments' expanding pre-clinical research activities. The group has two senior post-doctoral and two technical staff that focuses, primarily, on the longitudinal investigations of small animal models of disease. Cancer and brain disease are two areas currently under investigation with basic research into mechanistic aspects of disease progression and treatment being performed. A significant component of the pre-clinical work is formed in collaboration with other research groups within the Copenhagen area. This provides the opportunity for exciting multi-disciplinary projects to be performed with contributions from researchers with different scientific expertise and experience.

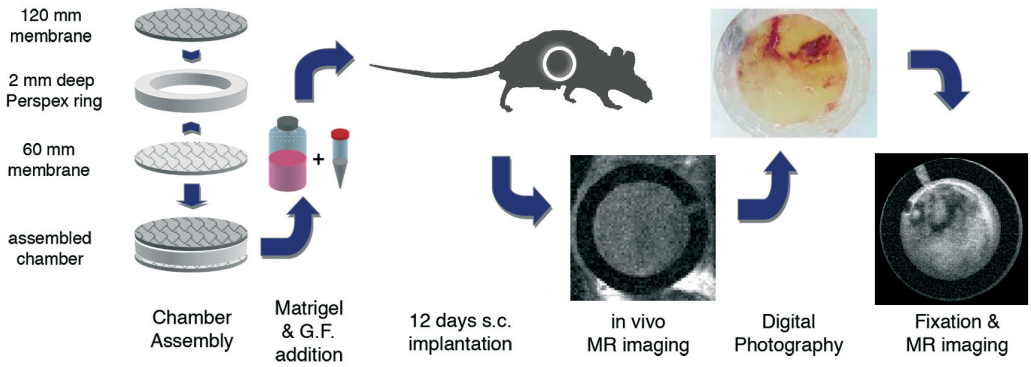
For a tumour to develop beyond approximately 1 mm^3, new blood vessels able to supply nutrients etc must also develop. The development of new blood vessels, known as angiogenesis, is obviously an essential step in tumour progression and is also an obvious target in cancer treatment. The group has been working in collaboration with the Institute for Molecular Pathology, University of Copenhagen, on two related projects. One project designed to develop MR methodology to investigate early vascular changes following administration of a drug targeted to tumour vasculature. The other project has been directed at developing a reproducible model of angiogenesis that could be readily investigated using MR.

The aim of the first study was to develop a method 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. To optimize the timing, the time course of the vascular effects should be characterized. Consequently, 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-means 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.



MRI studies of experimental meningitis: pre and post contrast (0.5 mmol/kg Gd-DTPA) T1W images, T2W images together with equivalent histological slices illustrating the evolutionary stages of the disease. Post-contrast T1W images were used together with the T2W images to grade the pathophysiological development of the meningitis model.

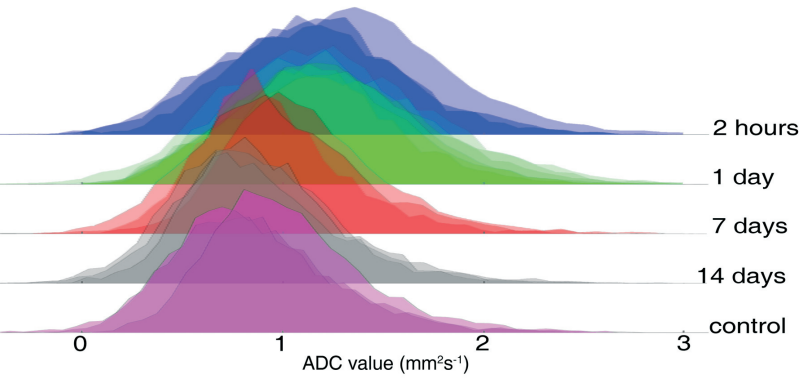
An in vivo angiogenesis assay that could be studied using MR methods would be of significant value in the screening and evaluation of anti- and pro-angiogenic agents. Such a model would facilitate the investigation of the influence of physiological factors upon angiogenesis and the validation of MR methods used



Development of a MR compatible in vivo angiogenesis assay: flow diagram indicating the different stages in the process.

to assess vasculature. Consequently, in the second project, a Matrigel angiogenesis assay was investigated and shown that high resolution in vitro and in vivo MR images could be obtained from the gel contained within a Perspex support. Furthermore, dynamic contrast enhanced imaging studies could also be performed. This ongoing work has demonstrated that the Matrigel implant model could, with refinement, be used to assess and quantify the effects of vascular-targeted agents. In addition, the model could also be used to investigate drug mechanism.

This year, a new collaborative study has been initiated with the State Serum Institute with the aim exploring the use of MRI as a means of monitoring experimental pneumococcal meningitis. Longer-term objectives include the development of a method of staging the disease by grading MR images of the brain obtained over a 48 hour period following infection. If successful, this would provide the opportunity to evaluate a wide range of therapeutic strategies designed both

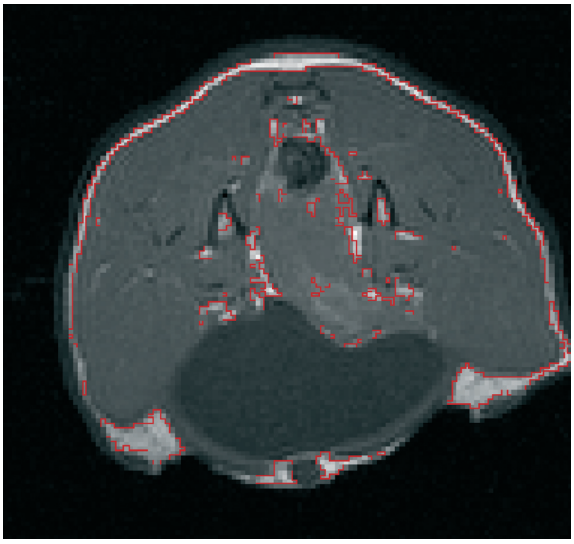


MR study of muscle damage following an electrotransfer gene delivery protocol. Normalised histogram representation of the summed muscle ADC values in 4 contiguous muscle slices, following an electrotransfer gene delivery protocol for all animals. Note the broader distribution and higher ADC values for the 2 hour group and the 'sharpening' of the distribution with time due to muscle repair which appears to be essentially complete within 14 days.

to cure the bacterial infection and minimise disease sequelae. Initial studies have demonstrated that MRI is well-suited to follow the progression of the disease and that the progression may be staged using MR imaging criteria. The study is about 50% completed and preliminary data will be presented at international meetings in 2004.

The group has previously developed a MR compatible electroporation system. This has been refined and applied to the study of the effects of electroporation in muscle. This is especially relevant since using electroporation-based methods, in vivo gene delivery can be achieved with high efficiency. Whilst such an approach could help fulfil the promise of gene therapy, the application of short, high voltage electric pulses results in high electric currents passing through the tissue for short periods of time, with consequent tissue damage. To achieve maximum gene transfer into muscle, minimal irreversible muscle fibre damage is essential. This project has used quantitative water diffusion measurements to investigate tissue damage that may occur as a result of the application of typical electrotransfer protocols for up to 14 days following the electrical pulses. The project has shown that water diffusion mapping is suitable for the quantitative assessment of tissue response to electroporation using MRI. Tissue repair, as assessed using tissue oedema as an indicator, appears to be mostly complete within 14 days.

As part of a Ph.D. project conducted mainly at the Royal Veterinary and Agricultural University, an animal model for diet-induced obesity and metabolic syndrome in humans is being established. This project involves collaboration with medical and technical personnel from the MR-department on the development of suitable imaging methodology for the measurement of the abdominal lipid distribution in pigs fed either a normal or high-fat diet. The animals are scanned twice, in this ongoing project, to monitor changes in lipid distribution.



Automated delineation of abdominal lipids in a porcine model of diet-induced obesity and metabolic syndrome.

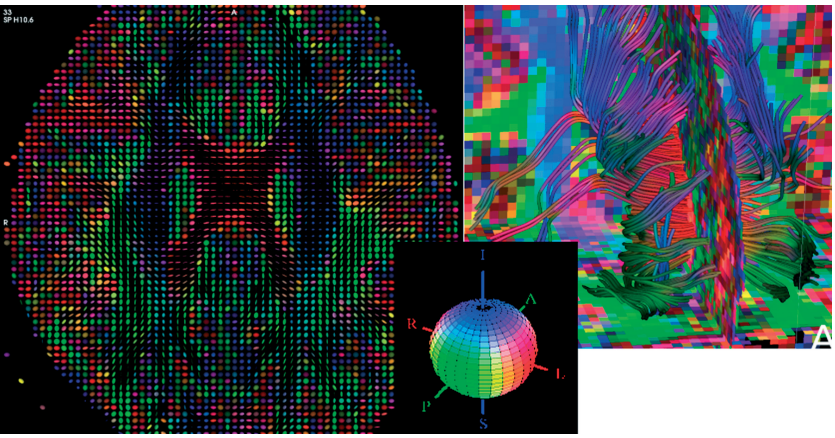
Clinical Brain Imaging

Neuropsychiatric Disorders

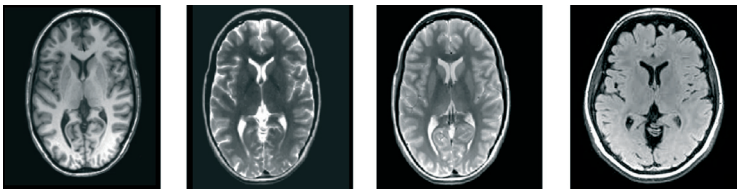
In this area of the program, research is directed at the longitudinal investigation of brain structure and function in prodromal and early stages of affective disorder (e.g., in monozygotic and dizygotic twins with very high risk to develop an affective disorder) and in different stages of schizophrenia (e.g., in drug-naïve first episode patients, in patients with disease onset in childhood and adolescence or adulthood, and in chronic patients).

Major depressive and bipolar disorder (MDD; BPD) are common and severe psychiatric illnesses, affecting respectively 4% to 8 % and 1.3% to 1.6 % of the general population. The risk of recurrences is high and 15% to 20 % of patients commit suicide. Although the etiology of affective disorder is unknown, genetic factors as well as environmental, especially stress-inducing, factors are involved. Heritability estimates for MDD range between 31% and 66% . The heritability of BPD is approximately 70%. The underlying pathophysiology of affective disorders is largely unknown. However, recent postmortem and functional and structural in vivo neuroimaging studies have provided accumulating evidence for the presence of functional and structural abnormalities in the brains of patients with affective disorder as compared to healthy controls.

Schizophrenia is a complex, chronic, and debilitating disease, in which different aspects of cognition and behaviour, including attention, perception, thought processes, emotion and volition are affected. The disorder afflicts approximately 1% of the general population and typically has its onset in young adulthood.



Images of fractional anisotropy and fibres crossing the corpus callosum were created with software developed at MGH Martinos NMR Center.



Differing MR techniques are used to obtain morphological information in the different projects: T1-, proton density-,T2-weighted, FLAIR.

Although its etiology is not known, genetic factors (~80% heritability) as well as environmental, such as intrauterine and perinatal, factors are involved. In vivo imaging studies have been pivotal for our understanding of schizophrenia as a brain disease. Studies of first-episode (drug-naïve) schizophrenia patients are important as they control to a large extent for effects of factors such as long-term hospitalization, neuroleptic treatment, and disease chronicity.

Generally, the MR investigations address the following questions: (a) which brain abnormalities are present before onset of an affective disorder, (b) which abnormalities are related to an increased (genetic) risk to develop affective disorder, (c) which abnormalities are present at illness onset, (d) which abnormalities emerge during the course of the illness, (e) which abnormalities progress in the first years of the illness, (f) how are these abnormalities and changes related to cognitive functions, pharmaceutical treatment, behavioural symptoms, and social and medical history, and (g) which abnormalities and changes are predictive of treatment response and clinical outcome. Questions (c) through (g) pertain to both psychiatric syndromes.

The following MR techniques are used in the different projects: structural MRI including T1, proton density and T2 weighted, FLAIR and diffusion tensor imaging (DTI) sequences. The latter is a novel technique that permits investigation of white matter microstructure. Additionally, in the schizophrenia projects, fMRI is used to investigate (frontal) brain function using a verbal working memory (N-back) task.

The senior researcher at the DRCMR responsible for coordinating the MR investigations is William Baaré. Patients and healthy controls are recruited and clinically evaluated by the psychiatry departments at the university hospitals of Rigshospital (affective disorders: Principal investigator: Prof. Dr. Lars Kessing) and Bispebjerg (Schizophrenia: Principal investigators: Professor Ralf Hemmingsen, Dr Birte Glenthoj and Professor Tove Aarkrog). Psychiatrist Maj Vinberg is the clinical researcher responsible for the

affective disorder project (A1). In this project healthy mono –and dizygotic twins (age > 18 years) with a high and a low risk of developing affective disorder are investigated. The height of the risk depends on zygosity and the diagnostic status of the cotwin (e.g., diagnosed with affective disorder or never received a psychiatric diagnosis). Four hundred potential subjects were identified by linking the Central Psychiatry Registry and the Danish Twin Registry, a possibility which is unique to Denmark. To date, 70 twins have undergone MR scanning.

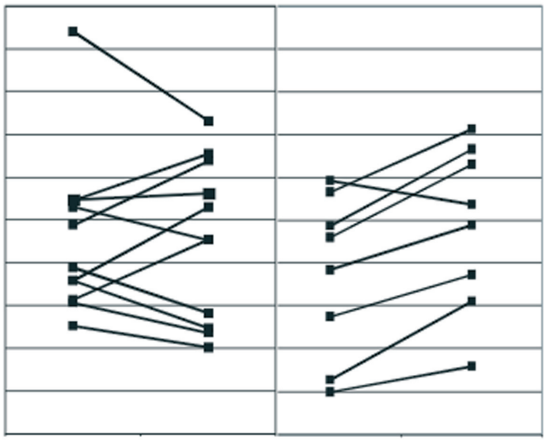
The verbal working memory task (NBack), characteristically, activates the parietal, (pre)frontal, and cingulate cortices

Clinical researchers responsible for the different schizophrenia projects are the psychiatrists Birte Glenthøj (S1: "Structural and functional brain abnormalities in drug naïve adult onset schizophrenia"), Katrine Pagsberg (S2: "Structural and functional brain abnormalities in early onset first-episode schizophrenia" and S3: "First episode psychotic children and adolescents: a 5 year follow-up study of brain structure and function"), Bettina Søholm (S4: "Pharmacological treatment of cognitive deficits in schizophrenic patients: The effects of central cholinergic augmentation on cognitive deficits, and psychopathology"), and Klaus Kristiansen (S5 "Structural and functional brain changes in drug-naïve first-episode schizophrenia patients: relation to cognitive function and anti-psychotic medication"). Data acquisition for projects S1 and S2 was completed in the end of 2002. For all other projects data acquisition started in 2003 and is ongoing.

In project S1, results indicate that, as hypothesized a priori, after only 3 months exposure to the typical drug zuclopenthixol the volume of the caudate nucleus has increased, while exposure to the atypical drug risperidone does not appear to exert this effect. This is the first study demonstrating this action in drug naïve patients after a short drug exposure.

In project S2 we have shown that abnormalities in ventricular and frontal white matter volumes are already present at the early onset of non-affective and non-organic psychosis in minimally medicated children and adolescents. Also, our finding of smaller intracranial volume in the subgroup of patients with schizophrenia suggests alterations in early brain development and supports current hypotheses implicating neurodevelopment in the pathophysiology of schizophrenia. In contrast to findings in adults, gray matter abnormalities appear not to be a key feature when the onset of illness takes place during childhood/adolescent brain maturation.

Caudate nucleus shown separately (in red in left panel) and in relation to the ventricular system (shown in green in right panel).



Caudate volume changes after 3 months medication with (left) the atypical drug risperidone and (right) the typical drug zuclopenthixol.

Clinical Brain Imaging

Brain Aging and Neurodegenerative Disorders

The Centre is the site of several studies of normal aging and the neurodegenerative disorders that afflict the elderly; and is a participating site in a broader multi-site investigation by European Union collaborators entitled, "Leukoaraiosis and Disability in the Elderly" (LADIS). The latter is an ongoing structural MRI study of the known changes that occur with aging in the white matter of the brain. The objective is to better describe the predictors and consequences of these changes. Older volunteers are scanned at entry into the study and again 3 years later and abnormalities in the white matter are measured. These measures are correlated with extensive neurobehavioral assessments. Egill Rostrup is the senior DRCMR investigator most closely involved with the LADIS studies.

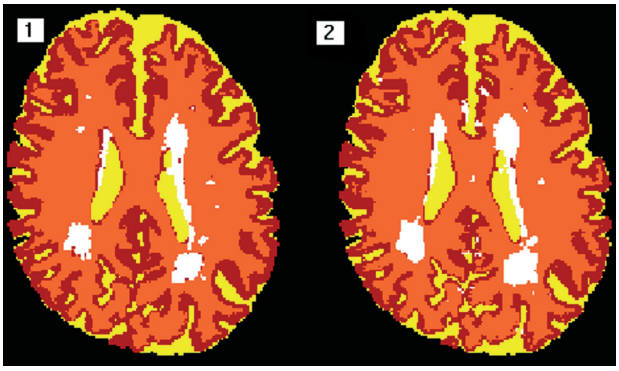
As part of the LADIS project, Charlotte Ryberg is focusing on studies of the corpus callosum, which is the major cerebral white matter structure carrying most interhemispheric connections. Initial studies in the Danish LADIS cohort have revealed a relationship between corpus callosum atrophy and cognitive decline, as well as an association between corpus callosum abnormality and the severity of white matter damage elsewhere in the cerebral hemispheres. These preliminary findings were presented at the 2003 meeting of the International Society for Vascular Behavioural and Cognitive Disorders.

Two important DRCMR subprojects have developed from the LADIS initiative, both involving the development of advanced methods for automated measurement of abnormalities in cerebral white matter. Tim Dyrby is developing and validating tissue segmentation methods that rely on artificial neural network algorithms. Other tissue segmentation methods are available that permit automated tissue segmentation of the normal tissues in the brain (gray matter, white matter, and cerebrospinal fluid). The new method under development at the DRCMR extends these by identifying and segmenting the white matter hyperintensities in the brain as well as the normal tissue types, thus providing a much more informative result in older individuals and patients, in whom such abnormalities are prevalent.

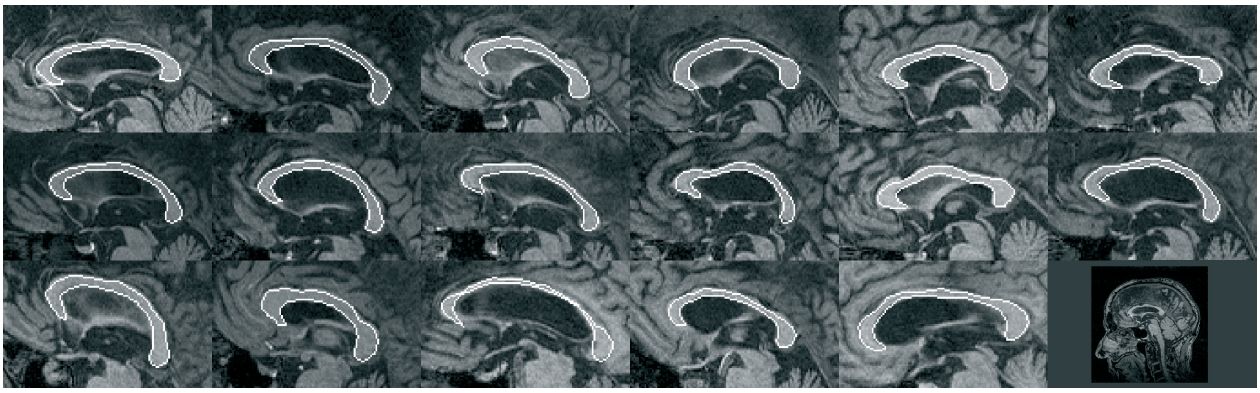
A second subproject of the LADIS investigation is led by Mikkel Stegmann, a collaborator from the Technical University of Denmark. This project involves the development and application of mathematical models for parameterisation of shape and appearance of MR data from corpora callosa. The resulting automated methods can then be used to examine, in a completely objective way, the variability in callosal morphology that occurs in the elderly LADIS subjects. This work was recently accepted for presentation at the annual SPIE meeting of the International Society for Optical Engineering at its International Symposium on Medical Imaging, in San Diego.

Ellen Garde and collaborators from DRCMR and from other University of Copenhagen hospitals (Glostrup and Rigshospitalet) continue their long-term (longitudinal) MRI investigation of elderly individuals. This study also focuses on white matter hyperintensities and recent findings confirm that increases in these abnormalities are associated with intellectual decline over a five-year period in 85 year olds. These results have been submitted for publication.

In addition to these large projects investigating normal aging, the DRCMR is involved in several other clinically-oriented projects investigating neurodegenerative disorders. Katja Krabbe of the DRCMR, together with collaborators from Bispebjerg Hospital, is completing a study of patients with Parkinson's disease and the related disorder, multiple system atrophy. This project employs several MR modalities with the aim of finding better methods for differential diagnosis of the disorders. Morphometric analyses of the data



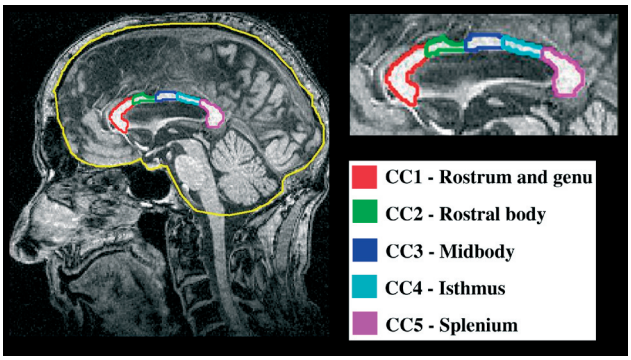
The difference between intensity histograms on images from different MR scanners makes automatic segmentation non-trivial. A general artificial neural network (ANN) has been developed to automatically segment the tissues: grey matter (brown), white matter (orange), CSF (yellow) and white matter lesions (white). The crucial thing making the ANN segmentation general is image pre-processing which is done using the Pipeline program. The left image shows a manually segmented brain while the right images shows an automatically segmented brain using the general ANN trained on two other brains. Note the good agreement even for the white matter lesions.



Fully automated registration of corpus callosum in mid-sagittal brain images. The results were obtained in a leave-one-out study of 17 subjects using 1.6 seconds of CPU time for each image. All results are cropped for display. The search area is illustrated in the lower right corner.

from this study are essentially complete; however analyses of MR spectroscopic and diffusion imaging data are continuing.

Terry Jernigan, who joined the DRCMR in 2003, initiated a new project that aims to develop clinically applicable functional MRI paradigms for probing brain systems affected early in several target neuropsychiatric disorders. The paradigms will be used to assess the functional integrity of brain systems involved in memory and including medial temporal and distributed neocortical structures. Initial efforts will be to examine the sensitivity of the methods at high field, the session-to-session stability of the results, and the effects of age on the pattern and intensity of brain activation. These studies should set the stage for evaluation of the methods for detecting early changes associated with Alzheimer's disease. Thomas Ramsøy has joined the project and is focusing on the development of fMRI paradigms that evoke activity in the peri-rhinal and entorhinal parts of the temporal lobe that show the earliest pathological changes in dementing patients.



Definition of the intracranial volume (ICV) as indicated by the yellow line. Callosal subsections are also defined in this midsagittal slice.

Functional MRI, methodological and applied projects

Functional MRI (fMRI) is a term that describes the application of special MR-imaging techniques to determine the location of brain areas involved in specific functions. These techniques are usually either sensitive to regional changes in brain blood flow (so called spinlabeling technique) or to changes in blood oxygenation (BOLD sequences). At the MR department interest in this field ranges widely from basic studies of the foundations of the methodology itself, to applied studies of basic cognitive functions.

In the methodological studies a mathematical model was developed to describe the relation between the regional blood oxygenation and a number of other physiological parameters, such as brain blood flow, hemoglobin properties and the blood levels of oxygen and carbon dioxide. The model was used to predict the BOLD response from physiological data based entirely on PET measurements in normal volunteers. By using PET measurements it was possible to obtain reference values for both blood flow and volume in the brain, which is not possible with current MR techniques. It was shown that the BOLD response is less sensitive to blood flow changes when the initial flow is elevated and how this effect is modulated by the concomitant changes in blood volume and oxygenation. Future work will be directed at improving the model, testing the effect of other physiological changes. In addition to a deepened understanding of the BOLD mechanism it is hoped that the model will be helpful

in interpreting brain mapping experiments in clinical situations where the physiological background may be not be controllable. Egill Rostrup currently leads this work.

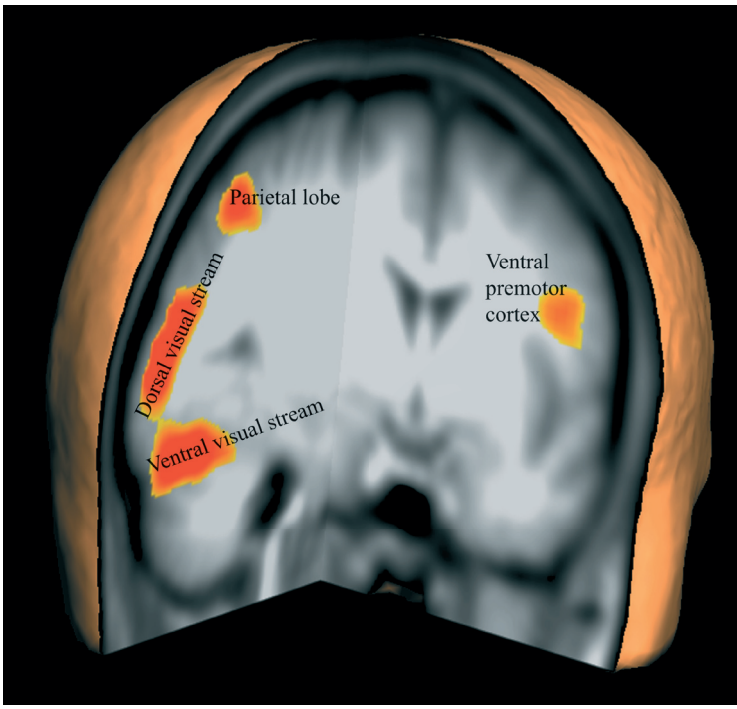
Methodological improvements also took place in the hardware and signal processing area where some very important work has been done to integrate fMRI and EEG data acquisition. This is a highly challenging task, because MR scanning creates electromagnetic fields of a much larger magnitude than those normally observed with EEG. Additionally, electromagnetic effects of cardiac pulsation are amplified by the high magnetic field. However by careful selection of hardware as well as of methods to remove artifactual signal from the EEG it has now become possible to detect high-quality EEG data during MR scanning. This new method, being developed by Torben Lund, opens a whole range of possibilities for combining the high spatial resolution of fMRI with the high temporal resolution of EEG. As a first approach it was shown possible to demonstrate brain regions in which cerebral blood flow is correlated to fluctuations in the well-known and spontaneously occurring frequency bands of the EEG. It may also be possible to map regions correlated to pathological EEG activity.

During 2003 the BOLD methodology was applied to a number of interesting areas with the aim of answering important neuropsychological questions.

One study is focused on determining whether specific neural systems are involved in discerning 3-dimensional from 2-dimensional visual experiences. Using colored glasses it was possible to switch from 2D to 3D vision, allowing for comparison of brain activity during these two states, even though the same picture is being projected to the subject inside the scanner. Kristoffer Madsen is conducting the study, and, as a spin-off from this project, a method for retinotopic mapping is now being implemented. This technique makes it possible to determine, as well as image, which part of the visual field each point in visual cortex relates to. This is expected to be of great importance in investigating patients with visual field defects, as well for distinguishing subspecialized areas of visual cortex.
In another study (project by Mark S. Christensen) fMRI has been used to approach one of the most essential questions about the human brain, the nature of consciousness itself. Using a specially designed visual display, it was possible to accurately determine the time at which subjects became aware of gradually displayed objects, and the concurrent brain activity changes could be determined. Activity was found not only in visual but also in premotor cortex. This is in accordance with a hypotheses (presented earlier by Prof. Cotterill, a collaborator on this project) stating that motor preparation activity below a threshold of actually performed movements is intimately linked to conscious experience.

Traumatic Brain Injury

Severe traumatic brain injury (TBI), predominantly caused by motor vehicle accidents, is the single most important source of death and long-term morbidity among younger age groups in the Western countries. The final outcome of traumatic brain injury is highly variable, ranging from full recovery to persistent vegetative state, and difficult to predict for the individual patient. Very often the acute injury is followed by periods of low blood pressure or lack of oxygen, causing global ischemic-hypoxic injury. Another type of widespread injury is diffuse axonal damage, which is caused by the traumatic event itself. These types of injury are not always well visualised by conventional imaging, but may be important determinants of outcome.



Areas highlighted in orange-red are areas showing increased activity when subjects become consciously aware of non-figurative visual objects. The image displays an average brain, where one quarter is removed to reveal the areas with more activity. The experiment is carried out as an event-related BOLD fMRI experiment.

A new project, run by Annette Skræp Nielsen, started in 2003 as a collaboration between the Department of Neurorehabilitation and the DRCMR. In this project adult patients with severe TBI, transferred from neurosurgical units for rehabilitation at Hvidovre Hospital are scanned 4-8 weeks post-injury, and again at follow-up after 6 months. The project applies newer MRI methods with the aim of obtaining a better characterisation of TBI patients in the subacute phase, and to identify key imaging parameters to improve the prognostic capabilities. Of particular interest are diffusion tensor imaging for quantification of diffuse axonal injury, contrast-based perfusion imaging for assessment of the hemodynamic status, and spectroscopy with whole-brain coverage for detection of hypoxic-ischemic changes.

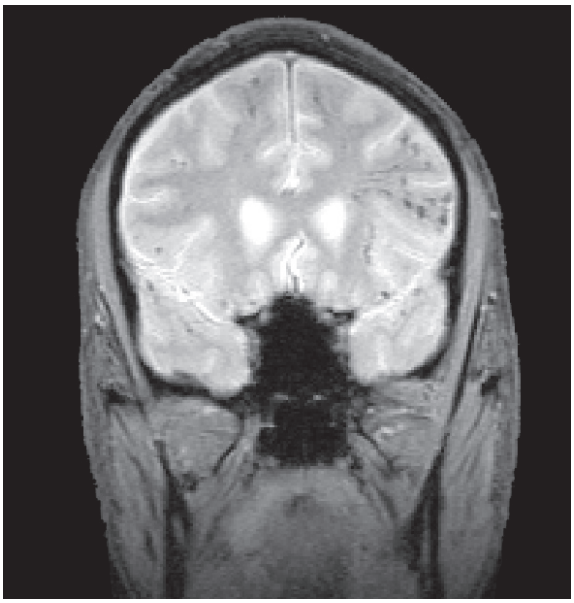
A total of 10 TBI patients, out of 30 planned, were scanned in 2003. As an addition to the project, patients that have been resuscitated from cardiac arrest are also included. This should make it possible to characterise the changes caused by pure ischemic-hypoxic events.

The association between imaging results and clinical outcome will be analysed taking into account other possible prognostic indicators such as apolipoprotein E genotype. The results of this project could provide important diagnostic, prognostic and pathophysiological information useful in the clinical management of brain injured patients. An additional benefit of the project is that it offers a detailed radiological investigation of each patient, which may often be requested not only the clinicians but also the patients relatives.

Multiple Sclerosis

The DRCMR has a long tradition of combining MR-research with research in multiple sclerosis (MS). In 2003 this tradition was not only continued, but the MS research programme was significantly improved and extended in several areas. Currently, there are five researchers involved full time in this area, and for the first time two simultaneous PhD projects have been planned.

In one ongoing PhD project Henrik Kahr Mathiesen adresses the essential question of the relation between MRI findings and clinical status of MS patients. A number of previous imaging studies have demonstrated that conventional measures, such as total number and volume of white matter lesions in the brain, are able to predict the patients symptoms only



Hemorrhagic white matter shearing lesions (diffuse axonal injury), a lesion type typically found in traumatic brain injury. Coronal T2 weighted gradient echo (FLASH) MR image. This 19 year old patient suffered severe head trauma in a motor vehicle accident 6 weeks previously.*

to a very limited extent. Nevertheless, these parameters are very often used in clinical trials, as “surrogate measures” of disability and disease activity. Newer MRI methods, such as diffusion imaging and spectroscopic imaging may have a higher pathological specificity. Diffusion tensor imaging (DTI) measures the diffusivity of water, directly reflecting the microstructure of the brain tissue, and by this technique abnormalities have been shown in otherwise “normal appearing white matter”. Similarly, by spectroscopic imaging it is possible to measure and image the distribution of neuronal metabolites, which should give a more direct picture of the tissue damage. In the current project a total of 36 patients (with either MS or optic neuritis) are being investigated serially at five time points during a period of 2 years. The first results of this large data material are now emerging, and in 2003 results of the first cross-sectional spectroscopic study were finished. Important methodological improvements were documented, since it was possible for the first time to obtain simultaneous whole-brain and regional measures (distinguishing cortical grey matter, white matter and white matter lesions) of neuronal metabolites. However, no significant correlation was found with standard clinical performance tests (‘EDSS’) and it is speculated that this may be because the clinical tests only samples a limited part of all brain functions, and that comparison with more extended neuropsy-

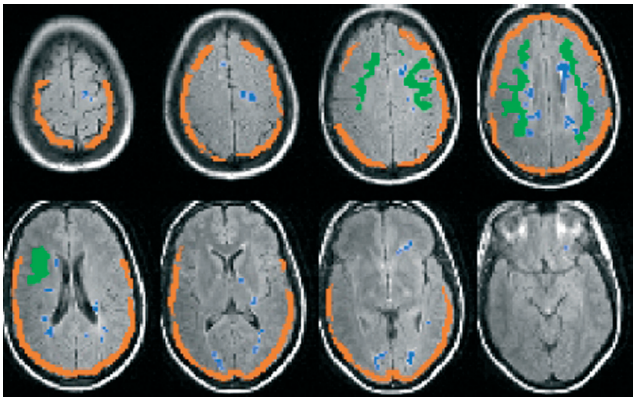
chological measures is needed. This hypothesis will be investigated further.

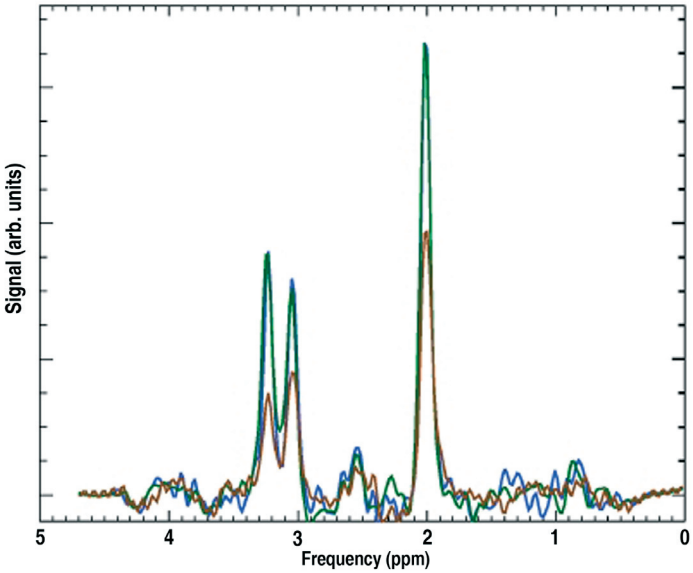
While the focus of the above project is to understand MS pathophysiology and shed light on the relation between structural and functional change, the DRCMR also participates in studies more directly aimed at elucidating current therapeutic questions. One such issue is the development of antibodies that counteract the effect of interferon-treatment in some MS patients. This is being investigated in a study initiated by the MS-research group at Rigshospitalet. In one group of patients the disease activity, as measured by MRI, is being compared to the level of antibodies, and preliminary results showed a correlation between high levels of antibodies and high disease activity on MRI, due to these patients relative immunity to treatment. Inclusion is now closed, and the final analysis will be submitted soon. A follow-up was initiated this year in which those patients with highest antibody levels will be treated with methylprednisolone, and their MRI disease activity and potential response to interferon treatment will be monitored.

The new high-field scanner (Siemens Trio, 3T), installed in the department in 2002, is now beginning to show its worth also in MS projects. The transition from conventional to high field is a very gradual process, first of all because many clinical projects run over a span of years, and cannot readily be moved from one scanner to another. Secondly, along with any clinical research project also comes the responsibility to provide diagnostic information by fully standardised techniques, and many clinical protocols have not yet been developed and/or tested at high field. To remedy this, and fully open the new scanner for MS research projects, a formal comparison of 1.5 and 3T scans was initiated by Kirsten Nielsen. In this project 20 patients with newly diagnosed optic neuritis are scanned sequentially on the same day in both scanners, and quantitative data regarding T2 lesion load as well as enhancing lesions will gathered and compared. In a pilot study suitable MRI techniques were selected for the high-field scanner, and important differences in the behaviour of T1-weighted sequences were confirmed.

When the clinical potential of the Trio scanner has been established by this project, its full potential in functional imaging can be exploited in future projects. We and other groups have previously shown remarkable changes in the activation pattern during the recovery from acute optic neuritis. These changes have been interpreted by some as adaptive changes that support the often quite effective recovery, and this hypothesis will be investigated further using retinotopic mapping, a more precise way of assessing cortical representations of the visual field. This project, which goes on in collaboration with the Department of Neurology, Glostrup, is now in its pilot phase in which retinotopic mapping is being tested in healthy volunteers.

Finally, the DRCMR participates in a number of international drug trials for MS-therapy. Most importantly, the department is the MR-analysis centre for the MECOMBIN and NORMIMS studies. Both of these studies are investigator driven trials assessing the therapeutic effect of simultaneous treatment with methylprednisolone and interferon-beta-1a (IFN). In the former study low dose IFN and methylprednisolone





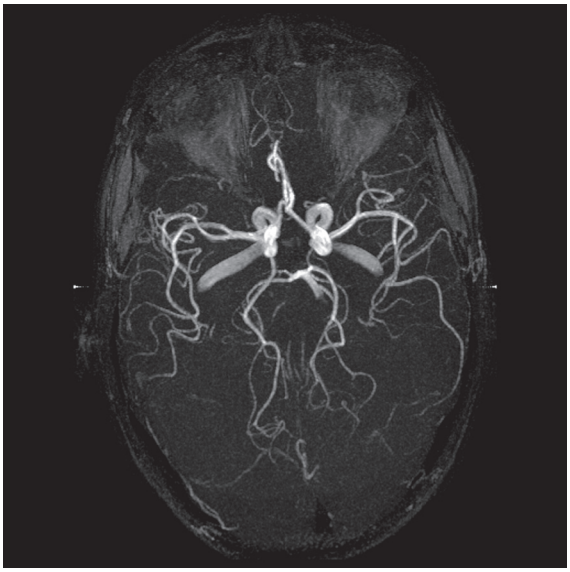
Spectroscopic imaging of multiple sclerosis. Spectra showing the signal from the metabolites choline, creatine and N-acetyl-aspartate are shown for brain regions chosen semi-automatically: Predominantly cortex (brown), normal appearing white matter (green) and lesions (blue).

is given to previously untreated patients, whereas in the latter, high-dose IFN and methylprednisolone is given to patients with residual disease activity in spite of IFN-treatment. Both studies will include 3-400 patients, and so far 30 MRI sites were approved for the MECOMBIN study and 7 for the NORMIMS. Image data are being processed using the in-house developed RIP software to delineate regions, and to calculate lesion load as one major MRI outcome variable. Other variables such as brain volume and brain parenchymal fraction are calculated following meticulous pre-processing to minimize the effect of inter-centre variability.

In addition to the analysis centre function, the department participates in a total of 5 international trials predominantly focusing on relapsing-remitting multiple sclerosis, and 2 trials investigating the treatment of "clinically isolated syndromes".

Cerebral Stroke

In this project group, 2003 was devoted to the analysis of a large data material collected on Stroke-in-progression (SIP) patients from the Department of Neurology, Hvidovre Hospital. A total of 41 patients were scanned acutely (<24 hours), after one week and at follow-up after 3 months, with a protocol including spectroscopy, perfusion and diffusion measurements. An extensive collection of clinical data is available from the same time points. Preliminary results confirmed the correlation between lesion size and clinical severity (Scandinavian Stroke Scale) in the acute stage, and at subsequent scans. Clinical recovery in the first week was seen predominantly in those in whom lesion size decreased, while increases in lesion size adversely affected the clinical status. The final clinical outcome, however, was not predictable by initial lesion size, or by the presence of non-infarcted areas with compromised blood supply (mismatch zones). These findings are of relevance for future therapeutic strategies such as thrombolysis, and suggest that clinical recovery is a multifactorial process, influenced by several factors other than lesion and mismatch volumes.



MR angiography is used in a omprehensive neuroradiological evaluation of ischaemic stroke to identify site(s) of vessel occlusion.

Neonatal Brain Maturation

Infants born prematurely are at risk of brain injury and neurodevelopmental deficits later in life. The pathogenesis of brain lesions is still controversial but apparently both infection in pregnancy and perinatal ischemia are implied in the development of white matter damage (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. Recent studies with single voxel spectroscopy have demonstrated that lactate (as a sign of insufficient oxygen supply to the brain) is significantly higher in premature infants with WMD at term-equivalent age, compared with premature infants at the same age with normal white matter.

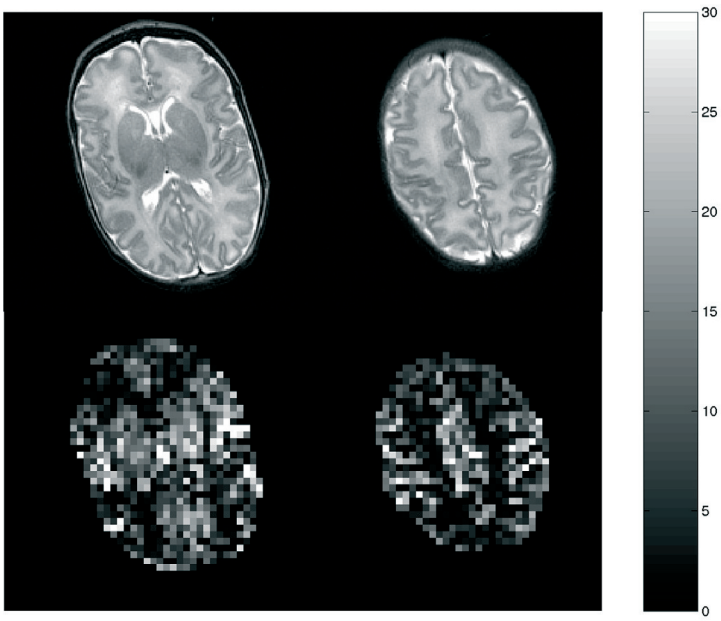
In an ongoing collaboration with the department of Paediatrics, a study headed by Maria J. Miranda aims to demonstrate an association between infection in pregnancy and white matter damage in the immature brain at term-equivalent age. The study started out on the centre's 1.5T scanner, but was quickly moved to the 3T scanner when that became available. The study aims at including 200 premature infants born at either

Clinical Brain Imaging

The experimental setup: a neonate in the 3T scanner with physiological monitoring and ear cups for noise protection.

Hvidovre Hospital or Rigshospitalet at a gestational age less than 33 weeks. The placenta is histologically and microbiologically examined by a pathologist, while blood from the umbilical cord is examined for bacterial endotoxins and several inflammation cytokines. These data will be correlated with brain lesions and lactate accumulation found in MR scans performed at term-equivalent age.

A unique tool available at the DRCMR is the arterial spin labelling (ASL) technique to non-invasively measure perfusion. Sick premature and term neonates have a vulnerable cerebral circulation. Impaired autoregulation of the cerebral blood flow may therefore be one of the main contributors to the development of brain damage in these infants. In the past years, studies of the cerebral circulation have been done using different invasive methods such as xenon-clearance, PET and SPECT while other non-invasive approaches for estimating CBF, e.g. Doppler ultrasonography and near infrared spectroscopy have not accomplished the primary expectations. Maria J. Miranda and Karam Sidaros have therefore headed a study to evaluate the feasibility of using ASL to measure neonatal cerebral perfusion. As this MR method is entirely non-invasive and safe, even in very young infants, serial measurements are possible, which might be essential for understanding the pathogenetical mechanisms of brain damage in sick neonates. The initial results of this study have indicated that with a minor modification of the ASL technique, the method is indeed suited for measuring neonatal perfusion. These results will be presented at several international meetings in 2004.

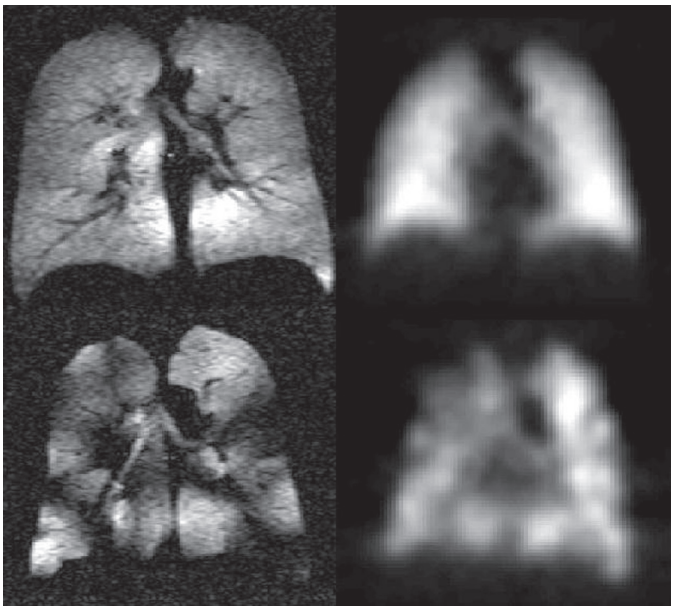


T2-weighted turbo spin-echo images (upper) and perfusion images (lower) at the level of the basal ganglia in preterm neonate scanned at term-equivalent age. The image intensities (see colour bar) represent perfusion in ml/100g/min as determined using arterial spin labelling.

Clinical Body Imaging

Pulmonary Function

Imaging of the lungs poses a number of difficulties with respect to traditional MRI. Large susceptibility differences at the air-tissue interfaces causes the MRI signal to decay very rapidly and in addition the density of the lung tissue is low compared to other tissues. During recent years a new MR method based on imaging an inhaled hyperpolarized gas has emerged.



Helium images acquired at the DRCMR (left) and conventional krypton images acquired at Rigshospitalet (right) showing the superb spatial resolution of the new helium technique for a healthy volunteer (top) and a smoker with chronic obstructive pulmonary disease (bottom). In addition, the new method involves no ionizing radiation, and may therefore be particularly suited for screening, pediatric scans and monitoring of treatment.

The DRCMR is one of the three clinical centers involved in the EU PHIL project on hyperpolarized ^{3}He MR lung imaging methodology and applications. The technique is unique in Denmark and relies on the inhalation of magnetized helium, which is a harmless gas. The aim of the PHIL project is to validate this new lung imaging method by comparing to conventional lung examination techniques: lung function test, CT scan and Krypton scintigraphy. The included subjects are patients diagnosed with chronic obstructive pulmonary disease (COPD) and lung healthy volunteers.

The hyperpolarized ^{3}He gas for the studies is produced by another PHIL partner in Germany and shipped to Copenhagen by air. The MR protocol includes morphologic imaging providing information about the ventilation distribution and diffusion imaging which has been shown to correlate to the alveolar sizes in the lung.

The project was very successful in 2003. Since March, 31 subjects were scanned at the DRCMR, nearly all resulting in very high quality images. Patient inclusion will continue until the end of February 2004. The results are being analysed together with results from the other participating centers. Specialists in radiology and nuclear medicine score the MR images as well as the images from CT and Kr scintigraphy studies in order to make detailed comparison of the techniques. Lise Vejby Søgaard and Trine Stavngaard are locally responsible for this project that also involves conventional lung imaging at Rigshospitalet.

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.

MR image of normal appearing triangular fibrocartilage in the wrist of a young man

In contrast, conventional radiography only shows the late signs of preceding synovitis.

In 2003, Marcin Szkudlarek defended his PhD study of ultrasonography in small extremity joints in rheumatoid arthritis. The study included a number of methodological investigations, comparison with clinical, histopathologic, radiographic and MRI findings, as well as longitudinal studies to investigate the sensitivity to change. On the basis of the studies the following was concluded in relation to finger and toe joints in patients with RA: 1) When properly standardized, US is a reproducible method of examination; 2) It is possible with US to detect and grade destructive and inflammatory changes; 3). US shows a high overall agreement with MRI for detection of destructive and inflammatory changes; 4) With MRI as a reference method, US is more sensitive and as specific as radiography for detection of destructive changes; 5) With MRI as a reference method, US is more sensitive and almost as specific as clinical examination for assessment of inflammatory changes.

Another PhD study, conducted by Bo Ejbjerg, is moving towards its final phase. In this study, MRI methodology is applied with special focus on small extremity joints, especially in the hand, which are often affected in rheumatoid arthritis. 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 methods; 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 unit can provide similar information as “conventional” expensive high-field MRI units.

In addition to research undertaken in the context of PhD projects, the rheumatology group participates in an important international collaboration concerning MRI definitions, scoring methods and validation in rheumatoid arthritis. In general MRI scoring methods of RA joints are insufficiently validated, and as a consequence of this an “OMERACT-MRI” study group have since 1999 worked on developing definitions of RA changes and on developing and testing scoring methods. OMERACT is an international forum with expertise in MRI in RA and in scoring methodology, which performs validation studies and seeks consensus within Outcome MEasures in Rheumatoid Arthritis Clinical Trials.

Finally, the group participates in a longitudinal multicenter 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.

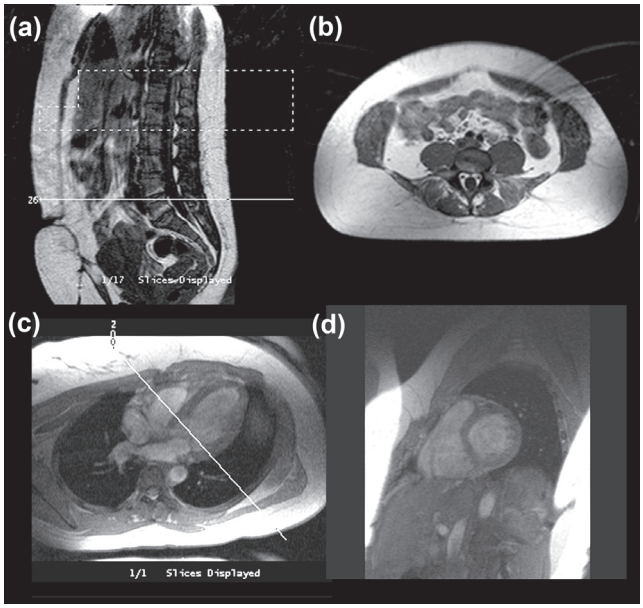
MR investigation of an 11 year old boy with pain in his lower leg after playing football. X-ray examination suggested the possible presence of a tumour. MR shows a stress fracture with callus formation.

Cardiac Function in Obesity and Disease

There is a growing worldwide epidemic of diseases driven by bad diet and lack of exercise. The influence of obesity on heart function is an area of research led by Dorthe Pedersen. Currently, two projects are being run, one concerning left ventricular function and geometry in obese subjects and potential anti-remodelling effects following weight loss. This project seeks to elucidate the influence of obesity and body composition on left ventricular mass and function and the influence of weight reduction. A second project is directed at investigating left ventricular mass and endothelial function in simple obesity. The project aims to elucidate the pathophysiology underlying increased left ventricular mass in simple obesity which can only be explained, in part, by increased blood volume and increased lean body mass. Thirty healthy obese subjects will be included and undergo cardiac and abdominal MRI, DEXA scans, endothelial functions test and blood samples once. The project is expected to begin early 2004, with an inclusion period of approximately one year.

Significant progress has been made in the first project and 58 obese patients have been included. All participants were examined at baseline, after 8 weeks and at one-year follow-up. All magnetic resonance data has been evaluated and data files from the first study have been received. Twenty-six healthy, normal weight control subjects will also undergo cardiac and abdominal MRI, DEXA scans, endothelial function test and blood samples. All MRI data will be evaluated here and serve as control reference to both projects. The inclusion of participants begins in January 2004.

Susette Krohn Therkelsen is also working in this area of research and has been using MRI to study 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. In collaboration with the cardiology laboratory at the University of Copenhagen, the study aims to measure right and left atrial as well as left ventricular dimensions and systolic function by 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. In addition a range of neurohumorale substances are measured along with atrial measures acquired with echocardiography and signal-averaged-p-wave duration, which is 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. Inclusion and examination of all 20 healthy volunteers, 60 patients with persistent atrial fibrillation and 20 with permanent atrial fibrillation is completed. Evaluation of the data is currently ongoing and the work will form the basis for a PhD thesis.



Study investigating the possible correlation between intra-abdominal fat and left ventricular mass.
(a). T1-weighted sagittal scout image indicating the level for image (b). T1-weighted 10 mm thick slice at the L4/L5 level. The image is used for evaluation of subcutaneous vs. intra abdominal fat deposit.
(c) Long-axis view of left ventricle in end-diastole where line indicate the level of image (d)
(d) Short-axis view of left ventricle in end-diastole by cinematographic gradient-echo technique. The entire left ventricle is covered by fifteen to seventeen 6 mm thick slices from which left ventricular geometry and function is estimated.

Other Activities

Consultation

The following staff members have acted as consultants for national and international agencies, boards and societies:

Lars G. Hanson:
- Reviewer for UK Mental Health Board

Terry Jernigan:
- Member of Special Emphasis Panel – Stress and Substance Abuse, Request for applications by National Institute for Drug Abuse, US National Institute of Health.
- Scientific reviewer for Brain Disorders and Clinical Neurosciences; Institutional Review Group; US National Institutes of Health
- Member of Editorial Advisory Boards: Neuropsychology; Psychiatry Research: Neuroimaging; Developmental Neuropsychology.

Olaf B. Paulson:
- Chairman, Department of Clinical Neuroscience and Psychiatry, University of Copenhagen
- Secretary of the Danish Society of Neuroscience
- Board Member of the Danish Alzheimer Association
- Chairman of the Research Committee of the Danish Alzheimer Association
- Member of the Danish Alzheimer Research Foundation
- Member of the European Federation of Neurological Societies Working Group on Brain Imaging
- Member of the Programme Committee for the Federation of European Neuroscience Society's annual meeting in Lisbon in 2004
- Member of the Executive Board of the European Society for Magnetic Resonance in Medicine and Biology
- Reviewer for the British Medical Research Council
- Reviewer for the Swedish Medical Research Council

Thomas Zoëga Ramsøy:
- Managing Editor: Science & Consciousness Review: www.sci-con.org
- Board member: Nordic Neuropsychological Society
- Administrator: Nordic Network for Consciousness Studies

Mikkel Østergaard:
- Consultant for the European Agency for the Evaluation of Medicinal Products (EMEA)
- Member of Editorial boards: Clinical Rheumatology; Scandinavian Journal of Rheumatology
- Member of Organizing Committee of the 10th Scientific Meeting of the European Society of Skeletal Radiology (ESSR), Århus 2003.
- Scientific committee membership: OMERACT-MRI in RA study group; OMERACT subcommittee on healing of erosions; EULAR-MRI in RA study group; OMERACT MRI in ankylosing spondylitis study group; OMERACT ultrasonography in arthritis study group; EULAR Working Party on Imaging in Rheumatology; EULAR Standing Committee on Clinical Studies incl. Therapeutic Trials (ESCISIT)

Journal Review

During 2003, DRCMR staff members have been reviewers for the following journals:

- Acta Neurologica
- Annals of the Rheumatic Diseases
- Arthritis and Rheumatism
- Cerebral Cortex
- Developmental Neuropsychology
- Journal of Cerebral Blood Flow and Metabolism
- Journal of Hypertension
- Journal of the International Neuropsychological Society
- Journal of Neurology
- Journal of Rheumatology
- The Lancet
- NeuroImage
- Neuropsychologia
- Neuropsychology
- Neurosciences
- Neurosurgery and Psychiatry
- Physics in Medicine and Biology
- Proceedings of the National Academy of Sciences
- Psychiatry Research: Neuroimaging
- Rheumatology
- Scandinavian Journal of Neurology
- Scandinavian Journal of Rheumatology
- Stroke

Training Activities

Received Training

The Centre strives to maintain a vigorous continuing-education program for staff at all levels within the Centre. Staff members are actively encouraged to attend relevant scientific and other professional conferences, and particular emphasis is given to sponsorship of Ph.D. students and junior staff at international symposia and workshops focusing on advanced theory and techniques.

Formal Instruction by DRCMR Staff

Throughout the year, many courses are organised and run locally for the benefit of staff, collaborators and other interested external researchers. In addition, staff contibute each year to a number of external training activities:

Outside Instruction

- Lars G. Hanson: Teaching, "Hospitalspraktik på MR-afdelingen", Technical University of Denmark, (coordinated locally by IK Andersen and LG Hanson)
- Lars G. Hanson: Teaching, Medical Imaging Course (MR Imaging), Technical University of Denmark, coordinated by J. Arendt Jensen.
- Lars G. Hanson: Teaching, Functional Imaging PhD Course, Rigshospitalet
- Karam Sidaros: Teaching, MR3 course at the University of Århus
- Karam Sidaros: External examiner, MR2 course at the University of Århus
- William Baaré: PhD course lecture: "Structural brain changes in schizophrenia: relationship to clinical symptomatology and cognitive functioning" at The University of Copenhagen, Graduate School of Neuroscience in collaboration with The National Danish Research Foundation: Center for Subjectivity Research. The Faculty of Health Sciences, Panum Institute, Course director: Josef Parnas.
- Lise Vejby søgaard: ("Hyperpolarisering") for "A kursus 'MR og metode", Dansk Selskab for Klinisk Fysiologi og NuklearMedicin (DSKNM) Bispebjeg Hospital.
- Trine Stavngaard: MR-course for physicians in nuclear medicine and clinical physiology: MRI of the lung with hyperpolarized 3-Helium, Dansk Selskab for Klinisk Fysiologi og NuklearMedicin (DSKNM) Bispebjeg Hospital.
- Trine Stavngaard: Course of lung physiology: Functional lung imaging, Rigshospitalet.

Individual Supervision by DRCMR Staff

- Lars G. Hanson: External evaluator, MR3 exam, University of Århus
- Lars G. Hanson: Supervision for physics colloquium, coordinated by S. Steenstrup, University of Copenhagen
- William Baaré: Research training provided to two undergraduate students: Elbrich Jagersma, Jon Wegner and one Ph.D. Student: K. Pagsberg
- Daniela Balslev: Co-supervisor together with Olaf B. Paulson for Stud. Med. Tanja Korfitsen OSVAL I project.
- Terry Jernigan: Supervision of 3 post-doctoral fellows; 5 Ph.D. students.
- Torben Lund: Supervision of 3 Master's thesis projects and 1 Ph.D. project
- Karam Sidaros: Supervision of 1 Master's thesis project.

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.

Awards

We are pleased to announce the following awards to DRCMR Staff in 2003:

- Professor Olaf B. Paulson received on February 25, 2003 the Lundbeck Foundation's 2002 Nordic Research Award for outstanding neuroscience research (see page 5).
- Daniela Balslev received the Mogens Fog Prize for the presentation: "The neural substrate of tool skills" at the 2003 Annual Meeting of the Danish Society for Neurology.
- Daniela Balslev received the Graduate Student Award for the paper "Tool proprioception at your fingertips, somatosensory representation for tool location" presented at the 4th Annual Meeting of the International Multisensory Research Forum.
- Mikkel Østergaard received the EULAR/Abbott Abstract Award 2003 for the abstract "Reducing costs, duration and invasiveness of Magnetic Resonance Imaging in rheumatoid arthritis by omitting intravenous gadolinium injection – does it affect assessments of synovitis, bone erosions and bone edema?" presented at the 4th Annual European Congress of Rheumatatology (EULAR), Lissabon, 2003.
- Mikkel Østergaard received the "Bevægeapparatets årtis Hæderspris 2003" awarded by the board of "Foreningen til Fremme af Bevægeapparatets årti" for musculoskeletal system research.

Publications

A large number of publications has resulted from the work performed by the research staff at the DRCMR during 2003. The most important of these publications are listed here according to category:

PhD Theses

- Marstrand J. Cerebral Hemodynamics measured with MR. Defended February 20th, 2003 at the University of Copenhagen, Faculty of Health Sciences.
- Szkudlarek M. Ultrasonography of small extremity joints in rheumatoid arthritis. Defended November 2003 at the University of Copenhagen, Faculty of Health Sciences.

Peer Reviewed Journal Articles

1. Andersen PB, Krabbe K, Leffers AM, Schmiegelow M, Holm S, Laursen H et al. Cerebral glucose metabolism in long-term survivors of childhood primary brain tumors treated with surgery and radiotherapy. J Neurooncol 2003; 62:305-313.
2. Baars BJ, Ramsoy TZ, Laureys S. Brain, conscious experience and the observing self. Trends Neurosci 2003; 26:671-675.
3. Bird P, Ejbjerg B, McQueen F, Ostergaard M, Lassere M, Edmonds J. OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging Studies. Exercise 5: an international multicenter reliability study using computerized MRI erosion volume measurements. J Rheumatol 2003; 30:1380-1384.
4. Conaghan P, Lassere M, Ostergaard M, Peterfy C, McQueen F, O'Connor P, Bird P, Ejbjerg B, Klarlund M, Shnier R, Genant H, Emery P, Edmonds J. OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging Studies. Exercise 4: an international multicenter longitudinal study using the RA-MRI Score. J Rheumatol 2003; 30:1376-1379.
5. Jernigan TL, Gamst AC, Fennema-Notestine C, Ostergaard AL. More "mapping" in brain mapping: statistical comparison of effects. Hum Brain Mapp 2003; 19:90-95.
6. Larsen R, Hilger KB, Skoglund K, Darkner S, Paulsen RR, Stegmann MB. Some issues of biological shape modelling with applications. Image Analysis, Proceedings, Lecture notes in computer science 2003; 2749:509-519.
7. Lassere M, McQueen F, Ostergaard M, Conaghan P, Shnier R, Peterfy C, Klarlund M, Bird P, O'Connor P, Stewart N, Emery P, Genant H, Edmonds J. OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging Studies. Exercise 3: an international multicenter reliability study using the RA-MRI Score. J Rheumatol 2003; 30(6):1366-1375.
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10. Olsen DB, Langkilde AR, Orngreen MC, Rostrup E, Schwartz M, Vissing J. Muscle structural changes in mitochondrial myopathy relate to genotype. J Neurol 2003; 250:1328-1334.
11. Ostergaard M, Hansen M, Stoltenberg M, Jensen KE, Szkudlarek M, Pedersen-Zbinden B et al. New radiographic bone erosions in the wrists of patients with rheumatoid arthritis are detectable with magnetic resonance imaging a median of two years earlier. Arthritis Rheum 2003; 48:2128-2131.
12. Ostergaard M, Peterfy C, Conaghan P, McQueen F, Bird P, Ejbjerg B et al. OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging Studies. Core set of MRI acquisitions, joint pathology definitions, and the OMERACT RA-MRI scoring system. J Rheumatol 2003; 30:1385-1386.
13. Peterfy C, Edmonds J, Lassere M, Conaghan P, Ostergaard M, McQueen F, Genant H, Klarlund M, Ejbjerg B, Stewart N, Bird P, Shnier R, O'Connor P, Emery P. OMERACT Rheumatoid Arthritis MRI Studies Module. J Rheumatol. 2003;30:1364-5.
14. Posthuma D, Baare WF, Hulshoff Pol HE, Kahn RS, Boomsma DI, de Geus EJ. Genetic correlations between brain volumes and the WAIS-III dimensions of verbal comprehension, working memory, perceptual organization, and processing speed. Twin Res 2003; 6:131-139.
15. Sellebjerg F, Jensen CV, Larsson HB, Frederiksen JL. Gadolinium-enhanced magnetic resonance imaging predicts response to methylprednisolone in multiple sclerosis. Mult Scler 2003; 9:102-107.
16. Stegmann MB, Ersboll BK, Larsen R. FAME--a flexible appearance modeling environment. IEEE Trans Med Imaging 2003; 22:1319-1331.
17. Stegmann MB, Larsson HBW. Motion-compensation of cardiac perfusion MRI using a statistical texture ensemble. Functional Imaging and Mod-

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21. Szkudlarek M, Court-Payen M, Strandberg C, Klarlund M, Klausen T, Ostergaard M. Reply. Eur Radiol 2003.

Peer Reviewed Journal Articles Omitted from The Previous Years' Annual Reports

1. Sellebjerg F, Jensen J, Jensen CV, Wiik A. Expansion of CD5 - B cells in multiple sclerosis correlates with CD80 (B7-1) expression. Scand J Immunol. 2002; 56:101-7.
2. Sellebjerg F, Giovannoni G, Hand A, Madsen HO, Jensen CV, Garred P. Cerebrospinal fluid levels of nitric oxide metabolites predict response to methylprednisolone treatment in multiple sclerosis and optic neuritis. J Neuroimmunol. 2002; 125:198-203.
3. Sorensen TL, Sellebjerg F, Jensen CV, Strieter RM, Ransohoff RM. Chemokines CXCL10 and CCL2: differential involvement in intrathecal inflammation in multiple sclerosis. Eur J Neurol. 2001; 8:665-72.

Book Chapters

- Jernigan TL. Anatomic Neuroimaging. In: Fogel B.S, Schiffer RB, Rao SM, editors. Neuropsychiatry. Baltimore MD: Lippincott Williams, 2003: 44-62.

Conference Proceedings

The DRCMR was represented at 18 meetings and conferences during 2003 with 39 abstracts.

- The Eleventh Scientific Meeting of the International Society for Magnetic Resonance in Medicine (10 abstracts)
- The 33rd Annual Meeting of the Society for Neuroscience (3 abstracts)
- The 9th Annual Meeting of the Organization for Human Brain Mapping (6 abstracts)
- The Annual Meeting of the Danish Society for Neurology (1 abstract)
- The Annual Meeting of the International Multisensory Research Forum (1 abstract)
- The 55th Annual Meeting of the American Academy of Neurology (1 abstract)
- The First Congress of the International Society for Vascular Behavioural and Cognitive Disorders (4 abstracts)
- The Seventh Congress of European Federation of Neurological Sciences (1 abstract)
- The International Congress on Schizophrenia Research (2 abstracts)
- The 20th Annual Meeting of the European Society of Magnetic Resonance in Medicine and Biology (1 abstract)
- The ISMRM Workshop on MR Technology to Assess MS Pathology In Vivo (1 abstract)
- The Annual Meeting of the American Psychosomatic Society (1 abstract)
- The 7th Annual Meeting of the European Federation of Neurological Societies (1 abstract)
- The European Congress of Obesity (1 abstract)
- The Sixth Annual International Conference on Medical Image Computing and Computer Assisted Intervention (1 abstract)
- The XIX Nordic Congress of Cardiology (1 abstract)
- The 24th Danish NMR Discussion Group Meeting (2 abstracts)
- The Sixth Annual Scientific Session of the Society of Cardiovascular Magnetic Resonance (1 abstract)

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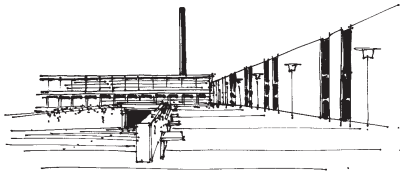

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