Welcome to the Exciting World of CMIV
Annual Scientific Report 2013
Dissertations
During 2013 several of the CMIV PhD students have finished their studies and defended their dissertations.

Equipment
Through unique collaborations with the industry it is possible for CMIV to always have the latest and most advanced equipment.

Organization
CMIV is governed by its Board of Directors, with representatives from academia, health care and industry.

Publications
The CMIV researchers have published numerous articles and conference proceedings in the past years.

Annual Accounts
Since CMIV is part both of the university and the county council the finances are also split in two parts.

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CMIV 2002-2012
When CMIV was initiated, the vision was to gather all the components of medical imaging and visualization in one place.

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CMIV Imaging Chain
CMIV conducts focused front-line research within multi-disciplinary projects providing solutions to tomorrow’s clinical issues.

Flagship Projects
During 2013 the CMIV scientific council decided to identify the three CMIV projects which together best represent the broad and multi-disciplinary research at CMIV. The flagship projects were chosen through a nomination procedure and the resulting projects complement each other in modalities, project stage and medical area.

Research Projects
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IT architecture, as well as a prioritized requirement set for corresponding IT tools. In October 2013 the first Nordic Symposium in Digital Pathology was arranged by CMIV in Linköping. Now the expectations of the second symposium in 2014 are high.

One example of the CMIV research’s importance for clinical routine is quantitative MRI imaging of “neuro” examinations that has moved into the radiology department. It is now an important link in the daily clinical workflow.

The result from all on-going activities and the added focus areas have rapidly gained wide attention and the unique patient-oriented clinical research now attracts researchers and clinicians from around the world.

The growing number of researchers and projects and the inflow of grants challenge the human and technical infrastructure. The planning and building of CMIV 3.0 has started and moving into new premises in 2015 can be a stairway to heaven for CMIV.

I am looking forward to the continued collaboration with the outstanding individuals at CMIV and the unique twinning of academic disciplines with great confidence.

ANDERS PERSSON, DIRECTOR OF CMIV

“Multi-disciplinary collaboration and a strong link to the clinic is the key to our success in medical imaging research and contribution to improved patient care.”

ANDERS PERSSON
When CMIV was initiated, the vision was to gather all the components of medical imaging and visualization in one place. And at the same time create a whole new type of research environment where scientists, technicians and medical doctors could work close together with immediate access to the patients. A place where there was no distance between research and clinical needs.

Launch of a new method for 3D virtual autopsies with a CT scan that only takes a few seconds – with no need to cut the body open. The method not only moves forensic science forward, the knowledge gained from working with high volume and high-resolution 3D images also benefits living patients. Plans for a new center start to take shape.
No Windows, an Amazing View

Four square meters and no windows, our first office was nothing to boast about. But when you are looking at CT images that in a short period of time will increase the number of coronary artery exams tenfold, the view is still pretty amazing.

Building with No Walls

When you’re first in the world to build a center that tears down traditional boundaries and allows people, ideas, creativity and production to flow freely, there are no blueprints or models to follow. Still progress is swift and the only thick walls in sight surround the CT and MRI scanners.
The new MRI scanner is in place and synthetic MR takes off. Synthetic MR is a software-based technology that reduces the examination time from one hour to a few minutes, greatly increasing patient comfort. Previously undetected conditions can also be visualized.

Functional magnetic resonance imaging fMRI is becoming increasingly important in brain surgery and the fight against neurodegenerative disease. A new toolbox helps detect areas of neural activity in the brain. Professor Anders Ynnerman is awarded the Akzo Nobel Science Award for his epoch-making contributions to visualization. SCAAR, a national register for heart patients, is also founded.
With so many exciting research projects underway, there’s been no time for the official opening of the center until now. The virtual theatre makes a grand entrance but it is the new Dual Source CT that steals the show. It can scan any beating heart, at any rate, allowing cardiovascular research to take a big leap forward.

**2006**

**A Big Leap for the Heart**

A New Method

Breakthrough for a new method rendering extremely large data volumes that allow immediate display of high-resolution, full-body scans. Director Anders Persson receives the Lennart Nilsson Award for revealing the hidden mysteries of the body and producing images that can be understood and interpreted by laymen and experts alike.

**2008**

**Hidden Mysteries Revealed**
Surgical Knife Replaced by Fingertips

The Virtual Autopsy table is launched dispensing with the need for invasive surgical procedures. Explore the inside of the human body in 3D using only your fingertips. CMIV is also one of the first centers in the world to install the Somatom Definition Flash. This year CMIV also wins the Athena Award for best clinical medical research in Sweden.

Exposing the Culprit

An advanced method based on MR images shows the quantities and distribution of subcutaneous and visceral fat in the body – the latter responsible for many modern day illnesses. This can prove helpful in understanding and treating endocrine system disorders. Professor Anders Ynnerman is honored with IVA’s gold medal. CMIV is first in Scandinavia to install a new type of 3 Tesla MR scanner.
The Bloodless Blood Trail

New method to measure and visualize blood flow with MR paves the way to replacing invasive methods. After more than ten years of continuous improvements, the CT radiation dosage is lowered by as much as 70%. Awards this year include the Knowledge Award, and the Thorax category in Siemens International CT Image Contest which is given to Petter Quick while ten out of the eleven Swedish papers accepted at the RSNA are submitted by CMIV.

Branching Out to Pathology

Pathology is one of the most recent scientific fields being digitalized to further the delivery of personalized medicine. The CMIV article on Parametric fMRI Analysis is one of the most popular downloads from the high impact journal Neuroimage.
2013 has been an eventful year at CMIV with many publications, awards and research grants. The research has blossomed and resulted in exciting meetings and conferences. Here you will find the highlights of the year.

Professor Anders Persson is Honored with the Combined Royal Colleges Award 2013

The Combined Royal Colleges medal is awarded each year for an outstanding contribution to the advancement of medical photography or the wider field of medical imaging. This year Professor Anders Persson, head of CMIV, was honored with the award. He received the medal for pioneering work in medical imaging. The medal was originally established in 1938 by the Royal Photographic Society in collaboration with the Royal College of Physicians of London, the Royal College of Surgeons of England and the Royal College of Obstetricians and Gynaecologists. The award ceremony was held at the Royal Society in London.

CMIV PhD Student Conference

This year the CMIV PhD conference was held at Storgården in Rimforsa. During the conference the PhD students presented their project in poster sessions, where projects and ideas were discussed with both other PhD students and senior researchers. The conference also included a workshop where mixed groups brainstormed about the future development of CMIV and ended with a valuable session on writing popular science with Monica Westman Svenselius, editor at Linköping University.
The Knut and Alice Wallenberg Foundation has Granted a CMIV Project With Four Year Funding

**THE CMIV PROJECT** “Seeing organ function – patient specific image data”, is one of 27 Swedish research projects with potential of new scientific breakthroughs, which together are granted over 770 million SEK by Knut and Alice Wallenberg Foundation. The CMIV project, with professor Anders Ynnerman as principal applicant has been granted with four year funding of 24.5 million SEK. Co-applicants are Orjan Smedby, Timo Ropinski, Magnus Borga, Tino Ebbers, Maria Engstrom, Markus Heilig, Matts Karlsson, Hans Knutsson, Peter Lundberg, Claes Lundstrom, Anders Persson and Karin Wardell.
3D Technologies
Reveal Hidden
Egyptian Treasures

During 2013 CMIV participated in a project together with the Interactive Institute Swedish ICT at Visualization Center C in Norrköping and Autodesk to create a digital copy of the mummy Neswaiu from Medelhavsmuseet in Stockholm. The result is now presented in a new exhibition where the visitors can unwrap and explore the mummy using an interactive touch table.

The mummy has been captured digitally in 3D using a combination of dual energy computed tomography (CT) and 3D photogrammetry using the Autodesk ReCap solution, resulting in a complete 3D model of the mummy, not just for the outside but also on the inside.

Apart from Neswaiu also the rest of the mummies at Medelhavsmuseet were scanned at CMIV. The novel CT methods developed at CMIV allowed a more detailed scanning of the mummies than has ever been possible before and therefore revealed details that were not previously known. The images present a unique possibility for the historians to explore the Egyptian culture without disturbing the mummies.
Nature Publication

During Spring 2013 a CMIV research group published a study in Nature Medicine. The aim of the study was to investigate which types of brown fat there are in humans. The results show, unlike earlier studies, that there are two types of brown fat in humans. Evidence for the existence of beige brown fat has been presented in earlier studies. However, this study also found evidence of classical brown fat, a type of brown fat that until now only was believed to be present in rodents. The research is a collaboration between scientists from Sahlgrenska Academy in Gothenburg and from CMIV in Linköping. At CMIV a magnetic resonance camera is used to localize the brown fat. The image is used as guidance when extracting the tissue samples, which are then analyzed on a molecular level in Gothenburg.

Anders Persson Receives Award at Röntgenveckan 2013

Anders Persson received the second place award for best independent presentation at Röntgenveckan 2013. The subject of his presentation was "High frequency of misplaced catheters in the thoracic region of patients treated and deceased in hospital care".

Swedish Research Council Grant to CMIV Researcher

The Swedish Research Council grants CMIV researcher Petter Dyverfelt four million SEK during four years for his project “A paradigm shift in the evaluation of vascular disease: Quantification of hemodynamic markers with novel 4D magnetic resonance flow imaging”.

This project will develop new techniques for measuring blood flow properties using 4D magnetic resonance flow imaging. Most vascular diseases are related to atherosclerosis. Atherosclerosis alters the blood flow mechanics which in turn damages the vessels and worsens the vascular disease. Finding new ways to monitor the blood flow will increase the understanding of the relation between blood flow and vascular disease and open up for new diagnostic possibilities.
CMIV IMAGING CHAIN

CMIV conducts focused front-line research within multidisciplinary projects providing solutions to tomorrow’s clinical issues. The mission is to develop future methods and tools for image analysis and visualization for applications within health care and medical research.

CMIV has a unique constellation in which research in the university provides the opportunity for clinical benefit in the county council while the industry benefits nationally and internationally. The activities aim to combine different demands were the university seeks publications in high quality journals and the county council wishes that the research and development comes to patient benefit. CMIV’s organization centrally located within the university hospital creates conditions that combine these requirements. Results from basic research in universities can be utilized in clinical research which can then result in scientific publications, and patient cure.

The research projects at CMIV are all part of the imaging chain. Projects move dynamically through the chain and researchers from different disciplines work together to reach the goal of patient benefit. Focused research and development in all steps of the chain is important to continue to improve quality of care.

Information is gathered using novel imaging equipment

Raw data is processed using complex calculations and algorithms
Important findings are visualized in a comprehensive way.

Images and findings are used in patient care.
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PROJECT NAME
Assessment of cardiovascular blood flow using 4D flow MRI

PROJECT LEADER
Tino Ebbers, Department of Medical and Health Sciences, Division of Cardiovascular Medicine & Department of Science and Technology, Division of Media and Information Technology

MAIN PROJECT PARTICIPANTS
Senior research leaders: Tino Ebbers, Carl-Johan Carlhäll, Jan Engvall, Petter Dyverfeldt
Post Doc: Jonas Lantz
PhD students: Sven Petersson, Jonatan Eriksson, Belén Casas Garcia, Mariana Bustamante

GRANTS
Swedish Research Council 2011-2013
European Research Council 2013-2017

KEY PUBLICATIONS
Assessment of Cardiovascular Blood Flow Using 4D Flow MRI

Despite the primacy of flow, cardiac diagnostics still rely almost exclusively on tools focused on morphological assessment. Flow characteristics are often assumed rather than measured directly. Suitable non-invasive tools for characterizing and measuring flow dynamics are needed to push our medical effectiveness to the next level.
The objective of this project is to develop the next generation of methods for the non-invasive quantitative assessment of cardiac diseases and therapies by focusing on blood flow dynamics, with the goals of earlier and more accurate detection and improved management of cardiac diseases. The project has developed a method for flow quantification using MRI which allows for simultaneous measurement of time-resolved, three-dimensional (time + 3D = 4D) blood flow velocity and turbulence intensity. This method reveals blood flow patterns in the heart and the large vessels.

“We are now working on optimizing the accuracy, measurement time, and robustness of 4D flow MRI and have good hope of bringing the technique to clinical use in the near future.”

Cardiovascular blood flow is still to a large extent unknown. In order to define relevant parameters, development of analysis and visualization approaches and studies of normal and abnormal blood flow have to be performed in chorus. Studying cardiovascular blood flow dynamics in patients and healthy subjects will improve our understanding of the roles of flow dynamics in health and disease, leading to improved cardiac diagnostics, novel assessments of pharmaceutical, interventional, and surgical therapies, and promoting exploration of new avenues for management of cardiac disorders.

Tino has studied blood flow with magnetic resonance imaging (MRI) for many years. In the beginning the analysis was time-consuming with low quality images and not suitable for a clinical setting.

“The magnetic resonance technique has advanced in recent years and it is now possible to analyse blood flow with high quality images fast enough for clinical purposes, continues Tino.

“At CMIV, we are one of the leading centres in the world when it comes to imaging blood flow dynamics in the heart.”

PROFESSOR TINO EBBERS
PROJECT NAME
Imaging of Brown Adipose Tissue

PROJECT LEADER
Magnus Borga, Department of Biomedical Engineering, Division of Medical Informatics

MAIN PROJECT PARTICIPANTS
Anders Persson, Olof Dahlqvist Leinhard, Thobias Romu, Nils Dahlström

GRANTS
KAW 2012-2017

KEY PUBLICATIONS

Imaging of Brown Adipose Tissue

Through a unique collaboration between researchers at CMIV and Sahlgrenska University Hospital the role of brown fat is unraveled. The vision is to find a way to reduce obesity related health problems.

**THE GENETIC COMPOSITION** of brown fat has been studied for several years at Sahlgrenska University Hospital. But it was not until the Sahlgrenska research group met the CMIV researchers Magnus Borga and Olof Dahlqvist Leinhard that the project reached new levels. Magnus and Olof have developed a method to distinguish fat from water in magnetic resonance imaging (MRI) a method applicable on localizing brown fat deposits in the body. The two research groups complement each other in a unique manner.

"We both bring competences to the project that the other group lack. The result is a fruitful collaboration for both groups," says Magnus Borga, Professor
in Medical Informatics and project leader of “Imaging of Brown Adipose Tissue”.

The human body contains different types of adipose (fat) tissue that play different roles in the metabolism. While white adipose tissue (WAT) acts as energy buffer, brown adipose tissue (BAT) converts stored energy (WAT) directly into heat that keeps us warm at least as infants and is also most likely of importance to us for longer than that.

Today’s sedentary lifestyle has generated a cluster of obesity related health problems commonly referred to as the metabolic syndrome. A positive energy balance will eventually lead to insulin resistance and ultimately type 2-diabetes, which in turn may cause e.g. heart attacks, stroke, kidney problems and also many types of cancers.

“The way we eat, we supply more energy than the body can use. If there was a way to increase the energy consumption without work it would revolutionize health care, continues Magnus.

In recent years, Brown Adipose Tissue (BAT) has emerged as a highly interesting object of study in the search for future solutions to many of the major health care challenges related to the metabolic syndrome. Also, recent publications have shown relations between BAT and osteoporosis and sarcopenia (age related loss of muscle mass).

The lack of efficient tools for studying BAT in vivo, however, is a serious limitation hindering large clinical studies related to BAT. Until recently the only available method for in vivo imaging of BAT was positron emission tomography, which requires injection of a radioactive substance in the subjects, clearly limiting its use in large prospective studies.

The overall aim of this project is therefore to develop and evaluate accurate automatic methods for high-resolution in vivo imaging, classification and quantification of BAT using quantitative magnetic resonance imaging and dual energy computed tomography.

–Manual assessment of the BAT images is extremely time consuming, making larger studies impossible. Also, the reproducibility is limited in manual work. Computers on the other hand are very useful when it comes to reproducibility and speed, says Magnus.

In parallel with the method development the project also studies the properties of brown fat and the possibilities to activate and even increase the amount of brown fat.

–We have shown that it is possible to alter the constitution and amount of brown fat in rats by exposure to low temperatures. We are now proceeding with studies on humans and the results look promising, Magnus explains.

The studies of brown fat involve professionals from multiple disciplines, patient recruitment and advanced equipment. Without a center as CMIV the project would be impossible to realize.

“If there was a way to increase the energy consumption without work it would revolutionize health care.”

PROFESSOR MAGNUS BORGÅ
The image illustrates how BAT can be detected in the neck and shoulders using MRI that can quantify the amount of fat and water in the tissue. WAT contains almost 100% fat and is indicated in yellow. BAT contains approximately 50% water and is indicated in red.
PROJECT NAME
Optimized flows and IT tools for digital pathology

PROJECT LEADER
Claes Lundström, Department of Science and Technology, Division for Media and Information Technology

MAIN PROJECT PARTICIPANTS
Senior research leaders: Claes Lundström, Peter Lundberg, Stergios Kechagias, Karin Wårdell, Daniel Fornberg, Nastaran Monsef, Ebo de Muinck, Per Carlsson, Lars-Åke Levin, Martin Hallbeck
PhD students: Kavitha Shaga Devan, Jesper Molin, Mattias Aronsson
Main clinical leads: Sten Torstenson, Janos Vasko, Lars Lundgren, Helen Richard, Edyta Johansson

GRANTS
VINNOVA 2013-2014

KEY PUBLICATIONS
Optimized Flows and IT Tools for Digital Pathology

In digital pathology the histology samples are scanned to create digital images of the tissue, which can be analyzed on a computer screen. While the pathologist is still responsible for the evaluation and diagnosis, the digital environment is a valuable tool for image analysis to detect, measure and grade diagnostic findings.

**Diagnostic Pathology is** of crucial importance for health care, especially cancer care. Pathologists analyze tissue from the patient to determine its characteristics (histology). This knowledge is used to find the correct diagnosis and therapy. Due to lack of pathologists the waiting time for the pathology report is often long, with an anxious wait and delayed therapy for the patient as a result.

Linköping and Kalmar are world pioneers in digitization of the histology samples. The work was initiated by pathologist Sten Thorstenson as a way to deal with neck problems caused by
tool for image analysis to detect, measure and grade diagnostic findings. This possibility is an advantage that is expected to have enormous impact. The CMIV research agenda in digital pathology tackles image analysis challenges such as correlating findings between radiology and histology in liver biopsies and carotid artery plaques, as well as breast cancer histological grading and lung cancer cytology screening. Furthermore, health economic effects are investigated and human-computer interaction aspects are explored.

Analyzes of the pathology department show that digitization of the workflow from referral, finished preparation and scanning of samples to the pathologist’s workstation may result in a better overview of the workload, less administration and shorter turnaround times. Digital pathology also entails unique opportunities for collaborations between hospitals both regionally and worldwide as the digital samples can be sent instantly.

“We believe that digitization of the pathology workflow has the potential to increase both efficiency and quality of care.”

ASSISTANT PROFESSOR
CLAES LUNDSTRÖM

Claes Lundström is the project leader of the CMIV project “Optimized flows and IT tools for digital pathology”. The project aims to design an optimal workflow for digitized pathology, to develop a prototype of the pathologist’s workstation and to create a platform for research and education within the field of digital pathology. CMIV heads the project consortium, which consists of nine county councils/care providers, the medical IT company Sectra and the industrial research institute Swerea IVF. The main funding source is VINNOVA (the Swedish Innovation Agency). CMIV efforts within the project are primarily focused on a number of research initiatives.

Today, most pathologists analyze histology samples in a microscope. In digital pathology the histology samples are instead scanned to create digital images of the tissue, which can be analyzed on a computer screen.

– A common delusion is that digitization means replacing the pathologists with computers. This is not an option, a machine can never have the diagnostic responsibility, explains Claes.

While the pathologist is still responsible for the evaluation and diagnosis, the digital environment is a valuable

hours in the microscope. Now digitization entails wider advantages.

– We believe that digitization of the pathology workflow has the potential to increase both efficiency and quality of care, says Claes Lundström assistant professor at Linköping University.

In order to realize this potential, cross-disciplinary research efforts are needed that can combine clinical expertise with knowledge in image analysis and human-computer interaction.

– To digitize medical images is nothing new, continues Claes. The radiology department went through a similar revolution 15 years ago and now no one looks back.

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The research within CMIV is based on innovations in medical image science and visualization. Future directions will strengthen the interdisciplinary approach to enhance the possibilities of image-based diagnosis and treatment. At CMIV research is conducted within several medical problem areas, combining a number of technologies for novel application within clinical routine, medical research and dissemination of information. Here you will find a selection of the research projects at CMIV.
THE MAIN FUNCTION OF our arteries is to distribute blood flow to the organs of our body. Arteries can sometimes become constricted and this may affect the blood flow to downstream vasculature. Today, the risk that a constriction affects the blood flow is assessed based on the size of the constriction. It has been known for quite some time that abnormal blood flow is both an indicator of arterial disease and a risk factor for disease progression. Unfortunately, appropriate tools for measuring these flow effects in humans have been lacking. Consequently, we still use measures such as the size of a constriction to assess the status of the blood flow. The purpose of this project is to develop methods for the determination of some of the most important aspects of blood flow.

Many arterial diseases are related to atherosclerosis. The atherosclerotic disease process starts when we are young with deposition of fat in the arterial wall. This early process does not affect the size of our arteries but it makes them stiffer. Arterial stiffness alters the pressure wave that the heart generates when it contracts. Altered pressure wave is a strong marker of several cardiovascular diseases. Today’s methods can only measure this in a few arteries, and the information that can be obtained represents an average. However, arterial stiffness varies within an artery. If we could measure those variations we could increase and improve the clinical applicability of pressure wave measurements.

The more advanced stages of atherosclerotic disease are characterized by large deposits of fat in the arterial wall. These deposits, plaques, constrict the arterial lumen. The plaques may rupture, which can cause stroke or a heart attack. The blood flow in constricted arteries can become turbulent. Several studies indicate that turbulent forces increase the vulnerability of the plaques and their risk of rupture. Today’s techniques for assessing the effects of flow on the vessel wall focus on forces that exist in normal...
blood flow in healthy arteries. However, methods that permit assessment of the impact of turbulent forces do not exist. We will develop methods for the determination of pressure wave velocity and the effects of turbulent flow on the vessel wall. In achieving our goals we plan to use an advanced magnetic resonance imaging (MRI) technique referred to as 4D flow MRI, which permits comprehensive assessment of time-varying three-dimensional (time + 3D = 4D) blood flows. This technique has the potential to unveil information about key aspects of blood flow. However, dedicated research efforts are needed to realize this potential.

Additionally, we want to be able to measure these aspects of blood flow in the coronary arteries, where many of the most dangerous vascular diseases happen. 4D flow MRI is today used primarily to study blood flow in the heart and the greater vessels. We will improve the technique for application in coronary arteries. Successful application of MRI in the coronary arteries requires that the motion of the arteries due to breathing and cardiac contraction be taken into account. If this is not done the images get blurry.

Being able to measure aspects of blood flow that have previously not been measurable will lead to an increased understanding of the interrelationship between blood flow and vascular disease. It will also open up for new ways to assess and risk-stratify vascular disease. This will offer improved care for the vast population of patients with vascular disease and financial benefits for the health care system.

4D flow MRI visualization of blood flow in the left and right carotid bifurcation (the forking of the arteries supplying the head and neck with oxygenated blood) of a normal volunteer using streamlines color-coded by flow speed. The carotid bifurcation comprises the common (square), internal (diamond) and external (asterix) carotid arteries. Arrow: Slow recirculating flow in the carotid bulb.
INVESTIGATIONS as well as the therapeutic measures undertaken are costly and carry a considerable risk for the patient. The response of chronically ischemic myocardial cells to therapy depends on many factors. Little is known, however, about the exact relation between these pathophysiologic factors and functional recovery of the myocardium for a given therapeutic strategy.

Therefore, the purpose of DOPPLER-CIP is to determine the optimal noninvasive parameters (myocardial function, perfusion, ventricular blood flow, cell integrity) for the prediction of left ventricular morphologic and functional remodeling in chronic ischemic patients.

DOPPLER-CIP is a multi-center observational study. All patients with ischemic heart disease included in this study undergo at least two noninvasive stress imaging examinations at baseline. The presence/absence of investigations as well as the therapeutic measures undertaken are costly and carry a considerable risk for the patient. The response of chronically ischemic myocardial cells to therapy depends on many factors. Little is known, however, about the exact relation between these pathophysiologic factors and functional recovery of the myocardium for a given therapeutic strategy.

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DOPPLER-CIP is a multi-center observational study. All patients with ischemic heart disease included in this study undergo at least two noninvasive stress imaging examinations at baseline. The presence/absence of
left ventricular (LV) remodeling will be assessed after a follow-up of 2 years, during which all cardiac events will be registered.

After completion, DOPPLER-CIP will provide evidence-based guidelines toward the most effective use of cardiac imaging in the chronically ischemic heart disease patient. The study will generate information, knowledge, and insight into the new imaging methodologies and into the pathophysiology of chronic ischemic heart disease.

In Linköping, almost all 192 patients have undergone at least three stress imaging tests. We will have an excellent opportunity to compare the different modalities in our local material. The patients in this study have helped us develop new MRI-based methods for the measurement of wall motion abnormalities and for 3D-visualization of intracardiac blood flow.
Atherosclerotic coronary artery disease is caused by changes to the wall known as plaque. The plaque consists of deposits of cholesterol, cells and calcium sometimes causing obstruction to the coronary flow. The diagnosis of coronary artery disease rests on the visualization of atherosclerotic plaque or limitations to flow. Invasive investigation should be reserved for patients with a high likelihood of significant disease. Various exercise tests are employed to uncover effects of obstruction that may be silent at rest. Myocardial blood flow may be visualized in different ways, most often using a gamma camera to trace the myocardial uptake of injected markers. The relationship between myocardial blood flow and the tracer molecules has been shown to be fairly linear within the range of normal resting coronary flow while uptake rolls off with increasing flow.

An alternative approach to calculating myocardial blood flow could be to use effects of angiographic contrast media in cardiac computed tomography (CT). Recent improvement in CT technology with higher temporal resolution and more advanced software has motivated a renewed interest in this method. There are a number of critical prerequisites for using this approach: the scanning of the left ventricle must be fast to be able to detect the short-lived phase of increase in attenuation that comes with the wash-in of contrast, the X-ray detector has to be large enough to allow coverage of the entire heart and reconstruction and evaluation of the recording need to be fast and accurate. Ideally, the contrast medium itself should not induce any change in coronary flow. A number of smaller studies have been published but the method still needs extensive validation.
before being incorporated into clinical practice.

Thus, the purpose of this study was to evaluate the variation in blood flow in cardiac segment determined to be normal or abnormal according to the gamma camera result. In addition, we wanted to compare CT blood flow values obtained with manual delineation of the cardiac wall with those obtained with automated software.

A positive but moderate correlation was found between CT and the gamma camera. Large variations in CT blood flow were detected which suggests that a single cut-off value for stress myocardial blood flow is inadequate to detect ischemic segments.
Magnetic Resonance and Carotid Ultrasound Observations

**Worldwide, the most common cause** of death is cardiovascular disease and the dominant cause of cardiovascular disease is atherosclerosis. Atherosclerosis is caused by accumulation of fat, primarily cholesterol in the wall of arteries. When the fat builds up in the arterial wall it causes thickening of the vessel wall and the thickened area bulges out into the vessel, causing narrowing of the artery. The areas with fat accumulation are called atherosclerotic plaques. Sometimes these plaques rupture causing a blood clot to form at the site of rupture. The clot completely occludes the artery and stops blood flow. This causes a heart attack if it happens in the arteries of the heart or a stroke if it happens in the arteries feeding the brain.

We have developed an imaging method to identify plaques that are at high risk of rupture. We anticipate that this method will allow us to identify patients with rupture prone plaques and treat them before they suffer from a heart attack or stroke. The method uses magnetic resonance imaging (MRI) and can measure how much fat and blood there is inside atherosclerotic plaques (Figure 1). Plaques with a high fat content and a lot of blood are

![Magnetic resonance image of a patient with atherosclerotic plaque in both carotid arteries. The plaque has caused a severe narrowing in the right carotid artery (arrow). The amount of fat in the plaques is shown in yellow and the amount of blood is in red.](image)

**Project Name**
Magnetic Resonance and Carotid Ultrasound Observations (MR CARUSO)

**Project Leader**
Ebo de Muinck, M.D., Ph.D, Department of Medical and Health Sciences, Division of Cardiovascular Medicine

**Main Project Participants**
Marcel Warmtes, Petter Dyverfeldt, Johan Kihlberg, Rodrigo Moreno, Daniel Forssberg, Toste Länne, Anne-Marie Landtblom, Darren Treanor

**Grants**
Swedish Heart and Lung Foundation

**Key Publications**
at higher risk of rupture since fat and blood increase inflammation inside a plaque and inflammation leads to rupture.

We also measure turbulence in the blood that flows through the arteries, which is a third factor that can contribute to plaque rupture. Atherosclerotic plaques lead to narrowing of arteries and when blood flows through such a narrowing there is a lot of turbulence immediately behind the narrowing. Turbulent blood flow acts on the vessel wall and increases inflammation inside the plaque, thereby increasing the risk of plaque rupture (Figure 2).

In this project we study patients who are scheduled for surgical removal of atherosclerotic plaque that has caused a narrowing in one of the arteries that leads to the brain (Figure 3). This surgical procedure is called ‘endarterectomy’. Before surgery, the patients undergo MRI of their carotid arteries and we measure the amount of fat and blood inside the plaque that is to be removed as well as the amount of turbulence caused by the narrowing. After surgery we study the plaque in a microscope. For this purpose the plaque is cut into a series of very thin sections and the amount of fat and blood as well as the amount of inflammatory cells is measured on each section. Then a 3D reconstruction of the plaque is generated based on these sections. This 3D rendering is compared with the MRI images by overlaying images.

We anticipate that the current study will result in an imaging method that will help identify patients with atherosclerotic plaques that are at high risk for rupture. These patients can then be treated to prevent plaque rupture and stroke.
Computer-Assisted Coronary CT Angiography Analysis

DESPITE WORLDWIDE EFFORTS to investigate and control cardiovascular risk factors, coronary artery disease remains the primary cause of death, in particular among Western nations. Examination of the coronary arteries was conventionally done by selective coronary angiography (CA) which requires flexible tubes to be inserted into the coronary vessels. This is a costly and invasive procedure and may cause severe complications in some patients. A new imaging technique, coronary computed tomography angiography (CCTA), which collects computed tomography (CT) scans after injecting contrast agent into a vein in the arm, is rapidly replacing the conventional exam because of the ability to reduce risk and discomfort to the patient. However, giving diagnosis based on the hundreds of images generated from the CT scan for each patient is not as easy as reading the CA images. It requires the radiologists to go through all slices while building an overview of the arteries based on their subjective observation instead of quantitative measurements. The aim of this work is to develop and evaluate a computer
tool that uses intuitive 3D visualization technique to present the coronary arteries. The tool uses the images from the new CCTA method and presents them in a manner similar to traditional catheter angiography. It also provides automatic quantification tools to measure the reduction of the vessel lumen.

In the first part of the project, a new image segmentation algorithm, called “virtual contrast injection” was developed based on the gray-scale fuzzy connectedness theory. It was used to separate the vessels from the heart chambers and find their centerlines. To build a fully-automatic workflow, additional methods such as finding the heart in a 3D volume were developed and integrated into an open source medical image visualization software, OsiriX.

To test the diagnostic accuracy of the software, 3D views that show if any narrowing of the arteries (stenosis) is present were performed. The results were compared with the conventional 2D method and an alternative commercial 3D method. The study show that the software developed in this project was as good at classifying coronary arteries as the conventional 2D method while the alternative commercial method was considerably less efficient.

Finally, we have developed a faster version of the “level set” algorithm, which is particularly suitable for defining (segmenting) blood vessels from surrounding tissue. The new method is 10-20 times faster than conventional methods without loss of accuracy, making it possible to quantitatively analyze stenosis without delays.
Using methods available in a radiological department, in particular different types of computed tomography (CT) methods. Since the trabeculae are often less than 0.2 µm thick, the limited resolution of the radiological methods may be a problem. Therefore, we have focused on developing new image processing techniques for as accurate measurements as possible in the available images.

Most analysis methods presuppose that you start by deciding, for each point in the volume examined, whether it consists of bone or other tissue, i.e. the region is divided into two regions (segmentation). We have found, however, that using methods that op-
erate directly on the original grayscale image are more reliable than those starting with a segmentation step. To study how the structure of the bone differs between different directions we use mathematical concepts called tensors. With these tools, it is also possible to test to what extent the traditional assumptions about trabeculae being shaped as rods or plates are valid.

In the future, we hope that these methods will be useful in particular to evaluate the effects of treatment against osteoporosis. With better tools to measure the structure of the bone trabeculae it will be possible to draw such conclusions at an earlier stage, hence the number of subjects and the observation times in clinical trials may be reduced.
DEFORMITY OF THE spine can be classified into different types. The most common are neuromuscular scoliosis, idiopathic scoliosis and congenital malformations. A progressive deformity leads to postural problems, pain and in the long run sometimes impairment of the heart and lungs. Scoliosis affects the spine by causing a sideways displacement of the vertebra, which can be observed on a frontal radiograph. However, the deformation of a scoliotic spine is not limited to a single plane. Instead there is a 3D deformity at hand, including a rotation and a structural change of the vertebrae in the spine over time. Despite the 3D nature of the deformity, clinical practice for assessing the deformity is to use measures based upon 2D imaging, where the Cobb angle is the most commonly employed measure.

Performing a full 3D assessment based upon 2D radiographs is a challenging task, although some successful examples have been reported in the literature. On the other hand, 3D
imaging, as provided by computed tomography (CT), provides excellent opportunities for performing 3D assessments of spinal deformities. Radiation dose has earlier been a major concern limiting the use of CT in clinical practice; however, today the dose has been significantly reduced due to improved detectors, imaging protocols and reconstruction algorithms. Thus, with the current state of the art CT scanners it is possible to acquire image data suitable for 3D assessments of spinal deformities.

We will develop methods both for description of structural changes of each vertebra and a 3D measurement of the curved spine. The methods are intended to be employed to quantify the severity of spinal structural changes, which allows for an improved diagnostic accuracy and for better monitoring of the disease. They also provide a better understanding of how the disease evolves and how different treatments reduce spinal deformities.

In particular, we are focusing on:
• Determining the relationship between the Cobb angle as observed from radiographs with the patient in standing and in supine position. This is relevant, since current clinical practice is based upon the Cobb angle from radiographs with the patient in standing position and not in lying down as is the case for CT examinations.
• Developing computerized methods based upon advanced image analysis, which can be employed for assessing various measures related to quantifying the 3D deformity in scoliosis. Automatic and robust methods are needed in order to limit the effects of intra- and inter-observer variability associated with manual methods.
• Determining the relationship between the Cobb angle and the axial vertebral rotation. This is relevant, since the axial vertebral rotation is of many clinicians considered as a differentiating factor between different types of scoliosis.
• Investigating how the axial vertebral rotation is affected by different surgical techniques for correcting spinal deformities.

Figure 2. Visualizing the scoliotic spine in 3D allows the viewer to observe the true 3D deformity at hand, i.e. not only a sideways displacement of the vertebrae but also a rotation and a deformation of the vertebrae.
**PROJECT NAME**
Whole body MRI-based fat and muscle measurement

**PROJECT LEADER**
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**GRANTS**
FORSS Research council of Southeast Sweden 2012-2014

**KEY PUBLICATIONS**

Romu T, Borga M, Dahlqvist Leinhard O. MANA – Multi Scale Adaptive Normalized Averaging. In proceedings of the 8th International Symposium on Biomedical Imaging (ISBI’11), Chicago, USA, 2011.


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**THE METABOLIC SYNDROME** is a disorder involving alterations of the normal biochemical processes of the body. High blood pressure, high blood sugar level, excess body fat around the waist and abnormal cholesterol increase the risk of heart disease, stroke and diabetes. In the metabolic syndrome several of these risk factors occur together, dramatically increasing the risk further. Body Mass Index (BMI), weight and waist circumference do not tell the whole story about the metabolic syndrome. A better understanding of the effect of drugs and different life styles requires biomarkers reflecting where and how the body stores fat, build muscles and reacts on physical exercise. Fat stored diffusively in and in between the internal organs is much more dangerous than fat stored as subcutaneous fat and weight gain due to increased muscle mass is rather positive than negative for your health.

Body composition measurement with magnetic resonance imaging (MRI) enables safe and accurate quantification of fat and how it is stored in the body. The technology can determine diffuse storage of fat in the liver, pancreas and muscles, fat stored between the internal organs in the abdomen, and subcutaneous fat. The technique also allows quantification of the volume of muscles.

In this project we develop a technique for detailed analysis of fat and muscle tissue in the body based on whole body MRI examination (see figure). Recent technical development of MRI scanners enables high-resolution images of the complete body without exposing the subject to ionizing radiation or other known health risks. The technique can be applied in large-scale research studies to provide a better understanding about different body composition phenotypes.

We apply the technique in a number of clinical studies. In one project we study fibromyalgia where we recently showed an increased fat content in the
thigh muscles of fibromyalgia patients. Another project regards whiplash associated disorders, where fat infiltration in deep neck muscles may affect the outcome of patient rehabilitation. We also study the effect of anti-obesity therapies and the role of abdominal and liver fat in diffuse liver disease.

Furthermore, we use the technique to provide better understanding of Sarcopenia, the decline of muscle tissue with age, which is one of the most important causes of functional decline and loss of independence in older adults.

Another important application area of the technique is imaging of brown adipose tissue (BAT). Recently, we demonstrated the presence of BAT between the shoulder blades in human infants. BAT is an organ that allows non-shivering thermogenesis in mammals and is a potential target for anti-obesity therapies.
where the sample is taken. If the biopsy is extracted from the wrong area there is a risk that important information is overlooked.

Many liver diseases are diagnosed when they are in an advanced stage and the liver is already seriously damaged. At that time, surgery is the only treatment option. In order for the patient to survive a liver tumor surgery, a healthy piece of the liver has to be left in the body. The liver is then growing during 4-5 weeks to regain almost full size and function. The first week after the surgery is a critical time since the small piece of liver has to manage the job of a full liver.

Liver Intrinsic Function Evaluation (4LIFE) is a four year research project that, with the help of magnetic resonance (MR, MRS and MRI), will develop new methods for diagnosing liver disease at CMIV. The new technology is expected to result in safer liver surgery. A goal for the project is to develop an intuitive and simple tool for evaluation of liver status, which further on will be able to simulate surgical procedures to foresee how they will affect the liver.

With the help of MR it is possible to measure several parameters in the liver without invasive procedures. The MR also enables a better overview of the liver status as whole than biopsies.

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Today, determination of how much of the liver to remove is difficult as only partially sampled liver tissue is extracted from the wrong area there is a risk that important information is overlooked. Many liver diseases are diagnosed when they are in an advanced stage and the liver is already seriously damaged. At that time, surgery is the only treatment option. In order for the patient to survive a liver tumor surgery, a healthy piece of the liver has to be left in the body. The liver is then growing during 4-5 weeks to regain almost full size and function. The first week after the surgery is a critical time since the small piece of liver has to manage the job of a full liver.
a rough estimate of the liver function can be made. Occasionally, patients may suffer from liver failure following radical surgery. On the other hand, some patients are wrongly judged unfit for surgery when the rough estimate suggests that they will not survive the procedure. With a better estimate of size and function in the liver residue more patients could have surgery. This project will develop a tool where data from different types of liver measurements may be gathered. The data will support the physician in determine how to treat the patient. All MR measurements are conveniently done at the same occasion.

The magnetic resonance technology may, among other things, be used to measure the amount of fat in the liver, measure the uptake of a contrast agent to get an idea of how well the liver works and measure levels of many different elements, including iron and phosphorus compounds.

One of the MR methods used is elastography. The examination shows fibrosis, formation of connective tissue, in the liver. The connective tissue makes the liver less flexible and impairs the function in fibrotic areas. During MR elastography vibrations are sent into the patient’s body. The vibrations are propagated differently depending on the flexibility of the tissue. Through registration of the different vibrations the MR-scanner can separate healthy from diseased tissue.
POPULAR SCIENTIFIC SUMMARY

PETER LUNDBERG

PRESTO-CAN for Three-Dimensional Functional MRI

THE MAGNETIC RESONANCE images (MRI) are not produced directly by the MRI scanner. Instead raw data from the scanner is temporary stored in the so called k-space. The raw data comes in to k-space as sinus waves of different frequencies. These frequencies can then be transformed into images by a mathematical operation. This is called reconstruction. Normally, the frequency measurements are performed in thin 2D slices of the body which are reconstructed and combined in a stack to form an image volume. Occasionally, k-space is measured directly in 3D with a square pattern called Cartesian sampling pattern (figure 1, left).

In contrast to the 3D Cartesian geometry, our method PRESTO-CAN samples k-space using a hybrid between a radial geometry and a Cartesian geometry (figure 1, right). The large

Figure 1 Left: 3D Cartesian sampling of k-space. Right: PRESTO-CAN sampling of k-space.
steps in the angular direction gives a fast recording of the important information located in the center of k-space.

The method was developed having functional MRI (fMRI) applications in mind. In fMRI, MRI-volumes are recorded during a time period when a person/patient performs a particular task. By analyzing the MRI time sequence, it is possible to detect brain activity. Accordingly, it is desirable with a high time resolution. PRESTO-CAN has shown to provide excellent temporal resolution and satisfactory image quality. We have also been able to demonstrate that it is indeed possible to detect neural activity with fMRI using PRESTO-CAN, see figure 2.

As seen to the right in figure 1, there are more densely sampled data in the inner part of k-space. It has been shown that by removing parts of the inner over-sampled k-space at certain time points, the time resolution can be further increased. However, this gives a more complicated sampling pattern and a non-trivial reconstruction. Consequently, we previously got disturbing image artifacts, which probably affected the fMRI-detection in a negative way. To eliminate these artifacts we have improved the image quality by implementing a recently published improved reconstruction technique.

A major advantage of the PRESTO-CAN sequence for neurological research is that it allows for whole brain coverage. We aim to demonstrate this in a comparative fMRI study between PRESTO-CAN and conventional techniques.

The rather simple geometry of PRESTO-CAN makes it easy to include standard procedures for speeding up the data acquisition further, such as parallel imaging which can be combined with unique 3D motion correction schemes. These possibilities will be investigated further.
Sleep is a naturally recurring state, which still is a mystery since the function and purpose of sleep is not fully understood. In this project we explore the networks of the human brain that are involved in the regulation of sleep and wakefulness. For this quest, patients with sleep disorders provide keys to the understanding of why we sleep and why we wake up.

By investigating patients with excessive sleepiness due to brain inflammation, von Economo in the early 20th century detected brain areas involved in the regulation of sleep and wakefulness. Almost a century later, scientists discovered an important sleep-regulating substance, orexin, which is produced in a certain area of the brain, the hypothalamus (see figure). Loss of orexin causes the sleep disorder narcolepsy. Patients with narcolepsy have involuntary sleep attacks during daytime and poor nighttime sleep.

Kleine-Levin syndrome is another sleep disorder where the patients can sleep for extremely long periods, up to several weeks. These sleep disorders often debut in the childhood or adolescence, but many patients are not diagnosed until adulthood. Thus narcolepsy and Kleine-Levin syndrome are under-diagnosed disorders and novel methods for early diagnosis are urgent. In addition, the relations between disease mechanisms and the patients’ symptoms
are still unresolved. The aim of the SAND:MAN project is to investigate the neurobiology of sleep disorders in order to improve the well-being of the affected patients by defining imaging biomarkers for early diagnosis and for assessment of treatment effects.

The neurobiology of sleep disorders is investigated by visualization of the neural function in brain areas that are important for the regulation of sleep and wakefulness. Such visualization is obtained by brain scanning, so called functional Magnetic Resonance Imaging (fMRI). By fMRI, the activity in the synapses of the nerve cells can be measured through the increased blood flow that arises in response to the activity. This blood flow response is, however, much slower than the synaptic activity. Therefore we simultaneously also measure the brain’s electrical activity by EEG. In this way we can measure faster neural responses. In addition, we measure the concentrations of signal substances that regulate synaptic activity in the brains of patients with sleep disorders.

In order to understand the function of such a complex system as the human brain it is necessary to formulate hypotheses of the neurobiological mechanisms that generate measured data. Here, these hypotheses are formulated using mathematical expressions that constitute mechanistic models of brain function. Accurate measurements of neural function combined with advanced mathematical modeling form a new approach to the studies of human brain function. In line with the early discoveries of von Economo, we expect that brain imaging in patients with sleep disorders could provide new views on the neurobiology that governs sleep and wakefulness.
In this project we approached this research question by investigating healthy individuals and patients with epilepsy by functional Magnetic Resonance Imaging (fMRI) and standardized language tests.

For most people the brain’s left hemisphere is dominant for language. This means that the left side of the brain executes language tasks, such as reading and talking. However, the brain’s right side is also often activated language function in generalized epilepsy: Inadequate suppression of the default mode network. Epilepsy & Behavior, 28, 26–35, 2013.


Language ability plays an important role when communicating with others. Although the most important areas of the brain that are involved in language function are identified, the relation between activation in these areas and language ability is not fully uncovered. That is to say, we do not know in detail the relation between the magnitude and extent of language activation as measured by brain scanning and individual performance on language tests. In this project we approached this research question by investigating healthy individuals and patients with epilepsy by functional Magnetic Resonance Imaging (fMRI) and standardized language tests.

For most people the brain’s left hemisphere is dominant for language. This means that the left side of the brain executes language tasks, such as reading and talking. However, the brain’s right side is also often activated.
during language tasks, but the role of the right hemisphere in language remains elusive. We have shown that the right side of the brain plays an important role in supporting language ability. We have also shown that patients with generalized epilepsy have subtle language deficits and that inability to suppress brain networks that are not used for language processing could explain language problems in epilepsy. This work adds value to the recently emerged research field of the brain’s resting state network or the default mode network. This network is engaged when we are at rest, when we are mind wandering and “thinking about nothing”. When performing executive tasks, such as language processing, this network should be suppressed for an optimal usage of the brain’s resources.

Language function in healthy subjects, axial slices. The left side is dominant; however, activation in the right hemisphere is also present.
magnetic resonance imaging (fMRI) study was set-up to investigate this group, now around thirteen years old. With fMRI you can measure brain activity. The method registers changes in blood flow in the brain, and blood flow increases when a brain area becomes more active and needs more energy. There is always activity in the brain, but the location depends on what the person is doing. When a person is engaged in a task, activity may be seen in language or attention networks. In contrast, when a person is at rest, brain activity in the so-called default mode network emerges. This network can be seen in the figure, it looks very sym-
metrical between the two brain halves. The default mode network is thought to be responsible for every day thought monitoring; when you are thinking about what you plan to do tomorrow or what is for dinner tonight. Since the network is active in persons that are not doing a task, it logically follows that its activity is suppressed, whenever a persons attention is drawn by a task. This suppression is what is shown in the figure.

We have plotted individual brain activation values for the part of the default mode network that is under the crosshair, called the inferior parietal lobe. The scatterplot shows that the control group in blue scored around 0; no activation or suppression thereof. The premature group in red scored significantly below 0. This means that the premature born children have more suppression of the default mode network. What does this imply? One explanation is that the premature born children experience the task as quite difficult, and need their full attention, in contrast to the control group. But if we take into account the previous findings about the initial cognitive setbacks of the premature born children which they later successfully overcome, this difference in network suppression could also represent a long-term strategy of the premature group. They learned to more efficiently direct their attention and brain resources towards a task. It is of interest to explore whether the whole network indeed functions differently between groups, and if the premature born children show more changes in brain activity that may point to different cognitive strategies. This will be linked to changes in brain anatomy, which may reveal the long-term impact of a very early birth.
Clinical, Psychosocial and Imaging Studies of Fatigue in Multiple Sclerosis

**PROJECT NAME**
Clinical, psychosocial and imaging studies of fatigue in multiple sclerosis

**PROJECT LEADER**
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**MAIN PROJECT PARTICIPANTS**
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**GRANTS**
Swedish Research Council (VR)

**KEY PUBLICATIONS**


**POPULAR SCIENTIFIC SUMMARY**

ANNE-MARIE LANDTBLOM AND MARIA ENGSTRÖM

**Clinical, Psychosocial and Imaging Studies of Fatigue in Multiple Sclerosis**

**MULTIPLE SCLEROSIS (MS) IS AN** inflammatory disease affecting the nerve cells of the brain and spinal cord. The disease damages the nervous system communication resulting in a wide range of physical and mental symptoms. Fatigue, extensive tiredness and exhaustibility, is a common symptom of multiple sclerosis (MS). Fatigue is often found to be a more decapitating symptom than paresis. In this project we have aimed to describe fatigue from an epidemiological, psychosocial (effect on employment), physiological (coupling to heat sensitivity), clinical (effect on cognition) and interventional (cryotherapy) point of view.

Fatigue can be either peripheral or central. The neuronal mechanisms are not fully uncovered but the hypotheses for central fatigue involve the feedback loops between the basal ganglia and the motor cortex.

We have used functional magnetic resonance imaging of the brain (fMRI) to investigate the neuronal

Figure 1. Differences in brain activation between MS participants and healthy participants in regions of interest in the brain. The red colour represents areas that were more activated in MS participants compared to controls, and the blue colour represents areas that were less activated in MS participants compared to controls.
activity involved in the enhancement of cognitive problems due to fatigue among patients with MS. In fMRI, changes to the blood flow in the brain are measured. Increased blood flow corresponds to increased activity in that area of the brain. The patients were performing verbal tasks during the scan. A control group of healthy participants were also investigated.

The patients were then examined in the same way after having a treatment with cryotherapy, i.e. having put on an active cooling garment with running cold water to lower the body temperature. The measurements were repeated to see if the cooling had improved the cognitive functions.

The fMRI experiments showed correlation between activation in specific areas of interest in the brain and perceived fatigue during the working memory tasks. The areas activated were the right substantia nigra and the left posterior parietal cortex. Neuropsychological investigations revealed clear effects on the working memory in the patients with MS and fatigue compared with the control group. It is important to describe fatigue to gain acceptance for this decapitating symptom. It is of great relevance to continue to investigate the physiological mechanisms behind the symptom. The results of this study have identified areas of the brain that are involved. The project will go on investigating the intervention effect of the cooling garment where the fMRI will be of great interest and can help in determining how fatigue acts physiologically.

Figure 2. Brain activation with positive correlation to perceived fatigue during the working memory task. The images show activation in regions of interest: the right substantia nigra and the left posterior parietal cortex.
Clinical, Imaging and Memory Investigation in Patients with the Kleine Levin Syndrome

**SLEEP DISORDERS IN** young individuals are acknowledged as a growing problem. Some disorders increase, especially delayed sleep phase syndrome (DSLP), but also narcolepsy as a consequence of the Pandemrix vaccinations. Some of the rarer sleep disorders are hard to diagnose, especially the periodically occurring hypersomnia, Kleine-Levin syndrome (KLS). The diagnostic tools used are mainly clinical, but in narcolepsy also laboratory.

We have developed laboratory tools to support the diagnosis of the Kleine-Levin syndrome, including neuropsychological testing to identify working memory deficits. We also used measures of cerebral blood flow in our diagnostic set up for KLS. Over the years we have gathered a large number of KLS patients from the Nordic countries (n=30) who take part in clinical and scientific procedures. This gives us the opportunity to compare young individuals with the disorder. Future goals are to investigate also other sleep disorders within a larger project, outlined by assistant professor Maria Engström and in collaboration with colleagues in Gothenburg, see Engström’s report the SAND:MAN project.

In this study we examined frequency, duration and type of sleep periods the patients had. We also performed basic investigations including blood flow measurements in the brain (fMRI), where increased blood flow corresponds to increased activity in that part.
of the brain. The fMRI measurements were combined with cognitive tests of the working memory, and also neuropsychological investigations. The tasks had varying difficulty and therefore required different effort levels. Measurements were also performed in resting state. Our results show that there are areas in the brain that are activated differently in patients with KLS compared with healthy individuals. The differences between patients with KLS and healthy controls were demonstrated in the resting state. In activated state during the working memory test, patients with KLS showed increased activation in some parts of the brain while other parts were less activated compared with healthy individuals. The differences in activation in these areas could be used to part the KLS patients from the healthy individual in most of the cases; hence the techniques have the potential to be developed into diagnostic tools of KLS.

As mentioned above our present goals are to investigate also other sleep disorders within a larger project. We also plan additional studies regarding genetics and physiology. For example we will investigate the role of body temperature in relation to sleep episodes.

Figure 1. Functional connectivity in the salience network. Neural processing is often performed by an integrated network of several regions in the brain. Functional connectivity studies investigate the interaction of regions within these networks. Yellow areas show the network in selected slices. Red and blue areas show connectivity differences. (A) Red colour denotes regions that are more strongly coupled to the network at a high effort level compared to a low effort level. Blue colour denotes regions that are more strongly coupled to the network at a low effort level. (B) Regions that are more strongly (red) respectively more weakly (blue) coupled to the network in patients with periodic idiopathic hypersomnia (KLS) compared to healthy individuals at the high effort level.

Figure 2. Typical working memory activation in healthy individuals and thalamic hyperactivation in KLS patients. In other parts of the brain KLS patients had less activation than healthy individuals.
Clinical and Imaging Studies of Multiple Sclerosis

**PROJECT NAME**
Clinical and Imaging studies of multiple sclerosis

**PROJECT LEADER**
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**GRANTS**
Swedish Research Council (VR)

**KEY PUBLICATIONS**

**POPULAR SCIENTIFIC SUMMARY**

ANNE-MARIE LANDTBLOM

MULTIPLE SCLEROSIS (MS) is an inflammatory disease affecting the nerve cells of the brain and spinal cord. The disease damages the nervous system communication resulting in a wide range of physical and mental symptoms. The symptoms may occur in isolated attacks or build up over time.

Together with inflammation, destruction of the insulating covers of nerve cells and the formation of lesions in the central nervous system are the main characteristics of MS. However, not all MS patients have the typical lesions in the brain. In fact, MS could be seen as a generic group for a variety of disease patterns and this perspective may help the endeavors to find more specific treatment in the future.

Since not all patients have lesions in their brain, they cannot be the explanation for the neuronal damage. Patients without lesions have almost equal disability from the disease. New methods that can look deeper into the cause of MS is therefore of great interest.

Using magnetic resonance (MR) technique we can measure the levels of different metabolites in the brain. High levels of some substances reflect healthy tissue whereas others reflect damage. Using this method we have followed MS patients treated with the pharmaceutical Copaxone. Copaxone has been shown to decrease the lesions and slows down the progression of the
disease. The results showed that the treatment slowed down the biochemical development of the disease. Brain lesions can be seen both in MS and cerebral arteriosclerosis and is therefore often hard to use as basis for a diagnosis. Since the possibility to discriminate these lesions would be a valuable tool for diagnosis we have performed a pilot project aiming to develop an MR method to determine such differences.

The project has until now examined about 10 patients with MS, 10 patients with known cerebral arteriosclerosis with ischemia, and a few patients with diagnostic problems, where MS or arteriosclerosis could not be decided from the clinical and laboratory study. Preliminary results revealed a trend that may help in differentiating these two conditions and this will be investigated further.
IN THIS PROJECT we explore the application of state-of-the-art signal processing techniques in volumetric visualization. The goal is to extract additional information that will provide more knowledge about the content inside the dataset.

One approach we have investigated is the use of existing knowledge about vessel shape together with adaptive data filtering to automatically adjust visualizations to local variations in the data. The primary application is varying concentrations of contrast agent in computed tomography angiography (CTA). The concentration of contrast agent affects the received signal. When working with CTA, the visualization of the entire vascular tree is prohibited by local changes in contrast agent concentration. These local changes are, in our approach, modelled by filters designed to detect and measure vessel-like structures. As a result, our algorithms...
are capable of visualizing the full cardiovascular tree by locally adapting the transfer function (figure 1).

Another approach we have investigated is to include knowledge from the user in the reconstruction step of the volume rendering pipeline. By doing so, we are able to prevent artifacts in the form of falsely classified samples due to interpolation effects that arise from the assumption of data continuity. Figure 2 illustrates the problems that arise from applying continuous data assumptions on data that are perceived as discrete.

In the figure, the rendering on the left corresponds to a high resolution reference image. The middle and right images are both renderings from downsampled version of the same data. Of these, the middle image applied a fully continuous model (the standard in many areas of medical imaging), whereas the image on the right applied a piecewise continuous data model. By utilizing the existing classification from the visualization pipeline also in the reconstruction step, the piecewise continuous data model can, for example, help prevent the construction of false tissue layers. An example of this is illustrated in figure 3, where a non-existent layer of dentine is shown between the (harder) enamel and (softer) surroundings of the tooth.

Figure 2. Comparison of standard continuous reconstruction (middle) and adapted, boundary aware, reconstruction (right) from a high resolution reference image (left).

Figure 3. Erroneous sheet artifacts commonly found in traditional volume rendering can be suppressed by utilizing classification information in the reconstruction step.
Tissue Classification Using Dual Energy CT and Iterative Reconstruction

Today’s computed tomography (CT) images are affected by artifacts caused by the X-ray spectrum. These artifacts are called beam-hardening artifacts. Due to the artifacts the CT-images are not completely quantitatively accurate. We have developed a mathematical method, an algorithm, which eliminates the artifacts. With our dual energy iterative reconstruction algorithm (DIRA) the pixels of the image can be classified into bone (red regions) and soft tissue (blue regions). Bone pixels carry information about percentages of compact bone, red and yellow bone marrow. Soft tissue pixels carry information about percentages of water, protein and lipid. It is also possible to reclassify a specific tissue, e.g. the liver can be classified into liver tissue, lipid and iron. Consequently, DIRA provides quantitative information that can be used for improved medical diagnosis and treatment. As an example, DIRA can be used for determination of lipid content in the liver or the composition of plaques in aorta. The method can also be used in radiation treatment planning of brachytherapy for prostate cancer.

To verify the method we applied DIRA to simulated projection data of a mathematical phantom of the human pelvic region by using "DRA-
SIM\textsuperscript{TM}, a CT-simulation tool provided by Siemens. The X-ray spectra used were 80 and 140kV and the geometry was basically the same as for the real CT-Scanner at CMIV.

Figure 1 shows conventionally filtered back-projection reconstructed images for 80kV in color which is equivalent to 0 iterations of DIRA (left) and after 4 iterations in DIRA (right). It is apparent that the beam-hardening artifacts corrupt the image causing streaks and shift of values after 0 iterations (left). These artifacts are to a large extent reduced after 4 iterations (right). The image for 140kV was improved in a similar way.

The soft tissue of the images for 80 and 140kV were then classified into the base material triplet lipid, protein and water (LPW), see figure 2. The classification based on the 4th iteration is consistent with the true values and provides quantitative information of the tissue. As mentioned above, such information can be used for improved medical diagnosis and treatment.
Digital images are omnipresent and are used in a broad spectrum of count- less applications, ranging from digital photography to medical diagnostics. A quite common problem is that the image data you collect is incomplete or distorted. Image reconstruction and image enhancement are fundamental methods of image processing, which normally focus on the so-called inverse problem, which is to reconstruct a high quality image from incomplete and noisy data. Usually these methods do not take into account that ultimately it is a human observer looking at a visualization of the image. When you look at printed photographs or when radiologists analyze images from a computed tomography (CT) scan, it is in fact a transformed version of the originally measured data that is shown. Normally image processing methods do not take into account this visualization process.

The goal of this project is to develop new methods to improve and reconstruct images while taking into account domain knowledge of the imaging and visualization process.

The enhancement of noisy images is determined by a balance between the deviation from the original image data and how “soft” and “clean” the result obtained should be perceived. In our approach, we use the transfer function that is used in the visualization process for determining this balance between deviation and smoothness. This leads to results that are superior to the traditional workflow where denoising and visualization are performed sequentially. The resulting non-linear system for image enhance-
ment replaces ad hoc methods and is based on an approach directly derived from the actual transfer function.

The case of incomplete data requires specific knowledge of the image acquisition process to formulate an optimal reconstruction method. A few existing systems use local imaging properties, such as the so-called point spread function, or special imaging techniques, such as projections, embedded in the image enhancement process. By integrating reconstruction and image enhancement in a joint approach, an optimal trade-off between the deviations in both sub problems is achieved.

By deriving image enhancement methods from knowledge of both the imaging and the visualization process, a new uniform approach is obtained. This approach will provide new insights into the theory of iterative image enhancement and is expected to lead to significant advances in the field, particularly for the non-linear functions above that are derived from fundamental principles. In this project, we extend our previous results on some sub-problems:

Combining analytical computed tomography (CT) reconstruction with algebraic methods, applying known solutions of regularization problems in terms of integral transforms on the CT image reconstruction, identifying the systematic connection between fundamental principles and diffusion formulations for image enhancement as well as understanding and modeling of the visualization process, particularly with feedback from the observer.

The overall aim of this project is to support radiologist to formulate accurate diagnoses from noisy image data. We develop image noise reduction tools which incorporate a transfer function into the filtering scheme, thus we not only take structural image information into account but also utilize the desired visualization window.
TECHNOLOGICAL ADVANCES IN medical imaging have largely improved the diagnosis of illness. However, these advances also impose a burden to physicians, since the amount of information acquired through medical imaging is usually huge. Medical image analysis techniques aim at helping physicians in the analysis of these data. The potential high impact in the public health systems has fostered the research in this area in the recent years. One of the aims of computer vision is to extract information from images. Since both areas deal with image analysis, it is not surprising that many tools that have been proven effective in computer vision applications in noisy conditions. Perception-based methods use psychological theories on how humans manually identify regions of interest in the images. One of the most versatile of these techniques is tensor voting. Tensors can be used for describing physical properties and geometry in a mathematical way. In tensor voting the information provided by individual tensors are propagated using - perception-based rules in order to detect regions of interest in the images. We have successfully used tensor voting for image denoising, edge detection and segmentation tasks in color images. This method may potentially be beneficial for problems in medical images, such as blood vessel segmentation, detection of bifurcations, detection of separation points and vortices in blood.
flow, tractography, and detection of nodes in trabecular bone. However, important theoretical extensions of tensor voting are still required to tackle these problems. These extensions are not straightforward due to the inherent complexity of the theory of tensors and the difficulty of proposing efficient implementations. In this line, the main aim of this project is to propose efficient theoretical extensions of tensor voting to make it suitable to different medical image applications.

An additional challenge for automated methods aiming at mimicking human’s performance in analysis of medical images is that, radiologists not only use their perception but also their extensive knowledge in radiology for detecting and assessing structures of medical importance. Combining perception-based methods and machine learning strategies is a promising approach for this issue, which will also be explored in this project.

Diffusion Tensor Image (DTI) of a section near the ventricles in the brain. The orientation of the depicted ellipsoids indicates the main direction of fibers in the white matter. Tensor voting could be used to extract the trajectory of fibers in order to create connectivity maps in the brain (tractography).
Optimizing Radiographic Procedures – Dose vs. Image Quality

BEFORE X-RAY EXAMINATIONS, the staff at the radiology department will take measures to minimize the radiation exposure and at the same time make sure that the image quality is sufficient for the radiologist to make a correct diagnosis. This process is called dose and image quality optimization. It requires that both the image quality and the patient absorbed dose can be measured and balanced against each other. An improved image quality may result in an increased absorbed dose for the patient. Our research shows that large dose reductions are possible without reducing clinical image quality.

Our objective is to develop and use computer simulations of the complete X-ray imaging system to predict image quality and absorbed doses in the patient. To reach this goal, we are developing a computer model of the imaging system, a so called virtual X-ray system, by searching for correlations between the subjective assessment of clinical image quality by the radiologist and of objective image quality by the computer model observer. The model observer is able to use all the information in the radiograph and compute an index of image quality depending on the diagnostic task (for example finding a lung- or breast tumor). The model observer can be used in a very cost-effective manner to search for settings on the X-ray unit that minimizes the patient exposure. A key part of the model is the database of patient like, three-dimensional volumes of different parts of the human anatomy. The image below is an example in chest imaging.

Our virtual model of the imaging system provides unique possibilities not just to assess existing X-ray systems, but also to explore future imaging systems before constructing expensive prototype systems. The research therefore gives important
design information to manufacturers of X-ray imaging systems.

An example of a model observer is the signal-to-noise ratio for a clinically relevant structure, for example a contrast-filled vessel. The signal-to-noise ratio measures how well this vessel can be detected (safely diagnosed) in a radiograph where the visibility of the vessel is limited by the noise in the image when a limited number of X-rays are used to form the radiograph. This is similar to the case of taking ordinary photographs under poor lighting conditions that will result in noisy images.

Our research aims to find optimal settings on the X-ray unit that maximizes the ratio of image quality per absorbed dose in the patient, i.e. maximizing the dose efficiency. Our investigations so far show a clear indication that dose reductions of up to 50% are possible using optimal settings in clinical practice.

The figure shows a simulated (computed) chest radiography to the left and a real radiograph of the same lung to the right.
Scan time reduction and automatic brain segmentation. After the initial prototype phase more hospitals became involved, among which a number in the US, to introduce synthetic MRI as a standard procedure into the clinical workflow. For example, in the radiology department at Linköping University Hospital synthetic MRI is now used as a standard protocol for MS patients and a research protocol for brain tumor patients. In the entire County Council of Västerbotten it is used as standard protocol for MS patients.

Currently an increasing number of evaluation projects are ongoing to validate the time reduction on the MR scanner and to assess the robustness of the technique on diseases such as multiple sclerosis (MS), hydrocephalus, cancer and dementia in clinical and research settings.
practice. Exciting new research ideas are worked out such as automatic MS lesion detection and brain myelination assessment. Also on other anatomies synthetic MRI is tested. Examples are the assessment of the prostate and of plaques in the large vessels. A new quantification sequence is developed which is so fast that the entire heart chambers can be measured within one single breath-hold.

In the history of MRI, general images were acquired which were subjectively interpreted by radiologists. With the advent of synthetic MRI we believe that this is going to change dramatically: Scan times will be shorter and the decision support will be more based on numbers and statistics. Automated analysis can make the work of the radiologist both faster and more objective. The technique is available on most scanner brands which will decrease the variation between different hospitals. Synthetic MRI is a clear example of excellent cooperation between university, hospital and commercial companies, made possible by CMIV.

Example of synthetic MRI on the brain: Based on a single acquisition different conventional images can be recreated such as a T2-weighted (A) or a T1-weighted (B) image. Additionally the sequence serves as input to automatic tissue segmentation, such as cerebrospinal fluid (C) or white matter (D). Automatic tissue segmentation enables objective patient monitoring.
perform simulations of the ways light absorbs and reflects, while still being able to interactively explore the data, is a computationally daunting task. Several approaches to this problem exist, but with the demand for interactivity, compromises with respect to the physical accuracy of the light transport in the volume have to be made. Our research therefore has focused on methods for high-quality illumination in interactive volume graphics.

**PROJECT NAME**
Methods for high-quality illumination in interactive volume graphics.

**PROJECT LEADER**
Anders Ynnerman, Department of Science and Technology, Division for Media and Information Technology

**MAIN PROJECT PARTICIPANTS**
Daniel Jönsson, Joel Kronander, Timo Ropinski

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**KEY PUBLICATIONS**


**AN ESSENTIAL INGREDIENT IN understanding of the structures found in volumetric data is the ability to interactively change rendering parameters and camera settings. In this project we strive to increase the clarity of images and improve the perception of depth and detail by developing efficient algorithms for shading of volumetric data in real time. However, being able to perform simulations of the ways light absorbs and reflects, while still being able to interactively explore the data, is a computationally daunting task. Several approaches to this problem exist, but with the demand for interactivity, compromises with respect to the physical accuracy of the light transport in the volume have to be made. Our research therefore has focused on**
developing efficient methods for simulating physically based light interaction of volumetric objects from computed tomography (CT) scans, mimicking the real world matter-light interaction, while still allowing interactive data exploration. This lifelike object-light interaction was previously not possible until we in this project were able to simulate realistic light interactions interactively using photon maps. The maps have a data structure that enables recording of the photons path history, thus avoiding costly recalculation of photon paths. The image below shows a screen shot of such an interactive rendering of a volumetric data set from at CT scan of hand.

We are now extending our methods to 4D CT scans and thereby enabling examination of the hand’s function with realistic shading. The key to this is to utilize correlation between the changes in time and the changes of light transport for individual photons.
limit the radiation dose the patients are exposed to.

Thanks to modern computers becoming more and more powerful, it is now possible to use advanced techniques and improved calculations on the CT data, resulting in high quality images. These so-called iterative techniques make it possible to use less X-rays in the CT scan and still obtain images of high quality.

An important research question is therefore how to lower the radiation dose as much as possible and still obtain images of high quality. These so-called iterative techniques make it possible to use less X-rays in the CT scan and still obtain images of high quality.

The main problem is that X-rays are associated with a risk of cancer. The benefit of a well performed CT outweighs this risk, but it is important to continue improving the technique to limit the radiation dose the patients are exposed to.

Thanks to modern computers becoming more and more powerful, it is now possible to use advanced techniques and improved calculations on the CT data, resulting in high quality images. These so-called iterative techniques make it possible to use less X-rays in the CT scan and still obtain images of high quality.

An important research question is therefore how to lower the radiation dose as much as possible and still obtain acceptable images. This is important to study in real patients. Therefore, the 400 patients involved in this project receive an extra CT scan with very low dose together with their
standard CT scan. The extra X-ray dose amounts to less than 1 mSv, which is about one third of the radiation dose we are exposed to each year from the earth and the sky.

The data from both the low-dose scan and the standard scan are stored in a digital archive. From this data, images can then be produced using both old and new techniques, in a number of ways. Generally, the low-dose images are of unacceptable quality when the old technique is used (see figure).

This project compares the best images we can reconstruct from low-dose data, using the best available iterative technique, with the standard-dose images. Since we have access to novel iterative techniques that are still in development, the research results will be relevant when these techniques are introduced on the market.

If the X-ray dose can be lowered in all or many of the very common CT examinations, CT will be a safer and more valuable technique, especially for patients that are young or have to go through many CT examinations.
Mostly homicides are analyzed and the imaging gives the police an early report allowing the traditional autopsy to wait for the crime scene investigation to finish. During the scan the body stays sealed in the bag preserving any evidence, as fibers and body fluids, present on the body. The images produced during the virtual autopsy are conveniently presented and easy to understand in court.

This project has focused on optimizing the total workflow for the postmortem imaging and developing a new type of software that can visualize full body data-sets and three-dimensional images.

A RECENT ADDITION to the autopsy workflow is the possibility of conducting postmortem imaging using computed tomography (CT) and magnetic resonance imaging (MRI) in a virtual autopsy. The results from these modalities can provide additional information to the autopsy report. The images give a fast overview of damages to the skeleton, air pockets and foreign objects that is not possible to achieve with conventional methods. Blood clots and bleedings can also be identified in the images.

At CMIV postmortem imaging has been used in routine work since 2003.
visualization. The conditions when scanning a dead body is not the same as for a living patient. When using the CT it is possible to use high radiation doses without concern for long term effects and there are no artifacts caused by movement. This allows images with high resolution. The bodies are scanned at two different energy levels at the same time, dual energy CT, improving soft tissue discrimination and visualization.

The MRI examinations are sensitive to the body temperature and it is difficult to generate images with good contrast when scanning a cold body.

At CMIV the clinically established protocols has been adjusted for optimal image quality at any given temperature. If a natural death is suspected the heart is examined using specific MRI protocols revealing heart attacks.

The number of autopsies performed is decreasing and natural deaths are rarely investigated. The virtual autopsy is therefore not only a useful complement to the traditional autopsy in the forensic investigation. It could be used instead of autopsy for natural deaths which would otherwise not be investigated to improve medical education, quality assurance and reliable mortality statistics. It is also an alternative when the invasive autopsy is not agreed by the next of kin due to personal or cultural reasons.
What enables us to follow a voice in the presence of other voices? A number of psychological theories compete to give the best answer to this question. The debate mainly concerns where the filtering of the irrelevant material, in this case the voices we don’t wish to follow, takes place: Some suggest that the filtering takes place early, before the irrelevant material is processed whereas others suggest that the filtering is late, after some processing. Our previous psychological research has repeatedly found a relationship between cognitive capacities and the capability to control the extent to which irrelevant sound is processed, and within the physiological/biological research tradition one has found outer hair cells of the ear to be involved in the filtering of irrelevant sound. Using functional magnetic resonance imaging (fMRI), the research project proposed here will juxtapose psychological and physiological/biological theories and methods to investigate whether there is a relation between cognitive capacities and the capability to control the outer hair cells’ response to sound. The relationship would show that cognitive abilities modulate the filtering of irrelevant material and that the filtering takes place at a very early stage in the information processing (i.e., the inner ear). The project has consequences for theories of selective attention and it has its most prominent application in the understanding and treatment of hearing impairment.
In the heart of CMIV you will find the medical staff and the radiological equipment. This is where most of the research examination is taking place and the patient examinations are carried out. CMIV is situated in the middle of the hospital close to the radiology department. Both regular patients and research patients are examined at CMIV. This closeness to the regular medical care is a great advantage for the research at CMIV.
MRI Research and Clinic Walk Hand in Hand

There is a close relationship between MR research and clinic at CMIV. Questions that arise during clinical work are passed on to become research projects. At the same time new methods may be tested in research project and used clinically when verified.

AT CMIV THERE are around 10 radiology nurses and biomedical analysts working with magnetic resonance imaging (MRI). They produce the images and process them according to the medical referral.

–There are extensive calculations involved in the production of MR images, says Johan Kihlberg, radiology nurse and team leader at CMIV.

–Depending on the medical question at hand it can require calculations of for example flow and volume or for identification of nerve fibers.

Johan is responsible for the MR research as well as development and maintenance of the clinical work. Half of his time is devoted to his own research as a CMIV PhD student.

The camera time at CMIV is split fifty-fifty between research and clinic. All types of MR examinations might end up at CMIV but the focus lies in abdominal, cardiac, blood vessel and neuro scans.

–We have experience and routine from the research scans in these areas and it’s therefore natural that we focus our resources on them, says Johan.

There is a close relationship between MR research and clinic at CMIV. Questions that arise during clinical work are passed on to become research projects. At the same time new methods may be tested in research project and used clinically when verified.

–In one of our research projects we have verified a method to measure liver fat with MR against the standard methods ultrasound and biopsies. Now we have taken the noninvasive MR method into clinical use, explains Johan.

MRI is based on a large magnet placing a magnetic field over the patient and a radio pulse turning on and off. A coil placed as close to the body as possible works as an antenna and takes up the signal emitted back from the body.

At CMIV there are two MR cameras with different field strength. The higher field strength, 3 tesla instead of 1.5, is an advantage in specific methods. For example in fMRI which is a method that measures brain activity the images will be much clearer and spectroscopy, a method to measure metabolites in the body the values will be more specific in the 3 tesla.

In the near future both MR cameras will be upgraded with the latest software from Philips. The 1.5T will be equipped with new, more effective coils and to the 3.0T phosphor spectroscopy technique will be added.
Assistant Nurses Caring for the Patients

The assistant nurses are in charge of the logistics and booking the examinations making sure that the work flow is efficient. Much of their work is about caring for the patients and making them comfortable.

Assistant nurses are also in charge of the logistics and booking the examinations making sure that the work flow is efficient. The clinical routine examinations made at CMIV are booked at the radiology department next door.

Carina Johansson and Mona Cederholm are in charge of the research booking at CMIV. They both have long experience from working as assistant nurses at the radiology department in Linköping. Now they are devoting half of their time to the research booking at CMIV while still working half time at the radiology department.

–We are a good team, the schedule is not always easy to work out but we solve it together, says Mona Cederholm.

As they are alternating weeks in the research booking there is always one of them on duty. Having full time focus on the booking has increased the efficiency at CMIV. The research projects are finished faster and empty slots are often filled with patients from other departments. The overview Mona and Carina have of the schedule makes them a valuable asset to the daily work flow.

–As we have the schedule overview and patient experience we often help out where ever needed at CMIV, continues Carina Johansson.

It is not unusual that patients are worried about their examination, both regarding the experience in the camera and what might be found in the images. This is an important responsibility for the assistant nurses.

–We sometimes spend hours on the phone calming patients down, explaining the procedure and convincing them to come in for their appointment, explains Carina and Mona.
LILIAN HENRIKSSON AND PETTER QUICK are radiology nurses at CMIV, both specialized in computed tomography (CT) with long experience in the field. They perform CT examinations on the radiologist’s ordination ensuring that the correct images are taken and processes the images to show the best view of what the radiologist is looking for. The method produces slices of data that stacked together can show images from any angle or in 3D depending on the purpose.

The CT at CMIV has two X-ray sources and two detectors. This has two main advantages explains Lilian Henriksson. First, the examination may be performed much faster than with regular CT. This is useful for example when analyzing a beating heart where the movement otherwise may disturb the images or if the patient is restless and unable of lying still. Second, if the X-ray sources are used at

Enlighten the Body with Computed Tomography

The radiology nurses perform CT examinations on the radiologists request. The method produces slices of data that stacked together can show images from any angle or in 3D depending on the purpose.
unnecessary radiation exposure. Several projects are working on lowering the radiation doses without compromising image quality. One of them is a method to scan scoliosis patients fast and at low radiation doses using dual energy, a method implemented in clinical use at the hospital. Another ongoing study investigates the possibility to use abdominal scans to simultaneously measure the bone density to identify osteoporosis.

–CMIV is now planning on replacing the current CT with the latest, even more advanced, model from Siemens. This will lead to new opportunities in research and development, Lilian concludes.

The technique is called dual energy and is often used to lower artifacts from metal implants. The machine simply produces faster and better images than a regular CT, explains Petter Quick.

Scanning larger patients is another advantage with the two X-ray sources. To penetrate a large body higher radiation doses than a single source machine can produce is required.

With the CT it is possible to scan the whole body. Any referral coming through the radiology department at the hospital may end up at CMIV. However, the majority of the CT examinations at CMIV are of the heart and blood vessels. In collaboration with the pathology department CMIV also performs postmortem scans of forensic cases to be used in virtual autopsies.

Apart from managing the advanced imaging techniques, another side of the job is to guide the patients through the procedure.

–If the patients understand the procedure it is easier for them to cooperate during the examination, says Lilian Henriksson.

The research studies performed on CT are done with patients already scheduled for a CT scan to avoid unnecessary radiation exposure. Several projects are working on lowering the radiation doses without compromising image quality. One of them is a method to scan scoliosis patients fast and at low radiation doses using dual energy, a method implemented in clinical use at the hospital. Another ongoing study investigates the possibility to use abdominal scans to simultaneously measure the bone density to identify osteoporosis.
The CMIV research school offers a doctoral program with both medical and technological entries and coherent research education. A basic principle for our doctoral program is the close connection between different disciplines as medicine and technology. Currently there are around forty PhD students admitted to the research school. Here a selection of them presents their research.
A Mechanistic Model for Blood Flow Regulation in Response to Neuronal Activity

Introduction

Blood flow to the brain is highly regulated, and changes in flow can indicate various neurological conditions.

The proposed model aims to explain these changes by integrating neuronal activity and hemodynamic responses.

Conclusion

The proposed model is able to describe the shape of the BOLD response. The neurobiological model performs even better, as it allows for a practical understanding of the factors involved in blood flow regulation.
Annette Karlsson

Assessing Muscle Volume Using Magnetic Resonance Imaging

During a 10 minute MR-scan images of a patient’s whole body may be taken. The method developed in our research can use these images to determine that patient’s muscle volume, both total muscle volume and the volume of separate muscle groups. The presented method can also determine the amount of fat within the muscle. Fat inside the muscle is a sign that the muscle is injured.

The muscle system is important for us as the muscles make it possible to walk and provides stability to the body. If the muscles are hurt or decreased in volume the result is immobility and pain. The possibility to measure the muscle volume and the amount of fat in the muscles is a useful tool in finding the right treatment and rehabilitation for patients. This automatic muscle volume method will be applied in a clinical study in order to investigate if the muscle volume in patients suffering from whiplash associated disorder is different from healthy controls.

However, measuring the muscle volumes of patients is not easily done. Scales and measuring tapes are not accurate since they do not discriminate between muscles and fat. With an MR-scanner, images are created where all the soft tissue, for example liver, fat and muscles may be shown separately. A pair of images where the first only shows fat tissue while the second shows all the tissue containing water is shown in Fig. 1.

For a trained human, it is easy to distinguish e.g. the liver from the muscles as the human knows where the liver is located and its shape. However, when calculating the volume of the muscles, each small image element must be included for each muscle group. This is too expensive why automatic solutions are needed.

For a computer, organs like the liver and the muscles look very similar as they have similar intensity values in the images (Fig. 1). The computer has no knowledge about where the liver is located or its shape. This method’s solution is to manually pre-define the muscle groups within an image, as shown in Fig. 2. When a new image with no pre-defined muscles is produced the old images are adapted so that they become as similar to the new image as possible. The adapted labels are in that process overlaid onto the new image and an automatic solution for the new muscles is achieved. The volume is calculated by a sum of all the small image elements. A typical result is shown in Fig. 3.

Figure 1. A paired magnetic resonance image where the left shows all the water within a whole body and the right shows all the fat.

Figure 2. Manually defined muscle groups where a trained human has marked the different muscles shown in different colors. Tissue with grey-color are not muscle tissue.

Figure 3. A typical result from the automatic method. The different muscle groups are shown in different colors. Grey color indicated that the automatic method has not considered that tissue as muscle tissue.
To study the distribution of various tissues within the human body we use a technique that separates water and fat in magnetic resonance (MR) images. An example of such images is seen in figure 1. By combining quantitative images where every pixel corresponds to an actual fat volume with automatic segmentation through anatomical atlases we study the amount of fat in different compartments in a cost-effective way.

White adipose tissue (fat tissue) volume is very hard to measure by imaging since it is the most variable tissue in the human body. Its volume can take up everything from a few per cent of a person’s total volume, to several times the volume of other tissues. Excess of adipose tissue carries a high risk of diabetes type 2, cardiovascular disease and cancer. However, the total amount of fat is not the strongest indicator of a higher risk. It has been shown that the central abdominal fat surrounding the liver, kidney, and intestine correlate with the risk of developing type 2 diabetes. The problem is that current methods, such as waist circumference, are not accurate enough to make predictions on an individual level. At the same time, more accurate image-based methods are too expensive.

We have created an inexpensive method for analysing water and fat separated images as well as protocols for speedy MRI acquisition. We can cover the abdomen in 5-6 min, and the entire body in less than 10 min, making it possible to add the sequences to existing protocols without much work. After the data acquisition the abdominal fat can usually be measured without user interaction, by a system which learns from prior examinations. However, no bodies are identical to each other, so we have developed tools for those few cases where the automatic method fails, and by using those tools the abdominal fat can be measured in 1-3 min. For every new case the method learns a bit more about the possible variations, so it will handle those variations better in the future.

Abdominal fat is not the only fat of interest. The same methods are used to measure the amount of brown adipose tissue, a tissue which burns energy to produce heat. They are also used for the amount of subcutaneous adipose tissue, the amount of liver and pancreatic fat and breast density, which is a strong predictor of breast cancer.
Liver disease is a growing problem in modern society and we need good tools to investigate the liver accurately. The liver is one of the largest organs in the human body and it handles many vital tasks. The main tasks of the liver are to process nutrients, remove toxins, make bile and build proteins. My research aims towards developing a collection of techniques that in the end can be used for better and safer liver diagnostics.

Many liver diseases develop unnoticed and once the symptoms become visible the disease has often advanced so far that an operation is the only option. Importantly, as the disease progresses there is a loss in liver function and tools that accurately measure this are in high demand. For instance, when surgeons plan liver surgery they need to be sure that there will be enough function left in the liver after the surgery, so that the risk of liver failure is minimal.

The conventional method of diagnosing many liver diseases suffers from several drawbacks. Currently this method involves taking a small sample of the liver, a biopsy, by using a needle. Since the sample is so small (about 10 to 20 microliters) it can be difficult to know if it is representative for the entire liver. Also, there is a small risk of complications with the procedure.

In our projects we use novel imaging techniques in magnetic resonance (MR) cameras in order to determine liver function. We measure the liver function by injecting a contrast enhancing agent in the patient’s blood flow and image the liver for about 30 minutes. In the figure you can see how the liver lights up in the images due to this contrast agent. Once the images are processed we use mathematical models to determine the liver function. The contrast agent is taken up by the liver but only in areas of the liver that are healthy enough. Basically the healthy parts of the liver are very bright in the images compared to the areas suffering from major disease.

The final goal of this project is to combine the results of the MR exam and present them in a simple to use tool that shows the condition of the liver, for instance to surgeons planning liver surgery or to medical doctors treating patients.

An example of the images we use to calculate liver function. This image shows how the contrast enhancing agent is taken up by the liver (the orange arrows points to the liver), and increases the intensity in the images over time.
Carina Stenman

An Alternative Workflow Method for Ultrasound Examinations

**ULTRASOUND IS OFTEN** a first choice for radiological examinations. It is a quick and safe diagnostic method. Thanks to recent technical progress in regard to image quality ultrasound is used to diagnose, for example, focal changes in the liver.

The most common way to document ultrasound examinations is to store still images. This method offers very limited possibilities for re-evaluation of an ultrasound examination. Especially when new clinical questions arise after the examination, re-evaluation is often not helpful. A possible solution is to use standardized examination protocols and store as cine-loops. The purpose of this project is to evaluate the introduced ultrasound method that is used at the radiology department in Linköping, with special consideration to reproducibility.

The Radiology department in Linköping uses a standardized method for ultrasound examinations. The examination is performed according to an examination protocol and then stored as cine-loops. Cine-loops are films where the scan covers 5-10 centimetres in 5-10 seconds depending on the target organ. The documentation should include both longitudinal and transversal views covering the whole organ or region of interest. The dynamic scans are saved in the Picture Archiving and Communication System (PACS) from where the films can be retrieved and reviewed on a later occasion at dedicated workstations.

The ultrasound examination is in suitable cases, such as technically uncomplicated normal ultrasound scans with a clear clinical question, performed by a radiographer. The advantage is that examinations performed by a radiographer can be evaluated later by a radiologist, thus increasing the availability of the radiologist for more advanced examinations.

A prerequisite for recommending this routine for general use is that no diagnostic information is lost in the process. The professional roles may become more clear-cut, with the radiographer concentrating on perfecting the examination technique and the radiologist on improving diagnostic skills, just as in other radiological modalities.
EVERY TIME WE do something, whether it is to breathe, solve a math problem or look at a picture, the nerves in different areas of our brain will be activated. The activity in the brain can be measured in a magnetic resonance scanner, using a technique called fMRI (functional magnetic resonance imaging). fMRI is often used in brain research as it is very safe for the person being examined. It measures changes in the level of oxygen in the different areas of the brain. When the nerves of an area start to signal each other they need more oxygen and nutrients. More blood is then sent to the brain area to deliver oxygen and nutrients. Since the oxygen level is controlled by the nerve signals it is used as a measurement of the activity in the brain. However, it is not completely known how the nerve signal governs the oxygen levels and it is not possible to measure.

We know that the time it takes for the blood and oxygen to get to the active area (about 10 seconds) is much longer than the time it takes for the electric nerve signal to get there (about half a second), and we want to find out what happens during that time. Therefore we are building computer models of the human brain which can fill the knowledge gap between nerve signal and oxygen level. The models can then be used for looking at the nerve signals even though all we can measure is the oxygen level. We hope that by using these models we can develop a good tool for diagnosing and investigating complicated brain disorders from fMRI images. One such disorder is KLS (Kleine-Levin Syndrome), or sleeping beauty syndrome. KLS is a sleep disorder where afflicted patients have periods of excessive sleep and various psychological symptoms. The cause of the disease is unknown. If you look at an anatomical picture of the brain of a person with KLS, no tumors can be seen, nor any areas of dead nerve cells or anything else that makes them different from a healthy person. But if you look at the activity in the brain when they solve certain tasks their pattern of activation is different. Using models of brain activation, we may be able to figure out what is different in KLS patients, as compared to healthy individuals. This will allow medical doctors to make better diagnoses.
Belen Casas

Improved Diagnosis and Management of Heart Disease by 4D Blood Flow Assessment; Stenotic Blood Flow

NARROWING OF THE valves of the heart, valve stenosis, prevents the valves from opening fully which obstructs the blood flow. The blood flow after the valve will be turbulent and produces a pressure drop across the valve. Such pressure drop will cause the heart to perform additional work to increase the driving pressure and maintain the blood flow through the vascular system. Over time, this causes adverse remodeling of the heart muscle. In many patients with valve stenosis, the heart’s short-term compensatory mechanisms become less and less effective, ultimately leading to heart failure. It appears that the pressure drop over the valve is a crucial marker of the severity of the stenosis.

The current gold standard for measuring the pressure drop is catheterization, but this is an invasive procedure and cannot be applied routinely. In practice, the pressure drop is instead estimated non-invasively based on ultrasound measurements. This approach, however, does only work well for severe stenoses since mild pressure drops are masked by a pressure recovery phenomenon downstream of the stenosis. The irreversible pressure drop over the stenosis is directly related to the amount turbulence and a method monitoring this would be useful in detecting also mild stenoses.

The aim of this project is to propose and validate a non-invasive method to estimate irreversible pressure loss based 4D magnetic resonance imaging (MRI) measurements of the turbulent blood flow. Such a method should be suitable for assessment of mild, moderate and severe stenoses. In particular, it would be especially helpful for assessment of moderate and mild stenoses, for which current non-invasive methods often fail to provide a correct estimate of the pressure drop.
Mariana Bustamante

Automatic Quantification and Visualization of Blood Flow in the Heart

**THE MAIN PURPOSE** of the project is to develop a semi-automatic method to quantify, analyze and visualize blood flow patterns in the whole heart. It is a part of HEART4FLOW, a collaboration between researchers in different areas, whose aim is to develop the next generation of methods for noninvasive quantitative assessment of cardiac diseases and therapies.

The project intends to reach its goal by optimizing the most promising technique for intracardiac blood flow assessment at the moment, 4D flow MRI, and to utilize this technique to improve understanding of intracardiac blood flow dynamics in health and disease.

Analysis of 4D flow data is extremely time-consuming, especially during the heart segmentation stage. In spite of this limitation, some approaches have used the information available in the acquisitions to analyze values like flow components, kinetic energy, linear momentum and early vs. late diastolic inflow.

All of these methods require segmentation of the heart’s chambers and large vessels, which present a problem in velocity MRIs, since the contrast between myocardium and blood is usually not very good (figure 1).

The first goal of the project is to develop a semi-automatic atlas-based segmentation method that can be used on 4D flow MRI data. A segmented 3D model of a heart, also called atlas, will be used as base for the registration and subsequent segmentation of the input heart image. Where available; other acquired MRI data, such as angiography or velocity information, will be used to improve the quality of the method.

A successful result will be a delineation of the cardiac chambers, large vessels and valves of the heart. Some manual interaction with the obtained delineation may be necessary to assure robustness.

The technique’s results will be validated visually on dilated cardiomyopathy patients and healthy volunteers, with a focus on blood flow analysis. Furthermore, the accuracy of volume flow through different valves can be assessed by using the continuity equation.

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**Figure 1.** Flow Magnitude (left) and Short Axis balanced (right)

**Figure 2.** Atlas-based segmentation of large vessels.
Advanced MRI Techniques for Functional and Stereotactic Neurosurgery

MANY BRAIN DISORDERS—e.g. tumors, vascular malformations and Parkinson’s disease—can be treated either surgically or by focused radiation. The treated areas are often small and it is of course vital not to harm the surrounding healthy tissue. This places extremely high demands on the accuracy of the tools used by neurosurgeons; for example the Leksell Gamma Knife (a Swedish invention) can deliver focused radiation with accuracy better than one millimeter.

To take full advantage of this accuracy you need to know where to direct it, which is why you need imaging. This project deals with the imaging technique known as Magnetic Resonance Imaging (MRI). It was developed in the early 1970’s by the chemist Paul Lauterbur and the physicist Sir Peter Mansfield, a feat for which they were awarded the Nobel Prize in physiology or medicine in 2003.

Since its introduction, the principles and applications of MRI have been subject to intense research. We strive to take these scientific land winnings and put them at the hands of those who make it matter—the neurosurgeons. Our emphasis is on segmentation, which means that an MR image is, more or less automatically, provided with a “map” that describes the locations of different anatomical and functional structures in the image. This map can comprise both the target of the treatment (e.g. a tumor) and normal, healthy, brain structures.

Accurate and robust segmentation methods have several clinical uses. The most obvious is to aid in defining the target of a treatment and identifying nearby structures which must be protected. To evaluate the effects of a procedure, new MR images are acquired and compared to the prior ones. Segmentation methods can facilitate this comparison by, for example, quantifying how much a tumor has shrunk. Yet another important application, specific to radiation therapy, is the need to accurately compute the radiation dose. This is something that typically requires additional X-ray imaging with little diagnostic gain, in particular for brain disorders. It is therefore desirable to do the dose calculations using only MR images. An important step in this direction is to use segmentation to identify tissue types that have different effect on the radiation (Figure).

A specific MR technique with an important role in this project is so called diffusion imaging, which provides means to segment nerve fibers by taking advantage of the fact that water travels easier along nerve fibers than across them. This could provide the neurosurgeon with a valuable insight into the wiring of the brain; allowing critical nerves to be spared, improving understanding of how epileptic seizures spread throughout the brain and facilitating treatment of conditions in which a nerve itself is the culprit (e.g. trigeminal neuralgia—one of the most painful conditions known to mankind).
Brain Mechanisms in Irritable Bowel Syndrome

IRRITABLE BOWEL SYNDROME (IBS) is a common chronic syndrome characterized by recurrent abdominal pain or discomfort associated with altered bowel habits. In the absence of generally agreed upon biomarkers, the diagnosis relies on symptom reports and exclusion of organic disease. The cause of IBS is not completely understood. Altered brain-gut interactions are thought to play an important role in the cardinal symptoms, particularly abdominal pain since it has been shown that hypersensitivity to distensions in the lower part of the bowel is present in some, but not all IBS patients. Increased knowledge about how the brain receives and processes the signal from the gastrointestinal tract is important to understand the basic mechanisms of IBS.

A growing number of brain imaging studies have demonstrated that IBS patients have an abnormal brain activity during rectal distensions but also during the expectation of rectal stimuli. In spite of intensive studies of the syndrome, there is currently no effective medical treatment available. However, several studies have demonstrated a beneficial effect of hypnotherapy in IBS. Despite that hypnotherapy treatment for IBS has been used successfully for more than 20 years, the neural mechanisms of pain relief after a course of hypnotherapy still remain unclear.

The objective of this project is to learn and further develop functional magnetic resonance imaging (fMRI) as a method to study the pathophysiological mechanisms in IBS. It aims to identify differences in brain response to standardized cued rectal distensions between IBS and healthy controls. Another aim is to explore in what way a course of hypnotherapy and educational intervention affect the brain response to standardized cued rectal distensions in IBS patients. The results show that there is a difference in how the brains of hypersensitive IBS patients respond, both to the rectal distension itself and to the expectation of distension compared to IBS patients with normal sensitivity and healthy individuals.

Gut directed hypnotherapy as well as disease related education resulted in symptom improvement and decreased bowel related anxiety. These subjective changes were correlated with changes in brain response. The present findings establish psychological therapy as an important strategy in IBS treatment.

Brain activation during expectation (A) and delivery (B) of rectal distension in hypersensitive IBS patients.
Pernilla Norberg

Quantification and Optimization of Lung SPECT Images

**CHRONIC OBSTRUCTIVE PULMONARY** disease (COPD) is characterized by poor airflow with shortness of breath and cough as a result. The disease is chronic and worsens over time. Reduced ventilation in lung regions affected by COPD is correlated to disease advancement.

As the lung behaves in an asymmetric manner, the regional differences are ideally studied with the use of imaging. Single-photon emission computed tomography (SPECT) is a technique for imaging organ function using radioactive isotopes and a detector collecting information around the subject (Figure 1). SPECT is being increasingly used as a tool in respiratory research. It is common to interpret lung SPECT images by visual inspection. However, quantitative measures obtained from a SPECT image have the potential of providing more information.

The aim of the project is to generate quantitative measures from ventilation lung SPECT images that could be useful together with visual assessment to identify mild lung function reduction. It is important to detect lung function reduction in an early stage to be able to prevent further degeneration. COPD is one of today’s most common diseases and more than 5% of the Swedish population are estimated to have COPD. The number of deaths due to COPD has been increasing since the 1970’s unlike stroke and heart disease.

We have proposed a method, the CVT-method, which measures inhomogeneity caused by lung function reduction using the relative standard deviation, CV.

To provide image quality sufficient for the quantitative task of maximising the separation between healthy and mild COPD activity distributions using the CVT-method, optimisation of acquisition and reconstruction parameter values is needed. Examples of parameter values are activity level of the radioactive isotope, choice of collimator designed for high resolution or high sensitivity, algorithm reconstructing two dimensional projections into three dimensional images, number of updates for the iterative reconstruction algorithm and parameter values for the noise reduction filter.

The method is capable of identifying early COPD in computer simulated images of an anthropomorphic phantom with lesions mimicking early COPD, with a very high probability. The CVT-method is also shown to be capable of identifying patients with severe COPD, also this with a high probability (Figure 2). While our results are promising, the ultimate test of its applicability to detect less advanced stages of lung function reduction in human subjects is one of our future aims.
THE GOAL of this work is to explore new visualization and tracking techniques for surgery, particularly neurosurgery. The main interest is in brain tumor surgery to provide the surgeon visual information regarding tumors and eloquent areas, e.g. speech, motor and visual areas.

A central problem for all neuronavigation systems is the fact that, once the operation has started, the brain will be deformed to such an extent that the MRI image acquired preoperatively will no longer be a geometrically correct map of the area where the operation is carried out. This “brain shift” problem has attracted considerable attention, and the solutions proposed often involve some kind of real-time imaging, e.g. by ultrasound, to which the preoperative image is morphed. However, since the most relevant information (tumor extent, functional centers, and vessels) usually is present only in MRI, the real-time images cannot replace the preoperative images.

If the correct deformation is applied to the preoperative MRI image we still have to render it in such a way that the surgeon will perceive the important structures in the right position. Since the tumor can be located totally inside the brain the selection of the opacity levels and rendering types plays an important role. For instance if the tumor is rendered totally opaque then it will look like it is outside the brain, this is due to the occlusion depth-cue that can be stronger in stereoscopy.
Stephanie Franzén

The Role of Hypoxia in the Development of Kidney Damage

ONE THIRD OF all diabetes patients develop kidney damage during the course of their disease. The underlying mechanisms are, however, not yet completely known. Diabetes complication such as cardiovascular events is today one of the most common causes of death in the industrial world, whereas one in four Americans have metabolic syndrome which is indicated by obesity, diabetes, high blood pressure and high levels of plasma cholesterol.

The kidneys main function is filtration of the blood, reabsorption of the filtered substances that are necessary such as glucose and sodium and excretion of substances that the body doesn’t need into the urine, i.e. proteinuria. Kidney damage has been demonstrated to be reversible with antioxidant and citrulline treatment. During the continued development of kidney damage the filtration rate reaches a top peak and then declines again with further increases in proteinuria, which at this stage is irreversible.

Our hypothesis is that oxygen metabolism is the main underlying mechanism for developing kidney damage. It is known that diabetic kidneys present decreased oxygen tension, i.e. hypoxia. We are investigating if the hypoxia is caused by the increased consumption of oxygen that is occurring in a diabetic state. Therefore, we have performed several studies investigating the changes in oxygen consumption and oxygen tension with different treatments and can with that conclude that oxygen metabolism plays a key role in the development of kidney damage in diabetes.

We have recently presented an optimized methodology with electron paramagnetic resonance (EPR) oximetry to repetitively monitor intrarenal oxygen tension and we are currently looking at a short term study investigating if kidney tissue hypoxia occurs directly after the onset of diabetes in a mouse model of diabetic nephropathy.

In conclusion, previous studies demonstrate that hypoxia plays an important role in the development of kidney damage in the diabetic state and treatments for reversing or slowing down the disease is necessary.
Chromatin Analysis in Breast Cancer Using Ensemble Method

PATHOLOGICAL DIAGNOSIS IS considered to be the ‘gold standard’ in the diagnosis of cancer and many other malignant as well as benign diseases. The practice of cytology and histology demands the wide use of perceptual and cognitive skills for the decision making process. Thus, pathologists often have to undertake a very complex decision making process in the diagnosis of diseases. As a solution to this problem, digital pathology is a revolutionary concept that is slowly and steadily being introduced in the field of anatomic and surgical pathology. Digital histopathological images are currently gaining wide acceptance in clinical routine.

Image analysis has the potential to play a critical role in the identification of novel therapeutic targets and creation of new disease classification systems which will be able to improve prediction of treatment response. In our project, we aim to use image analysis algorithms to perform Nottingham Histologic Grading (NHG) for breast cancer. NHG is a widely used classification system to decide how advanced the breast cancer is.

Breast cancer is one of the leading causes of death among women worldwide. Accurate and early detection has the potential to greatly reduce mortality rates. Thus, it is valuable to learn if and how image analysis and machine learning methods can contribute to precise and reproducible cancer grading. To achieve this, our study investigates one part of NHG where the shape of the nucleus and the chromatin is assessed to see whether chromatin texture of the nucleus can be exploited as an independent factor for automated nuclear grading in histology images. Such an investigation is in particular relevant, as the perception of texture may vary between pathologists, which can hinder objective quantification of chromatin distributions.
Jesper Molin

Smarter Digital Pathology Based on Diagnostic Tasks and Cognitive Processes

While no cure for cancer has yet been found, different treatment strategies have advanced rapidly during the last decades. The treatments have gone from a one-size fits all approach towards becoming more and more personalized. This development has put a pressure onto the diagnosing pathologists to deliver more detailed characterizations of the tumor biopsies. Together with the current lack of pathologists in Sweden this risk causing, if not severe implications, at least unnecessary emotional distress of patients waiting weeks on the lab results of their suspected cancer.

In recent years, the possibility of diagnosing cancerous tissue samples digitally has become available for clinical use. This makes it possible to create automatic systems that can aid and speed up the work of the pathologist. This project focuses on analyzing the thinking processes of the pathologist to gain new insights to how such automatic systems should be constructed and then using these insights to create prototype systems. Currently three different tracks are ongoing:

A think-aloud study has been carried out which has recorded pathologists’ verbal statements and interaction with a computerized interface when diagnosing cases. The data is currently being analyzed.

A human-centered system to count positive cancer cells has been conceived. The system assists the pathologist to estimate the growth rate of a cancer which is used to calculate survival rates, used by oncologists for treatment planning.

Finally, different input devices for pathologist are being tried out for navigating the digitized tissue samples to improve the ergonomics. The computer mouse is not adapted for long term panning and zooming in the Google maps-like tissue sample interface, why input devices from other professional computer users are tried out. Such devices include for instance multi-touch stylus tablets from the photo-editing industry or the 3D-mice from the computer aided design (CAD) industry.

An import focus of all tracks is a close collaboration with clinicians to guarantee that relevant problems are solved to improve turnaround time and accuracy of cancer diagnostics.

An interactive system that shows different amount of detail at different zoom levels that help pathologists to estimate the growth rate of cancer.
Stefan Lindholm

Scientific Visualization with Focus on Volume Rendering

THE PROJECTS we explore intend to exploit state-of-the-art signal processing techniques to improve volumetric medical visualization. A key goal of our work is to maintain a simple, functioning interface for the end user even for more advanced, parameter heavy, algorithms.

One of the investigated approaches targets visualization of contrast enhanced blood vessels. In short, we have developed algorithms that search for “vessel like structures” in the volumetric data. This information is then used to locally adapt the visualization in such a way that surrounding tissue does not occlude the studied vessels.

The vessel filter described above is one example of how local neighborhoods can be used to extract additional information from the data itself. Another valuable source of information is, of course, the physician that performs the examination. In another project we have investigated how the manual classification entered by the user during runtime can be used in the interpolation step of the visualization pipeline. By re-using this information, which is already in the system, it is possible to reduce the number of misclassified samples at tissue borders, and thereby significantly reduce a common type of artifact without increasing the complexity of the interaction. The approach is exemplified in the Figure providing improved distinction between the bone and (contrast enhanced) vessels.

![Figure. Comparison of standard continuous reconstruction (left) and adapted, boundary aware, reconstruction (right). Commonly occurring artifacts, such as the red sheet in the left image, can be reduced by using the already existing tissue classification also in the interpolation step of the visualization pipeline.](image-url)
Jacob De Geer

The Use of CT in Cardiac Imaging

There are a number of different ways to visualize myocardial perfusion. Traditionally, the most common way has been to use single-photon emission computed tomography (SPECT) but in recent years, more novel methods such as magnetic resonance imaging (MRI) and computed tomography (CT) have been introduced. With CT, there are a number of different approaches available but the one we have investigated is so-called dynamic CT perfusion (CTP) which utilizes continuous scanning during the contrast wash-in phase, with subsequent evaluation of the change in myocardial attenuation during this period. The purpose of the study was to compare the methods accuracy, using SPECT as reference method.

Our results showed only a moderate correlation between the methods, probably mainly due to the very different mechanisms involved. In addition, we observed a large variation in CTP blood flow in supposedly healthy cardiac segments, both within each patient but also between patients, leading to the conclusion that it is difficult to establish a single cut-off value for myocardial ischemia.

We also concluded that the CTP method itself was technically complex and hampered by small field of view, which in several cases caused accidental exclusion of large parts of the myocardium, rendering the exam useless.
During 2013 several of the CMIV PhD students have finished their studies and defended their dissertations. The PhD students are an important part of CMIV and we are proud to present their dissertations here.
The main function of the heart is to pump blood throughout the cardiovascular system by generating pressure differences created through volume changes. Although the main purpose of the heart and vessels is to lead the flowing blood throughout the body, clinical assessments of cardiac function are usually based on morphology, approximating the flow features by viewing the motion of the myocardium and vessels. Measurement of three-directional, three-dimensional and time-resolved velocity (4D Flow) data is feasible using magnetic resonance (MR). The focus of this thesis is the development and application of methods that facilitate the analysis of larger groups of data in order to increase our understanding of intracardiac flow patterns and take the 4D flow technique closer to the clinical setting.

Quantification of 4D Left Ventricular Blood Flow in Health and Disease

Jonatan Eriksson
Linköping University, Department of Medical and Health Sciences, Division of Cardiovascular Medicine

The genesis of atherosclerosis has previously been shown to be affected by the frictional load from the blood on the vessel wall, called the wall shear stress (WSS). Assessment of WSS can therefore provide important information for diagnoses, intervention planning, and follow-up. Calculation of WSS requires high-resolved velocity data from the vessel, which can be obtained using computational fluid dynamics (CFD). Since every vessel is unique, so is its WSS pattern. Hence the CFD simulations must be done in subject specific vessel models. Such can be created from anatomical information acquired with magnetic resonance imaging (MRI). In this work large eddy simulation (LES) was successfully used to simulate transitional flow in idealized as well as subject specific vessel models. It was shown that a scale resolving technique is to prefer for this application, since much valuable information otherwise is lost.

Turbulent Flow in Constricted Blood Vessels: Quantification of Wall Shear Stress Using Large Eddy Simulation

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Linköping University, Department of Management and Engineering, Applied Thermodynamics and Fluid Mechanics
Sven Petersson
Linköping University, Department of Medical and Health Sciences,
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Fast and Accurate 4D Flow MRI for Cardiovascular Blood Flow Assessment

The study of blood flow is essential in understanding the physiology and pathophysiology of the cardiovascular system. Small disturbances of the blood flow may over time evolve and contribute to cardiovascular pathology. Wall shear stress is the frictional force of blood on the vessel wall and has been linked to the pathogenesis of atherosclerosis and aneurysms. Time-resolved three-dimensional (3D) phase-contrast magnetic resonance imaging (MRI), often referred to as 4D flow MRI, is a versatile and non-invasive tool for cardiovascular blood flow assessment. The use of 4D flow MRI permits estimation of flow volumes, pressure losses, wall shear stress, turbulence intensity and many other unique hemodynamic parameters. In this thesis, the accuracy of 4D flow MRI-based turbulence intensity mapping and wall shear stress estimation was investigated by using numerical simulations of MRI flow measurements.

Gunnar Läthén
Linköping University, Department of Science and Technology,
Media and Information Technology

Level Set Segmentation and Volume Visualization of Vascular Trees

Medical imaging is an important part of the clinical workflow. With the increasing amount and complexity of image data comes the need for automatic (or semi-automatic) analysis methods which aid the physician in the exploration of the data. One specific imaging technique is angiography, in which the blood vessels are imaged using an injected contrast agent which increases the contrast between blood and surrounding tissue. In these images, the blood vessels can be viewed as tubular structures with varying diameters. Deviations from this structure are signs of disease, such as stenoses introducing reduced blood flow, or aneurysms with a risk of rupture. This thesis focuses on segmentation and visualization of blood vessels, constituting the vascular tree, in angiography images.
The main aim of this dissertation was to investigate the difference in neural language patterns related to language ability in healthy adults. The focus lays on unraveling the contributions of the right-hemispheric homologues to Broca’s area in the inferior frontal gyrus (IFG) and Wernicke’s area in the posterior temporal and inferior parietal lobes. The functions of these regions are far from fully understood at present. Two study populations consisting of healthy adults and a small group of people with generalized epilepsy were investigated. Individual performance scores in tests of language ability were correlated with brain activation obtained with functional magnetic resonance imaging during semantic and word fluency tasks. Performance-dependent differences were expected in the left-hemispheric Broca’s and Wernicke’s area and in their right-hemispheric counterparts.

Mind Your Language, All Right? Performance-Dependent Neural Patterns of Language

Helene van Ettinger-Veenstra
Linköping University, Department of Medical and Health Sciences, Division of Radiological Sciences

The Stack Mode Review of Volumetric Datasets: Applications for Urinary Stone Disease

Mats Lidén
Örebro University, School of Health and Medical Sciences

During the last decades the acquisition and visualization of radiological images have rapidly evolved. The increasing amounts of volumetric image data particularly from modern CT systems necessitate a constant evolution of the radiological visualization techniques. The dominating display mode for volumetric images has been the stack mode display since its introduction in computerized image review. In the increasing amounts of image data, the stack mode display needs to be analyzed so that the information content in the high resolution datasets can be transformed into clinically relevant information for the management of the individual patient. In the present thesis some aspects of the stack mode display were analyzed using for the most part the size estimation of urinary stones in unenhanced CT as a model.
Diffuse liver disease have the potential of causing chronic liver disease (CLD) and development of fibrosis, possibly culminating in cirrhosis with an increased risk for hepatocellular carcinoma, HCC. A liver biopsy may be needed to help establish the diagnosis. There are, however, well-known drawbacks with biopsies such as the risk of complications and inaccurate staging due to sampling error. Up to date, no non-invasive technique, either alone or in combinations, can compete with liver biopsy although there are promising possibilities in the magnetic resonance (MR) technique. The present study aims at demonstrating phosphorus metabolite concentration changes and alterations in uptake/excretion of a hepatocyte specific contrast agent in patients with diffuse liver disease by applying two non-invasive quantitative MR techniques and to compare the results with histo-pathological findings, with focus on liver fibrosis.

**Bengt Norén**
Linköping University, Department of Medical and Health Sciences, Division of Radiological Sciences

**Non-Invasive Assessment of Liver Fibrosis with 31P-Magnetic Resonance Spectroscopy and Dynamic Contrast Enhanced Magnetic Resonance Imaging**

Medical imaging plays an increasingly important role in modern healthcare. In medical imaging, it is often relevant to relate different images to each other, something which can prove challenging, since there rarely exists a pre-defined mapping between the pixels in different images. Hence, there is a need to find such a mapping/transformation, a procedure known as image registration. Over the years, image registration has been proved useful in a number of clinical situations. Despite this, current use of image registration in clinical practice is rather limited, typically only used for image fusion. This thesis aims to overcome some of the issues limiting the use of image registration, by proposing a set of technical contributions and two clinical applications targeted at improved clinical efficiency.

**Daniel Forsberg**
Linköping University, Department of Biomedical Engineering, Medical Informatics

**Robust Image Registration for Improved Clinical Efficiency: Using Local Structure Analysis and Model-Based Processing**
Through unique collaborations with the industry it is possible for CMIV to always have the latest and most advanced equipment. This is a prerequisite for the successful research carried out at CMIV.

CT
The Siemens SOMATOM Definition Flash is a scanner using two X-ray sources and two detectors at the same time. It enables scanning of every beating heart at any heart rate and at the lowest radiation dose possible. The CT provides one-stop diagnoses in acute care; even with large patients, regardless of condition, and heart rate. Dual-energy scanning is an amazing tool in exploration of new clinical opportunities.

MRI
The Philips Ingenia 3.0T is our most recently acquired MRI system with a 70 cm bore. It is equipped with Xtend gradient system (up to 45 mT/m - 200 T/m/s) and two parallel RF transmissions (Multitransmit 4D), which adapt RF signals to each patient. Multitransmit facilitates an increased image uniformity, contrast, and consistency, as well as faster imaging. A full range of receiver coils is available with analog-to-digital converters inside the coils (dStream RF). This samples the MR signal directly in the coil on the patient, and sends it to the reconstructor via a fibre-optic cable, resulting in up to 40% higher SNR, and a dynamic range that exceeds 185dB.

Our Philips Achieva 1.5T has a 60 cm bore and is equipped with Nova Dual gradients with capability (up to 66 mT/m – 160 T/m/s), a 16-channel Freewave data acquisition system, and the latest software release. A full research agreement with Philips Medical Systems allows all possible clinical as well as technical research applications.

In addition, we have access to a GE Signa 1.5T HDxt and Discovery 750 3.0T MRI system.

Ultrasound
CMIV has access to several clinical ultrasound scanners, Vivid E9 with Echopac BT 13 software for echocardiography and Siemens S2000 for vascular studies, as well as a dedicated scanner GE Logic E9 and a Vevo high frequency scanner for vascular research.
PACS

Sectra radiology PACS is a comprehensive workstation, designed to optimize the workflow. It ensures quick and easy access to patient data and images and provides instant access to all the tools needed integrated on the desktop – including RIS and clinical applications.

For storage and handling of echocardiographic image data (for both research and clinical use), one of the largest installations of the GE EchoPAC system in the world is available.

A number of advanced diagnostic workstations are available for clinical and research purposes.

Visualization

CMIV has its own Virtual Reality theatre with a capacity of 70 persons. The theatre is built around Barco Galaxy NW-12 projector (12,000 lumens light output, WUXGA (1920x1200) resolution.) The NW-12 has an integrated active Infitec 3D stereo filter, allowing for optimal 3D visualization with passive stereo glasses. Using a Barco XDS 150 and an EXTRON DMS 3600 DVI switch, all computers at CMIV’s network can be used for video conference system, allowing for 1080p HD conference meetings or video broadcasting. A Smartboard Interactive Whiteboard is available for interactive presentations and meetings.

Several Advantage Workstations from GE Medical Systems are available at the hospital. In addition to the theatre there is also a Sectra visualization table complete with Sectra PACS. The Visualization Table is a large interactive screen with an image display system that enables interaction with 3D human body images rendered from CT or MR.
Computed tomography scan of a young Brown Bear from the Swedish zoo Kolmarden. The scanning of the bear was performed during research collaboration between CMIV and Kolmarden. The aim of the project was to document and learn more about the physiology of wild animals. For CMIV the project was a unique opportunity to develop new methods without having to consider the radiation dose as most of the animals were not alive.
CMIV is governed by its Board of Directors, with representatives from academia, health care and industry. The Scientific Council, appointed among the senior researchers affiliated with CMIV, manages the research agenda of CMIV. The day-to-day operations of CMIV are handled by a group of core staff.

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<td>Henrik Haraldsson</td>
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<td>Markus Heilig</td>
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<tr>
<td>Camilla Josephson</td>
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<td>Susanna Walter</td>
<td>Olof Dahlqvist Leinhard</td>
<td>Umeå University, Diagnostic Radiology</td>
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The CMIV researchers have published numerous articles and conference proceedings in the past years. Here you will find a list of publications from the last five years. The list is however not complete as the network of researchers is complex and publication flow hard to overview.
2013 Peer-reviewed Original Articles


Model-based registration for assessment of spinal deformities in idiopathic scoliosis. Anders Ynnerman, C Scheidegger, T Ropinski, J Knutsson, accepted for publication in Physics in Medicine and Biology

vPSNR: a visualization-aware image fidelity metric tailored for diagnostic imaging. Claes Lundström, Mats Andersson, Hans Knutsson, accepted for publication in Physics in Medicine and Biology


Dual-energy computed tomography of a mouse.

Publications with authors from more than one faculty at LiU is marked with *. CMIV affiliated researchers are marked with bold and JIF > 5.


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CMIV Annual Scientific Report 2013

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Feature-enhancing zoom to facilitate Ki-67 hot spot detection. Jesper Molin, Kavitha Shaga Devan, Karin Wårdell, Claes Lundström, accepted to Digital Pathology, SPIE Medical Imaging, 2014.

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Engström M, Karlsson T. Brain and effort: brain activation and effort-related work.
ing memory in healthy participants and patients with working memory deficits. Front Hum Neurosci. 2013;7:40-17


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CT for diagnostik av kranskärlssjukdom, Studentlitteratur. Jan Engvall, Anders Persson, in press 2013


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J Lantz and M Karlsson: Large Eddy Simulation of LDL surface concentration in a subject specific human aorta, J Biomechanics vol 45(3):337-342, 2012 Number of citations: 1

*K Kindberg, H Haraldsson, A Sigfridsson, J Engvall, NB Ingels, T Ebbers and M Karlsson: Myocardial Strains from 3D DENSE MRI, BMC Med Imaging, vol 12(9), 2012 Number of citations: 1

J Renner, H Nadali Najafabadi, T Lanne and M Karlsson: Subject-specific aortic wall shear stress estimations using semi-automated segmentation, Clinical Physiology and Functional Imaging, Volume 32(6), 481-491, November 2012, Number of citations:.


Tissel A. Dahlqvist Leinhard O, Warnstjes JBM, and Lundberg P. Procedure for Quantitative 1H


Moreno R, Boga M, Smedby O. Generalizing the Mean Intercept Length Tensor for Gray-Level Images. Medical Physics 2012;39;4599-4612. DOI:10.1118/1.4730502


S. Landtblom AM, Lenn Lindholm, R. Lenn Persson, A. Borga M. Automatic Tuning of Spatially Varying Transfer Functions for Blood Vessel Visualization. IEEE Transactions on Visualization and Computer Graphics. 2012; (18) 12, 2345-2354 Number of citations: 2


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J Lantz, T Ebbers, J Engvall and M Karlsson: Large Eddy Simulation of Aortic Coarctation Before and After Surgery Artery 12, 18-20 October 2012, Vienna, Austria


Rodrigo Moreno, Magnus Borga, Orjan Smedby. Estimation of Trabecular Thickness in Gray-Scale Images Through Granulometric Analysis. SPIE Medical Imaging, Vol. 8141, 81412J. San Diego, USA, February 2012. DOI:10.1117/12.906754


Number of citations: 2

Simulations help us understand X-ray imaging (3 presentations. Topic: Physics in Radiology / Moderators: H. Borsmans (Leuven/BE), A. Persson (Linköping/SE) European Congress of radiology, 2012, March 5, 08:30 - 10:00


2012 Review-peer reviewed Articles

State-of-the-art of visualization in post-mortem imaging


Alexander Bock, Norbert Lang, Gianpaolo Evangelista, Ralph Lehrke, Timo Ropinski: Supporting Deep Brain Stimulation Interventions by Fusing


Stefan Diepenbrock, Timo Ropinski: From Imprecise User Input to Precise Vessel Segmentations, EG Visual Computing for Biology and Medicine - 2012.


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- G. Ahlman, M. Magnusson, O. Dahlqvist Leinhard, and Peter Lundberg. Increased temporal resolution in radial-Cartesian sampling of k-space by implementation of parallel imaging ESMRMB 2011, 28th Annual Scientific Meeting, Leipzig, Germany, October 6-8, 2011.

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Dahlqvist Leinhard, O., Jaworski, J., Aalto, E., Cronqvist, A., Tisell, A., Smedby, O., Landblom, AM., Lundberg, P. Is Increased normal White Matter Glutamate Concentrations a Precursor of Gliosis and Disease Progression in
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Advancing the state-of-the-art for Virtual Autopsie: initial forensic workflow study Isabella Scandurra, Camilla Forsell, Anders Ynnerman, Patric Ljung, Claes Lundström, Anders Persson, Studies in health technology and informatics 160 (Pt 1). 2010


Karlsson, T., Birberg-Thornberg, U., Duhêèn, K., & Gustafsson, P. (2010). LC-PUFA supplemented to mothers during pregnancy and breast-feeding improves cognitive performance in their children four years later—an rct study. Paper presented at the 9th biennial scientific meeting of the International Society for the Study of Fatty Acids and Lipids (ISSFAL); Maastricht, May 29 - June 2nd.


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“Phase Based Level Set Segmentation of Blood Ves-
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Joakim Rydell, Magnus Borga, Hans Knutsson,
“Robust Correlation Analysis with an Application


2008 Peer-reviewed Review Articles


ANNUAL ACCOUNTS

Since CMIV is part both of the university and the county council the finances are also split in two parts. These annual accounts are a summary of the two parts during the last five years.

During 2009 - 2013, the cost per year to operate CMIV’s infrastructure and R&D platform were approximately 12 million SEK. This was partially financed through a basic grant from the County council of Östergötland and Linköping University with 3.5 million, agreements with industry approximately 2 million, Wallenberg Foundation 1 million and clinical and research revenue from CT scan / MRI scans 6 million. The total turnover was approximately 30 million SEK per year.

The annual basic grant from Linköping University and the County Council of Östergötland is 3.5 million SEK distributed in 1 million each from technical and medical faculty and 1.5 million from the county council. The diagram shows an overview of how the grant is being used in the CMIV administration.

CMIV receives funding from research funds and the industry both directly to the R&D platform and to specific research projects. In addition, the affiliated researchers have their own funding; however these grants will not be presented here.

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<td>-13,632</td>
<td>-14,237</td>
</tr>
<tr>
<td>Cost of premises</td>
<td>-2,034</td>
<td>-2,145</td>
<td>-1,975</td>
<td>-1,683</td>
<td>-2,150</td>
</tr>
<tr>
<td>Misc. operating expenses</td>
<td>-8,876</td>
<td>-7,653</td>
<td>-9,549</td>
<td>-10,282</td>
<td>-5,557</td>
</tr>
<tr>
<td>Depreciation expenses</td>
<td>-5,336</td>
<td>-4,988</td>
<td>-5,883</td>
<td>-3,291</td>
<td>-4,937</td>
</tr>
<tr>
<td>Financial expenses</td>
<td>-185</td>
<td>-125</td>
<td>-403</td>
<td>-103</td>
<td>-112</td>
</tr>
<tr>
<td>Total Expenses</td>
<td>-33,187</td>
<td>-29,965</td>
<td>-32,455</td>
<td>-28,991</td>
<td>-26,993</td>
</tr>
<tr>
<td>Result of operations</td>
<td>2,389</td>
<td>2,666</td>
<td>345</td>
<td>-2,115</td>
<td>336</td>
</tr>
</tbody>
</table>

Numbers in thousands of SEK.
Basic grant overview 2009-2013
- 43% - Salaries, CMIV staff
- 21% - Research school
- 21% - Clinical Scientists
- 7% - Central administration
- 5% - Travels and conferences
- 3% - Office supplies and computers

Research funding 2009-2013
- 63 250 - External funds
- 38 700 - Industrial funds

Numbers in thousands of SEK