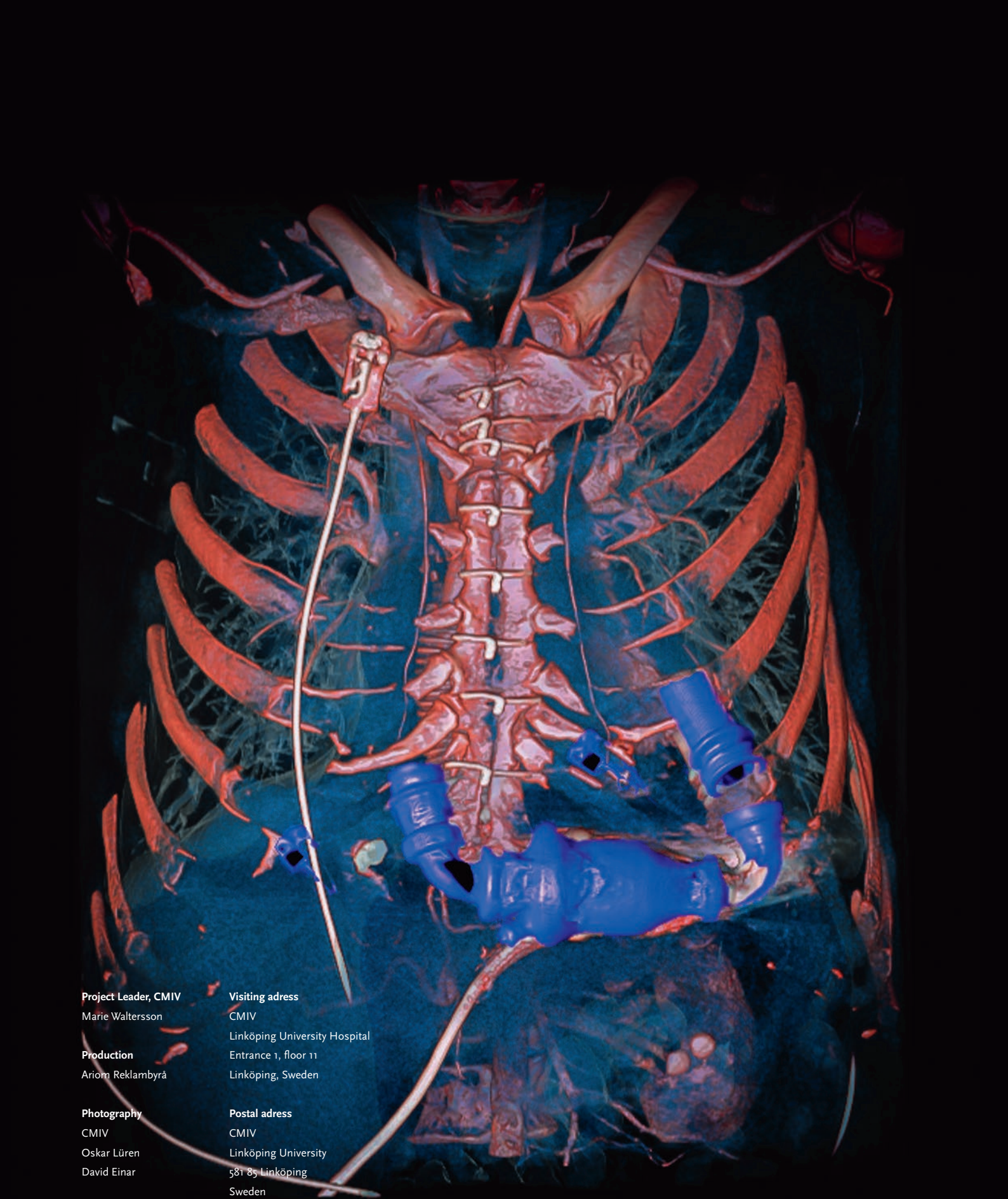
LINKÖPING UNIVERSITY

Welcome to the Exciting World of CMIV

Annual Scientific Report 2014



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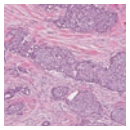

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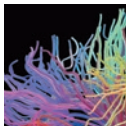

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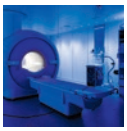

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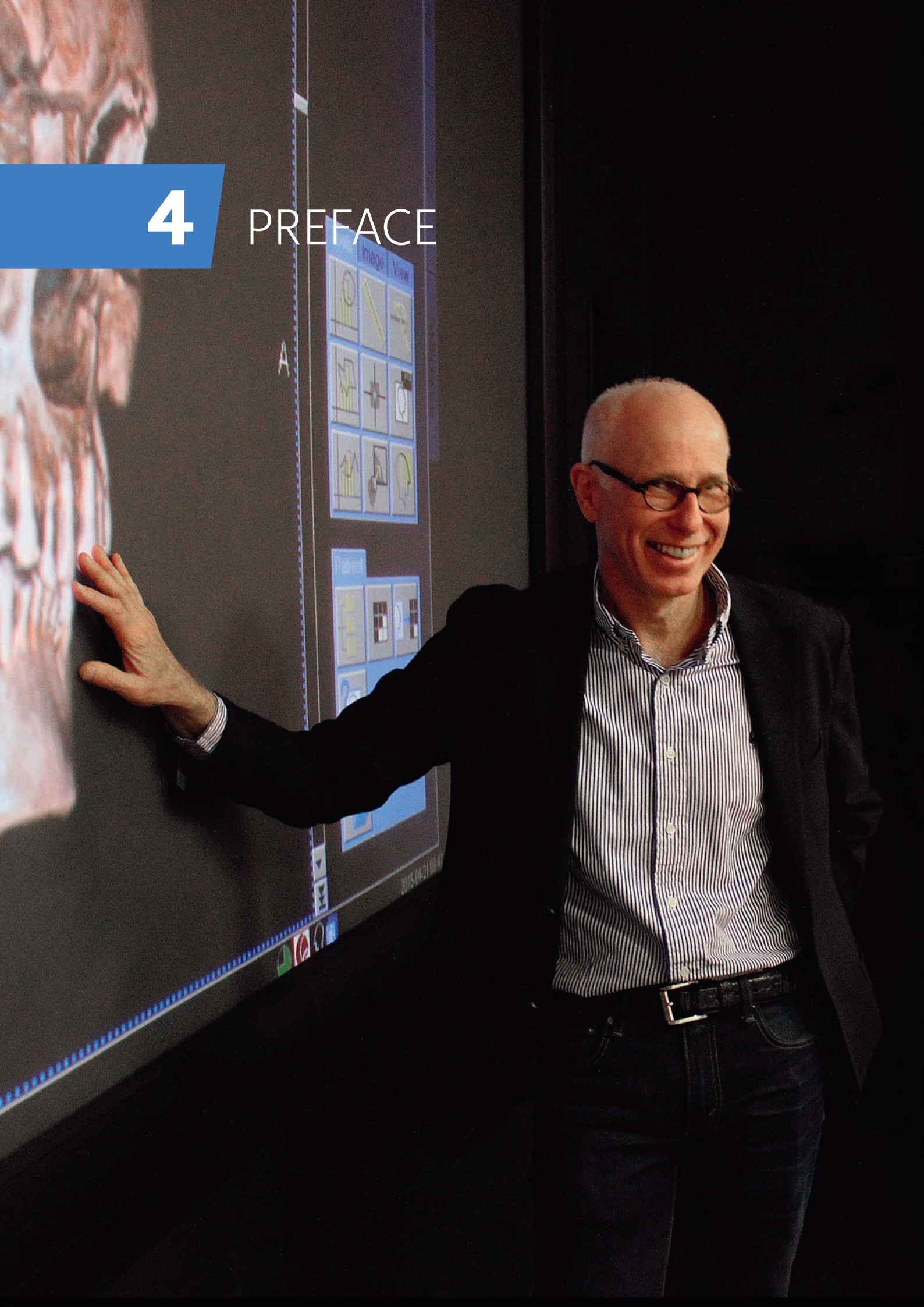
4 PREFACE



Exciting Times Ahead for CMIV

DURING 2014 OUR researchers and staff have continued to work with dedication to improve quality of care always with the patient in mind. The research at CMIV has continued to gain wide attention and the unique patient-oriented clinical research attracts researchers and clinicians from around the world.

It has become clear to us that the human and technical infrastructure plan that we stated in 2013 no longer fits: our research and clinical skills has already outgrown it. Since then flexible planning and creative thinking has resulted in alternative solutions that creates room for further expansion for CMIV.

The flagship projects of 2014 are "Assessment of Cardiovascular Blood Flow Using 4D Flow MRI", "Imaging of Brown Adipose Tissue" and "Optimized flows and IT tools for digital pathology". Three outstanding projects that together represent the multi-disciplinary research at CMIV.

For the first time a large part of the CMIV researchers have made an organized effort to unite their forces in a quest to visualize the functions of the human body in the project "Seeing organ function". The project received substantial funding from Wallenberg foundation last year and has great potential to enable ground breaking medical research on organ function.

Linköping through CMIV, Region Östergötland and Sectra continues to lead the way in digital pathology. The project "Optimized flows and IT tools for digital pathology" received two more years of funding from VINNOVA with the goal of introducing digitized solutions in clinical routine practice.

2015 will be the most active year during CMIV's lifespan. New exciting projects will be initiated such as the Swedish Heart-Lung Foundation study "SCAPIS" – Swedish CardioPulmonary bioImage Study. It is a unique research study involving all university hospitals in Sweden. The goal is to find risk markers that predict who is at risk of developing heart or lung disease and how to prevent it through customized and personalized treatment.

I am looking forward to 2015 where we will move in to the new building and the continued collaboration with the outstanding individuals at CMIV as well as the unique twinning of academic disciplines.

Anders Persson, Director of CMIV

6 CLINICAL PRACTICE

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

Johan Kihlberg, radiology nurse and team leader at CMIV is responsible for the MR research as well as development and maintenance of the clinical work.

The camera time at CMIV is split fifty-fifty between research and clinic and the focus lies in abdominal, cardiac, blood vessel and neuro scans.

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.

Assistant Nurses Caring for the Patients

The assistant nurses are in charge of the logistics and are 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 about the examination.

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.

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.

Enlighten the Body with Computed Tomography

Lilian Henriksson and Petter Quick are radiology nurses at CMIV, both specialized in computed tomography (CT) with long experience in the field. 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. 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 different energy levels it is possible to distinguish between different tissues and materials that would otherwise be impossible.

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.

8 HIGHLIGHTS 2014

2014 has been an eventful year at CMIV with new equipment, awards and research grants. The research has blossomed and resulted in exciting meetings and conferences. Here you will find the highlights of the year.

New CT at CMIV

THROUGH A UNIQUE collaboration with Siemens CMIV could install the new CT FORCE as one of the first centers in the world. The upgrade has lead to higher image quality, lower radiation doses and opened the opportunities for more advanced research projects. This investment will be a great benefit for healthcare, research and industry but above all for the patients.

- This equipment is stronger and faster than our previous CT. The whole body may be analyzed in a second, says Petter Quick, research nurse and application specialist.

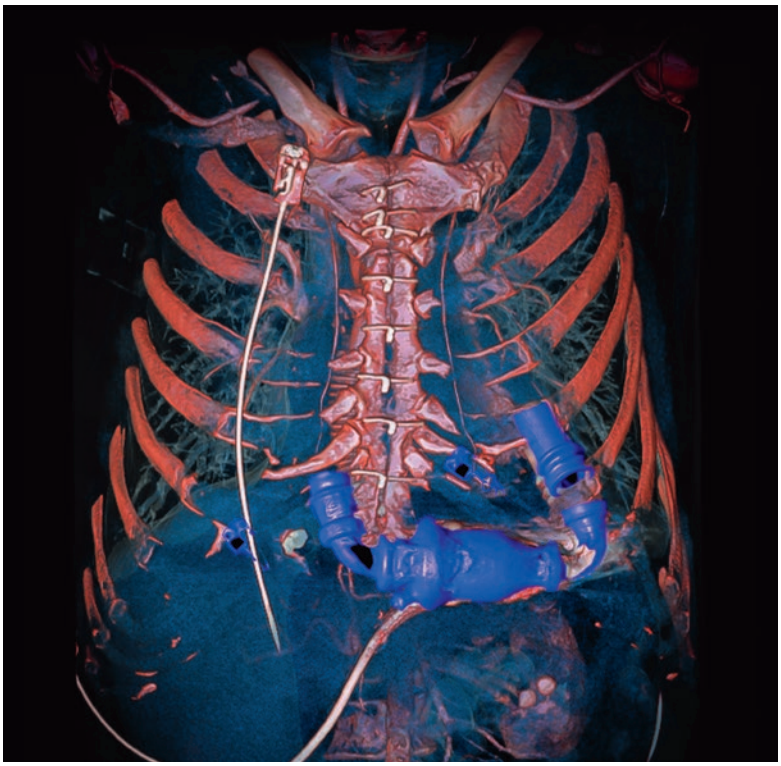
The high resolution minimizes quality problems due to patient movements, breathing or body volume. The new equipment also allows time resolved analyzes which will be explored in several research projects monitoring blood flow or joint movements.

- These projects are on the edge of what is possible but on the other hand, thats where CMIV wants to be, concludes 'Petter Quick.

VINNOVA Granted Funding for DigiPat3

THE SWEDISH INNOVATION agency VINNOVA granted continued funding for implementation of digitized pathology tools in clinical practice. The new project DigiPat3 will introduce the IT-tools and workflows developed in DigiPat2 in clinical practice at pathology departments. The project will also continue the development of innovative tools, education platforms and work on national collaborations regarding standardization and quality control.

DigiPat will be managed by a new consortium lead by Sectra. The other project members are CMIV/Linköping University, Equalis, the county councils of Gävleborg, Örebro, Värmland, Västmanland, Dalarna, Östergötland, Norrbotten, Jönköping and Stockholm, Sahlgrenska university hospital, Unilabs, LRI Instrument AB and Interactive Institute Swedish ICT.



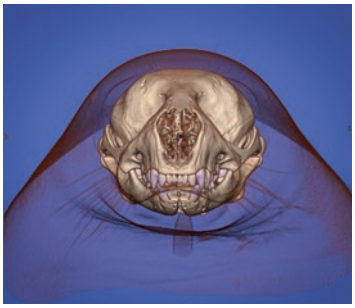
Anders Persson has received the Wellcome Image Award 2014 for his image of a mechanical heart pump inside a human chest.

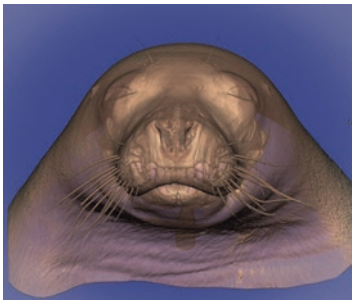
ANDERS PERSSON HAS received the Wellcome Image Award 2014 for his image of a mechanical heart pump inside a human chest. The image was created using dual energy computer tomography (DECT). Unlike a conventional computer tomography (CT) scan, DECT uses two sources of X-rays at different energies to scan the patient. These are then digitally reconstructed in three dimensions and can be rotated, sliced or magnified for greater clarity. DECT provides higher-quality images than conventional CT without the need for exposure to additional radiation. This technique is extremely useful for noninvasively investigating and diagnosing medical conditions and for performing virtual autopsies.

The Wellcome Image Awards celebrate the best in science imaging talent and techniques. This is the second time that an overall winner has been selected. It is one of 18 winning images chosen from those acquired by the Wellcome Images picture library since the 2012 Awards.

The Wellcome Trust is a global charitable foundation dedicated to achieving extraordinary improvements in human and animal health. It supports the brightest minds in biomedical research and the medical humanities.

BBC Medical Correspondent Fergus Walsh, who was a member of the judging panel and presented this year's awards, said: "Anders Persson's 3D image of a mechanical heart fitted inside a human chest is truly stunning. The juxtaposition of delicate human anatomy with the robust mechanical plumbing parts is dramatic, and the image is rendered so vividly in 3D that it appears to jump out at the viewer."



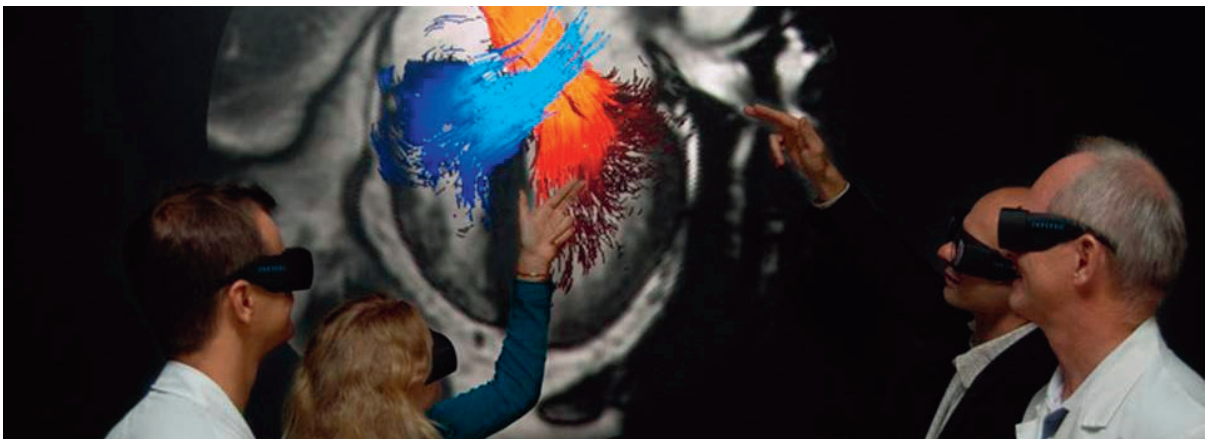


Anders Persson also received an award for his CT-image of a seal.

Nordic Symposium on Digital Pathology 2014

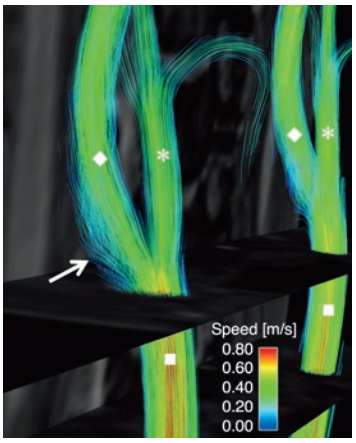
THIS YEAR THE Nordic Symposium on Digital Pathology was relocated to Linköping Konsert & Kongress to accomodate a growing audience, a poster exhibition and an industrial exhibition. During the meeting we had the opportunity to listen to outstanding presentations spanning from pioneering clinical implementations to exciting research outlooks. The exhibition was filled with the latest advances in digital pathology techniques and the program allowed plenty of time to explore and network. An interesting and appreciated element of the symposium was the digitization workshop where all participants had the opportunity to share experiences and discuss difficulties concerning digitization of pathology. The workshop resulted in fruitful discussions and insights from the Nordic countries, Australia, UK and Canada.

Parts of the scientific program was presented in Journal of Pathology Informatics.



RSNA Research & Education Foundation

ANDERS PERSSON HAS received a two year grant worth $145 000 from the RSNA Research & Education Foundation. The funding was granted for the educational project, "RadSim: Simulation Based Training Program for CT Protocol, Iterative Reconstruction and Dual Energy Applications". The CMIV project was selected together with six other projects from over 200 applications. It is highly unusual that a project outside of the US receives funding from the RSNA. The RSNA Research & Education Foundation's mission is to improve patient care by supporting research and education in radiology and related scientific disciplines through funding grants and awards to individuals and institutions that will advance radiologic research, education and practice.



American Heart Association's Scientific Sessions

DURING THE AMERICAN Heart Association's Scientific Sessions, November 16-19 2014 the CMIV researcher Petter Dyverfeldt held an invited talk about multi-dimensional bloodflow measurements in patients suffering from heart failure. The lecture was a summary of the work done on the subject at CMIV.

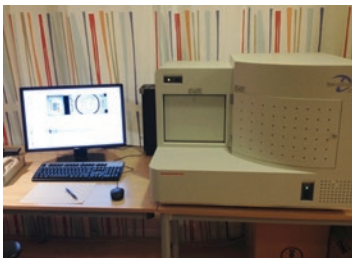
On the same conference Professor Ebo de Muinck presented his project "Direct in Vivo Quantification of Intraplaque Hemorrhage and Fat in Atherosclerosis by Magnetic Resonance Imaging" as a poster. It is not common for researchers outside of the US to be accepted for presentation.

CMIV Well Represented in the Big Announcement from VR

FOUR CMIV RESEARCHERS have received in total 13 million SEK from the Swedish Research Council.

- Tino Ebbers - A cardiovascular functional avatar: model-based analysis of advanced imaging data
- Maria Engström - Ab initio Mathematical Modeling of Mechanisms in the Human Brain
- Peter Lundberg - Hepatic Inflammation and Fibrosis (HiFi): Techniques for Early Disease Detection and Tissue Characterization
- Örjan Smedby - Fast vascular segmentation: skeleton-guided level sets combined with machine learning

Apart from these, also Mats Hammar received 6 million SEK for his CMIV associated project "Effects of resistance training in postmenopausal women on vasomotor symptoms, quality of life, white and brown adipose tissue, muscle mass, myokines, the immune system and length of telomeres".



Digital Pathology Glass Scanner

ONE OF THE LATEST TECHNICAL addition at CMIV is a pathology glass scanner from Hamamatsu. The scanner produces digital images of pathology glass slides that are traditionally examined using a microscope. Digitization is revolutionizing pathology departments worldwide increasing efficiency and quality of care. CMIV is involved in a VINNOVA project with aim to optimize work flows and IT-tools for digital pathology. The project members are in many aspects word leading in the field, booth regarding research and in clinical practice. The new scanner will support research and development within the field of digital pathology at CMIV.

Vetenskapsrådet

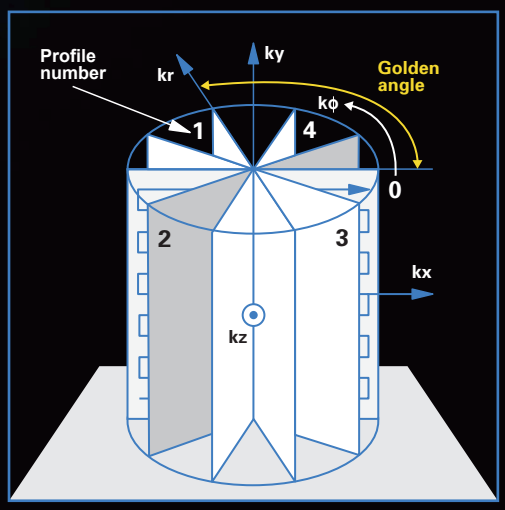
The Swedish Research Council Honours Young CMIV Scientist

THE CMIV RESEARCHER Fredrik Palm receives 18 million SEK from the Swedish Research Council grant for promintent young scientists. Fredrik is professor in experimental kidney medicine and will study why 15% of all diabetes patients develop renal disease within 10-15 years from diabetes debut.

12 CMIV IMAGING CHAIN

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. Since the start in 2002, CMIV has grown into the vision and it is now our everyday routine.

Information is gathered using novel imaging equipment

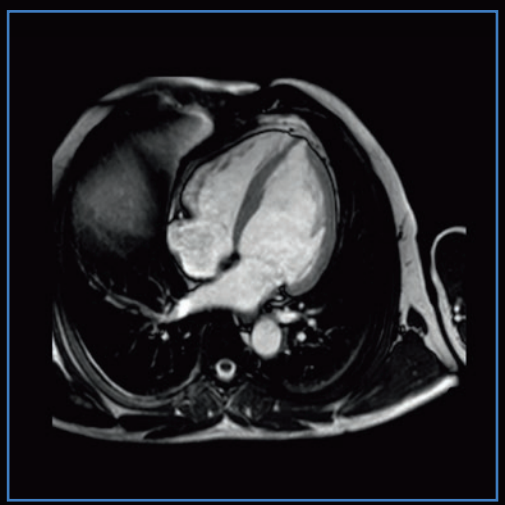


Raw data is processed using complex calculations and algorithms

TODAY, 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 region 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 region wishes that the research and development comes to patient benefit. CMIVs 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. In this way a technical solution in one medical field may be found useful in other fields as well. As it is or, moving back down the chain, inspire to new solutions no one even thought was possible.

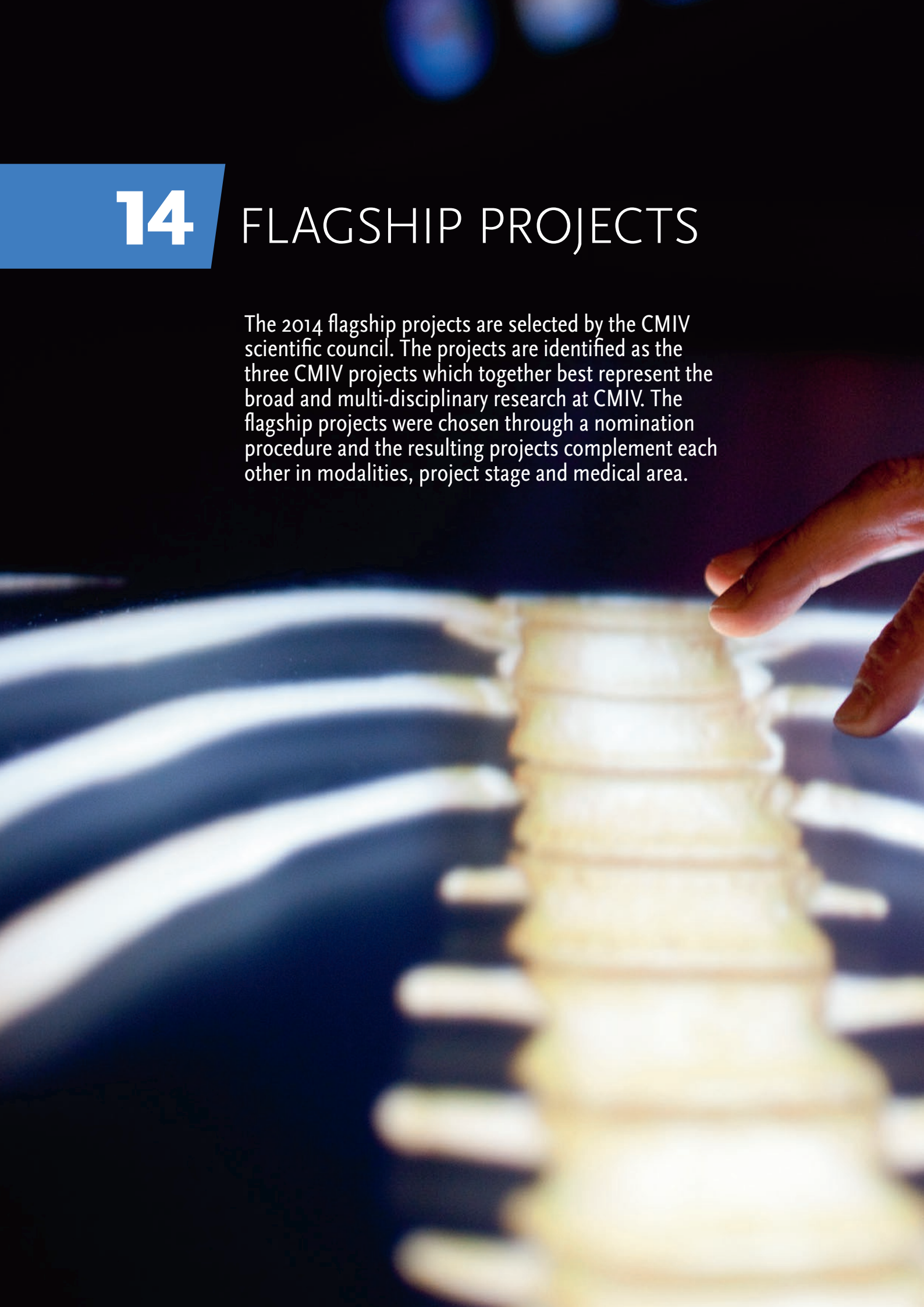


Important findings are visualized in a comprehensive way

Images and findings are used in patient care

14 FLAGSHIP PROJECTS

The 2014 flagship projects are selected by the CMIV scientific council. The projects are identified as 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.



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

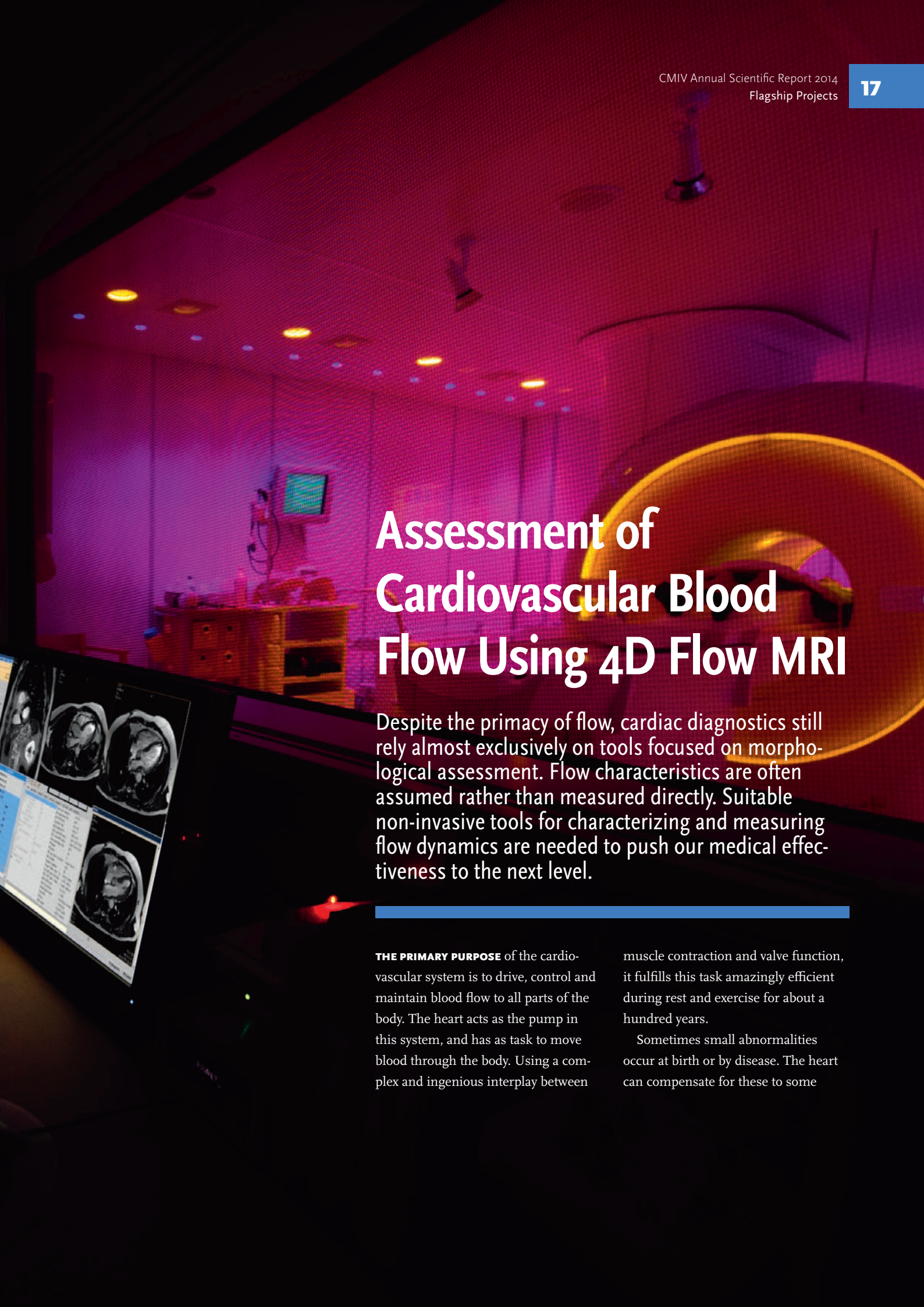
MAIN PROJECT PARTICIPANTS
Senior research leaders: Tino Ebbers, Carl-Johan Carlhäll, Jan Engvall, Petter Dyverfeldt
Post Doc: Jonas Lantz
PhD students: Sven Petersson, Jonatan Eriksson, Belén Casas Garcia, Mariana Bustamante

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

KEY PUBLICATIONS
Eriksson J, Bolger AF, Carlhäll C-J, and Ebbers T. Spatial heterogeneity of four-dimensional relative pressure fields in the human left ventricle. Magn Res in Med. 2015

Sigfridsson A, Petersson S, Carlhäll CJ, Ebbers T. 4D flow MRI using spiral acquisition. Magn Res in Med. 2012;68:1065-1073.

Markl M, Kilner PJ, and Ebbers T. Comprehensive 4D velocity mapping of the heart and great vessels by cardiovascular magnetic resonance. J Cardiovasc Magn Reson. 2011; 13(1): 7.



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 PRIMARY PURPOSE of the cardiovascular system is to drive, control and maintain blood flow to all parts of the body. The heart acts as the pump in this system, and has as task to move blood through the body. Using a complex and ingenious interplay between muscle contraction and valve function, it fulfills this task amazingly efficient during rest and exercise for about a hundred years.

Sometimes small abnormalities occur at birth or by disease. The heart can compensate for these to some

extent, but they can also lead to inefficient pump function and sometimes to a cascade of more severe abnormalities.

–We continue to lose ground against cardiovascular diseases. They are driven by obesity, diabetes and an aging population, says Tino Ebbers, Professor in Cardiovascular Physiology and project leader of "Assessment of cardiovascular blood flow using 4D flow MRI". Imaging that is focused on answering the most relevant questions, with an eye towards tangible improvements in diagnosis, therapy and outcomes can facilitate treatment of cardiac patients with higher quality and lower costs. 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.

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.

Analysing the heart ads an extra dimension to the imaging since it is in constant motion.

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.

"At CMIV, we are one of the leading centers 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

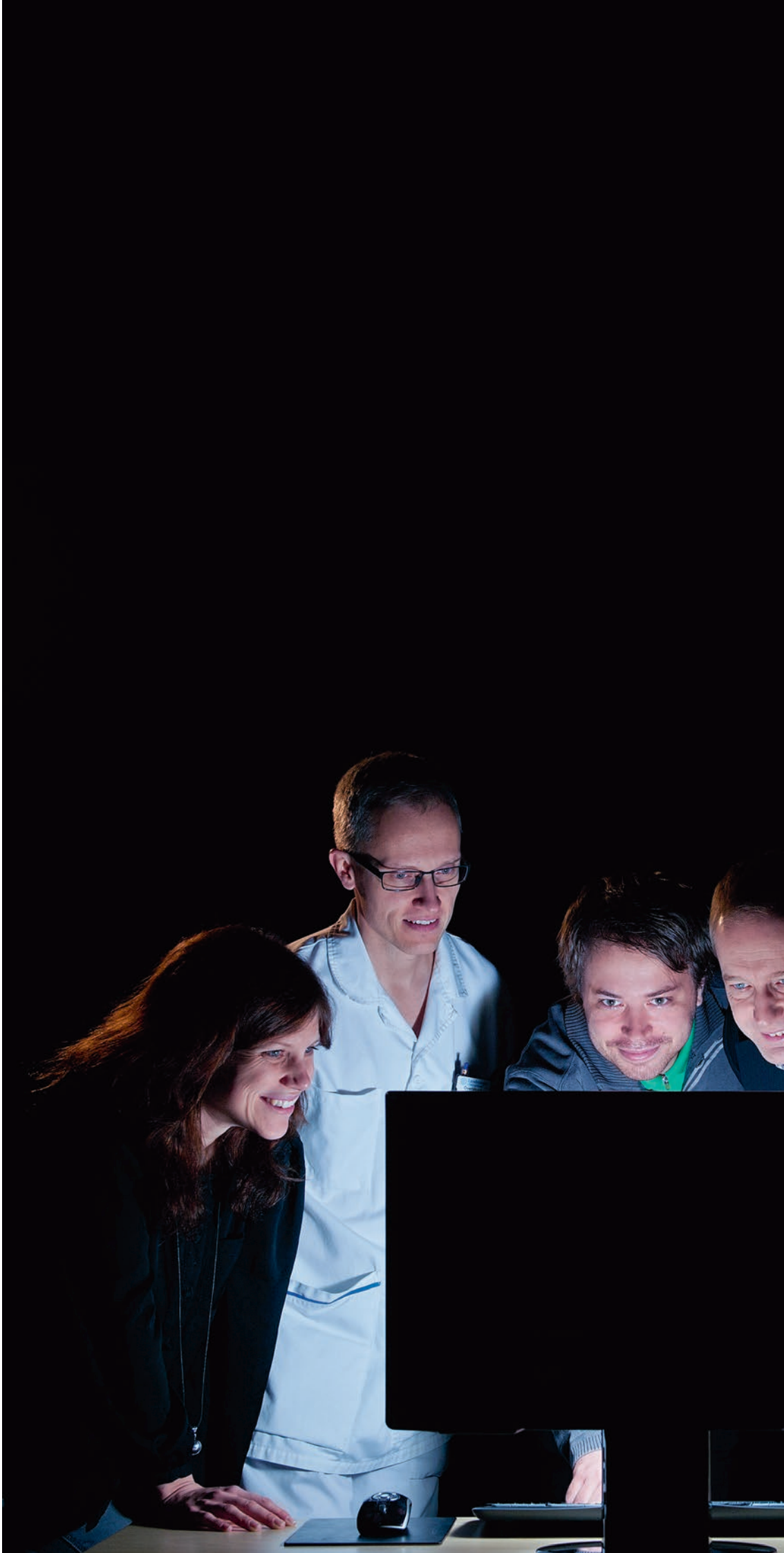
MAIN PROJECT PARTICIPANTS
Anders Persson, Olof Dahlqvist Leinhard, Thobias Romu, Nils Dahlström

GRANTS
KAW 2012-2017

KEY PUBLICATIONS
Martin E. Lidell, Matthias J. Betz, Olof Dahlqvist Leinhard, Mikael Heglind, Louise Elander, Marc Slawik, Thomas Mussack, Daniel Nilsson, Thobias Romu, Pirjo Nuutila, Kirsi A. Virtanen, Felix Beuschlein, Anders Persson, Magnus Borga, Sven Enerbäck, "Evidence for two types of brown adipose tissue in humans", Nature Medicine, 19(5): 631-634, 2013.

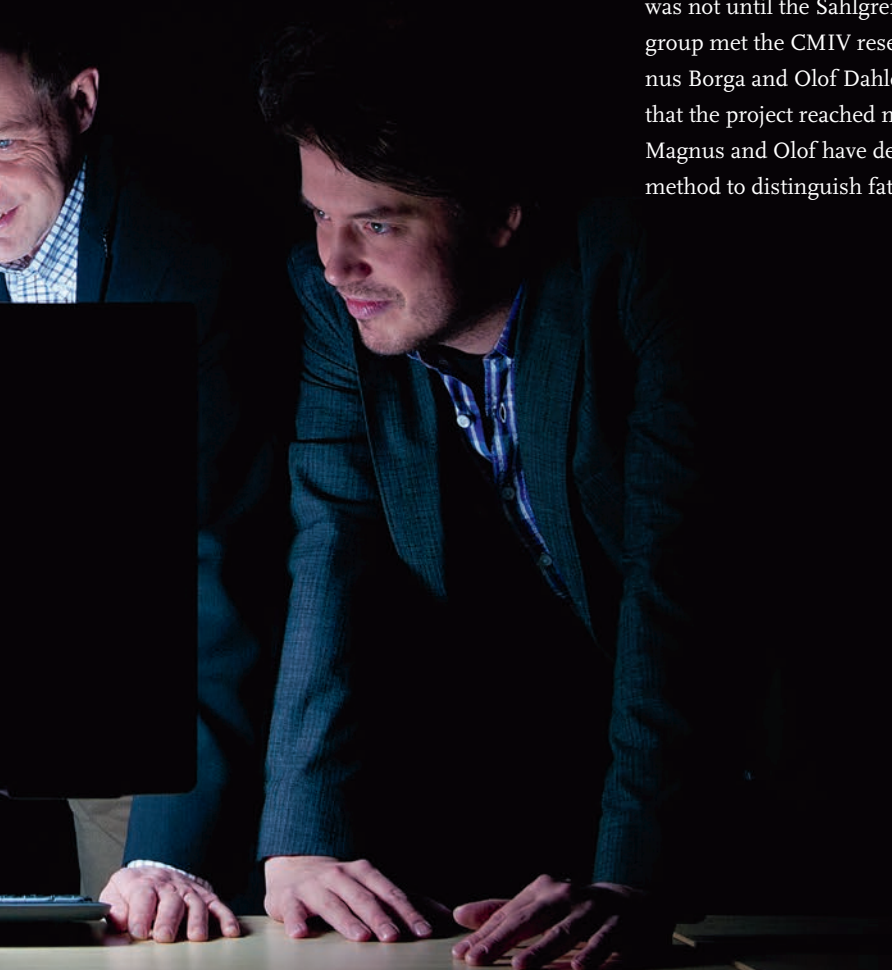
Magnus Borga, Kirsi A. Virtanen, Thobias Romu, Olof Dahlqvist Leinhard, Anders Persson, Pirjo Nuutila, Sven Enerbäck, "Brown adipose tissue in humans: detection and functional analysis using PET (Positron Emission Tomography), MRI (Magnetic Resonance Imaging), and DECT (Dual Energy Computed Tomography)", Methods of Adipose Tissue Biology, Methods in Enzymology, No. 537, 2014.

Thobias Romu, Louise Elander, Olof Dahlqvist Leinhard, Martin Lidell, Matthias Betz, Anders Persson, Sven Enerbäck, Magnus Borga, "Characterization of Brown Adipose Tissue by water-fat separated Magnetic Resonance Imaging", Journal of Magnetic Resonance Imaging, (Accepted), 2015.



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) act 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 life style 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.

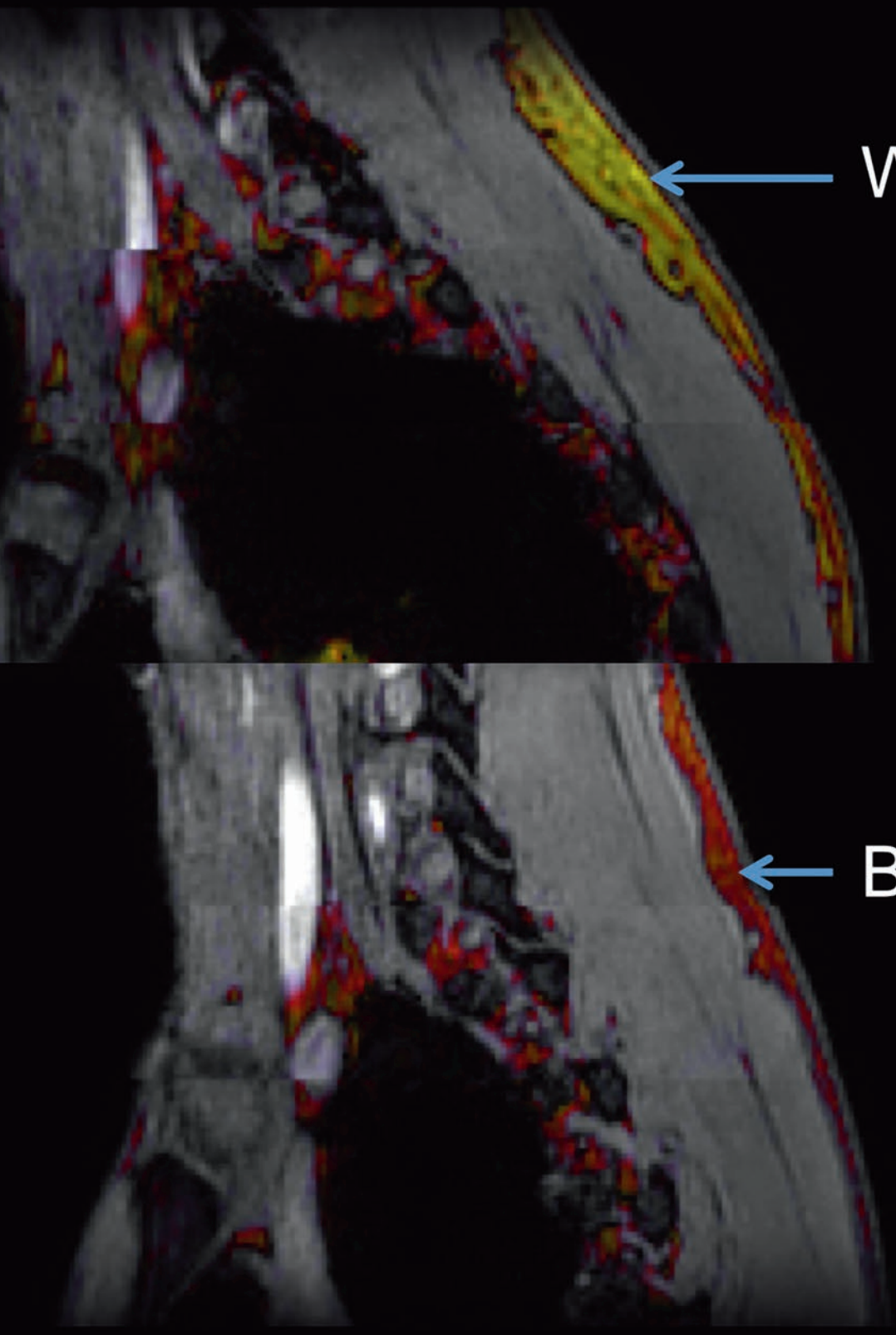
–Manual assessment of the BAT images is extremely time consuming, making larger studies impossible. Also, the reproducibility is limited in manual work. Computers on the other hand are very useful when it comes to reproducibility and speed, says Magnus.
In parallel with the method development the project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



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, Darren Treanor, Peter Lundberg, Stergios Kechagias, Karin Wårdell, Daniel Forsberg, Nastaran Monsef, Ebo de Muinck, Per Carlsson, Lars-Åke Levin, Martin Hallbeck
PhD students: Jesper Molin, Kavitha Shaga Devan, Mattias Aronsson
Main clinical leads: Anna Bodén, Sten Thorstenson, Arrigo Capitanio, Helen Richard

GRANTS
VINNOVA 2012-2014, 2015-2017

KEY PUBLICATIONS
Slide navigation patterns among pathologists with long experience of digital review
Jesper Molin, Morten Fjeld, Claudia Mello-Thoms, Claes Lundström
Histopathology 2014.

Evaluating Cell Nuclei Segmentation for Use on Whole-Slide Images in Lung Cytology
Daniel Forsberg, Nastaran Monsef
22nd International Conference on Pattern Recognition (ICPR), 2014.

Implementation of large-scale routine diagnostics using whole slide imaging in Sweden: Digital pathology experiences 2006-2013
Sten Thorstenson, Jesper Molin, Claes Lundström
Journal of Pathology Informatics 2014.

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

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, associate 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.

Claes Lundström is the vice project leader of the project "Optimized flows and IT tools for digital pathology". The project aims to design an optimal workflow for digitized pathology, to develop IT tools such as the pathologist's workstation, and to bring the resulting innovations out into the clinical reality. Apart from CMIV the project consortium currently consists of Sectra AB, eleven regional care providers, the Interactive Institute Swedish ICT, and LRI Imaging AB. 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 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.

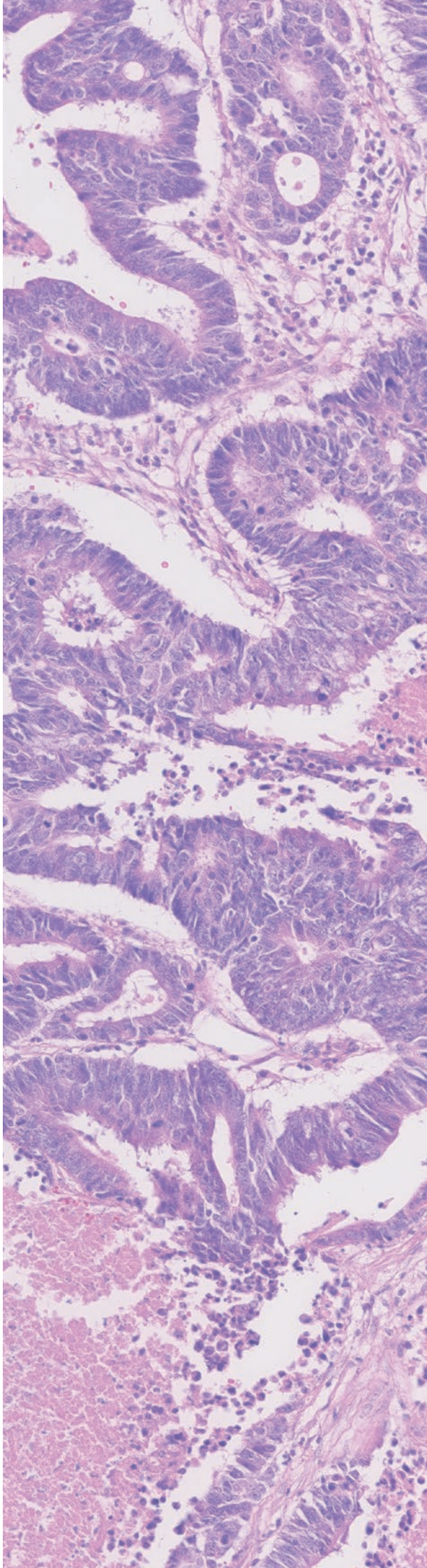
"We believe that digitization of the pathology work flow has the potential to increase both efficiency and quality of care."

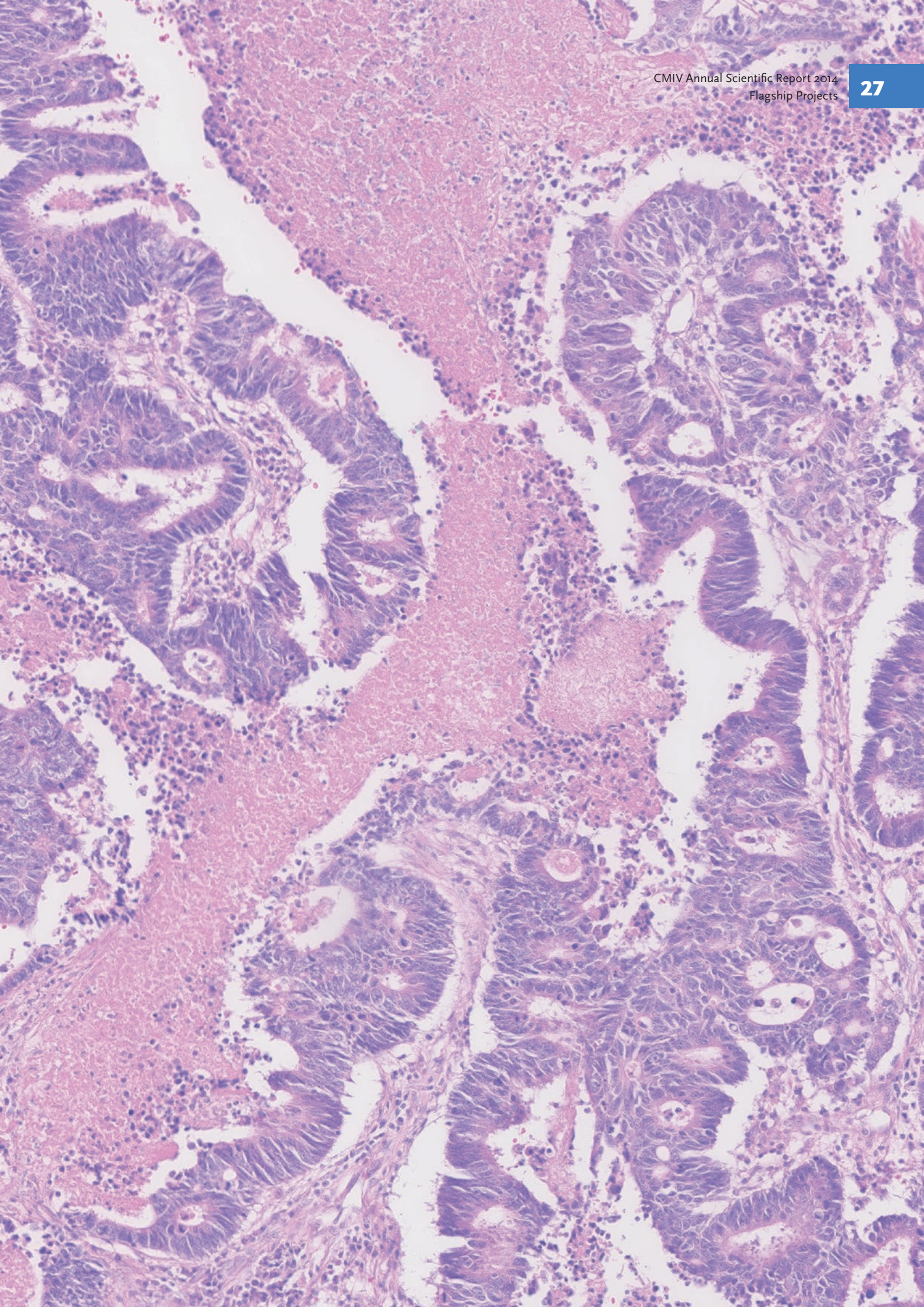
ASSOCIATE PROFESSOR CLAES LUNDSTRÖM

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 are now focusing on strengthening the research and finding digital solutions that will work in the clinical setting, says Claes.

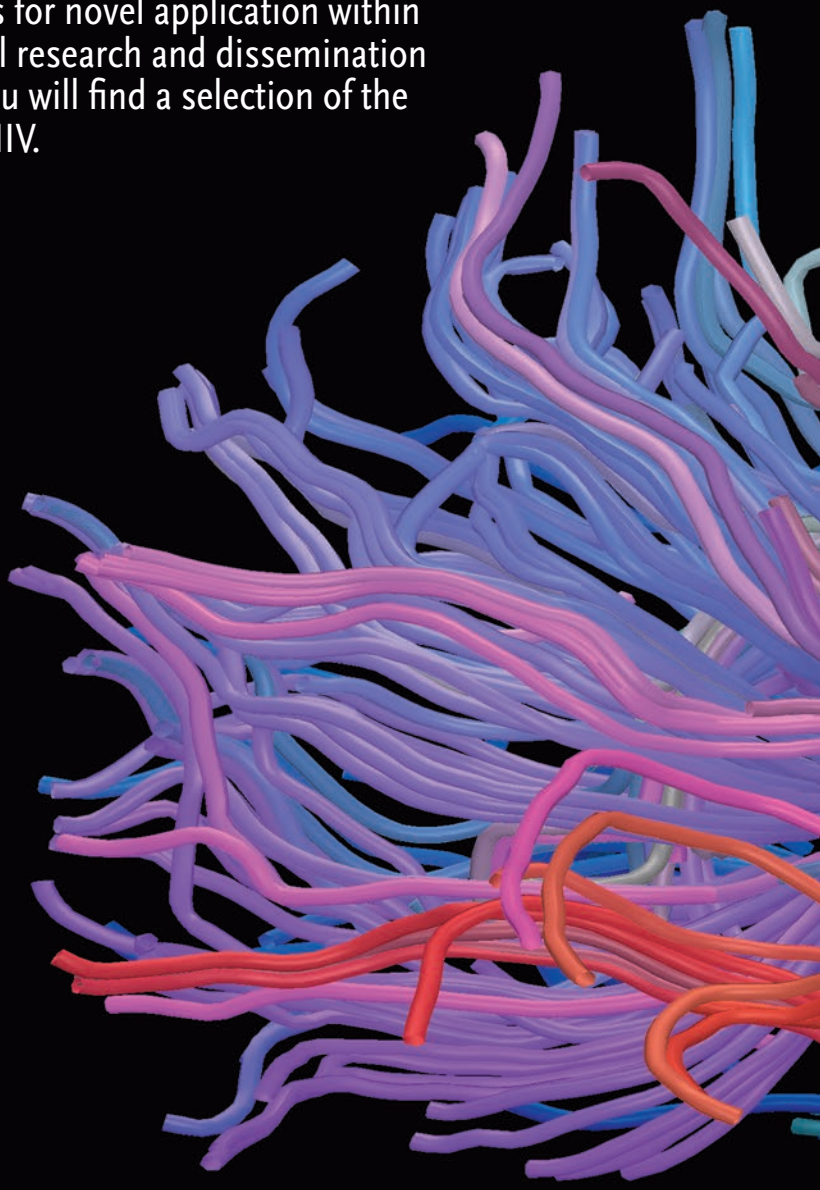
The pathologist's workstation is developed by Sectra AB in close collaboration with CMIV and pathologists to ensure novel solutions with high usability.





28 RESEARCH PROJECTS

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.



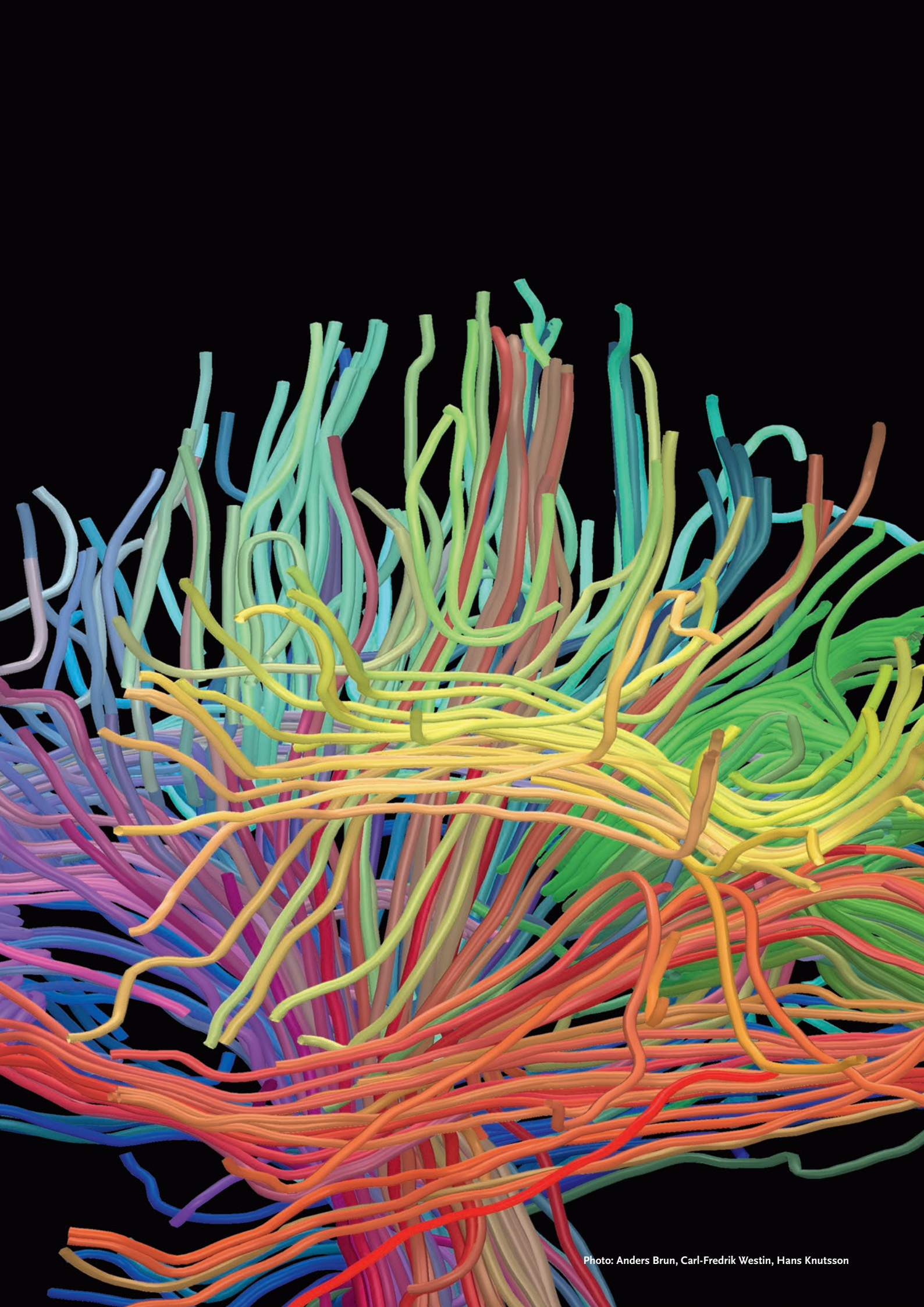


Photo: Anders Brun, Carl-Fredrik Westin, Hans Knutsson

POPULAR SCIENTIFIC SUMMARY
PETTER DYVERFELDT

Quantification of Hemodynamic Markers with Novel 4D Magnetic Resonance Flow Imaging

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 does make 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 also in normal

PROJECT NAME
Quantification of Hemodynamic Markers with Novel 4D Magnetic Resonance Flow Imaging

PROJECT LEADER
Petter Dyverfeldt, Department of Medical and Health Sciences, Division of Cardiovascular Medicine

MAIN PROJECT PARTICIPANTS
Magnus Ziegler, Jonas Lantz, Carl-Johan Carlhäll, Tino Ebbers, Ebo de Muinck, Toste Länne

GRANTS
Swedish Research Council

KEY PUBLICATIONS
Pulse Wave Velocity with 4D Flow MRI: Systematic Differences and Age-Related Regional Vascular Stiffness. Magn Reson Imaging 2014;32(10):1266–71.

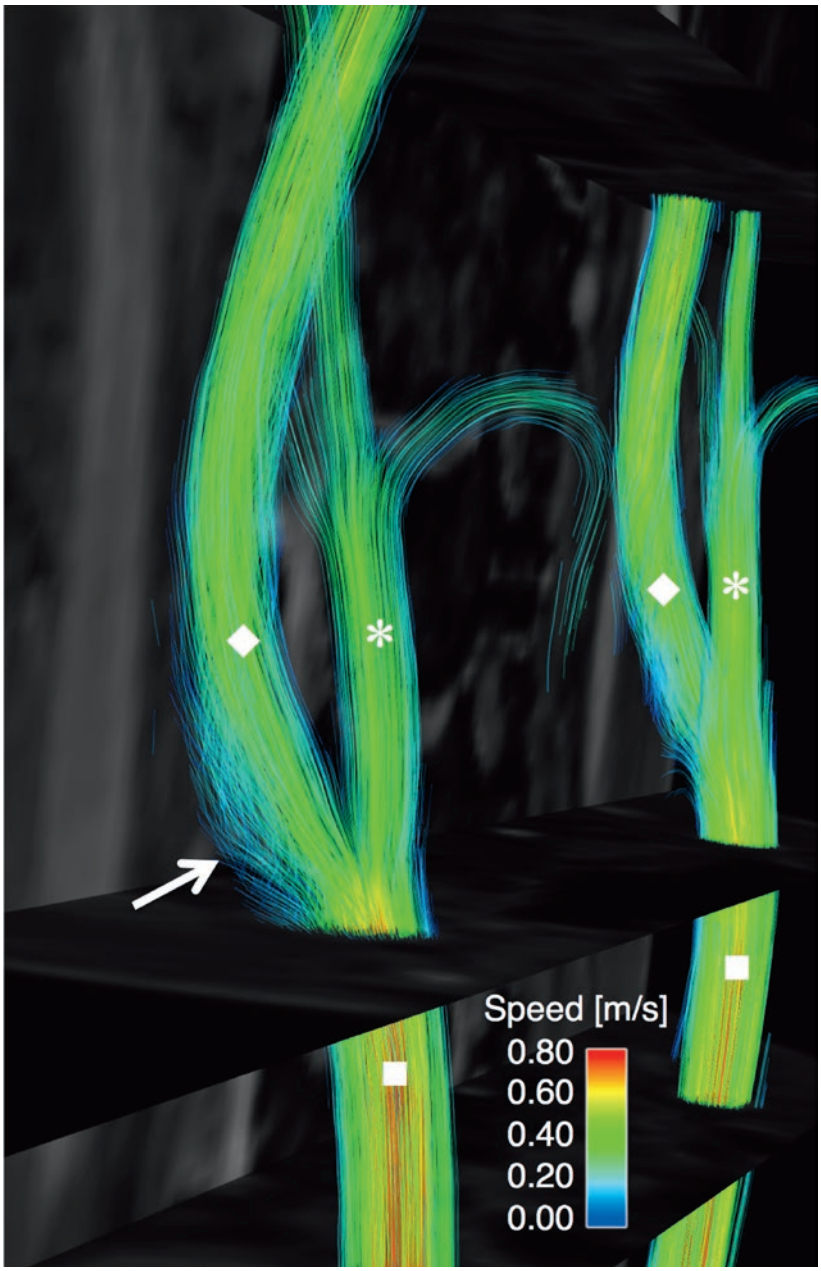
Hope MD, Sigovan M, Wrenn SJ, Saloner D, Dyverfeldt P. MRI hemodynamic markers of progressive bicuspid aortic valve-related aortic disease. J Magn Reson Imaging 2014;40(1):140-5.

Dyverfeldt P, Hope MD, Tseng EE, Saloner D. Noninvasive Magnetic Resonance Measurement of Turbulent Kinetic Energy for the Estimation of Irreversible Pressure Loss in Aortic Stenosis. J Am Coll Cardiol Img 2013; 6(1):64-71.

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.

POPULAR SCIENTIFIC SUMMARY
TINO EBBERS AND JAN ENGVALL

DOPPLER-CIP

PROJECT NAME
DOPPLER-CIP

PROJECT LEADER
Tino Ebbers and Jan Engvall, Department of Medical and Health Sciences, Division of Cardiovascular Medicine

MAIN PROJECT PARTICIPANTS
Johan Kihlberg, Petter Dyverfeldt, Eva Olsson, Carl-Johan Carlhäll, Lars-Åke Levin, Magnus Husberg, Magnus Janzon

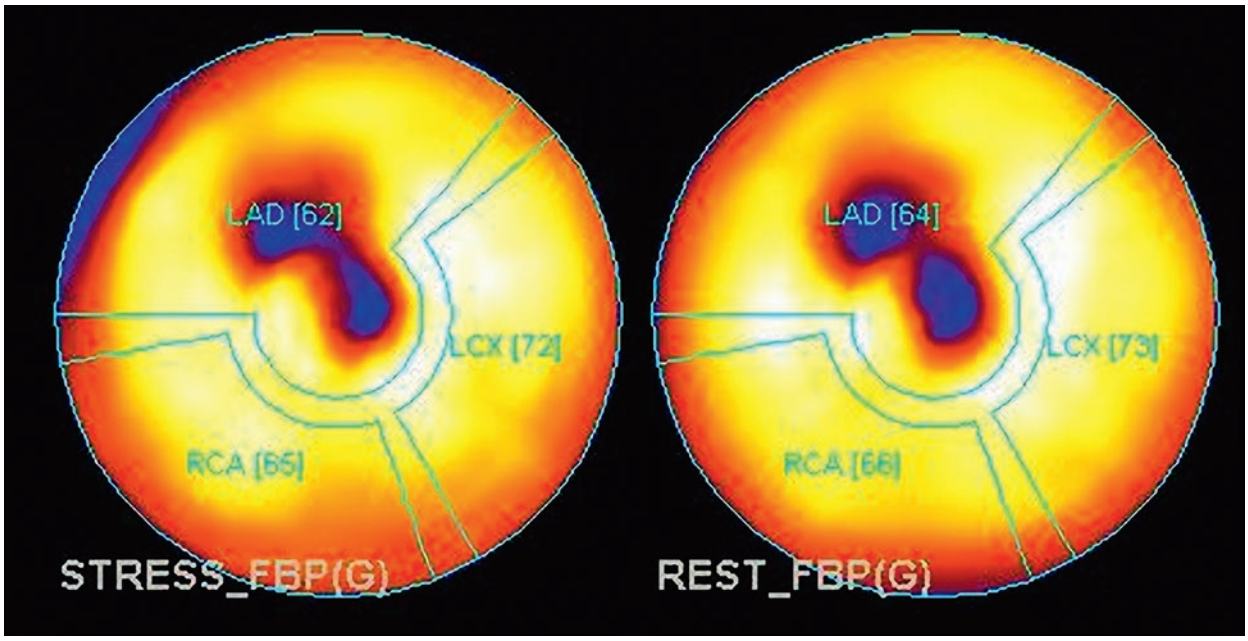
GRANTS
EU grant, 2010-2014

KEY PUBLICATIONS
Rademakers F, Engvall J, Edvardsen T, Monaghan M, Sicari R, Nagel E, Zamorano J, Ukkonen H, Ebbers T, Di Bello V, Voigt JU, Herbots L, Claus P, D'hooge J. Determining optimal noninvasive parameters for the prediction of left ventricular remodeling in chronic ischemic patients. Scand Cardiovasc J. 2013 Dec;47(6):329-34. doi: 10.3109 and 14017431.2013.857039.

CORONARY ARTERY DISEASE is the most prevalent cause of cardiovascular disease. It is defined by the narrowing and occlusion of coronary arteries with subsequent imbalance between myocardial oxygen consumption and supply. This imbalance causes either myocardial cell death (infarction) or chronic ischemia (viable myocardium), both leading to changes in the shape of the heart (morphologic remodeling) and functional deterioration. In the long term, patients suffer from heart failure or die.

Restoring blood flow to a region of chronic ischemia can stop the process of remodeling and allow partial or full recovery of function. The current therapeutic approaches are either to restore blood flow by mechanical dilatation of the stenosed coronary vessel (i.e., balloon angioplasty, PCI) or by surgically bypassing the stenosis (coronary artery bypass grafting). Preprocedural 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/or 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.

The study will close on March 31, 2015, and will have a closing event in Leuven, Belgium, April 25-26 2015. Several manuscripts are in preparation from the different core-labs. Based on evidence-based efficiency of different imaging technologies, researchers at Center for Medical Technology Assessment, CMT in Linköping will provide a cost-effectiveness analysis of the methods used to image coronary heart disease.

POPULAR SCIENTIFIC SUMMARY
JAN ENGVALL AND ANDERS PERSSON

Measuring Cardiac Perfusion Using Dynamic CT Adenosin Testing

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

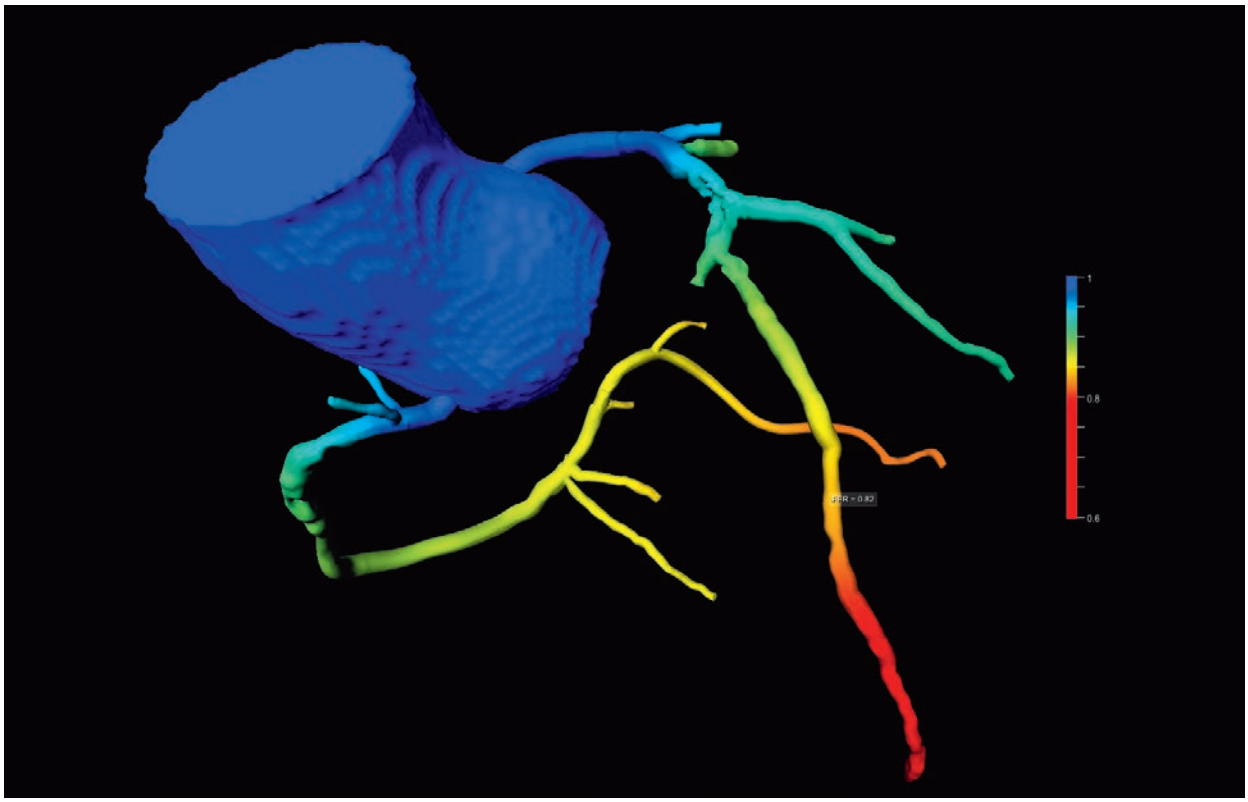
PROJECT NAME
Measuring cardiac perfusion using dynamic CT adenosin testing

PROJECT LEADER
Jan Engvall, Department of Medical and Health Sciences, Division of Cardiovascular Medicine and Anders Persson, Department of Medical and Health Sciences, Division of Radiological Science

MAIN PROJECT PARTICIPANTS
Jakob de Geer, Marcus Gjerde, Petter Quick

GRANTS
Magnus Bergvalls stiftelse

KEY PUBLICATIONS
DeGeer J, Gjerde M, Olsson E, Brudin L, Persson A, Engvall J. Large variation in blood flow between left ventricular segments, as detected by Adenosine stress dynamic CT perfusion. Clinical Physiology and Functional Imaging 2014 May 19. doi: 10.1111/cpf.12163

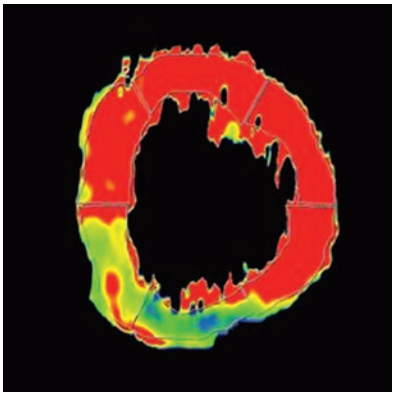


comes with the wash-in of contrast, the X-ray detector has to be large enough to allow coverage of the entire heart and reconstruction and evaluation of the recording need to be fast and accurate. Ideally, the contrast medium itself should not induce any change in coronary flow. A number of smaller studies 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.

The study now continues along two different paths: one repeating the study with an improved CT-scanner with a larger detector, and the other along the path of using non-invasive calculation of fractional flow reserve, to improve the prediction of significance of coronary stenoses detected by CT.



POPULAR SCIENTIFIC SUMMARY
EBO DE MUINCK

Magnetic Resonance and Carotid Ultrasound Observations

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 Warntjes, Petter Dyverfeldt, Johan Kihlberg, Rodrigo Moreno, Daniel Forsberg, Toste Länne, Anne-Marie Landtblom, Darren Treanor

GRANTS
Swedish Heart and Lung Foundation

KEY PUBLICATIONS
Moreno R, Koppal S, de Muinck ED. Robust estimation of distance between sets of points. Pattern Recognition Letters 2013;34:2192-2198.

Sandeep Koppal, Marcel Warntjes, Jeremy Swann, Petter Dyverfeldt, Johan Kihlberg, Rodrigo Moreno, Derek Magee, Nicholas Roberts, Darren Treanor, Ebo D de Muinck. Direct in vivo Quantification of Intraplaque Hemorrhage and Fat in Atherosclerosis by Magnetic Resonance Imaging. American Heart Association Annual Scientific Sessions 2014, November 15 – 19, Chicago IL, USA.

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. 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 at higher risk of rupture since fat and blood increase inflammation inside

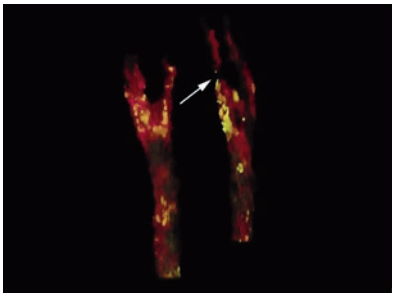


Figure 1. Magnetic resonance image of a patient with atherosclerotic plaque in both carotid arteries. The plaque has caused a severe narrowing in the right carotid artery (arrow). The amount of fat in the plaques is shown in yellow and the amount of blood is in red.

a plaque and inflammation leads to 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 (Figure 2).

In this project we study patients who are scheduled for surgical removal of atherosclerotic plaque. Before surgery, the patients undergo MRI of their carotid arteries and we measure the amount of fat and blood inside the plaque as well as the amount of turbulence. 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 (Fig. 3).

We have now validated the MRI method for quantification of fat and blood in plaques using 3D histology volumes from five patients who underwent MRI before carotid endarterectomy surgery. We have established that the volume of fat and blood in the plaque as measured by 3D histology correlates strongly to the fat and blood fraction as measured by MRI throughout the plaque. Thus, we show that fat and blood measured from Dixon MRI reliably quantifies the extent of hemorrhage and fat in atherosclerotic plaques as validated by 3D histology.

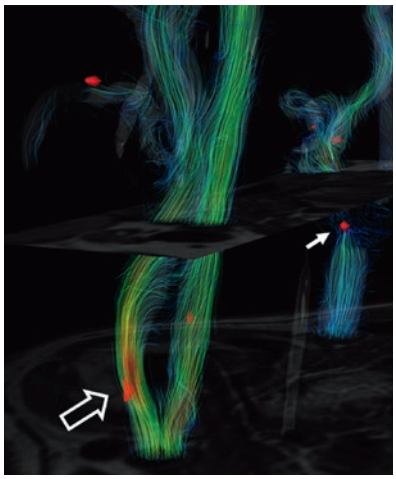


Figure 2. MRI turbulence data from a patient with carotid artery stenosis. The intensity of turbulence is graded according to a color scale, showing areas with a lot of turbulence in red and yellow downstream from a carotid artery stenosis (solid arrow) and at the outer wall of the contra-lateral internal carotid artery (open arrow).

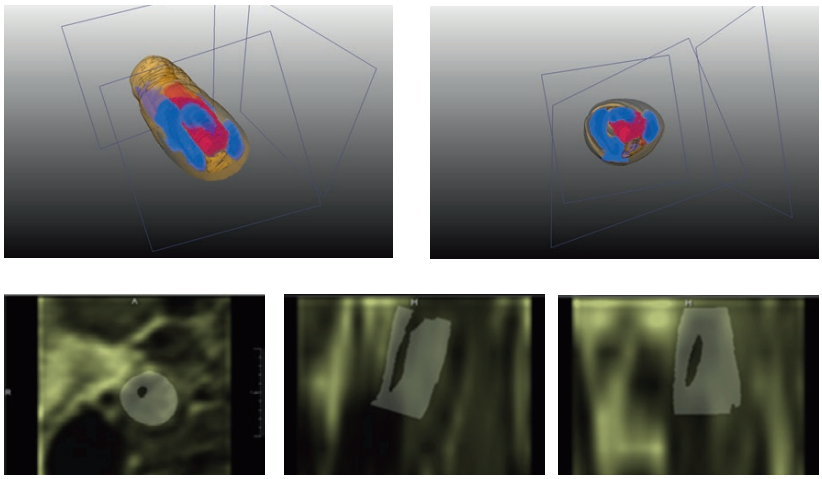


Figure 3. A-B 3D histology rendering of the atherosclerotic plaque showing the areas of internal hemorrhage (red) and lipid rich necrotic core (blue) within the lesion (yellow). C-E Spatial registration of 3D histology over 3D T1 weighted black blood sequence in an orthographic representation.

POPULAR SCIENTIFIC SUMMARY
ÖRJAN SMEDBY

Computer-Assisted Coronary CT Angiography Analysis

PROJECT NAME
Computer-Assisted Coronary CT Angiography Analysis

PROJECT LEADER
Örjan Smedby, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS
Chunliang Wang, Anders Persson, Hans Frimmel, Rodrigo Moreno

GRANTS
Swedish Heart-lung fundation 2008-2009
Swedish Heart-lung fundation 2010-2011
Swedish Heart-lung fundation 2012-2013
VR-NT 2012-2014

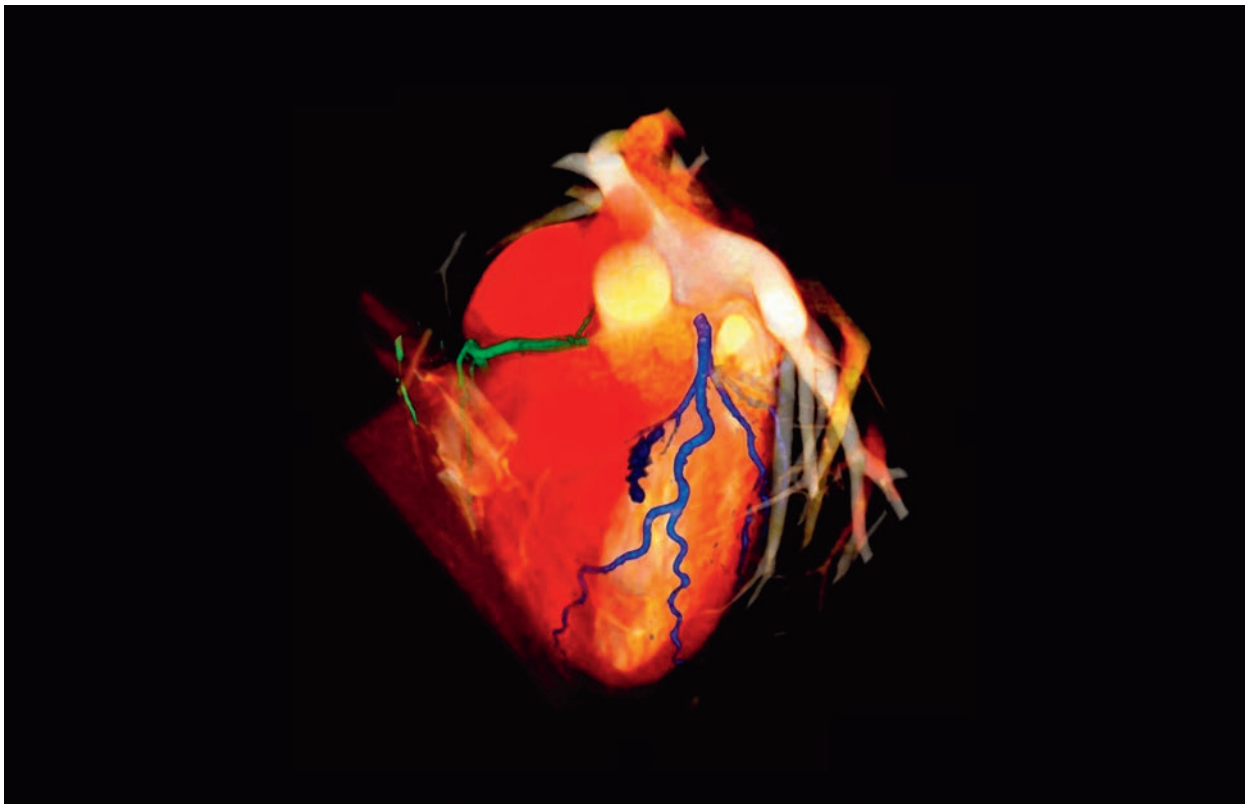
KEY PUBLICATIONS
Wang C, Smedby Ö. Integrating automatic and interactive methods for coronary artery segmentation: let the PACS workstation think ahead. Int J Comput Assist Radiol Surg. 2010 May;5(3):275-85. DOI:10.1007/s11548-009-0393-z

Wang C, Persson A, Engvall J, De Geer J, Fransson SG, Björkholm A, Czekierda W, Smedby Ö. Can segmented 3D images be used for stenosis evaluation in coronary CT angiography? Acta Radiol. 2012 Oct 1;53(8):845-51. DOI:10.1258/ar.2012.120053

Wang C, Frimmel H, Smedby Ö. Fast level-set based image segmentation using coherent propagation. Medical Physics 2014;41(7):073501. DOI:10.1118/1.4881315

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 (catheters) to be inserted into the coronary vessels. This is a costly and invasive procedure and may cause severe complications in some patients.

Coronary computed tomography angiography (CCTA), which collects computed tomography (CT) scans after injecting contrast agent into a vein in the arm, has to a great extent replaced the conventional invasive catheter exam, due to 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.



3D rendered coronary CT angiography from our software. The left coronary artery (blue) and right coronary artery (green) were segmented using the "virtual contrast injection" method.

The aim of this work is to develop and evaluate computer tools that use 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 work flow, additional methods such as finding the heart in a 3D volume were developed and integrated into 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 shows 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.

POPULAR SCIENTIFIC SUMMARY
ÖRJAN SMEDBY

Quantitative Assessment of Trabecular Bone Structure

PROJECT NAME
Quantitative assessment of trabecular bone structure

PROJECT LEADER
Örjan Smedby, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS
Rodrigo Moreno, Eva Klintström, Magnus Borga, Torkel Brismar (KI)

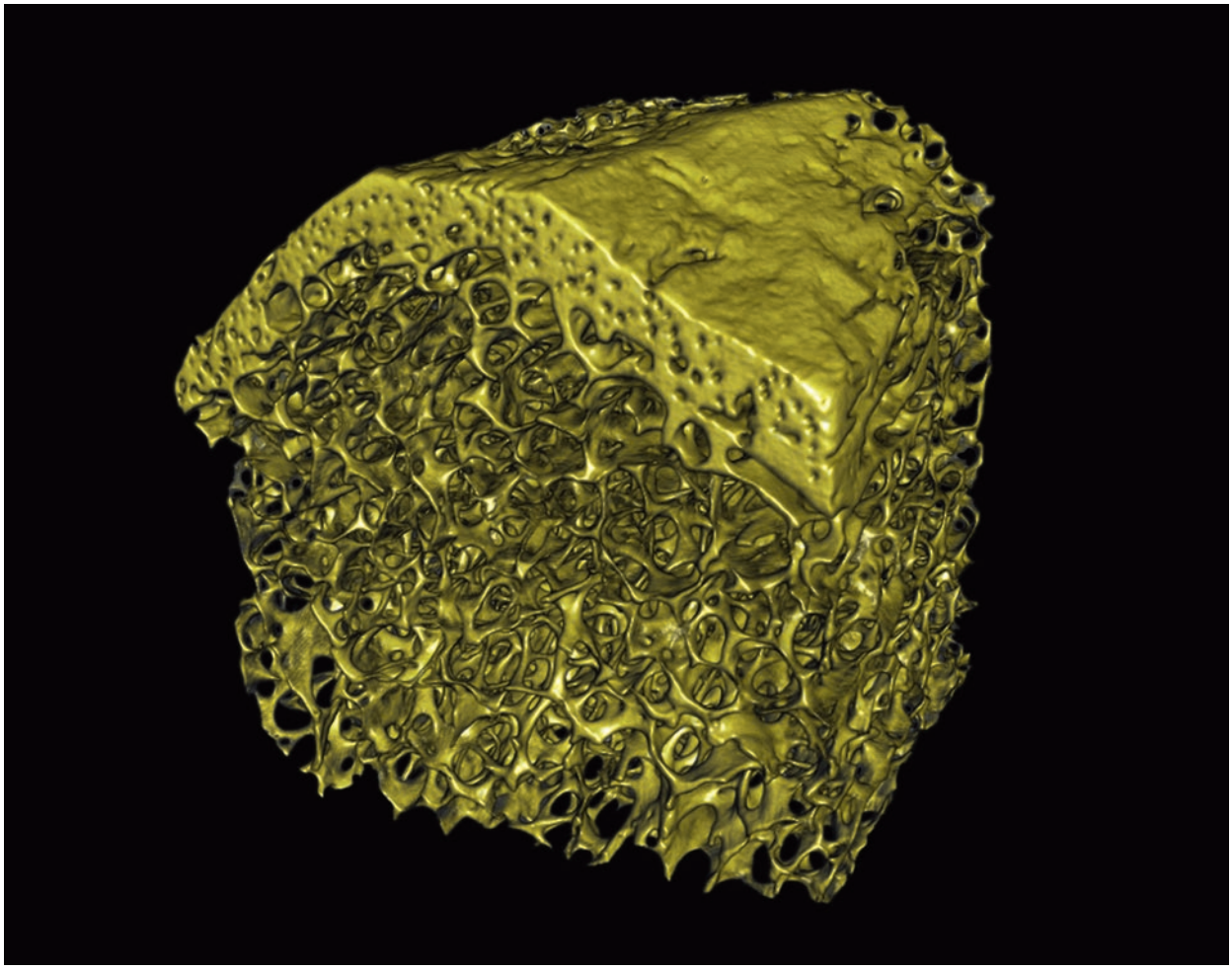
GRANTS
Swedish Research Council (VR-NT) 2007-2009

KEY PUBLICATIONS
Klintström E, Smedby Ö, Moreno R, Brismar TB. Trabecular bone structure parameters from 3D image processing of clinical multi-slice and cone-beam computed tomography data. Skeletal Radiology 2014;43(2):197-204. DOI:10.1007/s00256-013-1766-5

Moreno R, Borga M, Klintström E, Brismar T, Smedby Ö. Correlations between fabric tensors computed on cone beam and micro computed tomography images. Computational Vision and Medical Image Processing IV: VIPIMAGE 2013. 2013:393. DOI:10.1201/b15810-73

Klintström E, Smedby Ö, Klintström B, Brismar TB, Moreno R. Trabecular bone histomorphometric measurements and contrast-to-noise ratio in cone-beam computed tomography. Dentomaxillofacial Radiology 2014;43:20140196. DOI:10.1259/dmfr.20140196

PATIENTS SUFFERING FROM osteoporosis have an increased risk of fractures. To study this in patients, one usually measures the amount of calcium in the bone, which is reduced in osteoporosis. However, the condition is also characterized by a change in the internal structure of the bone, which may be more important for its strength than the reduced calcium content. The internal structures of the bone are called trabeculae, and they are usually portrayed as either narrow rods or flat plates. Earlier, the 3D microstructure could only be studied in bone specimens removed from the body, where properties such as the spacing and thickness of the trabeculae and the number of branching points can be measured. This project aims to study this structure in the living human by 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). In other words, an image with many shades of grey is first converted into one consisting of only two: black and white. We have found, however, that using methods that operate 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.

POPULAR SCIENTIFIC SUMMARY
HANS TROPP AND HANS KNUTSSON

Quantitative Musculoskeletal Imaging for Assessment of Idiopathic Scoliosis

PROJECT NAME
Quantitative Musculoskeletal Imaging for Assessment of Idiopathic Scoliosis

PROJECT LEADER
Hans Tropp, Department of Clinical and Experimental Medicine, Division of Orthopaedics and Hans Knutsson, Department of Biomedical Engineering, Division of Medical Informatics

MAIN PROJECT PARTICIPANTS
Ludvig Vavruch and Daniel Forsberg

GRANTS
VR 2008-2013
VINNOVA 2012-2014

KEY PUBLICATIONS
D. Forsberg, C. Lundström, and H. Knutsson. Eigenspine: Computing the Correlation between Measures Describing Vertebral Pose for Patients with Adolescent Idiopathic Scoliosis. Computerized Medical Imaging and Graphics, vol. 38, iss. 7, pp. 549-557, 2014.

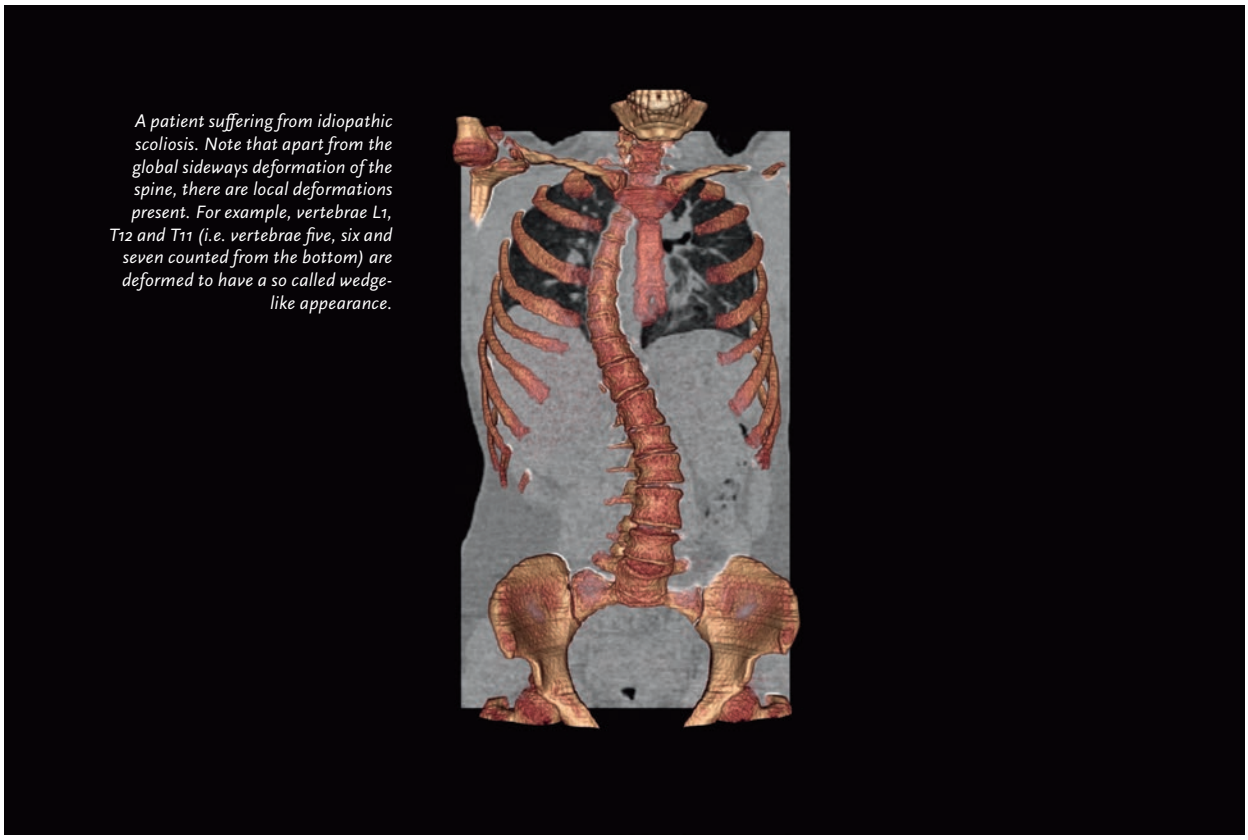
D. Forsberg, C. Lundström, M. Andersson, and H. Knutsson, "Model-based registration for assessment of spinal deformities in idiopathic scoliosis", Physics in Medicine and Biology, vol. 59, iss. 2, pp. 311-326, 2014

D. Forsberg, C. Lundström, M. Andersson, L. Vavruch, H. Tropp, and H. Knutsson, "Fully automatic measurements of axial vertebral rotation for assessment of spinal deformity in idiopathic scoliosis", Physics in Medicine and Biology, vol. 58, iss. 6, pp. 1775-1787, 2013

SPINAL DEFORMITIES, SUCH as idiopathic scoliosis, are not only causing changes in posture but can also be associated with severe pain, breathing complications, as well as heart complications. Treatment options include braces for mild to moderate cases of idiopathic scoliosis, whereas severe cases often require surgery, both to halt progression and to preferably correct the already existing deformity.

Choice of treatment, monitoring of progression, follow-up after surgery are all activities that to a large extent are based upon a single measure called the Cobb angle. The Cobb angle measures the angle of the spine as seen on frontal radiographs. However, although widely used in clinical practice, the Cobb angle is incapable of fully describing spinal deformities. This has motivated researchers and clinicians to pursue the development of new techniques to better describe and assess spinal deformities, which in turn will allow a better understanding of scoliosis on an individual level and, thus, be able to device personalized treatment plans.

To achieve this, we have focused our research on the combination of metrics describing the local deformation of each vertebra with metrics describing the overall deformation of the spine.



A patient suffering from idiopathic scoliosis. Note that apart from the global sideways deformation of the spine, there are local deformations present. For example, vertebrae L1, T12 and T11 (i.e. vertebrae five, six and seven counted from the bottom) are deformed to have a so called wedge-like appearance.

For imaging, we are utilizing 3D imaging, as provided by computed tomography (CT), which provides excellent opportunities for measuring and assessing spinal deformities. Current state-of-the-art CT scanners with new low-dose examinations make the use of CT clinically feasible from a dose perspective.

Thus far, our work has focused 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 supine position as is the case for CT examinations.
- Developing computerized methods based upon advanced image analysis, which can be employed for measuring various metrics 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.

Future work will focus on:

- 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. In this study, we will collaborate with University Medical Center Utrecht in the Netherlands.

POPULAR SCIENTIFIC SUMMARY
DANIEL FORSBERG

4D Orthopedic Kinematics

DISLOCATION OF THE kneecap is one of several different knee problems that can cause significant negative impact on the life of an individual. The initial treatment is to engage the patient in physical therapy and/or provide a knee brace. However, if this treatment is unsuccessful or if the condition is very severe (the kneecap has been dislocated on multiple occasions), then surgery is needed. This typically includes a reconstruction of the medial patellofemoral ligament (a ligament on the inside of the knee, stabilizing the kneecap). The purpose of the surgery is to stabilize and thereby restore the "normal" motion pattern/range of the kneecap. Surgery is considered successful if the kneecap feels stable and if the patient no longer experiences dislocations. Today there exist no standardized methods for precise quantification of the kneecap's motion during continuous flexion and extension of the knee. The lack of quantitative metrics makes it very difficult to evaluate the large number of different surgical techniques that exists for treating patients suffering from dislocation of the kneecap. This is what we intend to remedy.

PROJECT NAME
4D Orthopedic Kinematics

PROJECT LEADER
Daniel Forsberg, Department of Science and Technology, Division for Media and Information Technology

MAIN PROJECT PARTICIPANTS
Maria Lindblom, Anders Persson and Håkan Gauffin

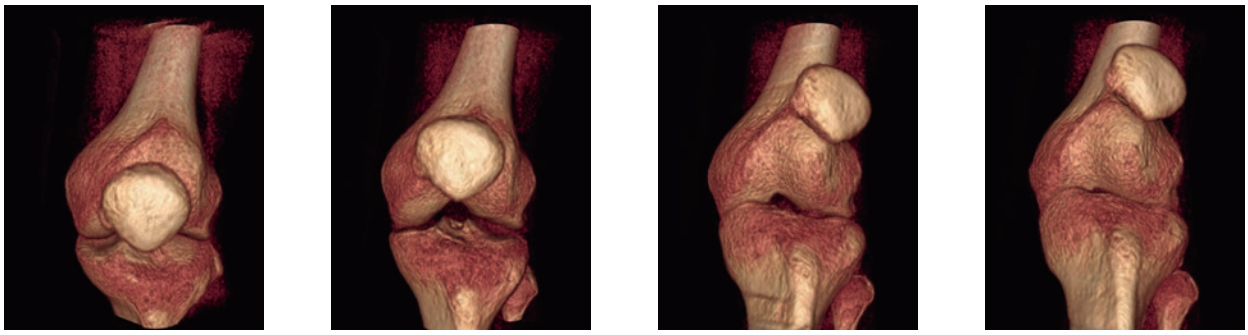


Figure 1 Preoperative imaging using CT for a patient with right knee prone to dislocation of the kneecap. Note how the kneecap moves to the side as the patient reaches full extension of the knee.

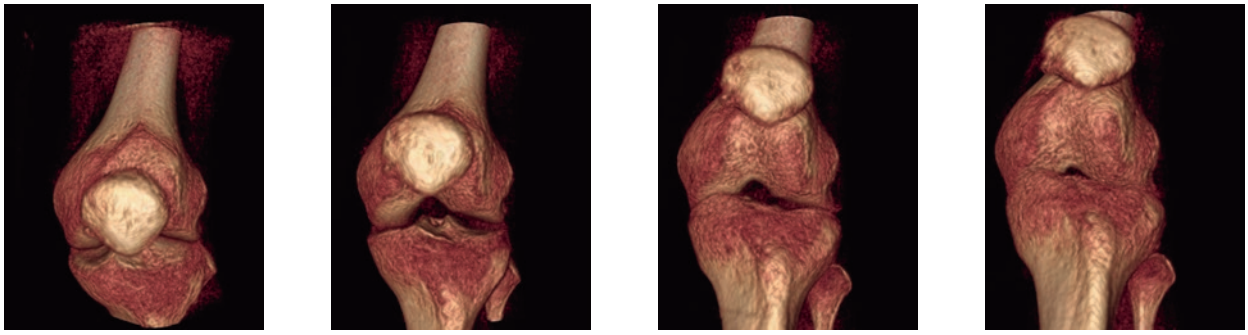


Figure 2 The same patient after reconstructive surgery. Now the kneecap stays much closer to the center of femur as the knee is extended.

Over the last few years, computed tomography (CT) imaging has undergone a remarkable development. Today, state-of-the-art scanners can image the knee with a spatial resolution of 0.4x0.4x0.4mm3 and a temporal resolution of less than a second. Further, improved detector technologies and new image reconstructions algorithms ensure that the dose is kept as low as reasonably achievable. This presents CT as a relevant technique for imaging the knee to allow a quantitative assessment of the continuous motion of the kneecap during flexion and extension of the knee.

Aided by the use of CT to obtain 4D datasets, i.e. a time sequence of 3D datasets, we aim to:

- Define metrics for quantifying the kneecap's motion pattern along with developing a method for measuring these metrics. By employing image analysis we intend the developed method to require as little user interaction as possible.
- Study the motion pattern of kneecaps from patients prone to dislocation of the kneecap and compare with control patients to determine what a healthy respectively pathological motion pattern/range of the kneecap is.
- Investigate how surgery affects the motion pattern of the kneecap for patients who have undergone surgery using the gracilis tendon (a tendon on the inside of the knee) to reconstruct the medial patellofemoral ligament.
- Evaluate the use of the developed method for assessing other knee problems, e.g. patients with injured anterior cruciate ligaments.

POPULAR SCIENTIFIC SUMMARY
OLOF DAHLQVIST LEINHARD

Whole Body MRI-Based Fat and Muscle Measurement

PROJECT NAME
Whole body MRI-based fat and muscle measurement

PROJECT LEADER
Olof Dahlqvist Leinhard, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS
Magnus Borga, Professor, Thobias Romu, PhD Student, Anette Karlsson, PhD Student, Thord Andersson, PhD Student, Patrik Tunon, MSc Student

GRANTS
FORSS Research council of South-east Sweden 2012-2014

KEY PUBLICATIONS
Lidell M, Betz M, Dahlqvist Leinhard O, Heglind M, Elander L, Slawik M, Mussack T, Nilsson D, Romu T, Nuutila P, Virtanen K, Beuschlein F, Persson A, Borga M, Enerbäck S. Evidence for Two Types of Brown Adipose Tissue in Humans. Nature Medicine, Volume 19(5):631-634, 2013, DOI:10.1038/nm.3017.

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.

Dahlqvist Leinhard O, Johansson A, Rydell J, Smedby Ö, Nyström F, Lundberg P, Borga M. Quantitative Abdominal Fat Estimation Using MRI. 2008 19th International Conference on Pattern Recognition, ICPR 2008 , art. no. 4761764.

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.

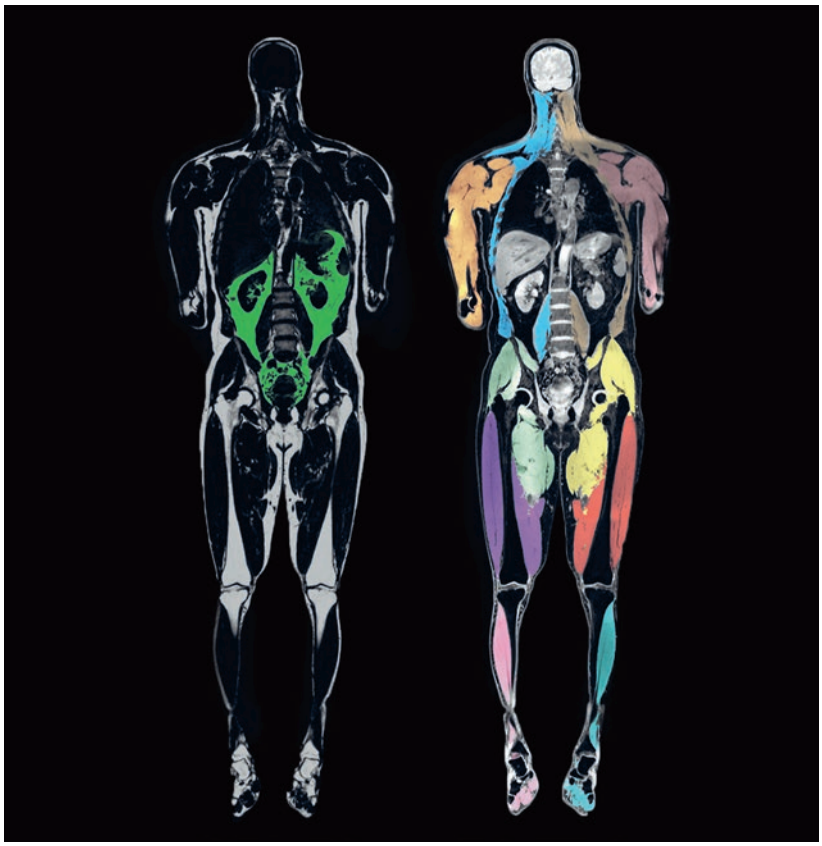
In this project we develop a technique for detailed analysis of fat and muscle tissue in the body based on whole body MRI examination (see figure). Recent technical development of MRI scanners enables high-resolution images of the complete body without exposing the subject to ionizing radiation or other 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.



Automatically segmented whole body fat and water separated dataset from a 10 minutes MRI examination where abdominal fat (left) and different muscle groups (right) are shown in different colors.

POPULAR SCIENTIFIC SUMMARY
PETER LUNDBERG

Liver Function Evaluation

PROJECT NAME
Liver Function Evaluation

PROJECT LEADER
Peter Lundberg, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS
Per Sandström, Stergios Kechagias, Örjan Smedby, Olof Dahlqvist Leinhard, Nils Dahlström, Mikael Forsgren, Thobias Romu, Johan Kihlberg, Gunnar Cedersund, Bengt Norén, Torkel Brismar

GRANTS
Swedish Research Council (VR) 2008-2010/2011,
Swedish Research Council (VR) 2012-2014/2015,
VINNOVA 2013-2017,
Swedish Research Council (VR) 2015-2018

KEY PUBLICATIONS
Norén B, Forsgren MF, Dahlqvist Leinhard O, Dahlström N, Kihlberg J, Romu T, Kechagias S, Almer S, Smedby Ö, Lundberg P (2013) Separation of Advanced from Mild Hepatic Fibrosis by Quantification of the Hepatobiliary Uptake of Gd-EOB-DTPA Eur Radiol 2013 Jan;23(1):174-81. doi: 10.1007/s00330-012-2583-2. Epub 2012 Jul 27.

Dahlqvist Leinhard O, Dahlström N, Kihlberg J, Sandström, P., Brismar TB, Smedby Ö, and Lundberg P. (2012) Quantifying differences in hepatic uptake of the liver specific contrast agents Gd-EOB-DTPA and Gd-BOPTA: a pilot study. Eur Radiol. 2012 Mar;22(3):642-53. Epub 2011 Oct 9.

Forsgren MF, Dahlqvist Leinhard O, Cedersund G, Lundberg P (2014) Physiologically Realistic and Validated Mathematical Liver Model Revels Hepatobiliary Transfer Rates for Gd-EOB-DTPA Using Human DCE-MRI Data PLoS ON, 2014 Apr 18;9(4):e95700. doi: 10.1371/journal.pone.0095700. eCollection 2014.

LIVER FUNCTION EVALUATION is a research project that with the help of magnetic resonance (MR, MRS and MRI), will develop new methods for diagnosing liver disease. 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 a whole than biopsies, as they only show status at the location 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 the liver has to manage the job of a full liver.

Today, determination of how much of the liver to remove is difficult as only 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

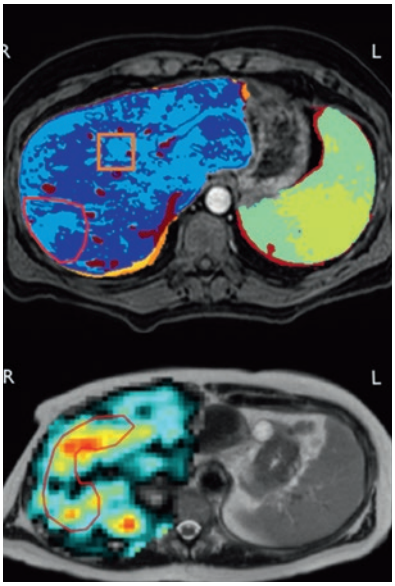
procedure. With a better estimate of size and function in the liver residue more patients could have surgery.

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.

Another important technology we use in the project is modeling of the system biology using the kinetics of a hepatocyte specific Gd-contrast agent ('EOB'). Modeling allows us to separate different grades of dysfunction in the liver. Yet another important technique that we predict will be highly useful is digital pathology, which we aim to use for determining four important contributors to hepatic function: fat storage, iron storage, degree of fibrosis, and degree of inflammation.



The uptake of hepatocyte specific contrast agent through a range of transport mechanisms is shown. On the lower panel the regional liver elasticity is shown; elasticity is a mechanical tissue property that is determined by the degree of fibrosis.

POPULAR SCIENTIFIC SUMMARY
PETER LUNDBERG

PRESTO-CAN for Three-Dimensional Functional MRI

PROJECT NAME
PRESTO-CAN for three-dimensional functional MRI

PROJECT LEADER
Peter Lundberg, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS
Maria Magnusson,
Olof Dahlqvist Leinhard,
Helene van Ettinger-Veenstra

GRANTS
Swedish Research Council (VR), Cancerfonden, Knowledge foundation.

KEY PUBLICATIONS
Magnusson M, Dahlqvist Leinhard O, Brynolfsson P, Thyr P, Lundberg P. 3D Magnetic Resonance Imaging of the Human Brain — Novel Radial Sampling, Filtering and Reconstruction. In: Proceedings of the 12th IASTED International Conference on Signal and Image Processing, Acta Press, 2010.

Magnusson M, Dahlqvist Leinhard O, Brynolfsson P, Lundberg P. A 3D-plus-time radial-Cartesian hybrid sampling of k-space with high temporal resolution and maintained image quality for MRI and fMRI. In: Proceedings of the 19th Scientific Meeting & Exhibition of ISMRM, Montréal, Québec, Canada, 2011.

Magnusson M, Dahlqvist Leinhard O, van Ettinger-Veenstra, H, Lundberg P. FMRI Using 3D PRESTO-CAN - A Novel Method Based on Golden Angle Hybrid Radial-Cartesian Sampling of K-Space In: Proceedings of the 20th Scientific Meeting & Exhibition of ISMRM, Melbourne, Australia, Montréal, 2012.

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 steps in the

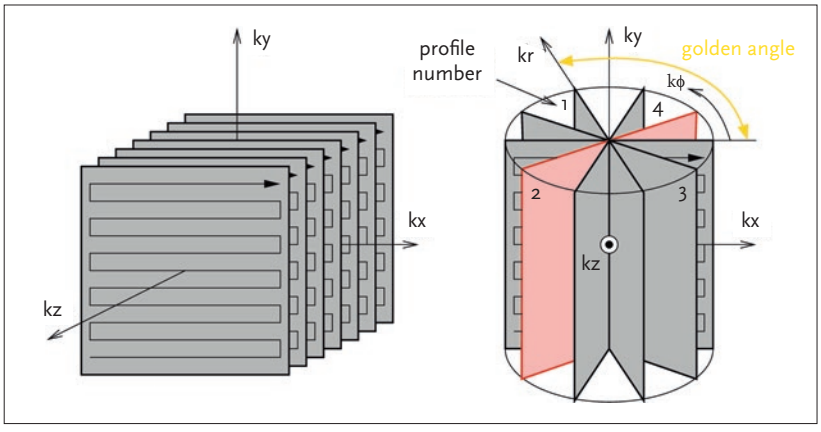


Figure 1 Left: 3D Cartesian sampling of k-space. Right: PRESTO-CAN sampling of k-space.

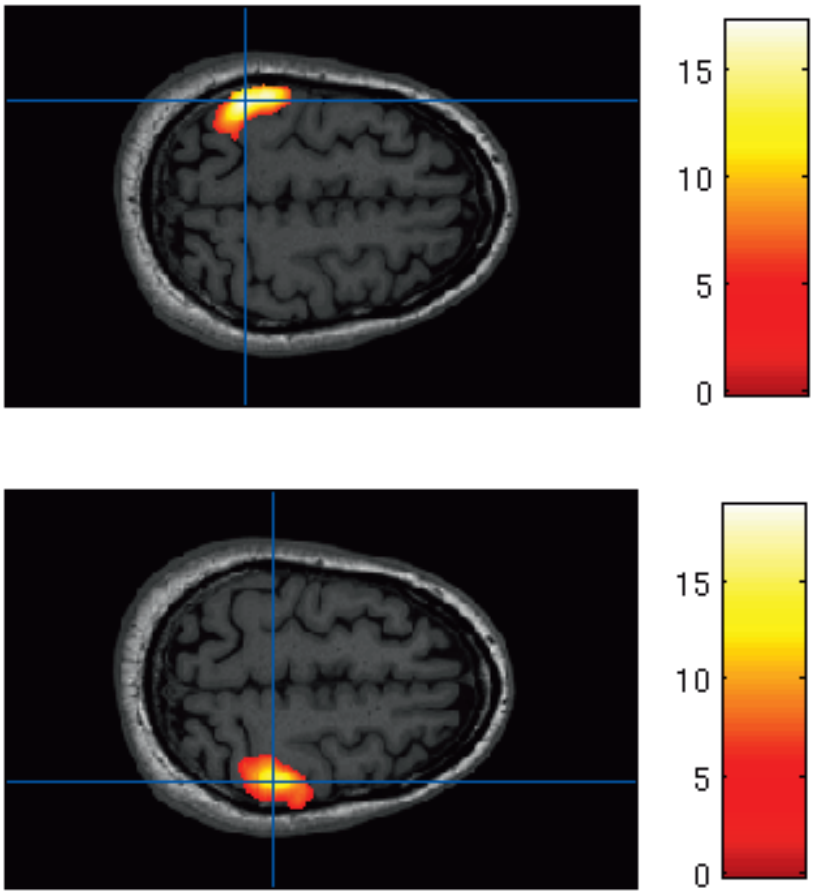


Figure 2 fMRI-activation computed from MRI-data based on PRESTO-CAN. Left: activation in left fingers motor cortex. Right: activation in right fingers motor cortex.

angular direction gives a fast recording of the important information located in the center of k-space.

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 temporal resolution can be further increased. However, this gives a more complicated sampling pattern and a non-trivial reconstruction. PRESTO-CAN has shown to provide excellent temporal resolution and satisfactory image quality.

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.

A major advantage of the PRESTO-CAN sequence is that it allows for whole brain coverage. We are currently performing a comparative fMRI study between PRESTO-CAN and conventional techniques, like EPI. Figure 2 shows left and right fingers fMRI-activation computed from MRI-data based on PRESTO-CAN.

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.

POPULAR SCIENTIFIC SUMMARY
MARIA ENGSTRÖM

Sleep Abnormality Network Description: Modeling and Analysis in Neuroimaging

PROJECT NAME
Sleep Abnormality Network Description: Modeling and Analysis in Neuroimaging (SAND:MAN)

PROJECT LEADER
Maria Engström, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS
Karin Lundengård, Natasha Morales-Drissi, Martin Ulander, Peter Lundberg, Anders Tisell, Sofie Tapper, Thomas Karlsson, Henriettae Ståhlbrandt, Anne-Marie Landtblom, Tove Hallböök, Atilla Szakacs, Niklas Darin

GRANTS
The Research Council of South East Sweden (FORSS), The Kleine-Levin Syndrome (KLS) foundation

KEY PUBLICATIONS
M. Engström, T. Karlsson, A-M Landtblom. Thalamic Activation in the Kleine-Levin Syndrome. Sleep, 37:379–386, 2014.

M. Engström, A-M Landtblom, T. Karlsson. Brain and effort: brain activation and effort-related working memory in healthy participants and patients with working memory deficits. Frontiers in Human Neuroscience, 7;140:1–17, 2013.

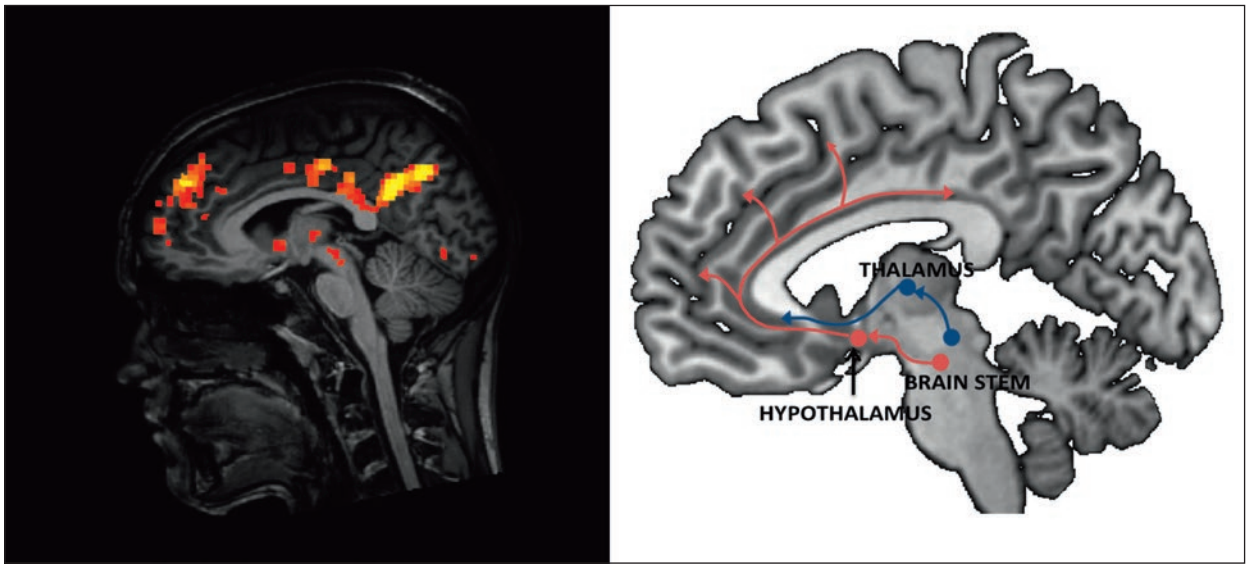
M. Engström, P. Vigren, T. Karlsson, A-M Landtblom, Working memory in 8 Kleine-Levin Syndrome patients: An fMRI study. Sleep, 32:681-688, 2009.

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



Left panel: Brain activation in one narcolepsy patient. *Right panel: Schematic image of brain areas that regulate sleep and wakefulness.*

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 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 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.

This project is directly linked to the project "Ab initio mathematical modeling of mechanisms in the human brain", which develop novel methods for mechanistic modeling of brain signals measured by fMRI and EEG.

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.

POPULAR SCIENTIFIC SUMMARY
MARIA ENGSTRÖM

Ab Initio Mathematical Modeling of Mechanisms in the Human Brain

PROJECT NAME
Ab initio mathematical modeling of mechanisms in the human brain

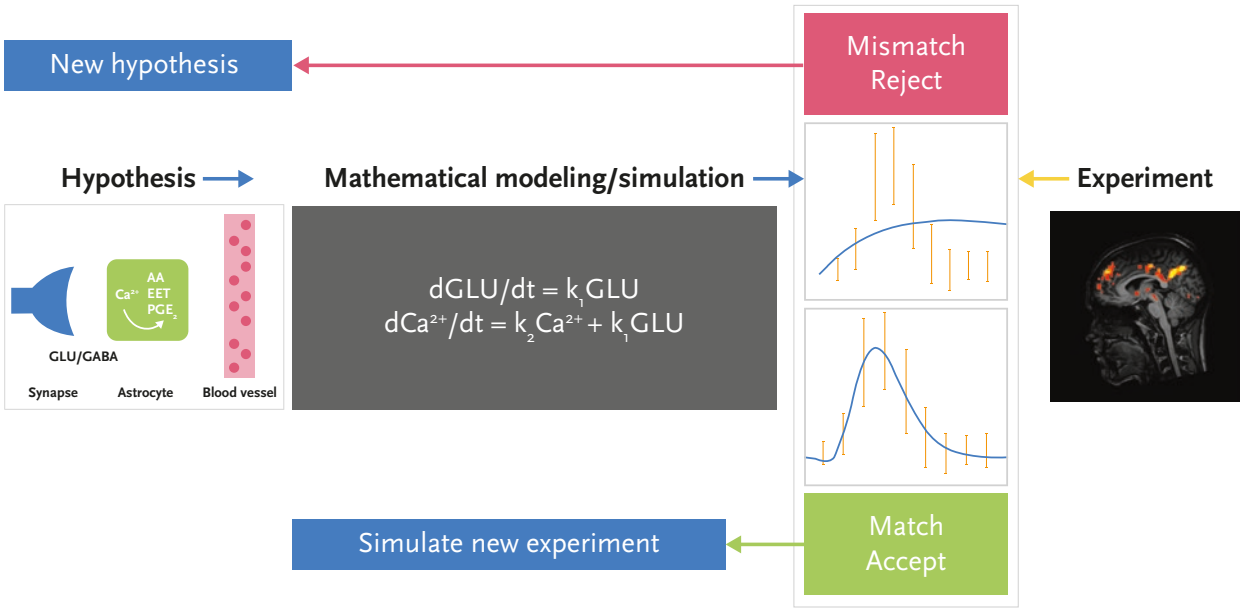
PROJECT LEADER
Maria Engström, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS
Karin Lundengård, Natasha Morales-Drissi, Sebastian Sten, Gunnar Cedersund, Fredrik Elinder, Susanna Walter

GRANTS
Swedish Research council

BY FUNCTIONAL MAGNETIC resonance imaging (fMRI), brain activity can be visualized and time dependent signals of the brain at work can be recorded. Despite the fact that fMRI is widely used in both research and health care, the relation between brain activity and the recorded signals remains elusive. The aim of this project is to investigate different theories that explain the relationships between brain activity and the fMRI signal. These theories are based on what is known about the neurobiology of the brain. Here, we investigate the neurobiology behind the fMRI signal by mathematical mechanistic modelling using systems biology, which offers an elegant approach to systematically investigate different theories on brain function. In this way, we hope to increase the understanding of how the brain works and increase the sensitivity in studies of patients with brain disorders.

Several theories, or hypotheses, of the neurobiology behind the fMRI signal are described in the literature. In the first phase of the project we investigate the "metabolic" and the "neurotransmitter" hypotheses, which



currently are the most supported. According to the metabolic hypothesis, it is assumed that activated nerve cells have an increased energy demand and thereby an increased need for oxygen and glucose. Since oxygen and glucose are transported to the brain by the blood, the increased energy demand is followed by increased blood flow. According to the neurotransmitter hypothesis, on the other hand, it is assumed that neurotransmitters, which are released when the brain is activated, trigger the release of substances that in turn influence the blood flow.

In this project we "translate" these hypotheses that describe neurobiological processes to mathematical expressions, so called differential equations. The mathematical models are then fitted to experimental data, which could be the fMRI signal but also measurements of blood flow or glucose or neurotransmitter concentrations. By fitting the mathematical model to experimental outcome, we can evaluate if the model can or cannot explain data. Once we know that the models can explain data, we can use the model to predict brain function in response to different stimuli or predict brain function when some part of the communication between nerve cells and blood vessels does not work.

In the future we will use the mathematical models to investigate brain function in clinical studies. For this purpose, this project is directly linked to the project "Sleep abnormality network description: Modelling and analysis in neuroimaging", which investigates patients with sleep disorders.

POPULAR SCIENTIFIC SUMMARY
MARIA ENGSTRÖM

Functional MRI Studies of Normal and Impaired Language Function

PROJECT NAME
Functional MRI studies of normal and impaired language function

PROJECT LEADER
Maria Engström, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS
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GRANTS
Henry och Ella Margareta Ståhls stiftelse

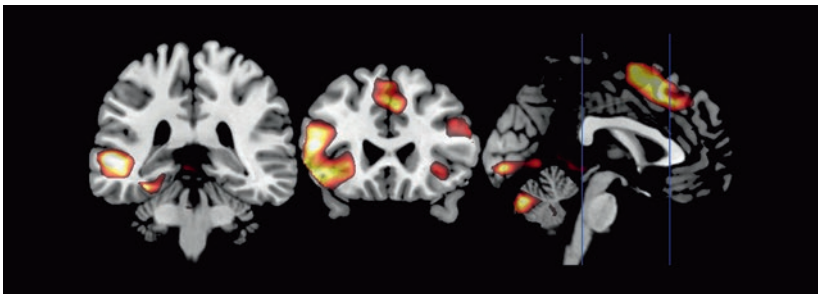
KEY PUBLICATIONS
H. Gauffin, H. van Ettinger-Veenstra, A-M Landtblom, D. Ulrici, A. McAllister, T. Karlsson, M. Engström. Impaired language function in generalized epilepsy: Inadequate suppression of the default mode network. Epilepsy & Behavior, 28:26–35, 2013.

H.M. Van Ettinger-Veenstra, M. Ragnehed, A. McAllister, P. Lundberg, M. Engström. Right-Hemispheric Cortical Contributions to Language Ability in Healthy Adults. Brain and Language, 120:395–400, 2012.

H.M. Van Ettinger-Veenstra, M. Ragnehed, M. Hällgren, T. Karlsson, A-M Landtblom, P. Lundberg, and M. Engström. Right-hemispheric brain activation correlates to language performance. NeuroImage, 49:3481-3488, 2009.

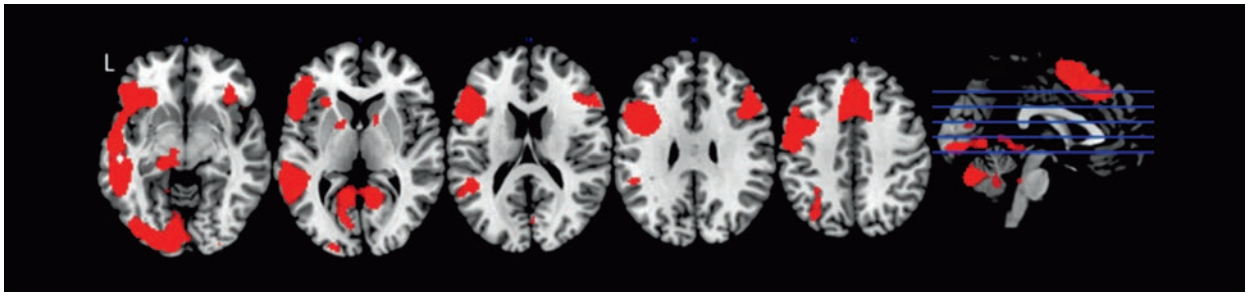
LANGUAGE ABILITY PLAYS an important role when communicating with others. Although the most important areas of the brain that are involved in language function are identified, the relation between activation in these areas and language ability is not fully uncovered. That is to say, we do not know in 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.



Language function in healthy subjects, coronal and sagittal slices: Brain activation is observed in typical language areas of the brain i.e., Broca's and Wernicke's areas, but also in medial frontal regions.

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.

POPULAR SCIENTIFIC SUMMARY
NINA NELSON

Functional Neuroimaging in Former Preterm Children with Very Low Birth Weight

IF A CHILD is born preterm with a very low birth weight, it enters a life full of obstacles. After its struggle to survive, there is a struggle to keep up with its peers at school, as many preterm born children experience cognitive deficits, including language problems. These deficits are often related to risks for early brain injuries, and associated white matter disease. These injuries together with adverse effects of other perinatal complications are responsible for a changed brain development in preterm born children.

In southeast Sweden, a group of preterm children with very low birth weight and a group of full-term born children as a control group was followed over time. Our interest in this functional magnetic resonance imaging (fMRI) study was to investigate components of reading ability in these groups, as reading is essential for school performance.

With fMRI, the activity level of the brain can be measured by looking at changes in blood flow transporting oxygen to active brain regions. During fMRI, our group of children did a series of language tasks, tapping semantic, orthographic, and phonological skills, all essential for reading ability.

As expected, the preterm very low birth weight group showed signs of

PROJECT NAME
Functional neuroimaging in former preterm children with very low birth weight

PROJECT LEADER
Nina Nelson, Department of Clinical and Experimental Medicine, Division of Pediatrics

MAIN PROJECT PARTICIPANTS
Carin Widén, Ingemar Leijon, Maria Engström, Thomas Karlsson, Helene van Ettinger-Veenstra

altered development of their brain, and in effect altered pattern of activation during language processing. The preterm group had smaller brains, lower performance on language tasks and a performance IQ task. Moreover, this group showed increased activation in the left lower part of their frontal lobe, an area important mainly for phonological and semantic processing. It is likely that the brains of the preterm group try to compensate for cognitive deficits, by increasing processing power (engaging additional brain regions compared to a control group). But this group might also have a different functionality of specialized areas as an effect of their preterm birth, with certain regions of the brains being less well developed.

Tentative results also show an indication of less activity for preterm children in brain regions important for attention and voluntary control during tasks. The direct connection between these fronto-parietal regions - important for communication between brain regions - develops during childhood. We hypothesize that children born preterm lag behind in development of these connections. As an effect, they may show impaired ability to focus on their task, and thus show lower performance than the term-born group; this would be an alternative explanation to impaired cognitive functioning.

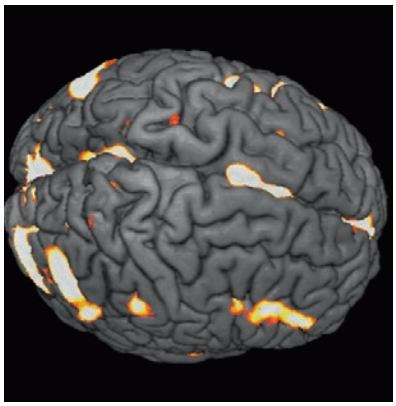


Figure 1. Sites of brain activity correlating (positively or negatively) with language tasks without regard to birth weight. (Head is facing rightward).

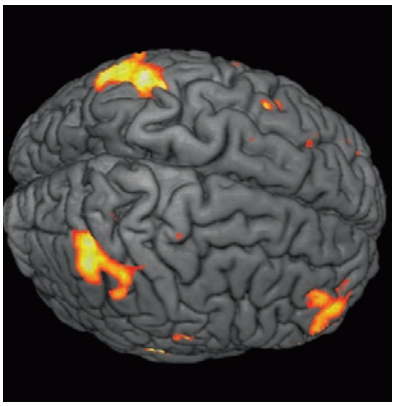


Figure 2. Difference in brain activity during language processing between normal birth weight and very low birth weight children in the fronto-parietal network.

POPULAR SCIENTIFIC SUMMARY
ANNE-MARIE LANDTBLOM AND MARIA ENGSTRÖM

Clinical, Psychosocial and Imaging Studies of Fatigue in Multiple Sclerosis

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

PROJECT LEADER
Anne-Marie Landtblom, Department of Clinical and Experimental Medicine, Division of Neurology
Maria Engström, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS
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GRANTS
Swedish Research Council (VR)

KEY PUBLICATIONS
Flensner G, Ek AC, Söderhamn O, Landtblom AM. Sensitivity to heat in MS patients: a factor strongly influencing symptomology – an explorative survey. BMC Neurol 2011;11:27.

Flensner G, Landtblom AM, Söderhamn O, Ek AC. Work capacity and health-related quality of life among individuals with multiple sclerosis reduced by fatigue: a cross-sectional study. BMC Public Health. 2013 Mar 15;13:224. doi: 10.1186/1471-2458-13-224.

Engström M, Flensner G, Landtblom AM, Ek AC, Karlsson T. Thalamo-striato-cortical determinants to fatigue in Multiple Sclerosis. Brain & Behaviour, 2013 November; 3(6): 715–728.

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

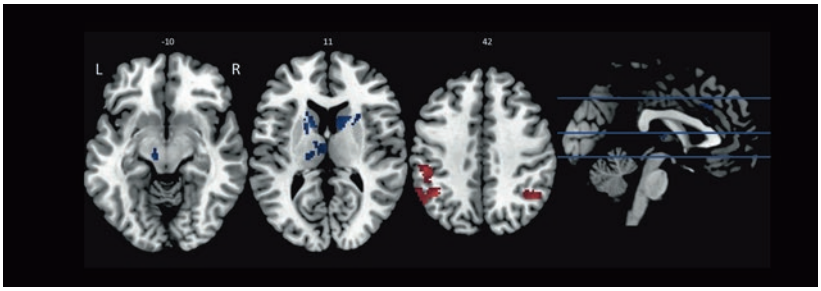

Figure 1. Differences in brain activation between MS participants and healthy participants in regions of interest in the brain. The red colour represents areas that were more activated in MS participants compared to controls, and the blue colour represents areas that were less activated in MS participants 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 decapacitating 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.

Analysis of results after intervention with a cooling garment is ongoing; here fMRI analysis is of great interest and can help in determining the physiological background of fatigue.

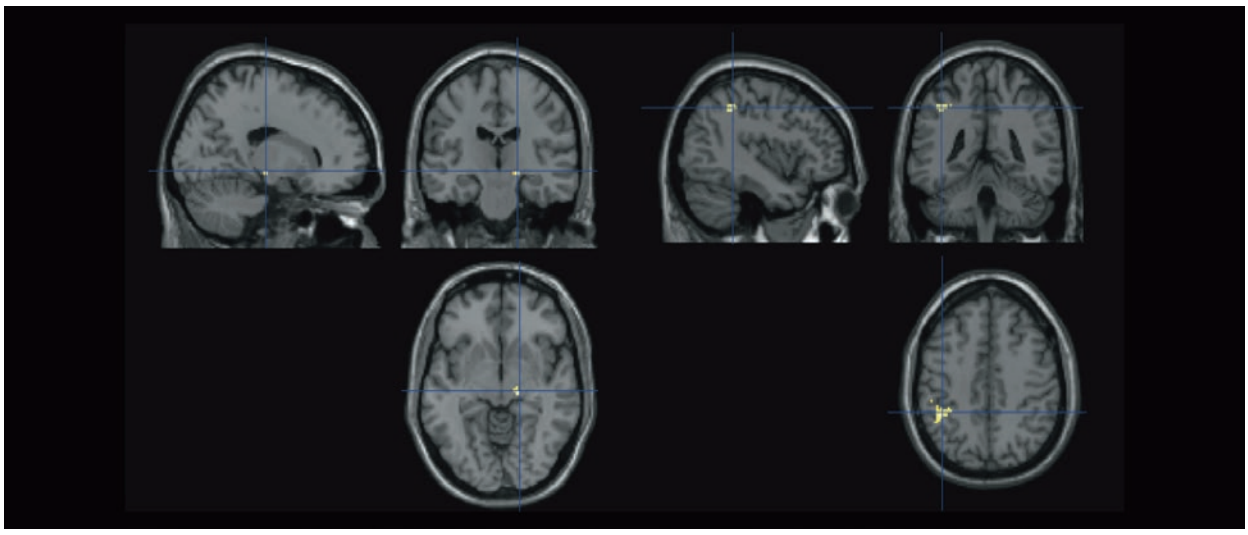

Figure 2. Brain activation with positive correlation to perceived fatigue during the working memory task. The images show activation in regions of interest: the right substantia nigra and the left posterior parietal cortex.

POPULAR SCIENTIFIC SUMMARY
ANNE-MARIE LANDTBLOM AND MARIA ENGSTRÖM

Clinical, Imaging and Memory Investigation in Patients with the Kleine Levin Syndrome

PROJECT NAME
Clinical, imaging and memory investigation in patients with the Kleine Levin syndrome

PROJECT LEADER
Anne-Marie Landtblom, Department of Clinical and Experimental Medicine, Division of Neurology
Maria Engström, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS
Peter Lundberg, Thomas Karlsson, Olof Dahlqvist Leinhard, Anders Tisell, Patrick Vigren

GRANTS
Kleine Levin Foundation, USA

KEY PUBLICATIONS
Vigren P, Tisell A, Engström M, Karlsson T, Leinhard Dahlqvist O, Lundberg P, Landtblom AM. Low thalamic NAA-concentration corresponds to strong neural activation in working memory in Kleine-Levin syndrome.PLoS One. 2013;8(2):e56279. Epub 2013 Feb 25.

Engström M, Karlsson T, Landtblom AM. Reduced thalamic and pontine connectivity in Kleine–Levin syndrome. Frontiers in Neurology 2014;5:42.

Engström M, Karlsson T, Landtblom AM. Thalamic activation in the Kleine-Levin syndrome. SLEEP, 2014;37(2):379-386.

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 associate professor Maria Engström and in collaboration with col-

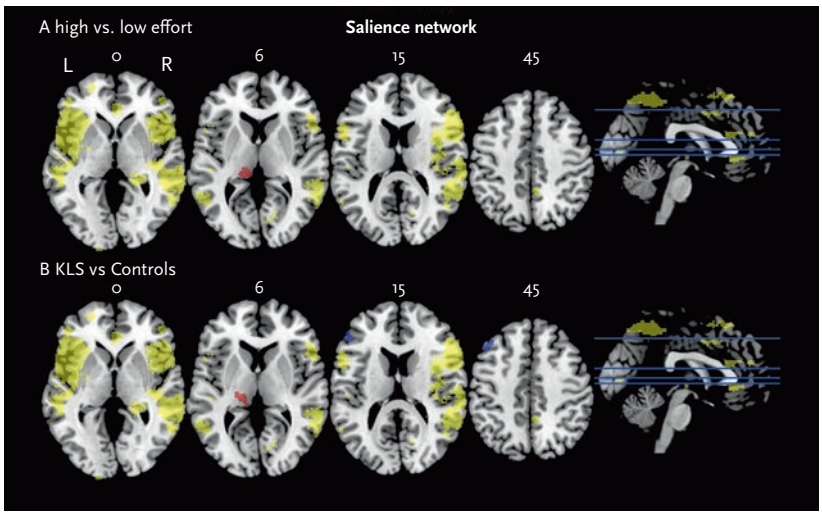

Figure 1. Functional connectivity in the salience network. Neural processing is often performed by an integrated network of several regions in the brain. Functional connectivity studies investigate the interaction of regions within these networks. Yellow areas show the network in selected slices. Red 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.

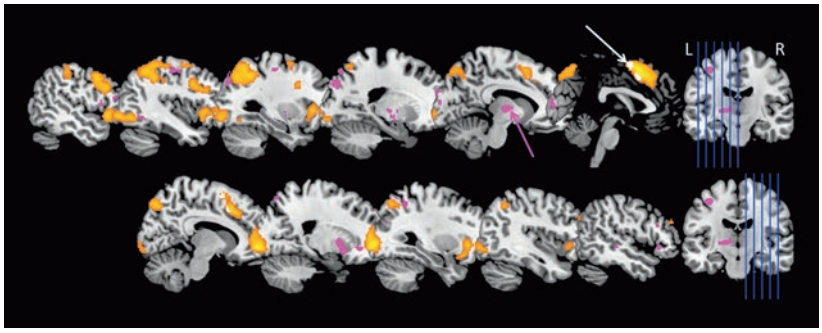

Figure 2. Typical working memory activation in healthy individuals and thalamic hyperactivation in KLS patients. In other parts of the brain KLS patients had less activation than healthy individuals.

leagues in Gothenburg, see Engström's report the SAND:MAN project.

In this study we examined frequency, duration and type of sleep periods that the patient 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.

POPULAR SCIENTIFIC SUMMARY
ANNE-MARIE LANDTBLOM

Clinical and Imaging Studies of Multiple Sclerosis

PROJECT NAME
Clinical and Imaging studies of multiple sclerosis

PROJECT LEADER
Anne-Marie Landtblom, Department of Clinical and Experimental Medicine, Division of Neurology

MAIN PROJECT PARTICIPANTS
Peter Lundberg, Olof Dahlqvist Leinhard, Marcel Warntjes, Anders Tisell, Örjan Smedby

GRANTS
Swedish Research Council (VR)

KEY PUBLICATIONS
Tisell A, Leinhard OD, Warntjes JB, Aalto A, Smedby Ö, Landtblom AM, Lundberg P. Increased concentrations of glutamate and glutamine in normal-appearing white matter of patients with multiple sclerosis and normal MR imaging brain scans. PLoS One. 2013 Apr 17;8(4):e61817. doi: 10.1371/journal.pone.0061817.

West J, Aalto A, Tisell A, Dahlqvist Leinhard O, Landtblom AM, Smedby Ö, Lundberg P. Normal and Diffusely Abnormal White Matter in Patients with Multiple Sclerosis, Assessed with Quantitative MR. PLOS one 2014 Apr 18;9(4):e95161. Doi:10.1371/journal.pone. 0095161. eCollection 2014.

Warntjes M, Tisell A, Landtblom AM, Lundberg P. Effects of gadolinium contrast administration on automatic brain tissue segmentation of multiple sclerosis patients. Am J Neurorad 2014;35(7):1330-6

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.

Inflammation is, together with destruction, destruction of the insulating covers of nerve cells and the formation of lesions in the central nervous system 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 only 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

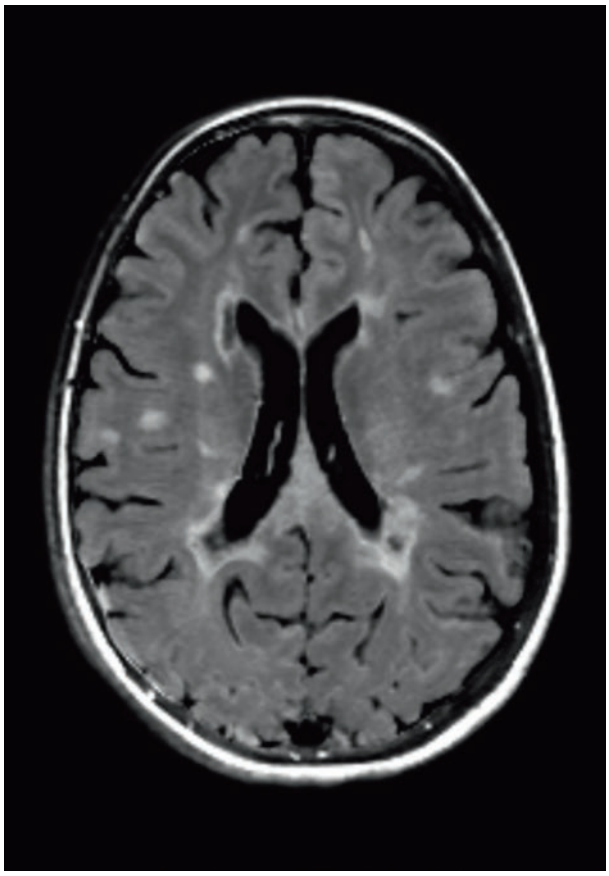

Figure 1. Image of the brain using MRI with conventional technique, showing lesions in the brain which can be a sign of MS, arteriosclerosis or insignificant signs in a healthy person over the age of 40.

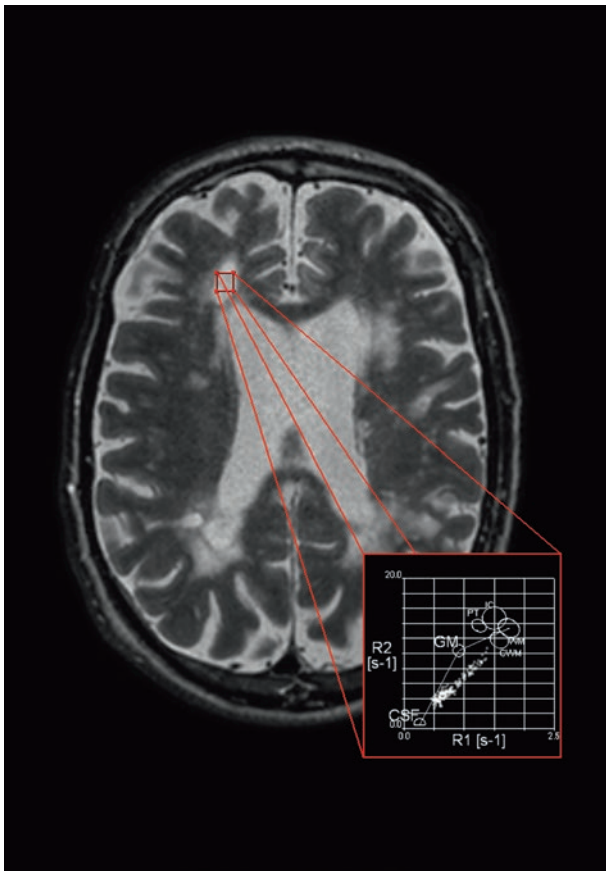

Figure 2. MR based method to discriminate between different types of brain lesions. Image by Örter and Warntjes, 2008.

disease. The results showed that the treatment slowed down the biochemical development of the disease.

Unspecific lesions in cerebral white matter can be seen both in MS and cerebral arteriosclerosis and is therefore often hard to use as basis for a diagnosis. A possibility to discriminate these lesions regarding their origin would be a valuable tool for diagnosis and we have therefore performed a pilot project aiming to develop an MR method to determine such differences.

This 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. The project will proceed further including cooperation with Uppsala University.

POPULAR SCIENTIFIC SUMMARY
CLAES LUNDSTRÖM

A Signal Processing Approach to Direct Volume Rendering

PROJECT NAME
A Signal Processing Approach to Direct Volume Rendering

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

MAIN PROJECT PARTICIPANTS
Stefan Lindholm, Anders Ynnerman

GRANTS
Swedish Research Council (VR) via Swedish e-Science Research Center (SeRC)

KEY PUBLICATIONS
S. Lindholm. "Medical Volume Visualization Beyond Single Voxel Values". PhD Thesis, Linköping University, 2014.

S. Lindholm, D. Jönsson, C. Hansen, A. Ynnerman. "Boundary Aware Reconstruction of Scalar Fields". In IEEE Transactions on Visualization and Computer Graphics, 20(12):2447-2455, 2014.

S. Lindholm, D. Forsberg, A. Ynnerman, H. Knutsson, M. Andersson, C. Lundström. "Towards Clinical Deployment of Automated Anatomical Regions-Of-Interest". Eurographics Workshop on Visual Computing for Biology and Medicine, 2014.

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

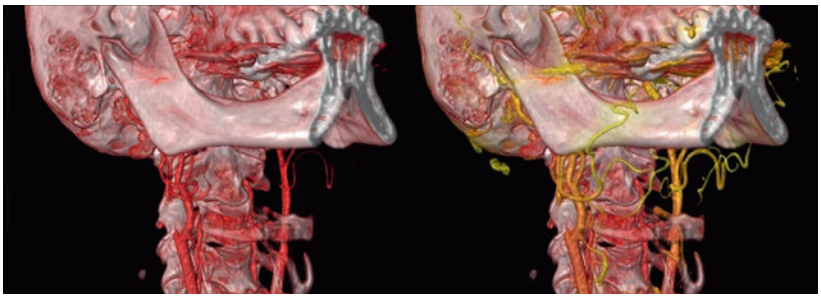

Figure 1. Enhanced vessel visualization using locally adaptive transfer functions (right) better depicts the full vascular tree than standard methods (left).

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 down sampled 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.

POPULAR SCIENTIFIC SUMMARY
GUDRUN ALM CARLSSON

Tissue Classification Using Dual Energy CT and Iterative Reconstruction

PROJECT NAME
Tissue Classification using Dual Energy CT and Iterative Reconstruction

PROJECT LEADER
Gudrun Alm Carlsson, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS
Alexandr Malusek, Maria Magnusson, Michael Sandborg

GRANTS
Cancerfonden 2013-2014

KEY PUBLICATIONS
Magnusson, M., Malusek, A., Muhammad, A. and Alm Carlsson, G. Iterative Reconstruction for Quantitative Tissue Decomposition in Dual-Energy CT. In: Proceedings of the 17th Scandinavian Conference, SCIA 2011, Ystad, Sweden, May 2011, (pp. 479-488). Springer Berlin/ Heidelberg.

Malusek, A., Karlsson,M., Magnusson, M., and Alm Carlsson, G. The Potential of Dual-energy Computed Tomography for Quantitative Decomposition of Soft Tissues to Water, Protein and Lipid in Brachytherapy. Physics in Medicine and Biology 58, no. 4 (February 21, 2013): 771.

Malusek, A., Magnusson, M., Sandborg, M., Westin, R. and Alm Carlsson, G. Prostate tissue decomposition via DECT using the model based iterative image reconstruction algorithm DIRA. Accepted at the SPIE conference Physics of Medical Imaging, San Diego, California, USA, February 16-20, 2014.

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 are first classified into bone and soft tissue. 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 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

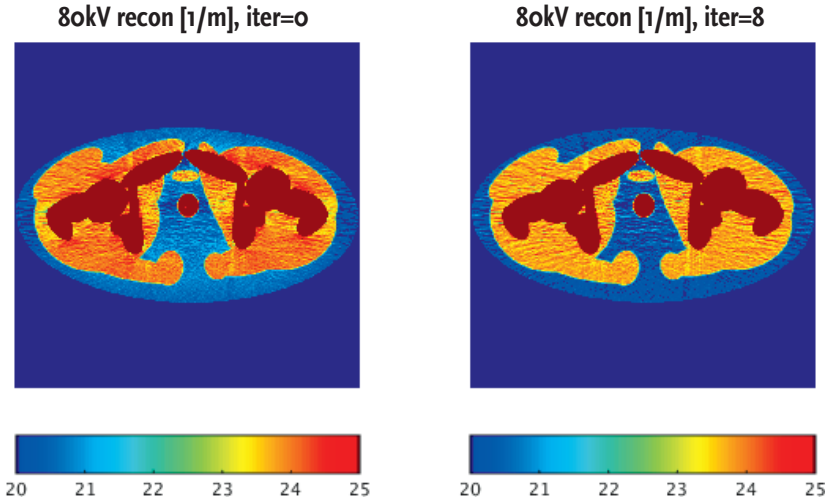

Figure 1. Suppression beam hardening artifacts in the human pelvic region from iteration 0 to iteration 8 in DIRA.

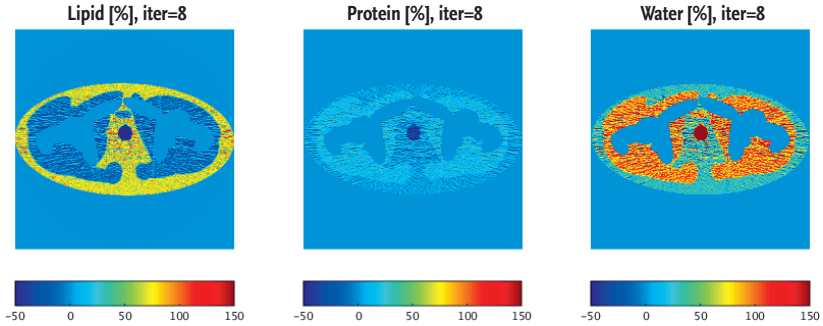

Figure 2. Soft tissue classification into lipid, protein and water (LPW) after 8 iterations of DIRA.

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 "DRASIM", a CT-simulation tool provided by Siemens. The X-ray spectra were 80 and 140kV, photon noise was included, and the geometry was basically the same as for the real CT-Scanner at CMIV. Figure 1 shows conventionally filtered back-projection 80kV reconstructed images of the human pelvic region after 0 iterations in DIRA (left) and after 8 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 8 iterations (right). The image for 140kV was improved in a similar way.

One key point in DIRA is to classify the soft tissue of the reconstructed images for 80 and 140kV into the base material triplet lipid, protein and water (LPW). The classification based on the 8th iteration is consistent with the true values and provides quantitative information of the tissue, see figure 2. As mentioned above, such information can be used for improved medical diagnosis and treatment. Ongoing research includes more advanced segmentation, test of different noise levels and implementation on parallel CPU architecture.

POPULAR SCIENTIFIC SUMMARY
RODRIGO MORENO

Medical Image Analysis Through Tensor Voting

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, also have been adapted to images acquired through medical imaging modalities and vice versa.

Many problems in medical image analysis have not completely been solved due to low resolution and noise present in the images. Using perception-based methods for this type of problems is promising given the largely reported success 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

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MAIN PROJECT PARTICIPANTS
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GRANTS
Swedish research Council 2013-2015

KEY PUBLICATIONS

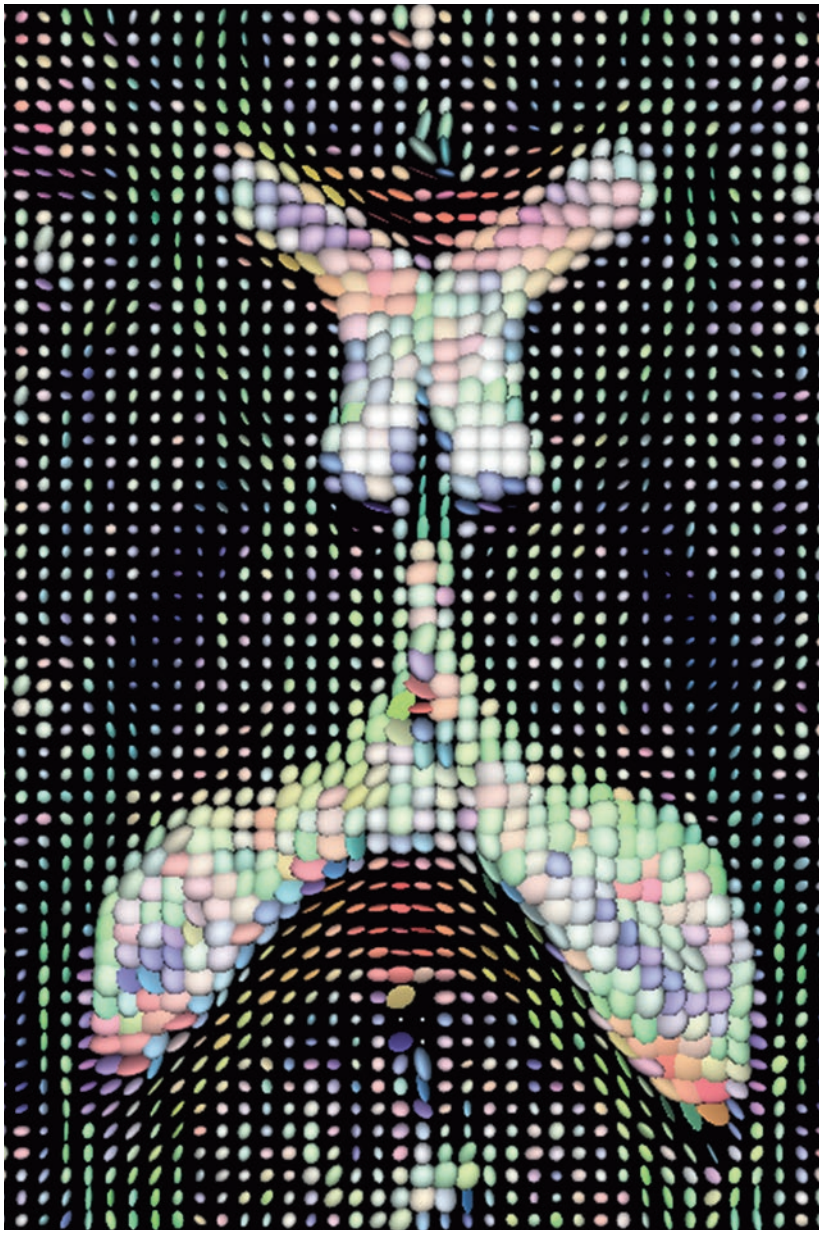
Jörgens, D., Moreno, R. Tensor Voting: Current state, challenges and new trends in the context of Medical Image Analysis. Schultz, T., Hotz, I. (Eds) Springer, in press.

Moreno, R., Garcia, M.A., Puig, D. Tensor voting for robust color edge detection. In Advances in low-level color image processing, Celebi, E., Smolka, B. (Eds), Springer, 2014, pp.279-301.

Moreno, R., Garcia, M. A., Puig, D., Pizarro, L., Burgeth, B., Weickert, J. On improving the efficiency of tensor voting. IEEE Transactions on Pattern Analysis and Machine Intelligence, Vol. 33, No. 11, 2011, pp. 2215-2228.

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).

POPULAR SCIENTIFIC SUMMARY
MICHAEL SANDBORG

Optimizing Radiographic Procedures – Dose vs. Image Quality

PROJECT NAME
Optimizing radiographic procedures – dose vs. image quality

PROJECT LEADER
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MAIN PROJECT PARTICIPANTS
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KEY PUBLICATIONS
Alexandr Malusek, Ebba Helmrot, Michael Sandborg, J-E Grindborg and Gudrun Alm Carlsson. In-situ calibration of clinical built-in KAP meters with traceability to a primary standard using a reference KAP meter. Phys. Med. Biol., 2014 (59), 7195-7210.

Michael Sandborg, Anders Tingberg, Gustaf Ullman, David R. Dance and Gudrun Alm Carlsson. Comparison of clinical and physical measures of image quality in chest and pelvis computed radiography at different tube voltages. Med. Phys., 2006, 33(11), 4169-4175.

Markku Tapiovaara and Michael Sandborg How should low-contrast detail detectability be measured in fluoroscopy? Med. Phys., 2004, 31(9), 2564-2576

MINIMIZING RADIATION EXPOSURE and at the same time making sure that the image quality is sufficient to make a correct diagnosis is called 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.

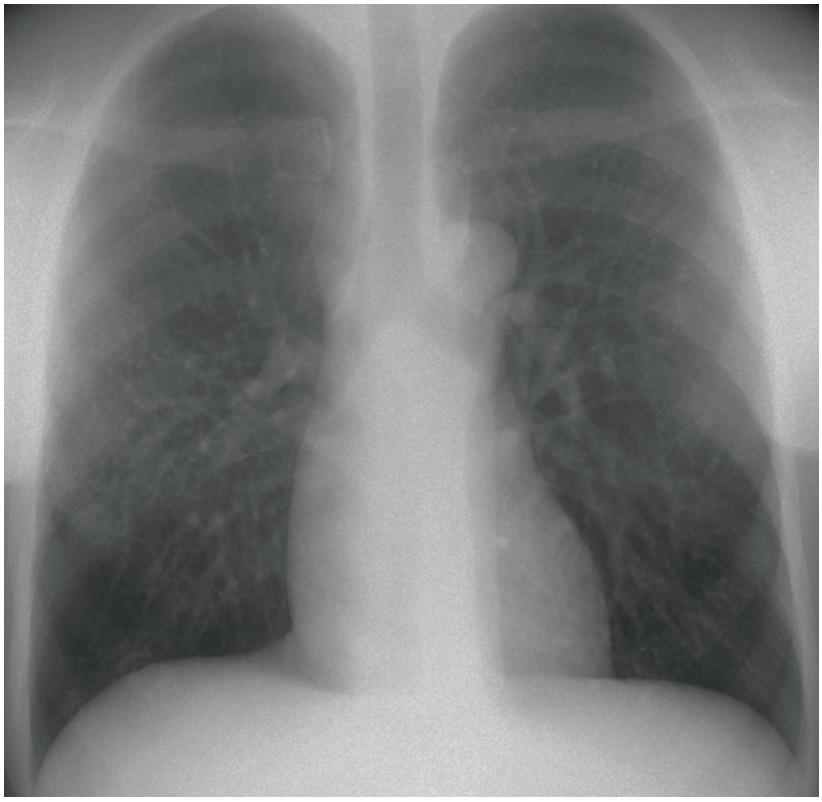
Our objective is to develop and use computer simulations of the complete X-ray imaging system to predict image quality and absorbed doses in the patient. To reach this goal, we are developing a computer model of the imaging system, a so called virtual X-ray system, by searching for correlations between 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 computes a detectability index for a 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. Figure 1 is an example in chest radiography.

Our virtual model of the imaging system provides unique possibilities not just to assess existing (today's) 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 in x-ray fluoroscopy. The signal-to-noise ratio measures how well this vessel can be detected (safely diagnosed) in a fluoroscopy image sequence 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.

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. Studies so far show clear indications that dose reductions up to 50% are possible using optimal settings in clinical practice.



A simulated virtual chest radiograph.

POPULAR SCIENTIFIC SUMMARY
MARCEL WARNTJES

Clinical Implementation of Synthetic MRI

SYNTHETIC MRI IS A technique to quantify physical properties of a patient using Magnetic Resonance Imaging (MRI). Based on these physical properties a range of conventional MR images can be recreated as well as tissue can be recognized and assessed automatically. This means that a relatively short scan time of 5-7 minutes is sufficient to reproduce a large part of a normal MR examination and, additionally, to provide more objective means of patient follow-up.

A close collaboration between researchers at CMIV and the university hospitals in Linköping, Umeå, Örebro, Uppsala and Gothenburg ensured the clinical relevance of the technique. A number of technical and clinical studies were performed to validate the various aspects of synthetic MRI on scan time reduction and automatic brain segmentation. A spin-off company, SyntheticMR AB, was created to ensure an installable, safe product including the necessary regulatory requirements. After this initial prototype phase more hospitals became involved, among which a number in the EU and US, to introduce synthetic MRI as a standard procedure into the clinical workflow. For example, Sahlgrenska University Hospital and the entire County Council of Västerbotten use it as standard protocol for MS patients. Queen Silvia Hospital in Gothenburg and Cincinnati Children's Hospital apply the approach for their pediatric scanning.

General Electric (GE) Healthcare announced at the RSNA conference in 2014 that they will release an embedded version of synthetic MRI in their coming new Pioneer scanner. Even Philips Healthcare showed it in their booth as a works in progress. Currently an increasing number of evaluation projects are ongoing to validate the time reduction on the MR scanner and to assess the robustness of technique on diseases such as Multiple Sclerosis, hydrocephalus, cancer and dementia in clinical practice. Exciting new research ideas are worked out such as automatic MS lesion detection

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KEY PUBLICATIONS

Multi-parametric representation of voxel-based quantitative magnetic resonance imaging
M Engström, JBM Warntjes, A Tisell, AM Landtblom, P Lundberg. PLoS One 2014;9:e111688

Novel Whole Brain Segmentation and Volume Estimation Using Quantitative MRI.
J West, JBM. Warntjes and P Lundberg. Eur Radiol 2012;22:998-1007

Rapid Magnetic Resonance Quantification on the brain: Optimization for Clinical Usage.
JBM Warntjes, O Dahlqvist Leinhard, J West and P Lundberg. Magn Reson Med 2008;60:320-329

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 generally 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 the major 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.

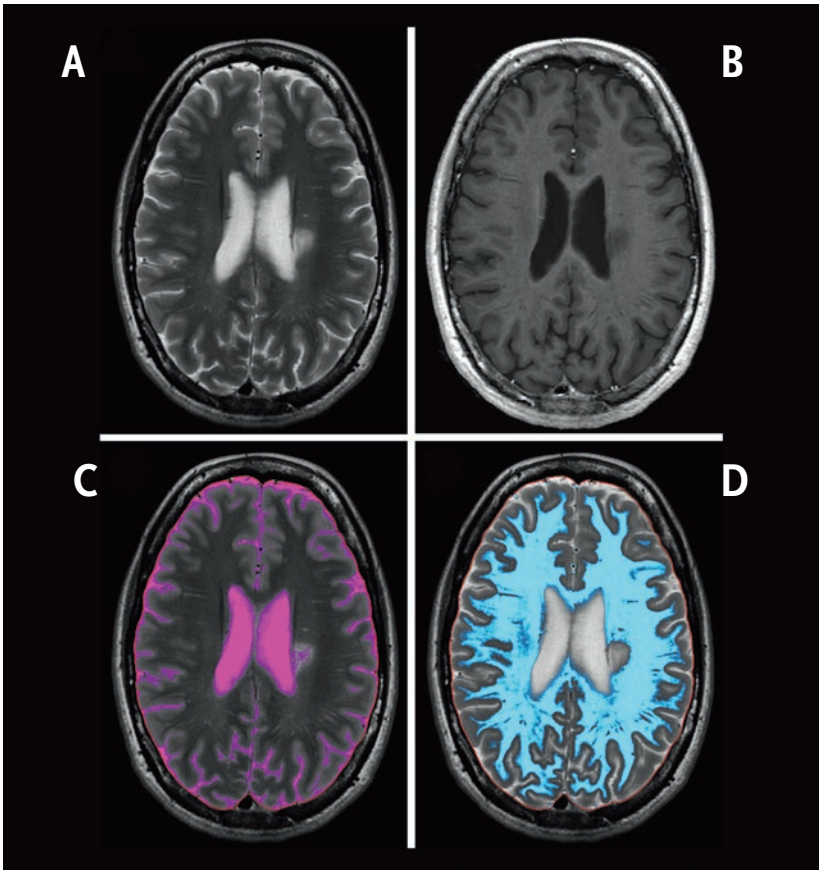

Figure 1. Example of synthetic MRI on the brain: Based on a single acquisition different conventional images can be recreated such as a T2-weighted (A) or a T1-weighted (B) image. Additionally the sequence serves as input to automatic tissue segmentation, such as cerebrospinal fluid (C) or white matter (D). Automatic tissue segmentation enables objective patient monitoring.

POPULAR SCIENTIFIC SUMMARY
ANDERS YNNERMAN

Methods for High-quality Illumination in Interactive Volume Graphics

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

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

GRANTS
The Swedish Research Council 2011

KEY PUBLICATIONS
Efficient Volume Illumination with Multiple Light Sources through Selective Light Updates, Erik Sundén, Timo Ropinski, IEEE Pacific Visualization, To appear - 2015

Historygrams: Enabling Interactive Global Illumination in Direct Volume Rendering using Photon Mapping, Daniel Jönsson, Joel Kronander, Timo Ropinski, Anders Ynnerman, IEEE Transactions on Visualization and Computer Graphics (TVCG), Volume 18, Number 12, page 2364--2371 - December 2012.

Efficient Visibility Encoding for Dynamic Illumination in Direct Volume Rendering, Joel Kronander, Daniel Jönsson, Joakim Löw, Patric Ljung, Anders Ynnerman, Jonas Unger, IEEE TVCG, Volume 18, Number 3, page 447-462 – 2012.

AN ESSENTIAL INGREDIENT in understanding 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 they reduce the physical accuracy of the light transport in the volume in order to maintain interactivity. Our research is therefore focused on developing efficient methods for simulating physically based light interaction of volumetric objects from computed

Displaying a computed tomography scan of a mummy. By applying advanced shading and light setups it becomes intuitive to understand the shape, location and size of internal structures of the mummy.

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 that did not change when altering light transport parameters.

By utilizing recent advances in hardware we have also shown how to perform selective light updates and reduce the memory footprint of a widely used light transport algorithm. This enables the user to create advanced light setups as shown in the screen shot above, which displays an interactive rendering of a CT scan of a mummy.

We are now extending our methods to time-varying CT scans and thereby enabling examination of organ functions with accurate shading. The key to this is to utilize the correlation between the changes of the data in time and incorporate the information in the light transport computation.

POPULAR SCIENTIFIC SUMMARY
ANDERS YNNERMAN

Seeing Organ Function

PROJECT NAME
Seeing Organ Function

PROJECT LEADER
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MAIN PROJECT PARTICIPANTS
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GRANTS
KAW

THE MAIN CAUSE of death in our part of the world is cardiovascular disease and the fastest growing cause of death is degenerative brain diseases, including dementia. In the diagnosis of cardiovascular diseases anatomical measurement of arterial constriction may be supplemented with patient-specific estimates of the constriction effects on blood pressure and flow. MRI Measurements of the three-dimensional blood flow provides a deeper insight into disease mechanisms in e.g. heart failure. The overall objective of this project is to create image-based patient-specific models that explore organ function through simulation, enable breakthroughs in research on organ function and, by extension, to use patient-specific functional organ models in the diagnostic workflow. The project is divided into four sections Data collection and enrichment, Image Based organ simulation, Interactive multidimensional organ visualization and Systems integration.

To diagnose degenerative brain diseases the centers that control brain functions and the connections between them needs to be localized. New MRI techniques can provide this information and provide the basis for

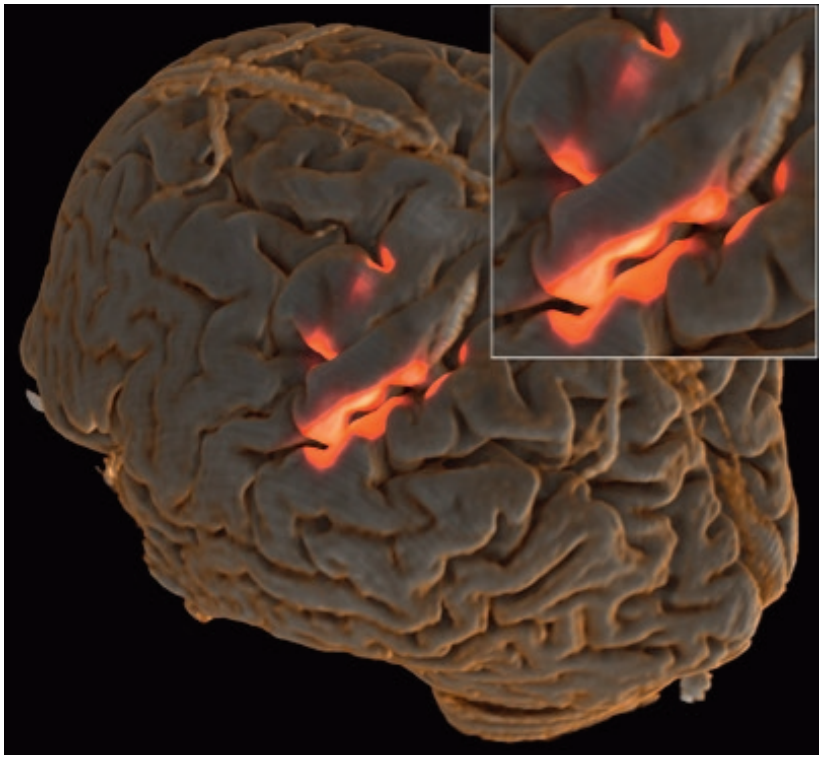

image-based measure of the degree of disease in e.g. Alzheimer's disease. In this project, we hope to contribute to the health care fight against all these diseases.

The project takes into account the complex mathematical concepts (vectors and tensors) that constitute the functional data and will specifically study the relation between form and function of the body's organs. An important problem for the subproject Data collection and enrichment is to integrate functional and structural information from different scales. Quantitative MR imaging of neurotransmitters in the brain and of the substance (myelin) that surrounds nerve fibers are other important elements.

Image based organ simulation will create patient-specific models of macroscopic and microscopic blood flow as well as the electrical activity of the heart and brain cells.

Interactive multi-dimensional organ visualization aims to create new visual representations to increase physicians and medical researchers' understanding of the functional information, for example by fusing data of different types from various image sources. System Integration, finally, combines the results from the three technical sub-projects into integrated tools for studying cardiac and brain function. This includes image-based models of the function of the individual patient's heart and integration of data about brain activity, relations between the various centers and the concentration of neurotransmitters.

POPULAR SCIENTIFIC SUMMARY
ANDERS PERSSON

Low-Dose Computed Tomography Below 1 milliSievert

PROJECT NAME
Low-Dose Computed Tomography Below 1 milliSievert

PROJECT LEADER
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MAIN PROJECT PARTICIPANTS
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KEY PUBLICATIONS
Kalra M, Woisetschläger M, Dahlström N, Singh S, Lindblom M, Choy G, Quick P, Schmidt B, Sedlmair M, Blake MA, Persson A. Radiation Dose Reduction with Sinogram Affirmed Iterative Reconstruction Technique for abdominal CT. J Comput Assist Tomogr, 2012, 36(3):339-346.

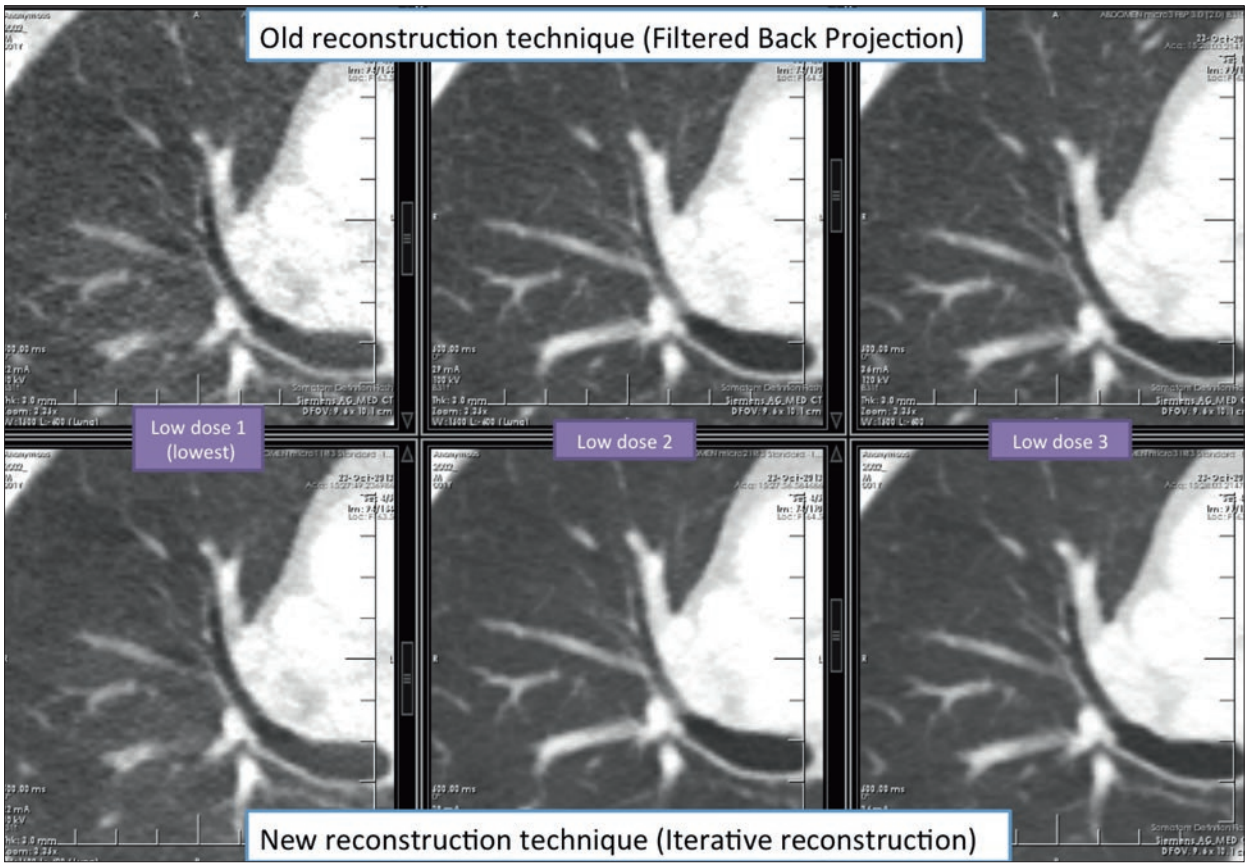
Kalra M, Woisetschläger M, Dahlström N, Singh S, Digumarthy S, Do S, Pien H, Quick P, Schmidt B, Sedlmair M, Shepard J-A O and Persson A. Sinogram-Affirmed Iterative Reconstruction of Low-Dose Chest CT: Effect on Image Quality and Radiation Dose. American Journal of Roentgenology, 2013, 201(2), W235-W244.

MEDICAL IMAGING IS USEFUL and necessary when examining and taking care of patients. X-rays have been used for more than a hundred years for imaging of the chest and skeleton. With the invention of Computed Tomography (CT) X-ray in the 1970's, X-rays could be used to image all parts of the body. The first machines could produce only a few images (slices) of a limited region, e.g. the patient's head, but since the mid-90's a CT machine can scan the whole patient, and nowadays this takes just a few seconds.

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.

POPULAR SCIENTIFIC SUMMARY
ANDERS PERSSON

Forensic Science – Virtual Autopsy

PROJECT NAME
Forensic Science - Virtual Autopsy

PROJECT LEADER
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MAIN PROJECT PARTICIPANTS
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GRANTS
KK-stiftelsen 2008-2010
RMV forskningsfond 2008-2010
RMV forskningsfond 2009
Konung Gustav V:s och Drottning Victorias frimurarstiftelse 2008-2012

KEY PUBLICATIONS
Ljung P, Winskog C, Persson A, Lundström C, Ynnerman A. Full Body Virtual Autopsies Using A State-of-the-art Volume Rendering Pipeline. IEEE Transactions on Visualization and Computer Graphics. 2006;12(5):869-876.

Persson A, Lindblom M, Jackowski C. A state-of-the-art pipeline for postmortem CT and MRI visualization: from data acquisition to interactive image interpretation at autopsy. United Kingdom: Informa Healthcare; Acta Radiologica. 2011; 52 no. 5 522-536.

C. Jackowski, N. Schwendener, S Grabherr, A. Persson. Postmortem cardiac 3T magnetic resonance imaging: Visualizing the sudden cardiac death? Journal of the American College of Cardiology, 2013; Volume 62, Issue 7, 13 August 2013, Pages 617–629.

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 cloths and bleedings can also be identified in the images.
At CMIV postmortem imaging has been used in routine work since 2003. 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 post mortem imaging and developing a new type of software that can visualize full

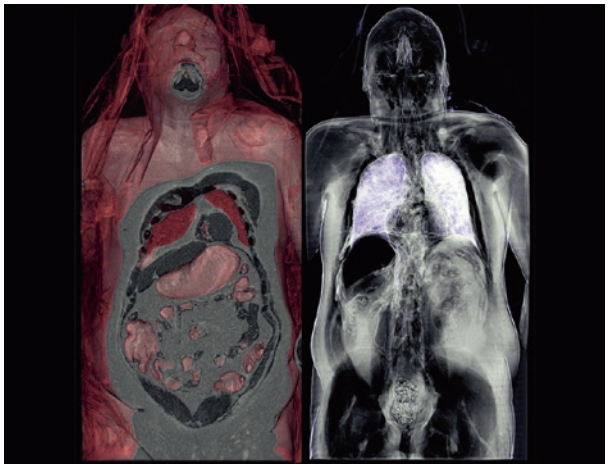


Figure 1. Postmortem Dual Energy computed tomography angiography. The captured data rendered with two different translucencies settings so that soft tissue and air in the body can be visualized by volume rendering 3D.

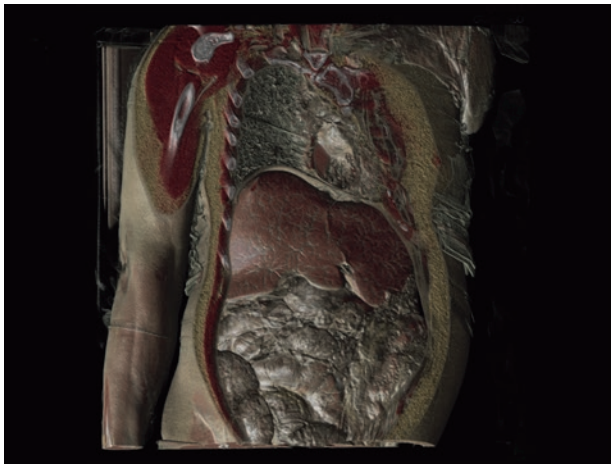


Figure 2. Postmortem Dual Energy computed tomography of a deceased person. Soft tissue rendered with different colours and different translucencies. Part of the anterior tissue virtually removed from the body so that the underlying organs can be studied.

body data-sets and three-dimensional 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.

84 POSTMORTEM IMAGING

Since 2003 CMIV performs postmortem imaging of murder victims to complement the forensic autopsies made at the National Board of Forensic Medicine (RMV) on behalf of the police, district attorney or court. This is an appreciated collaboration by all parts resulting in improved diagnostics and high quality research. In 2015 an SBU report will be published investigating the possibility to use the technique to replace clinical autopsy.

Start the Day with Postmortem Imaging

Maria Lindblom is a radiologist at the University Hospital in Linköping. She specializes in emergency radiology, skeletal injuries and children. However, every once in a while she comes in early to work with a forensic case. Maria started working with postmortem imaging during her residency in radiology.

–Before I chose radiology I was thinking of being a coroner so when the opportunity came to combine radiology with forensic investigations I didn´t hesitate, says Maria Lindblom.
In Sweden, the forensic autopsies are carried out by the National Board of Forensic Medicine (Rättsmedicinalverket, RMV) on behalf of the police, the district attorney or the court. Relevant cases from the Linköping district are sent to CMIV for postmortem imaging. All murder victims and children, who die outside of the hospital, are analyzed with computed tomography(CT) and sometimes magnetic resonance tomography(MR) before the regular autopsy. In respect for the patients these investigations take place early in the morning before the regular schedule.

– RMV calls us the day before to schedule an appointment. The next morning two forensic technicians bring the body in. It is kept in the bag to preserve any evidence until the autopsy begins, Maria explains. Since the body is sealed in, we don´t know much about it before we begin the examination.

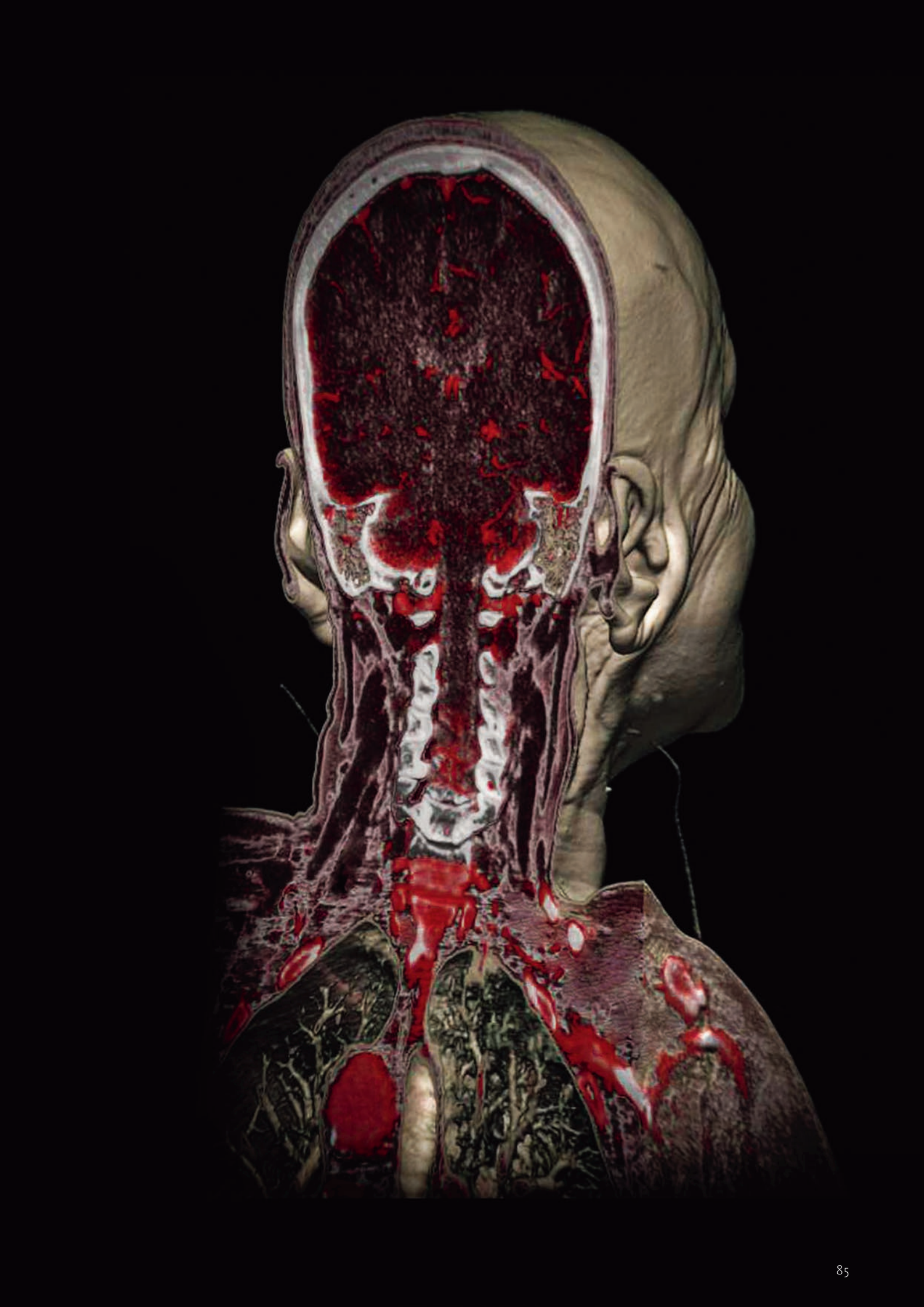
–We have produced a standard protocol for the whole body using dual energy over the chest to improve soft tissue contrast. We also do sequences over the teeth to help with identification.

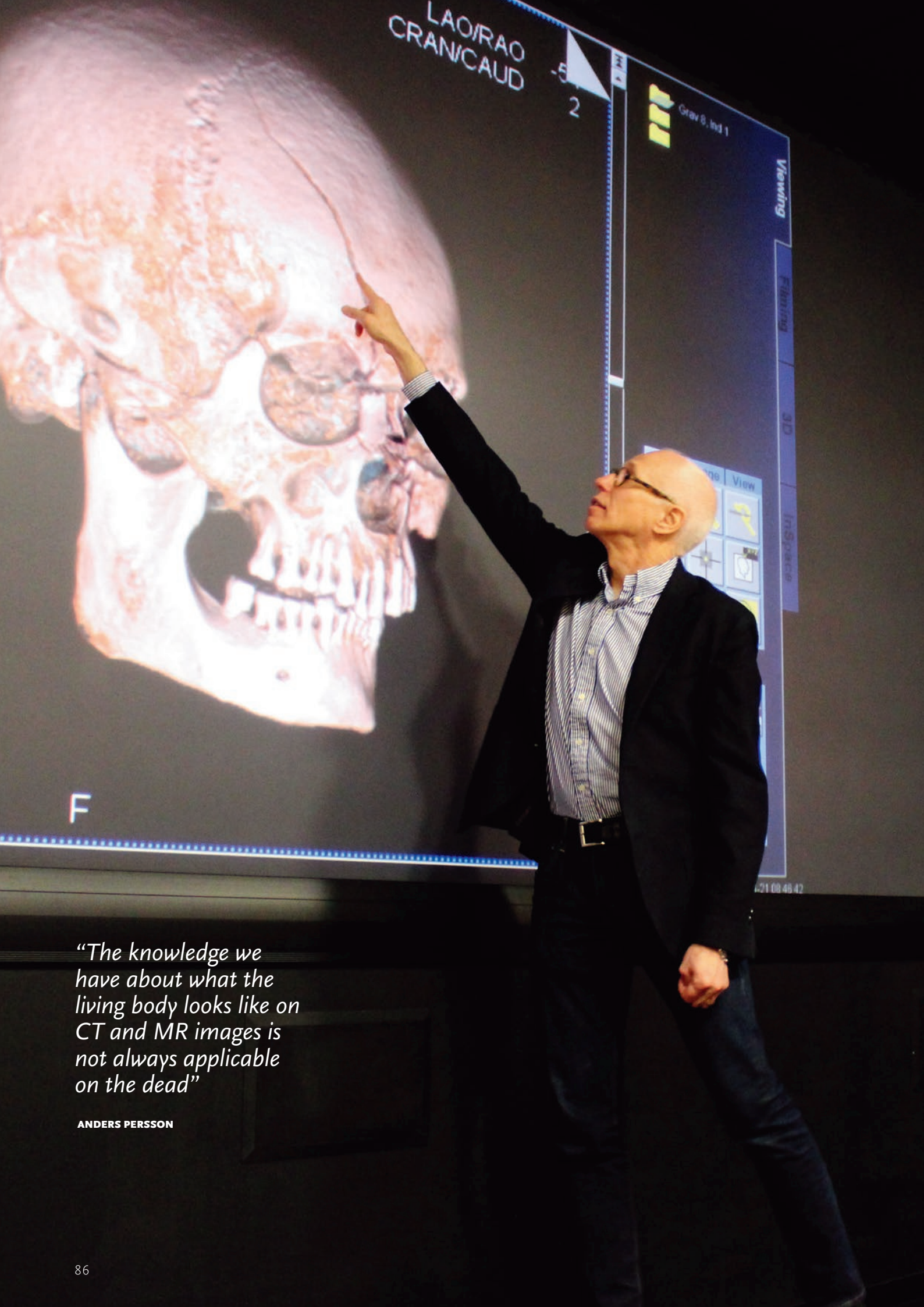
–When we have analyzed the images we have a dialog with the coroner about the findings. The coroner might also come back to us as new questions arise during the autopsy, says Maria.
Maria Lindblom and Anders Persson do most of the postmortem imaging analyses at CMIV. As special knowledge is needed to interpret the results the group of radiologists is kept small.

Fruitful Collaboration for Research and Crime Solving

In 2003 the director of RMV Lennart Ramler met with Anders Persson, director of CMIV. Lennart had just returned from a conference in Umeå,where he had learned about postmortem imaging.

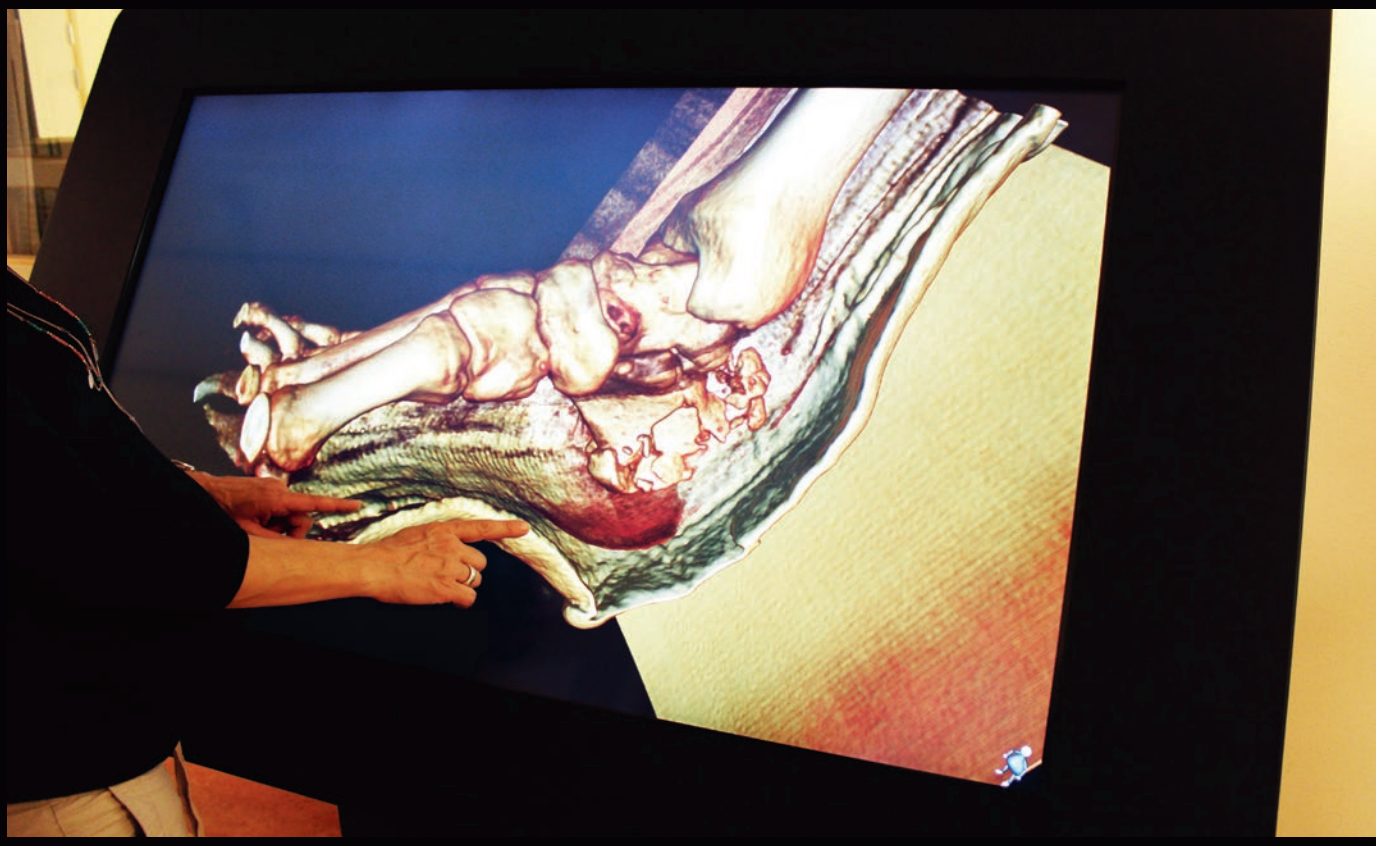
–He was very enthusiastic; a project for postmortem imaging was starting up in Bern and he turned to me to discuss the possibility to start a similar project in Linköping, says Anders Persson.
This was the start of a fruitful collaboration between RMV and CMIV. RMV needed to develop new methods to





"The knowledge we have about what the living body looks like on CT and MR images is not always applicable on the dead"

ANDERS PERSSON



complement the autopsy and CMIV was interested in enhancing their techniques but did not have the material.

–We started out with a couple of test subjects, a victim of a car crash and a deceased child. We immediately saw the benefits from the imaging, Anders continues. In the car crash victim we could see the skeletal damage very distinctly. In the child the post mortal gas was visual which is nearly impossible to see during the autopsy.

After the first successful experiments several research projects were started to develop reliable methods for routine use.

The Winding Road to Visualization

–After a while we realized that it wasn't that easy to work with the images. The CT scans produced large whole body images and we didn´t have equipment that was powerful enough to visualize the findings, says Anders.

A new research project was started to solve the visualization problem. A couple of researchers from Visualization Center C in Norrköping went to Princeton to find a new method to move data. The solution was to load only the part of the image that was in view in every moment. This method has revolutionized the visualization of CT images.

–Together with the Interactive Institute ICT and Visualization Center C, we made a prototype that used the new method to visualize CT images. Someone suggested that we should use a larger screen and then we added the touch functionality.

It was now possible to look inside the body in 3D, twisting and turning the images using only the fingertips. And so the visualization table was born. In 2009 the prototype was shown at the World Expo in Shanghai. The table drew considerable media attention during the following years.

At the Other End of the Line

Today, the director of RMV in Linköping is coroner Johan Berge. He and his staff of coroners, autopsy technicians, investigators and forensic assistants are all involved in the collaboration with CMIV.

–I find the collaboration very rewarding. Anders and Maria have a positive attitude and a real interest in our work, says Johan Berge. Both organizations benefit. Our methods are modernized and improved while CMIV get the opportunity to conduct front line research in the field.

The coroner on duty consults with the radiologist at CMIV over the phone and may look at the images at the same

time. During the autopsy, however, the coroner rarely looks at the images.
-I wish we could use the images more but right now it is not practical due to the unclean environment during the autopsy, Johan explains.

RMV sends around 20-30 cases to CMIV every year. It is mainly homicides and young children. It would be useful with postmortem imaging in more cases but it is both a financial question and a matter of capacity at CMIV.

–The vision nationally at RMV is to scan all relevant cases which would mean 20-30% or 1000-1500 cases per year. In Linköping that would be around 150 cases per year, explains Johan.

–We would like to scan all accidents, for example victims from traffic and workplace incidents. It would improve our diagnosis and statistics, continues Johan.

CSI or the Real Thing?

One of the advantages with the imaging technique is the possibility to do measurements in the image. When Johan finds a knife injury during the autopsy he can go back and ask Anders or Maria to go to that specific location in the image and measure the depth and angles of the wound. This information can then be used to role out or strengthen the suspicion of a murder weapon.

Digital images also opens up for the opportunity to consult weapon specialists in other countries, for instance, to match a pellet pattern to a specific rifle. The images from CMIV are used as a complement during trials when the coroner presents the evidence. They are often more visual and easier to handle for the audience than autopsy photos.

–All in all, postmortem imaging cannot replace the forensic autopsy but enhance findings and make the investigations better, concludes Johan Berge.

What We Know and Need to Know more about

Postmortem imaging in clinical autopsies are rare in Sweden while it has been used for a long time in forensic investigations to find postmortem gas, fractures and bullets. In fact, clinical autopsies are becoming more and more rare altogether.

–The lack of clinical autopsies is seriously affecting the quality of the cause of death statistics in Sweden. Cause of death based on only a clinical assessment is not as reliable and the wrong conclusions are often drawn, says Anders Persson.

Autopsies may reveal systematic faults in diagnostics and treatment choices and help improve care for future patients. The cause of death statistics is also the base in many research studies and its accuracy is crucial for the results.

In 2015 a new SBU report will be published investigating the possibilities for postmortem imaging to replace or complement clinical and forensic autopsy. The scientific analysis is carried out by Professors Anders Persson from CMIV and Anders Eriksson, Umeå University.

–If we could do postmortem imaging in the cases where no autopsy is performed it has the potential to drastically improve the reliability of the statistics, says Anders.

The report shows that postmortem imaging has great potential but to be able to use the technique, reliable research is needed proving that the images can show what the autopsy does.

–The knowledge we have about what the living body and its conditions look like on CT and MR images is not always applicable on the dead. We need more knowledge through high quality research studies, Anders sums up.

"Postmortem imaging cannot replace the forensic autopsy but enhance findings and make the investigations better"

JOHAN BERGE

90 THE CMIV RESEARCH SCHOOL

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 thirty PhD students admitted to the research school. Here a selection of them presents their research.


Sjuksköterska
Lilian Henriksson
Röntgensjuksköterska
Legitimerad
Röntgensjuksköterska

SUPERVISORS
Magnus Borga, Olof Dahlqvist Leinhard, Ola Friman

PROJECT
Fat- and Water Imaging Project
Quantitative Muscle Project
Brown Adipose Tissue Project

BACKGROUND
Master of Science, Engineering Biology, specialization in Biomedical Engineering
The Institute of Technology, Linköping University, 2005-2011

Research Engineer, Department of Biomedical Engineering, Linköping University, Linköping 2011-2012

Anette Karlsson

Assessing Muscle Volume Using Magnetic Resonance Imaging

WE HAVE DEVELOPED a method that can determine a patient's entire muscle volume, as well as the volume of separate muscle group based on images from a 10 minute MR-scan. The method can also determine the amount of fat within the muscle, which is a sign that the muscle is injured.

A muscle that is hurt or decreased in volume may cause 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 is for example 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.

Scales and measuring tapes are not accurate enough for measuring muscle volume since they do not discriminate between muscles and fat. With an MR-scanner, on the other hand, 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 figure 1.

For the human eye, 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 (figure 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. 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 figure 2.

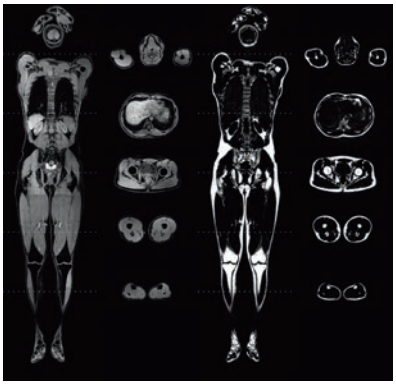


Figure 1. A paired magnetic resonance image where the left shows all the water within a whole body and the right shows all the fat.

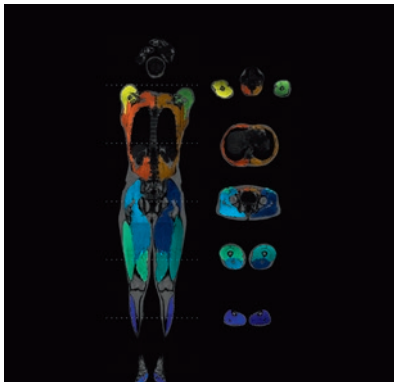


Figure 2.. A typical result from the automatic method. The different muscle groups are shown in different colors. Grey color indicated that the automatic method has not considered that tissue as muscle tissue.

SUPERVISORS
Magnus Borga
Olof Dahlqvist Leinhard

BACKGROUND
MSc from Linköping University

Thobias Romu

Quantitative Water-Fat Imaging

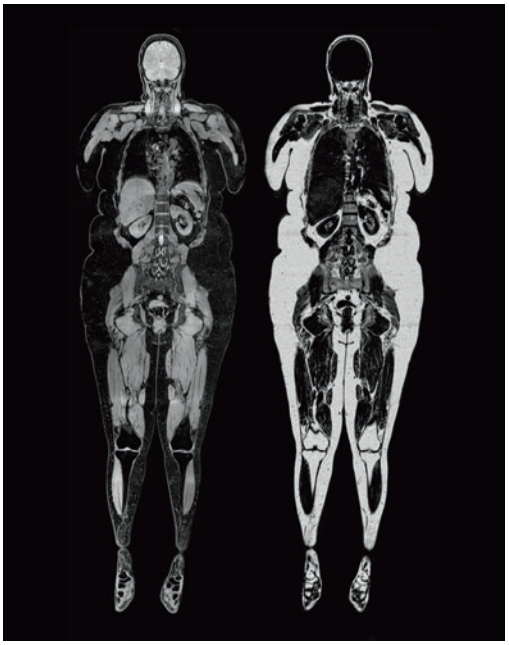
TO STUDY THE distribution of various tissues within the human body we use a technique that separates water and fat in magnetic resonance (MR) images. An example of such images is seen in the figure. We calibrate the images in a way that every pixel in the fat image corresponds to the actual adipose tissue concentration. Furthermore, we use automatic segmentation through anatomical atlases to 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 total volume varies from a few per cent of a person's total volume, to several times the volume of other tissues. An application of regional adipose quantification is that excess of visceral adipose tissue (belly fat) indicates a heighten risk of diabetes type 2, cardio vascular disease and cancer, whilst subcutaneous adipose tissue may even act protectively. Thus, it becomes important to separate the two fat compartments when assessing the risk of obesity.

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, competing image based methods are too expensive and time consuming.

We have created an inexpensive method for analyzing water and fat separated images as well as protocols for speedy MRI accusation. 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 cost. 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 method is used to measure the amount of brown adipose tissue, a tissue which burns energy to produce heat. It is also used to quantify the subcutaneous adipose tissue volume, the liver and pancreatic fat concentration as well as the breast density, which is a strong predictor of breast cancer.



A water and fat image from a set of images covering the whole body.

SUPERVISORS
Bengt Norén (co-supervisor),
Gunnar Cedersund (co-supervisor),
Olof Dahlqvist Leinhard (co-supervisor),
Peter Lundberg (supervisor)

PROJECT
Non-Invasive Liver Biopsy (NILB)
Liver Intrinsic Function Evaluation (LIFE & 4LIFE)
Hepatic Inflammation and Fibrosis (HiFi)

BACKGROUND
Master of Science (MSc), Engineering Biotechnology, Systems Biology, Linköping University 2006 – 2011

Applications Engineer (October 2012–Present)
Wolfram MathCore AB

Research Assistant/Engineer, County Council of Östergötland, CKOC, Department of Radiation Physics 2009–2012

Mikael Forsgren

Determining Hepatic Function in Diffuse and Focal Disease Using Multimodal Magnetic Resonance Imaging

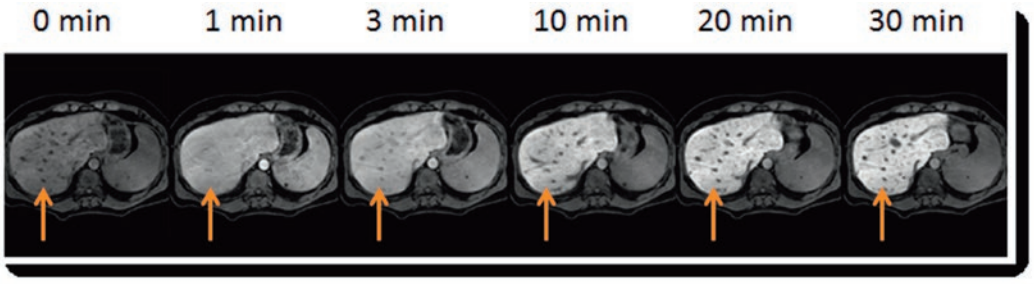
THE LIVER IS one of the largest organs in the human body and it handles many vital tasks such as processing nutrients, removing toxins, and assembling proteins. In our modern society diseases affecting the liver are a growing problem and there is a need for novel techniques that can be used for accurate non-invasive investigation of the liver. Such diagnostic techniques are the primary focus of my research.

The conventional methods of diagnosing many aspects of liver disease suffer from several drawbacks. One of these methods 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.

A problem with many liver diseases is that they develop undetected and once the symptoms become noticed 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 loss 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.

In our projects we use a set of novel magnetic resonance (MR) imaging methods in order to determine liver function. For instance, we measure liver function by injecting a contrast enhancing agent in the blood 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. 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. Once the images are processed we use mathematical models to determine liver function.

The goal of my projects is to be able to present a comprehensive understanding of the status of the liver, to for instance surgeons planning liver surgery, or to doctors treating patients, by combining our set of liver specific MR methods.



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 as contrast is being accumulated in the liver.

SUPERVISORS
Staffan Wirell (co-supervisor), Marcus Ressner (co-supervisor), Örjan Smedby (supervisor)

BACKGROUND
Bachelor of Science in diagnostic radiography nursing 2001

Master of Diagnostic imaging and physiology, 2008

Medical Ultrasound, 2009

Licentiate of Medical Science, 2011

Radiology nurse and sonographer, Department of Radiology, County Council of Östergötland, Linköping 2000-present

Carina Stenman

An Alternative Workflow Method for Ultrasound Examinations

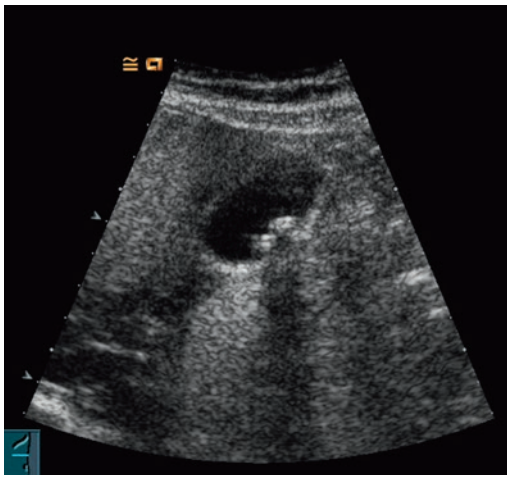
ULTRASOUND IS OFTEN a first choice for radiological examinations. It is a quick and safe diagnostic method. Thanks to recent technical progress in regard to image quality ultrasound is used to diagnose, for example, focal changes in the liver.

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.



SUPERVISORS
Jan Engvall, Tino Ebbers, Anders Persson

PROJECT
Cardiovascular blood flow assessment, Determining Optimal non-invasive Parameters for the Prediction of Left Ventricular morphologic, Early detection of cardiac effects induced by treatment for breast cancer, Heart4flow

BACKGROUND
Nursing degree from the University College of Health and Caring Sciences, Uppsala, in 1996

Bachelor degree 2000, Master of nursing in 2003, Linköping University.

Region Östergötland, Department of Medicine, Norrköping, 1996-1999,

Department of Radiology, Norrköping, 1999-2004.

2004-present CMIV, Linköping, radiographer responsible for the MRI scanners.

Johan Kihlberg

Determining Hepatic Function in Diffuse and Focal Disease Using Multimodal Magnetic Resonance Imaging

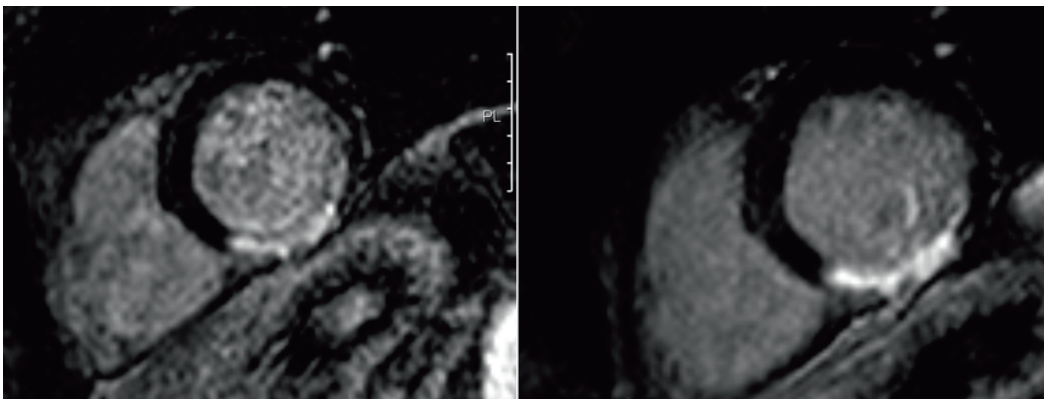
The treatment of myocardial infarction has advanced enormously in the last decade but it is still one of the leading causes of death. The larger the scar that the infarction results in, the more likely it is that patients develop heart failure. Preventive treatment with ACE-inhibitors and diuretics is used to unload cardiac work and improve survival. When an exact determination of infarct size is required, magnetic resonance (MR) is the best method. Still, many difficulties with cardiac MR exams remain, especially problems related to motion artifact. MRI is however, versatile and approaches requiring breath hold may be replaced by single-shot acquisitions, thus avoiding motion artifact.

An important parameter which has to be determined in the cardiac MRI exam is the inversion time which is critical for scar imaging. We have developed a sequence allowing a simulation of relaxation that in effect allows any inversion time to be used in scar imaging. We could show that synthetic scar images had a good agreement with the conventional images in terms of scar size. Scar size determines systolic pumping function.

We have developed "Displacement the Encoding with Stimulated Echoes" (DENSE) which measures the displacement of the cardiac wall during systole. In my studies, DENSE has been validated for its ability to detect scar in 125 patients participating in the "Doppler-Cip" study. The results are very promising, allowing the determination of significant scar with a sensitivity of 95% and specificity of 80%.

A competing MRI technique that can measure cardiac strain is "tagging", which can be analyzed with the software "Harmonic Phase", (HARP). Since HARP is considered the gold standard, we have compared DENSE with HARP.

Many diseases and treatments may cause cardiac deformation. Therefore, it is interesting to follow a pathophysiological process with an accurate method like DENSE. One such condition is irradiation of the breast to treat cancer. We investigate these patients with DENSE before, during and after treatment. The overarching goal is to reduce radiation to avoid cardiac impairment in both short and long term.



Synthetic image of a myocardial scar using the adaptive inversion time technique to the left and the conventional late gadolinium image to the right.

SUPERVISORS
Maria Engström, Gunnar Cedersund, Fredrik Elinder, Susanna Walter

PROJECT
SAND:MAN

BACKGROUND
BSc Biology with mathematics

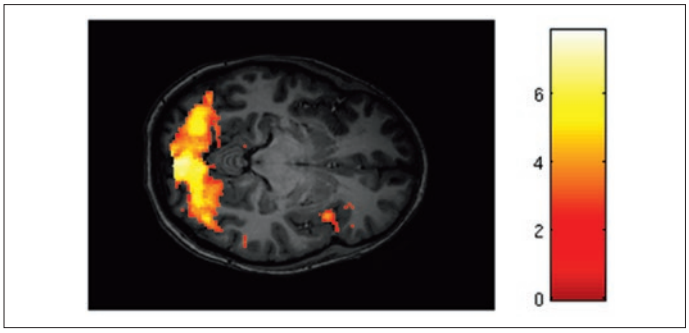
MSc Biology, Molecular genetics and physiology

Karin Lundengård

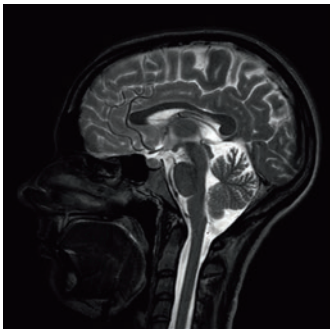
Building Computer Models of the Brain to Look at How Hungry Neurons Control the Blood Supply

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, since it is safe for the person being examined.
When we think of brain activity, we usually think of it as the electrical signals that neurons send to each other, but unfortunately the scanner cannot measure those electrical signals. Instead 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 transport 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 (less than 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 get a better understanding for how the brain works and develop a good tool for diagnosing and investigating complicated brain disorders from fMRI images.



fMRI image where the active areas in the visual centra are highlighted as the person is looking at a picture.



Anatomical image of the brain.

SUPERVISORS
Tino Ebbers (supervisor)
Petter Dyverfeldt (co-supervisor)
Jonas Lantz (co-supervisor)
Carl-Johan Carlhäll (co-supervisor)

PROJECT
Cardiovascular blood flow assessment

BACKGROUND
MSc in Biomedical Engineering
August 2010-March 2013, Linköping University (Linköping, Sweden)

MSc in Telecommunication Engineering
October 2003-March 2010, Universidad de Oviedo (Oviedo, Spain)

Systems engineer trainee
April 2010-July 2010, EADS Astrium (Madrid, Spain)

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.

SUPERVISORS
Tino Ebbers, Carl-Johan Carlhäll, Petter Dyverfeldt

PROJECT
Cardiovascular blood flow assessment

BACKGROUND
MSc Computer Science
Uppsala University, Sweden,
2010–2012

Computer Engineering
Simon Bolivar University, Venezuela,
2001–2006

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 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.

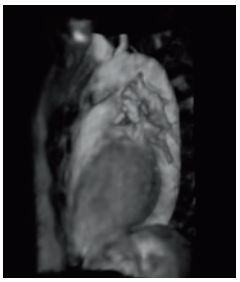


Figure 1: 3D rendering of a flow magnitude image

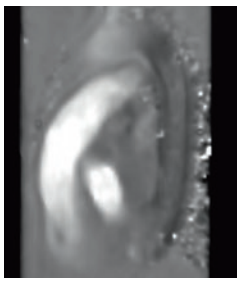


Figure 2: Flow velocity

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 (see fig. 3).

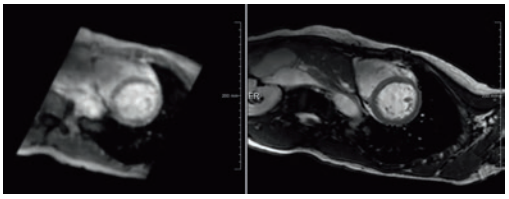


Figure 3: Flow Magnitude (left) and Short Axis balanced (right)

The first goal of the project was to develop an automatic atlas-based vessel segmentation method that can be used on 4D flow MRI. Atlas-based segmentation involves deforming an already labeled image by means of registration in order to extrapolate the labels into another unsegmented image. In this study, atlas-based segmentation was used in combination with registration between the timeframes of the 4D flow MRI dataset in order to obtain a 4D segmentation of the great thoracic vessels.

The atlas also includes information about 2D plane locations at which flow volume analysis will be performed.

In future projects, a 3D atlas of a heart 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.

SUPERVISORS
Hans Knutsson (supervisor), Mats Andersson (co-supervisor)

BACKGROUND
M.Sc. in Engineering Physics, KTH Royal Institute of Technology 2007–2012

Research Scientist, Elekta Instrument AB, Stockholm, Sweden (2012–present)

Jens Sjölund

Advanced MRI Techniques for Functional and Stereotactic Neurosurgery

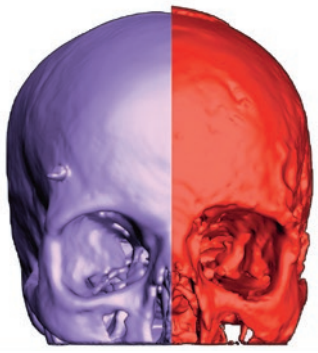
MANY BRAIN DISORDERS–e.g. tumors, vascular malformations and Parkinson's disease–can be treated either surgically or by focused radiation. The treated areas are often small and it is of course vital not to harm the surrounding healthy tissue. This places extremely high demands on the accuracy of the 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).



Bone segmented from X-ray imaging (CT) in purple and from MRI in red.

SUPERVISORS
Susanna Walter (supervisor)
Maria Engström (co-supervisor)
Magnus Ström (co-supervisor)

BACKGROUND
2004 Medical degree, Karolinska Institute, Stockholm, 2004

Residency in internal medicine and gastroenterology and hepatology, Heart and Medicine Center, Department of Gastroenterology, County Council of Östergötland, Linköping, 2006 – present

Mats Lowén

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.

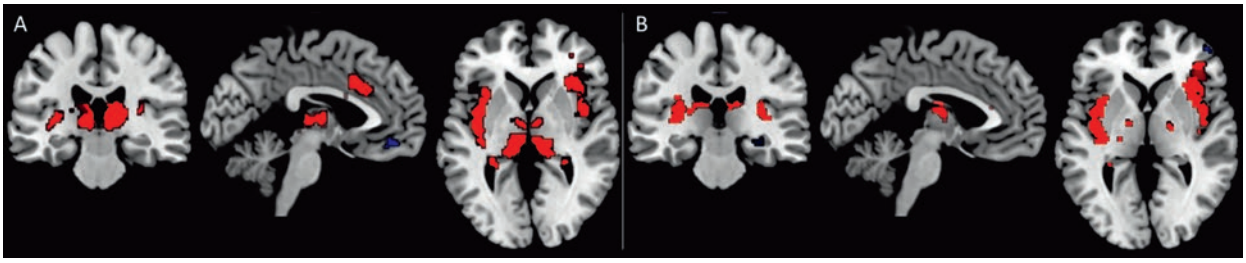
The cause of IBS is not completely understood. Altered brain-gut interactions are thought to play an important role in the cardinal symptoms, particularly abdominal pain since it has been shown that hypersensitivity to distensions in the lower part of the bowel is present in some, but not all IBS patients. 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.

SUPERVISORS
Prof. Michael Sandborg
Co-supervisors:
Prof. Örjan Smedby
Prof. Anders Persson
Docent Hannibal Sökjer

BACKGROUND
Diagnostic radiographer, Bristol School of Radiography in Great Britain April, 1980.

Diagnostic Radiographer Nairobi, Kenya 1980-1985

Radiology department Vrinnevi Hospital in Norrköping 1986-2014 during which I graduated with a Bachelor´s (2008) and Master's (2013) degree in Medicine.

Radiology Department in Linköping March 2014-present

Bharti Kataria

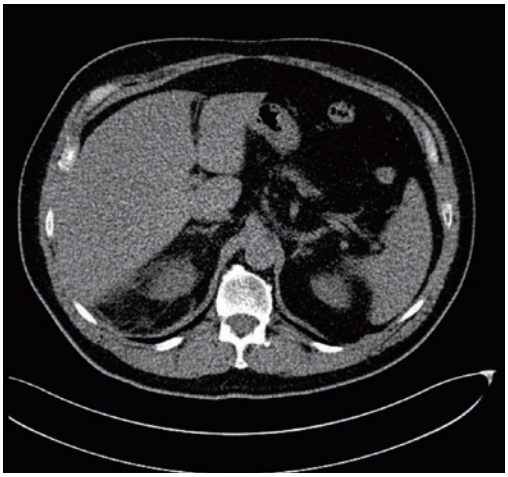
Evaluation of Optimization Methods for Abdominal Computed Tomography

FOR ALL DIAGNOSTIC radiology examinations using radiation there is a desire for the best possible image quality (AHARA principle) and at the same time endeavor to keep the radiation dose as low as reasonably achievable (ALARA principle). The higher the dose the better the image quality as image noise is reduced, but this is not always necessary to make a diagnosis.

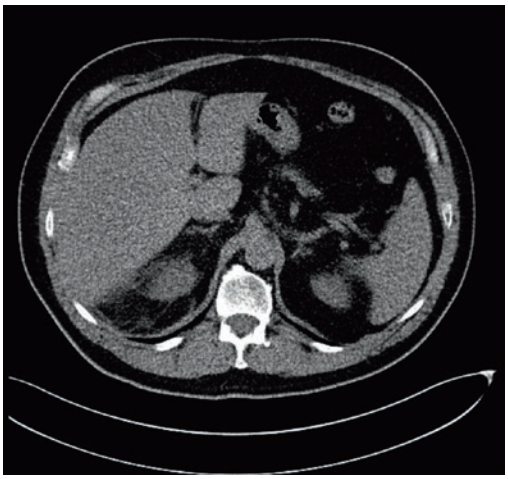
The main subject of this project is the relationship between radiation dose and image quality in abdominal Computed Tomography (CT) examinations, which deliver a high radiation dose to the patient. The purpose is to find ways of optimizing abdominal CT examinations by evaluating the dose reduction potential of different reconstruction and post-processing methods and the diagnostic value of a low-dose CT.

The first study evaluated the dose reduction potential of an iterative (mathematical) reconstruction method, SAFIRE, which reduces image noise and thereby allows 5-9% dose reduction. Further investigation of this algorithm and other post-processing methods using visual grading experiments will reveal the amount of dose reduction that is possible in order to optimize abdominal CT examinations.

Optimization is also about choosing the best imaging method to facilitate the diagnostic process by shortening time from presentation to treatment. Therefore evaluation of a low-dose abdominal CT to determine its diagnostic value compared to two other methods will be studied. The value of this project is to optimize protocols and reduce the radiation dose to all future patients undergoing abdominal CT examinations.



Filtered Back Projection 35 mAs



SAFIRE 35 mAs

Siemens SOMATOMForce

SUPERVISORS
Hans Tropp, Nils Dahlström, Daniel Forsberg, Per Aspenberg, Staffan Wirell

PROJECT
Quantitative musculoskeletal imaging for assessment of idiopathic scoliosis

Ludvig Vavruch

Idiopathic Scoliosis – Deformity in Three Dimensions.

SCOLIOSIS IS A deformity of the spine with curvatures in the frontal plane as well as in the sagittal plane. In addition, the vertebras in the deformity are rotated in the axial plane. Thus, scoliosis is a three dimensional spinal deformity. Traditionally the severity of each curvature has been evaluated by measuring the Cobb angle from standing radiographs. This angle is measured between the endplates of the vertebras in each curvature.

It is desirable to be able to measure the vertebra rotation in order to fully understand the scoliotic curve. There are methods for doing this using ordinary radiographs although these methods are difficult to perform and not very precise.

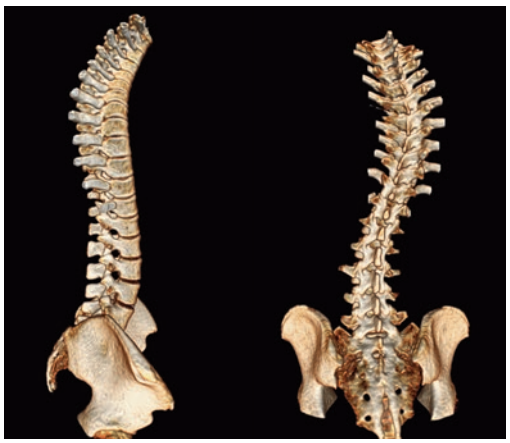
Since scoliosis is a three dimensional deformity, the importance of three dimensional imaging has been pointed out as a necessity to better understand the condition, as well as getting better preoperative information.

One way to obtain three dimensional images is to use low dose computed tomography images of the spine and then make three dimensional reconstructions. Using this technique it is easy to assess the spinal deformity as well as make precise measurements of each vertebra with concern to vertebral rotation and vertebral morphology.

The Cobb angle changes when going from standing to supine position (lying down). This is due to lesser gravitational loads in the supine position compared to when standing up. Since the patient is lying down during the CT examination we want to investigate how the Cobb angle changes from standing to supine position. This enables further studies based on images taken from low dose CT, in supine position.

The vertebras in scoliosis are not just rotated, they are also deformed. Therefore we will analyze how the morphology is changed in scoliotic vertebras compared to vertebras from a control group without any known back disorder. We hope to obtain a better understanding of the etiology of idiopathic scoliosis.

At our clinic most scoliosis patients undergo corrective surgery with an anterior approach. This is an established technique, but little is known about the changes in three dimensions as a result of the surgery. To learn more images from preoperative low dose CT are compared with postoperative low dose CT images in three dimensional reconstructions.



SUPERVISORS
Örjan Smedby, Sandro Rossitti, Karin Wårdell, Anders Ynnerman

PROJECT
Augmented Reality in the Operating Room (ARIOR)

BACKGROUND
Degree in Systems and Computation Engineering (Licenciatura) University of Algarve, Portugal 1996-2002

Masters in Computer Graphics and Virtual Environments University of Minho, Portugal 2004-2006

Research/ Development in Computer Graphics Faunhofer-Institut für Graphische Datenverarbeitung, Darmstadt, Germany 2003

Research/ Development in Computer Graphics Centro de Computação Gráfica, Guimarães, Portugal 2003-2005

PhD Program Image Guided Diagnosis and Therapy. Medizinischen Universitäat Innsbruck, Austria 2008-2010

Filipe Marreiros

Visualization and Tracking for Surgery

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 tracking, e.g. by ultrasound, intra-operative MRI or camera stereovision systems. Our approach is to use a multi-view camera (three cameras) system to track brain superficial blood vessels and extract their 3D centerlines position. The intraoperative information is used to guide a deformation applied to the preoperative image, in order to compensate for brain shift. This deformation is necessary 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 pre-operative MRI image, it is still necessary 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.

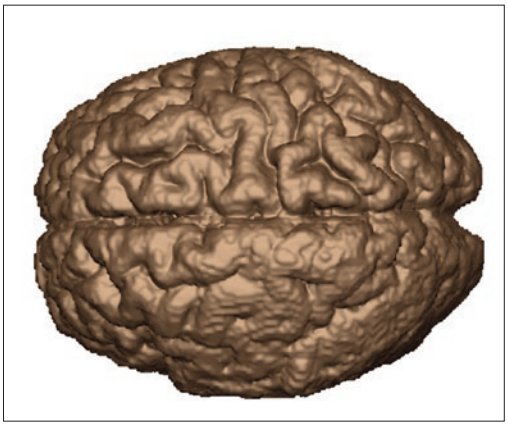


Figure 1. Pre-operative situation before brain shift.

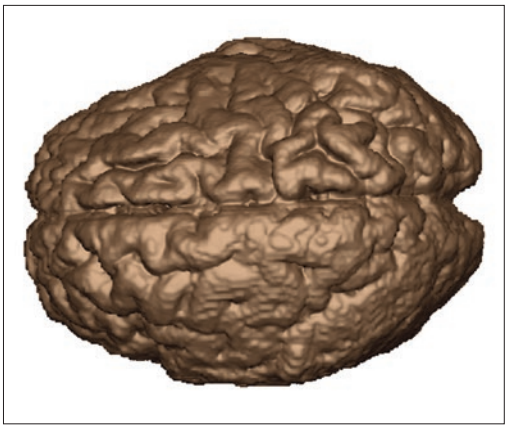


Figure 2. Intra-operative situation. Volume deformation for compensation of brain shift.

SUPERVISORS
Professor Fredrik Palm, IMH
Professor Mårten Segelmark, IMH
Professor Anders Persson, CMIV

BACKGROUND
MSc. in Biomedicine, started PhD in June 2012

Stephanie Franzén

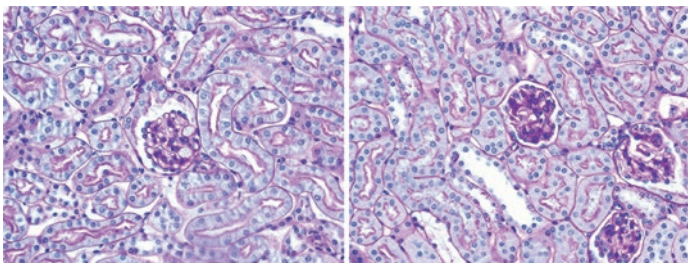
The Role of Hypoxia in the Development of Kidney Damage

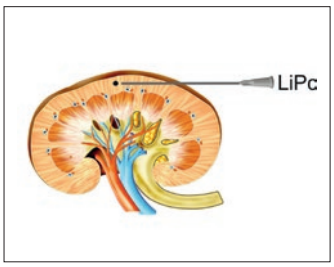
ONE THIRD OF all diabetes patients develop kidney damage during the course of their disease. The underlying mechanisms are, however, not yet completely known. Diabetes complication such as cardiovascular events is today one of the most common causes of death in the industrial world, whereas one in four 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. In early kidney damage the filtration rate is increased i.e. glomerular hyperfiltration, and there is a small leakage of proteins to the urine, i.e. proteinuria. This has been demonstrated to be reversible with antioxidant and citrulline treatment. Continued development of kidney damage causes the filtration rate to reach a top peak and further on decline with elevated 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 and lithium phthalocyanine (LiPc) probes to repetitively monitor intrarenal oxygen tension and can with this method conclude that intrarenal tissue hypoxia occurs before the clinical marker for kidney damage, proteinuria. This indicates that tissue oxygenation plays an important part in the development of kidney damage, and monitoring of tissue oxygenation may be used as an initial marker for indications of kidney disease.





SUPERVISORS
Morten Fjeld, Claes Lundström

PROJECT
Digital Pathology

BACKGROUND
Linköping University: Engineering degree in Applied Physics and Electrical Engineering with a minor in French, combined with a Master's degree in Biomedical Engineering, 2007-2012

Polytech'Montpellier: Exchange year at Electronique, Robotique et Informatique Industrielle, 2009-2010

Jesper Molin

Smarter Digital Pathology Based on Diagnostic Tasks and Cognitive Processes

NEW CANCER 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 pressure on the diagnosing pathologists to deliver more detailed characterizations of the tumor biopsies. Together with the current lack of pathologists in Sweden this risks causing, if not severe implications, at least unnecessary emotional distress of patients waiting weeks on the lab results of their suspected cancer.

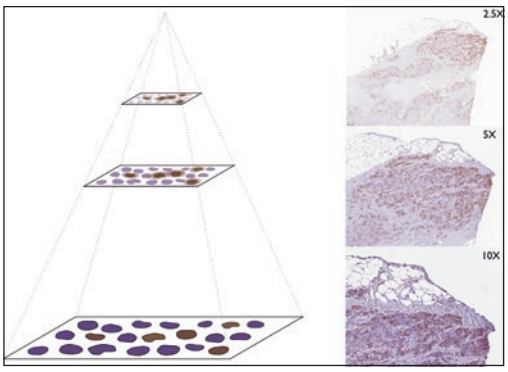
In recent years, the possibility of diagnosing cancerous tissue samples digitally has become available for clinical use. This makes it possible to create automatic systems that can aid and speed up the work of the pathologist.

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 and evaluate their performance.

So far three subprojects have been completed. We started out reviewing the current state of the art in digital pathology and analyzed navigation patterns when pathologist performed diagnoses with a prototype digital workstation. Based on these findings, we have developed two prototype systems. First, we implemented support for four different input devices and performed a comparative user study. Second, we developed a new image processing based visualization technique to help pathologists estimate the proliferation rate of breast cancer.

The findings from these projects are now used to develop new interactive visualization systems to facilitate the incorporation of results from image processing algorithms. The goal is to develop generic design patterns that can be used to put existing algorithms in use, rather than developing new algorithms.

These projects use a human centered design approach to assure that the outcomes can be used in routine clinical practice. A few of the solutions have already found its way out in clinical practice and are today used in pilot installations in Swedish pathology labs.



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

SUPERVISORS
Anders Persson (principal supervisor)
Jan Engvall (ass. supervisor)
Örjan Smedby (ass. supervisor)
Michael Sandborg (ass. supervisor)

Jakob De Geer

The Use of CT in Cardiac Imaging

DURING THE LAST decade coronary computed tomography (CCTA) has become an important tool in the work up of coronary heart disease, especially in cases where the pre-test likelihood has been deemed low to intermediary.

However, as technology evolves a number of methods have emerged which take the diagnostic value of CT in coronary artery disease even further.

In one study we have evaluated dynamic CT perfusion, using SPECT as a reference. 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.

Another emerging technology is the evolution of software being able to estimate the fractional flow reserve (FFR), i.e. the pressure drop over a stenosis, using CCTA data only (cFFR). FFR is the ratio between pre- and poststenotic flow in the coronary arteries and has hitherto been determined by measuring pre- and poststenotic pressure during invasive coronary angiography. A ratio of < 0.80 is considered to constitute a significant stenosis and thus, FFR is a valuable tool when determining whether the patient needs treatment or not. However, invasive procedures are costly and potentially risky. If the cFFR technology proves reliable, it could be an important tool in the triage to invasive procedure.

In a small retrospective pilot study, we have compared invasively obtained FFR-values with those derived from CCTA in the same patient. The result showed a sensitivity and specificity for significant stenosis of 0.80 and 0.76 respectively. Spearman rank correlation between the methods was 0.77 and the intraclass correlation coefficient was 0.73. The same method is also being further evaluated in an on-going prospective study.

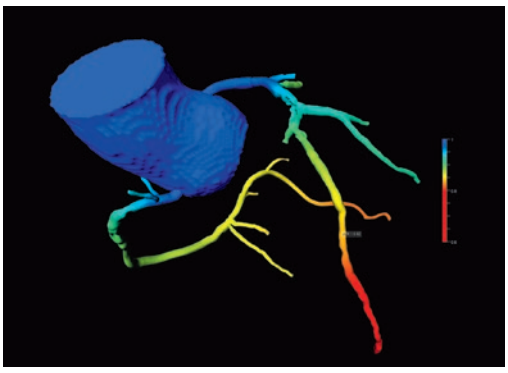


Figure 1 CT-based fractional flow reserve (cFFR) colour with cFFR = 0.82 in the LAD. The point of cFFR evaluation is freely adjustable.

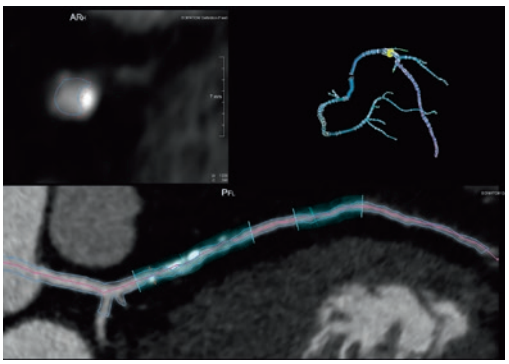


Figure 2 Overview of segmentation process, with the left anterior descending artery (LAD) in cross-sectional and curved MPR view, and the coronary tree mesh. Stenotic segments are manually defined. Vessel contours are automatically outlined but can be manually adjusted.

SUPERVISORS
Örjan Smedby, Torkel Brismar, Rodrigo Moreno

PROJECT
Quantification of osteoporosis with computed tomography

Eva Klintström

Quantification of Osteoporosis with Computed Tomography

FRACTURES RELATED TO osteoporosis are common in Sweden, in particular among women. This means suffering for the individual and great costs for the community. In order to be able to minimize the number of fractures, it is important to detect osteoporosis at an early stage. The technique most frequently used for diagnosing osteoporosis is DXA (dual energy X-ray absorptiometry). With this method it is possible to measure the mineral content, but it is not possible to describe the internal structure of the bone. There are several studies showing that also the internal structure of the bone is of great importance for bone strength and risk for bone fractures.

The aim of this project is to investigate the possibility to use the X-ray method computed tomography (CT) to image and measure the internal structure of bone, which would give a more complete picture of the osteoporosis. The aim is to find methods to measure osteoporosis and bone structure in patients. We started, however, with imaging small pieces of bone from the human forearm.

We have used 15 pieces of bone, all cubes with a side of 10-15 mm. The cubes were placed in test tubes filled with water, and the tubes were placed in a paraffin cylinder to mimic soft tissue. Imaging was performed with different types of CT methods and compared with the results from a method called micro-CT, which is considered the reference method. Micro-CT can only be used on small samples and in animal testing.

After imaging with the different X-ray methods, extensive image analysis is required. This analysis aims to identify all the small bone structures inside the bone. We analyse how many, how thick, how far apart the bone parts are, how many branches they have, how many free ends there are and the total amount of bone. For this purpose, a segmentation method is used that makes it possible to differentiate bone from the other structures, like blood vessels, fat and marrow inside the bone.

One of the tested methods, CBCT (cone beam CT), showed a very high correlation with micro-CT when analysing the bone pieces. CBTC is most often used in imaging teeth, jaws and people in need for implants in the jaws. The machine can also be used in diagnosing finger fractures both ordinary imaging and 3D visualisation.

In future studies, we want to compare the bone structure in the jaws with DXA results on patients examined for osteoporosis.

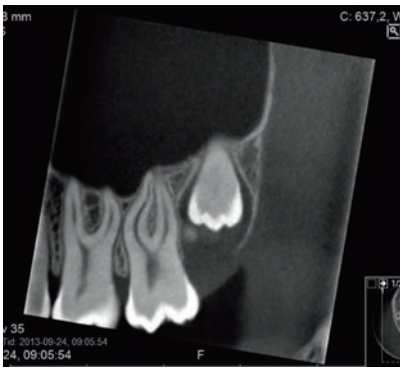


Figure 1. Teeth in left upper jaw imaged by CBCT.

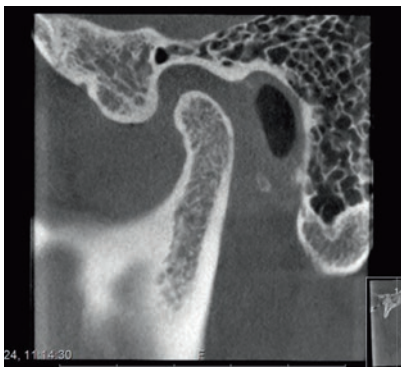


Figure 2. Left jaw and ear cells imaged by CBCT.

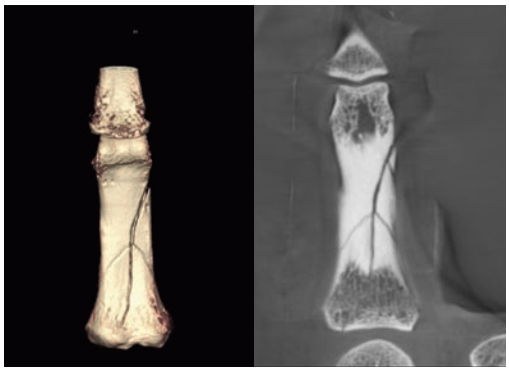
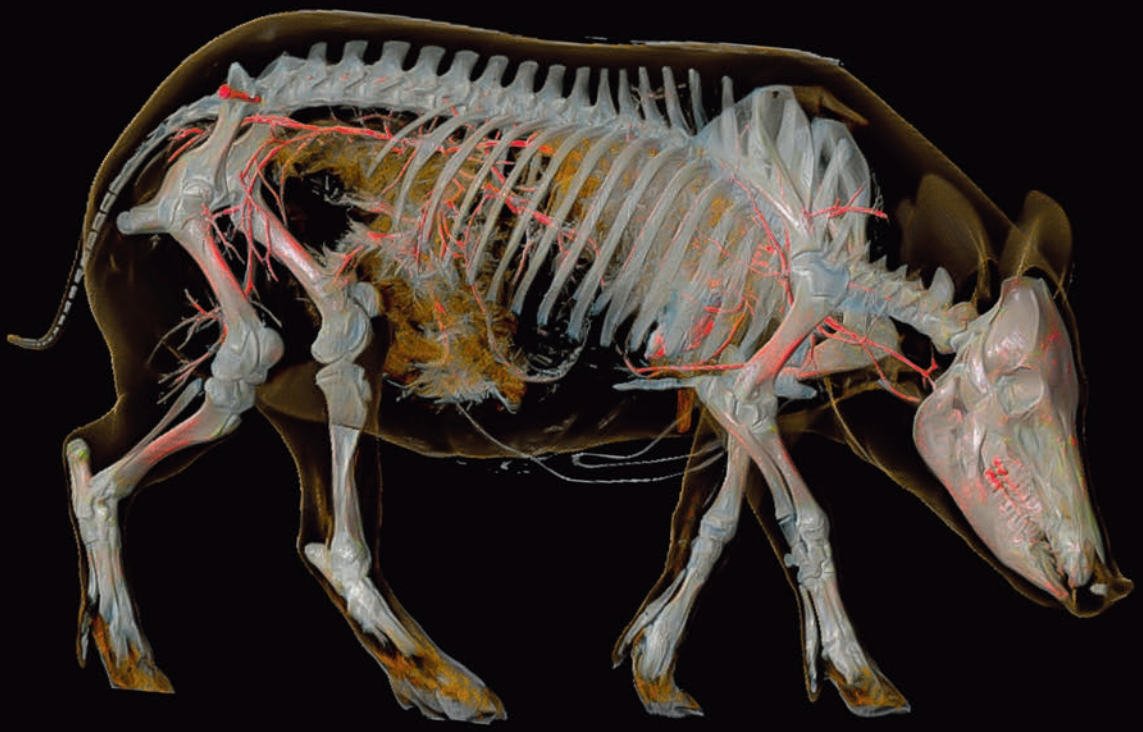


Figure 3. Left fractured first finger, CBCT image and 3D from CBCT.



110 DISSERTATIONS

During 2014 four of the CMIV PhD students have finished their studies and defended their dissertations. The PhD students and the research school are an important part of CMIV and we are proud to present their dissertations here.

Stefan Lindholm
Linköping University, Department of Science and Technology,
Division of Media and Information Technology

Medical Volume Visualization Beyond Single Voxel Values

Medical visualization involves many complex decisions for both the user and the imaging algorithms. This thesis aims to improve medical volume visualization through a series of technical contributions to aid such decision processes. Improvements are achieved by using more data, beyond single voxels, in the associated visual analyses. Simultaneous visualization of multiple data sources and different data formats is rapidly becoming a necessity. This is due to both the growing number of data producing image acquisition techniques as well as the increase in geometric data representations that can be created. Maintaining high rendering performance under these circumstances is challenging, but necessary, to support an exploratory visualization process. This thesis proposes two algorithms to address this challenge: a multi-volume approach that applies binary-space partitioning to solve painters' algorithm geometrically and a rendering algorithm for hybrid data that improves the management of the available graphics memory.

Janne West
Linköping University, Department of Medical and Health Sciences,
Division of Radiological Sciences

Quantification and Optimisation of Lung Ventilation SPECT Images

Magnetic resonance imaging (MRI) is a sensitive technique for assessing white matter (WM) lesions in multiple sclerosis (MS), but there is a low correlation between MRI findings and clinical disability. Because of this, other pathological changes are of interest, including changes in normal appearing white matter (NAWM) and diffusely abnormal white matter (DAWM). Even so, the mechanisms leading to permanent disability in MS remain unclear. In contrast to conventional MRI, quantitative MRI (qMRI) is aimed at the direct measurement of the physical tissue properties, such as the relaxation times, T1 and T2, as well as the proton density (PD). QMRI is promising for characterizing and quantifying changes in MS and for brain tissue segmentation. The present work describes a novel method of qMRI for the human brain (QMAP), and a segmentation method based on this. The developed methods were validated in control subjects and MR phantoms.

Pernilla Norberg
**Linköping University, Department of Medical and Health Sciences,
Division of Radiological Sciences**

Quantification and Optimization of Lung Ventilation SPECT Images

Currently, lung function tests are the gold standard for lung function measurements. Since the outcome of a lung function test is a summation of the status of the whole lung, significant changes in lung function may occur before a deviation from the norm can be identified. A method that can reliably detect lung abnormalities earlier in a disease process would therefore be beneficial. Regional differences in the lung are ideally studied by imaging methods. Heterogeneous ventilation in lungs of allergic individuals, cigarette smokers, asthmatics and chronic obstructive pulmonary disease (COPD) patients has been demonstrated using various imaging techniques such as single photon emission computer tomography, SPECT. The amount of heterogeneous ventilation is correlated to disease advancement. The CVT-method, that measures heterogeneity using the coefficient of variation (CV) caused by lung function reduction in lung SPECT images, was developed and optimized. Lung function in patients and healthy volunteers was evaluated using the CVT-method.

Khoa Tan Nguyen
**Linköping University, Department of Science and Technology,
Division of Media and Information Technology**

Supporting Quantitative Visual Analysis in Medicine and Biology in the Presence of Data Uncertainty

The advents of technologies have led to tremendous increases in the diversity and size of the available data. In the field of medicine, the advancements in medical imaging technologies have dramatically improved the quality of the acquired data, such as a higher resolution and higher signal-to-noise ratio. In addition, the dramatic reduction of the acquisition time has enabled the studies of organs under function. At the same pace, the progresses in the field of biology and bioinformatics have led to stable automatic algorithms for the generation of biological data. As the amount of the available data and the complexity increase, there have been great demands on efficient analysis and visualization techniques to support quantitative visual analysis of the huge amount of data that we are facing. This thesis aims at supporting quantitative visual analysis in the presence of data uncertainty within the context of medicine and biology. We present several novel analysis techniques and visual representations to achieve these goals.

114 EQUIPMENT

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 new Siemens SOMATOM Force enables routinely performed exams at low kV settings (70-90 kV), even in adults. This is due to the system being equipped with powerful generators and X-ray tubes. The low kV settings allow for substantial reductions in contrast medium dose. Improvements have been made on the detector side as well with an increased number of detector rows and upgraded collimation.

The Force renders images with high spatial resolution and soft-tissue contrast. It contains two X-ray sources and two detectors which can be used simultaneously. This in combination with a broader detector enables faster scans than before. High speed scanning is necessary for cardiac examinations as well as for restless patients. The two X-ray sources also provide the possibility for dual energy examinations with improved spectral separation.

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 45mT/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 E 9 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

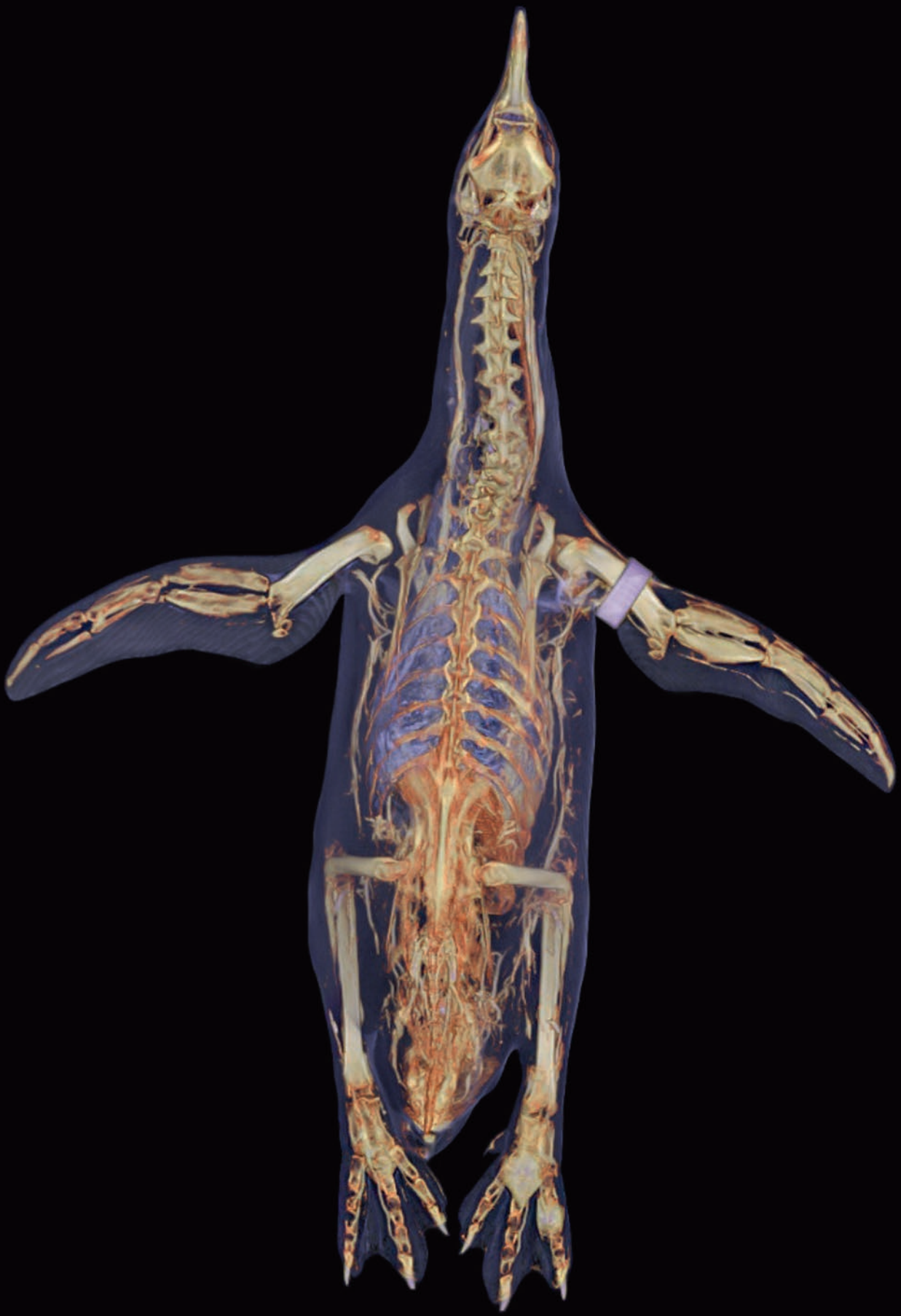
CMIV has its own Virtual Reality theatre with a capacity of 70 persons. The theatre is built around Barco Galaxy NW-12 projector (12 000 lumens light output, WUXGA (1920x1200) resolution.) The NW-12 has an integrated active Infitec 3D stereo filter, allowing for optimal 3D visualization with passive 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.

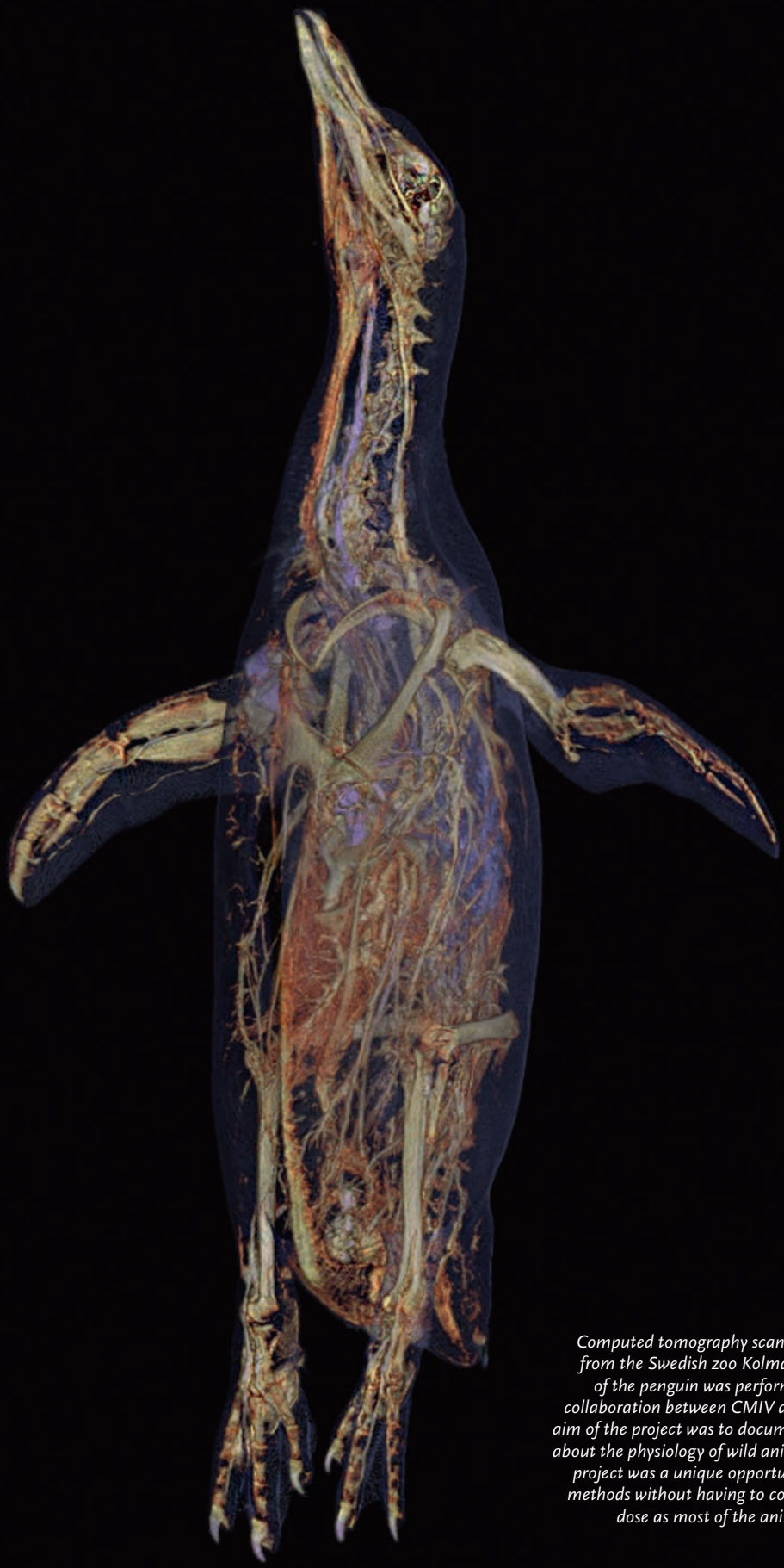
Several Advantage Workstations from GE Medical Systems are available at the hospital.

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.

Digital Pathology Scanner

The latest technical addition at CMIV is a pathology glass scanner from Hamamatsu. The Nanozoomer 2.0 HT convert glass slides into high-resolution digital data by high-speed scanning and has a capacity of scanning up to 210 glasses automatically.





Computed tomography scan of a young penguin from the Swedish zoo Kolmården. The scanning of the penguin was performed during research collaboration between CMIV and Kolmården. 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.

118 ORGANIZATION

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.

Researchers

Gudrun Alm Carlsson	IMH, Radiological sciences
Mats Andersson	IMT, Medical informatics
Magnus Borga	IMT, Medical informatics
Carljohan Carlhäll	IMH, Cardiovascular medicine
Åsa Carlsson Tedgren	IMH, Radiological sciences
Olof Dahlqvist Leinhard	IMH, Radiological sciences
Nils Dahlström	IMH, Radiological sciences
Petter Dyverfeldt	IMH, Cardiovascular medicine
Tino Ebbers	IMH, Cardiovascular medicine
Anders Eklund	IMT, Medical informatics
Maria Engström	IMH, Radiological sciences
Jan Engvall	IMH, Cardiovascular medicine
John-Peder Escobar Kvitting	IMH, Cardiovascular medicine
Daniel Forsberg	ITN, Media and information technology
Håkan Gustafsson	IMH, Radiological sciences
Markus Heilig	National Institutes of Health/ National Institute of Alcohol Abuse and Alcoholism
Camilla Josephson	IEI, National economy
Hans Knutsson	IMT, Medical informatics
Matts Karlsson	IEI, Applied thermodynamics & fluid mechanics
Thomas Karlsson	IBL, Disability research
Anne-Marie Landtblom	IKE, Neurology
Peter Lundberg	IMH, Radiological sciences
Karljohan Lundin Palmerius	ITN, Media and information technology
Claes Lundström	ITN, Media and information technology
Toste Länne	IMH, Cardiovascular medicine
Maria Magnusson	ISY, Computer vision
Alexandr Malusek	IMH, Radiological sciences
Rodrigo Moreno	IMH, Cardiovascular medicine
Ebo de Muinck	IMH, Cardiovascular medicine
Nina Nelson	IKE, Pediatrics
Peter Nilsson	IFM, Chemistry
Eva Nylander	IMH, Cardiovascular medicine
Håkan Olausson	IKE, Neurology
Fredrik Palm	IMH, Drug research
Anders Persson	IMH, Radiological sciences
Hans Ringerz	IMH, Radiological sciences
Timo Ropinski	ITN, Media and information technology
Michael Sandborg	IMH, Radiological sciences
Örjan Smedby	IMH, Radiological sciences
Hans Tropp	IKE, Orthopaedics
Helene Veenstra	IMH, Radiological sciences
Susanna Walter	IKE, Gastroenterology
Chunliang Wang	IMH, Radiological sciences
Marcel Warntjes	IMH, Cardiovascular medicine
Karin Wårdell	IMT, Biomedical instrumentation
Anders Ynnerman	ITN, Media and information technology

Phd Students

Thord Andersson	IMT, Medical informatics
Ida Blystad	IMH, Radiological sciences
Mariana Bustamante	IMH, Cardiovascular medicine
Belèn Casas Garcia	IMH, Cardiovascular medicine
Olivier Cros	IMT, Medical informatics
Jakob De Geer	IMH, Radiological sciences
Mikael Forsgren	IMH, Radiological sciences
Stephanie Franzen	IMH, Drug research
Diana Fraser	IKE, Psychiatry
Gustaf Johansson	IMT, Medical informatics
Daniel Jönsson	ITN, Media and Information Technology
Anette Karlsson	IMT, Medical informatics
Bharti Kataria	IMH, Radiological sciences
Johan Kihlberg	IMH, Radiological sciences
Eva Klintström	IMH, Radiological sciences
Sofia Kvernby	IMH, Cardiovascular medicine
Johan Kälvesten	IMH, Radiological sciences
Stefan Lindholm	ITN, Media and Information Technology
Mats Lowén	IKE, Medical Gastroenterology and Hepatology
Karin Lundegård	IMH, Radiological sciences
Filipe Marreiros	ITN, Media and Information Technology
Jesper Molin	Chalmers and Sectra AB
Tan Khoa Nguyen	ITN, Media and Information Technology
Pernilla Norberg	IMH, Radiological sciences
Eva Olsson	IMH, Radiological sciences
Thobias Romu	IMT, Medical informatics
Kavitha Shaga Devan	IMT, Biomedical Instrumentation
Jens Sjölund	IMT, Medical informatics
Carina Stenman	IMH, Radiological sciences
Jens Sjölund	IMT, Medical informatics
Freddie Åström	ISY, Computer vision

Scientific Council

Carljohan Carlhäll	IMH, Clinical Physiology
Olof Dahlqvist Leinhard	IMH, Radiological Sciences
Nils Dahlström	IMH, Radiological Sciences
Petter Dyverfeldt	IMH, Clinical Physiology
Maria Engström	IMH, Radiological Sciences
Jan Engvall	IMH, Clinical Physiology
Hans Knutsson	IMT, Medical Informatics
Maria Kvist	CMIV
Peter Lundberg	IMH, Radiological Sciences
Claes Lundström	ITN, Media and Information Technology
Fredrik Palm	IMH, Drug research
Anders Persson	IMH, Radiological Sciences
Örjan Smedby	IMH, Radiological Sciences
Chunliang Wang	IMH, Radiological Sciences
Karin Wårdell	IMT, Biomedical Instrumentation
Anders Ynnerman	ITN, Media and Information Technology

Core Staff

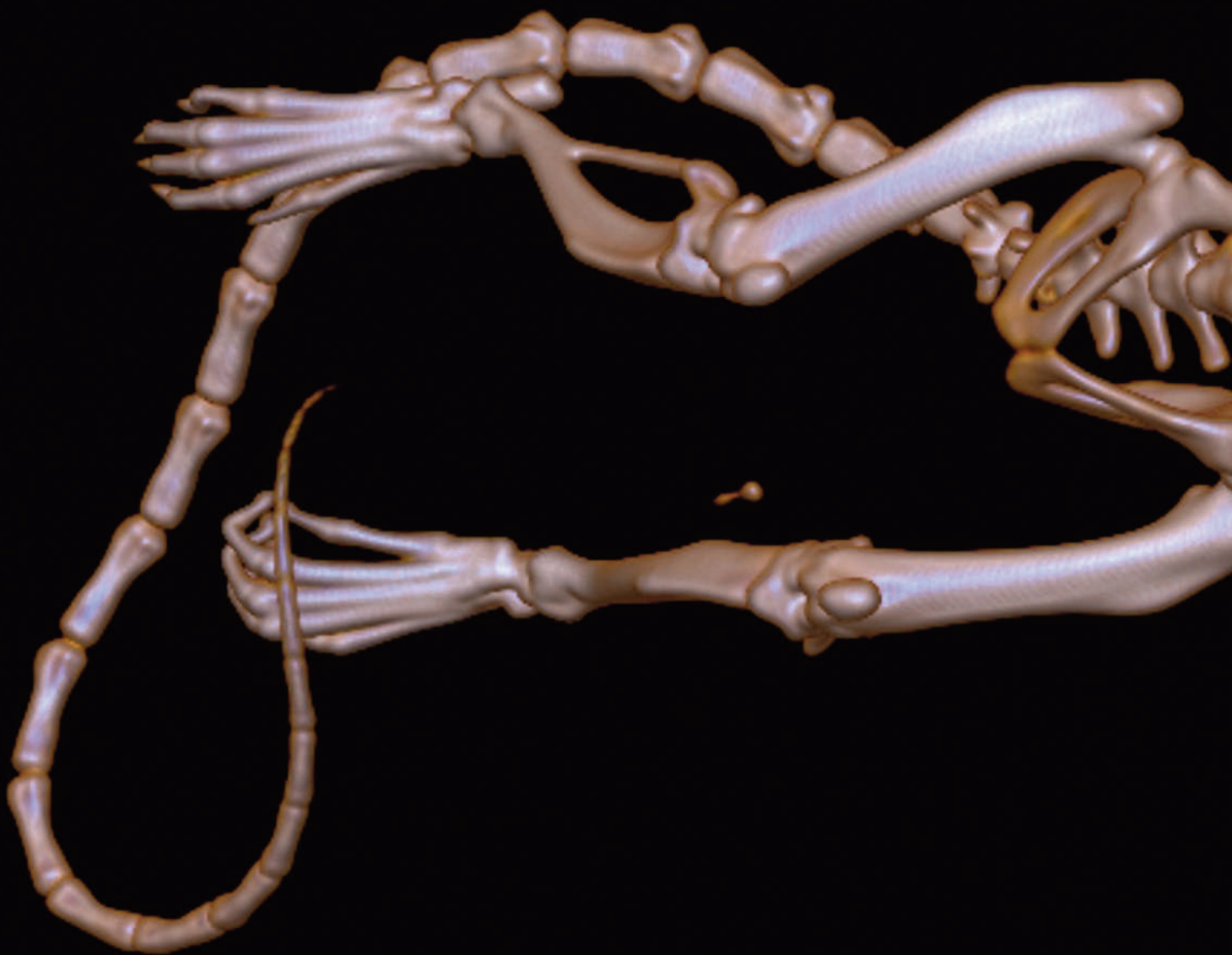
Anders Persson	Director
Maria Kvist	Research Coordinator
Marie Waltersson	Research Coordinator/Communicator
Björn Broo	IT Manager
Olof Dahlqvist Leinhard	Director of Doctoral Studies
Catrin Nejdeby	Financial Administrator
Marcel Warntjes	Clinical Scientist
Petter Dyverfeldt	Clinical Scientist
Suzanne Witt	Clinical Scientist

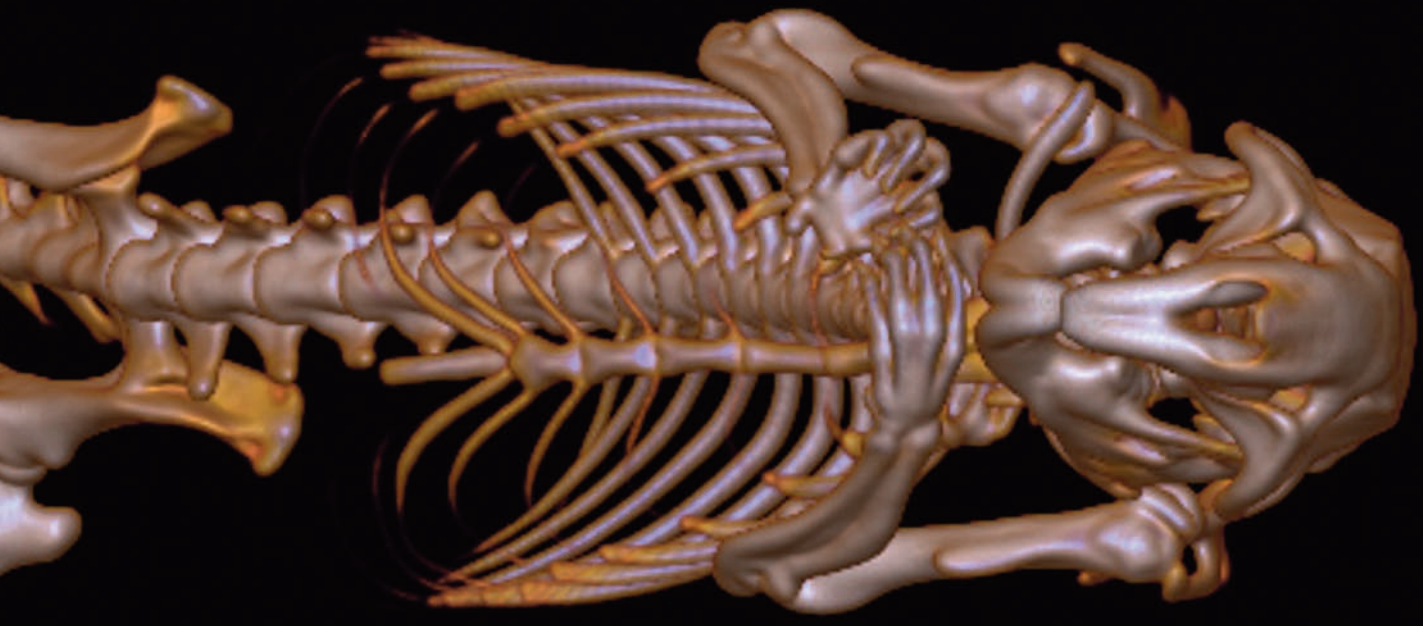
Board of Directors

Jakob De Geer	IMH, Medical Radiology
Curt Karlsson	Linköping University
Torbjörn Kronander	Sectra AB
Jan Kåredal	County Council of Östergötland, Diagnostic Center
Hans Gösta Ringertz	IMH, Medical Radiology
Thobias Romu	IMT, Medical Informatics
Anders Ynnerman	ITN, Scientific Visualization
Katrine Åhlström Riklund	Umeå University, Diagnostic Radiology

120 PUBLICATIONS

As the CMIV researchers are also affiliated to a home department at Linköping University or another university and their research is primarily registered there it can be difficult to overview. We have made an attempt at putting together a list with the publications produced during 2014. Although not complete it still shows a good representation of CMIV.

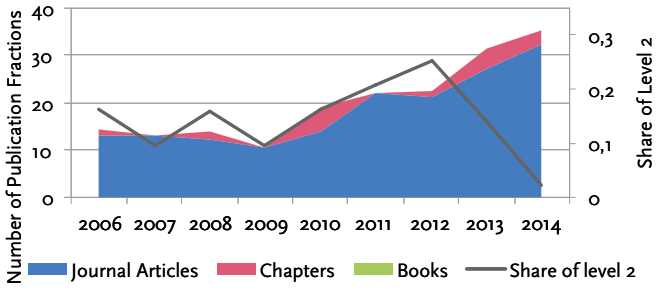




Bibliometric analysis

The bibliometric analysis has been provided by the Linköping University Library, department of Publishing Infrastructure. The citation data used in the analysis has been supplied by CWTS, Leiden University; data source: Thomson Scientific/ISI.

Number of fractionalized publications



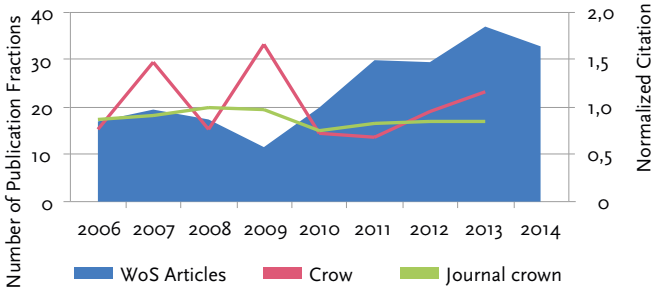
Norwegian model	2006-2014	
	Number of publications	Number of fractions
Journal articles - refereed	301	164,6
Chapters - other academic	28	17,4
Books - other academic	0	0,0

Comment: Proceeding papers are included if they have been published in an approved publication channel, and are counted as chapters or journal articles.

Results	
Publication points	226,1
Average number of publications points per year	25,1
% author shares level 2	14%
Author shares, sum	182,0

% author shares level 2: Percentage of fractionalized publications published in journals/publishers of the highest scientific quality.

Impact



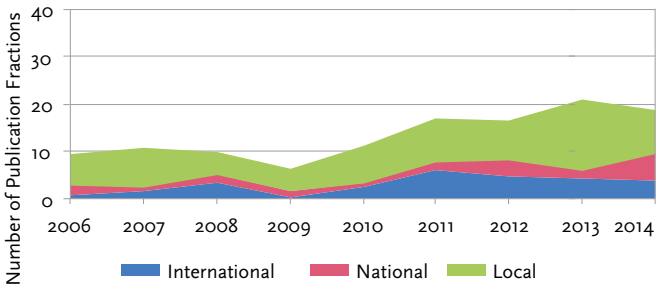
Citation analysis	2006-2013	
"Publications in Web of Science (excluding Conference Proceedings Index)"	Number of publications	Number of fractions
Articles, reviews, letters	166	83,4

Results	
Field-normalized citation rate (crown)	1,22
Share of top 10%	17%
Share of uncited publications	21%
Field-normalized journal citation rate (journal crown)	1,09
Journal Impact Factor (JIF) ranking, mean	0,66

Crown: A measure of the impact of the articles included in the analysis. Provides a comparison value with an international average for the same field, year and article type, and where the value 1 corresponds to a world average. Share of top 10%: The percentage of publications that are among the 10% most cited in the subject area during the time period

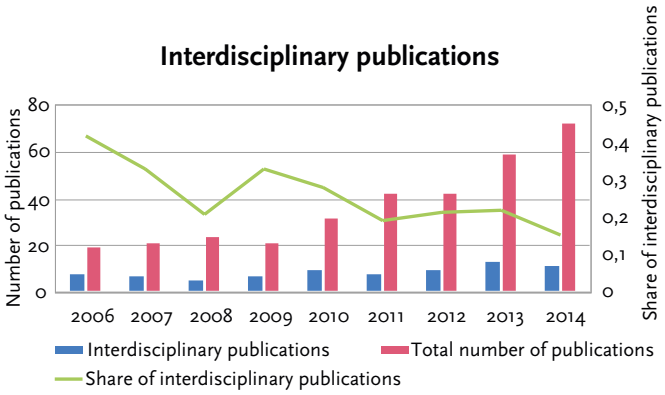
Journal Crown: A measure of the impact of the journals that the department published in. JIF Ranking mean: All journals within each subject category are ranked based on the JIF, and the number indicates how the journal in question is placed in the rankings. Ex 0.8 indicates that the journal is among the 20% highest ranking.

Fractionallized journal articles in WoS: Co-authorships



Co-authorship	2006-2014
Share of articles with international co-authors	22%
Share of articles with national co-authors	17%
Share of articles with local co-authors	61%

Interdisciplinary publications



Interdisciplinary authorship (LiU faculties)	2006-2014
Publications with interdisciplinary authorship	
Number	77
Share	23%

Publications 2014

*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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130 ANNUAL ACCOUNTS

The economic growth has continued and during 2014 CMIV had a turnover of more than 48 million. The financial results for CMIV in 2014 was 4.1 million SEK in surplus.

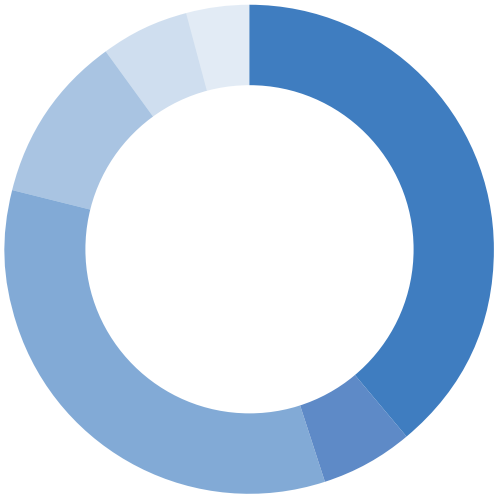
In the fiscal year 2014, several efforts have been made in priority areas. The center has been able to install a new type of CT as one of the first in the world. The modality has met all requirements and expectations and enables set research objectives to proceed. Economically, the new equipment will mean savings in contrast medium consumption.

During 2014 CMIV had two major ongoing grant projects, 3T MRI scanner and digital pathology. The project Optimized Flows and IT Tools for Digital Pathology was completed in 2014 with good results. During the year, investments were made in the 3T MRI corresponding to the final part of funds from the Knut and Alice Wallenberg Foundation of 6 million SEK.

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.

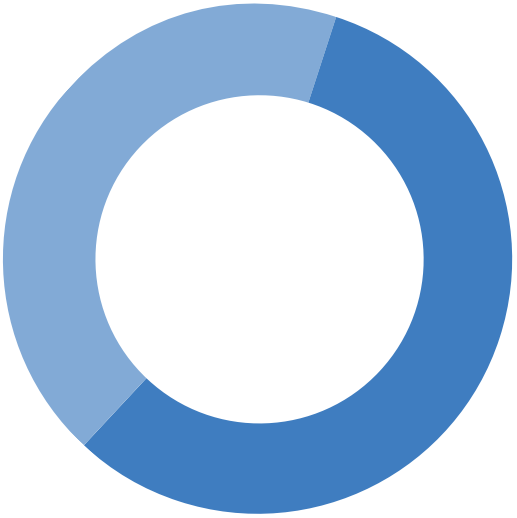
Year	2010	2011	2012	2013	2014
Total revenue	**26 876**	**32 800**	**32 629**	**35 576**	**48 762**
Expenses					
Staff expenses	-13 632	-14 645	-15 102	-16 756	-19 507
Cost of premises	-1 683	-1 975	-2 145	-2 034	-2058
Misc. operating expenses	-10 282	-9 549	-7 653	-8 876	-17 334
Depreciation expenses	-3 291	-5 883	-4 938	-5 336	-5 629
Financial expenses	-103	-403	-125	-185	-102
Total Expenses	**-28 991**	**-32 455**	**-29 963**	**-33 187**	**-44 630**
Result of operations	**-2 115**	**345**	**2 666**	**2 389**	**4 133**

Numbers in thousands of SEK.



Basic grant overview 2010-2014

- 39% - Salaries, CMIV staff
- 6% - Research school
- 34% - Clinical Scientists
- 11% - Central administration
- 6% - Travels and conferences
- 4% - Office supplies and computers



Research funding 2010-2014

- 66 150 - External funds
- 50 500 - Industrial funds

Numbers in thousands of SEK

Linköping University

Region Östergötland

SECTRA

PHILIPS

SIEMENS

Bayer