

Welcome to the exciting world of CMIV

ANNUAL SCIENTIFIC REPORT 2021



The image shows a 3D image of the heart and lung vessels from our photon counting detector CT, NAEOTOM Alpha, by Anders Persson, CMIV.

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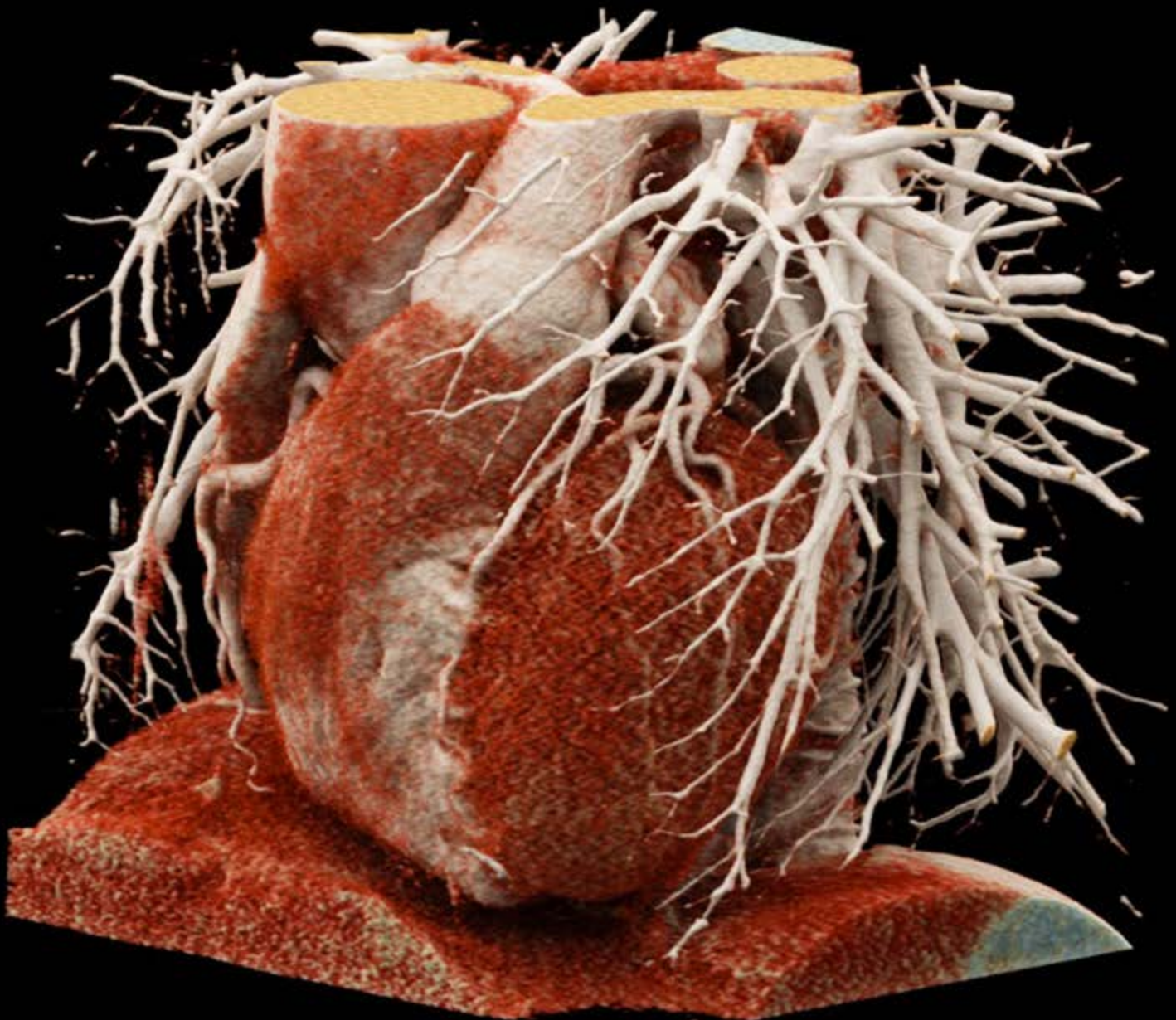


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The CMIV research efforts lead to a steady stream of scientific publications. This is an overview of the 2021 production.

150

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Preface



C OVID-19 has spread rapidly throughout the world, prompting CMIV to take unprecedented measures in response. These measures have adversely affected the healthcare in our region and society. Clinical examinations have been prioritized at CMIV and operating restrictions were imposed to protect health and safety of CMIV's researchers and clinical employees. The researchers have been able to work remotely from home most of the time and this has made it possible to further expand the clinical translational research. At the end of September, we could finally put an end to the remote work and return and meet in person again. The most important creative meeting place, our coffee room is now more filled with people than before. Despite the challenging situation during the year I see amazing accomplishments, both from CMIV as a whole but also from individual research groups and supporting staff.

In August, a new high-end modality was installed, the world's first photon-counting computed tomography (CT) with Quantum Technology that has the potential to revolutionize CT. The system has replaced the previous photon-counting prototype at CMIV. The amount of active ongoing research projects has increased to exceed 140. Among these the scientific council has elected the three flagship projects of 2021. As usual they complement each other and well represent CMIV in showing different areas and how we work close to the clinic combining technical and medical knowledge.

The first project "Advanced Quantitative MRI of the Brain" is a new and promising technique to diagnose and prognose disease, but also a way of determining treatment and monitoring the chosen therapy.

The second project Medical Digital Twin (MeDigiT) is a platform with the aim of facilitating the use of personalized digital models in healthcare as well as for education of healthcare professionals, patients, and the general public. The platform is a meeting place for stakeholders in the subject of medical digital twins where technical solutions and applications may be discussed.

The third flagship project "Musculoskeletal Imaging Using Computed Tomography" is above all focusing on the new technology with our photon counting CT.

All in all, 2021 has been an exceptional yet demanding year. Nevertheless, many new research projects were initiated during the year and research activities developed to new heights. Without the fantastic collaboration between all stakeholders; university, health care, industry, individual research groups and supporting staff, these steps would not have been possible to take.



Anders Persson
DIRECTOR OF CMIV

Highlights

As always, a lot of things have happened during the past year. The CMIV infrastructure expanded with the installation of the world's first photon counting detector computed tomography, NAEOTOM Alpha with Quantum Technology, which was inaugurated in November. Here you can read about this and more highlights of the year.

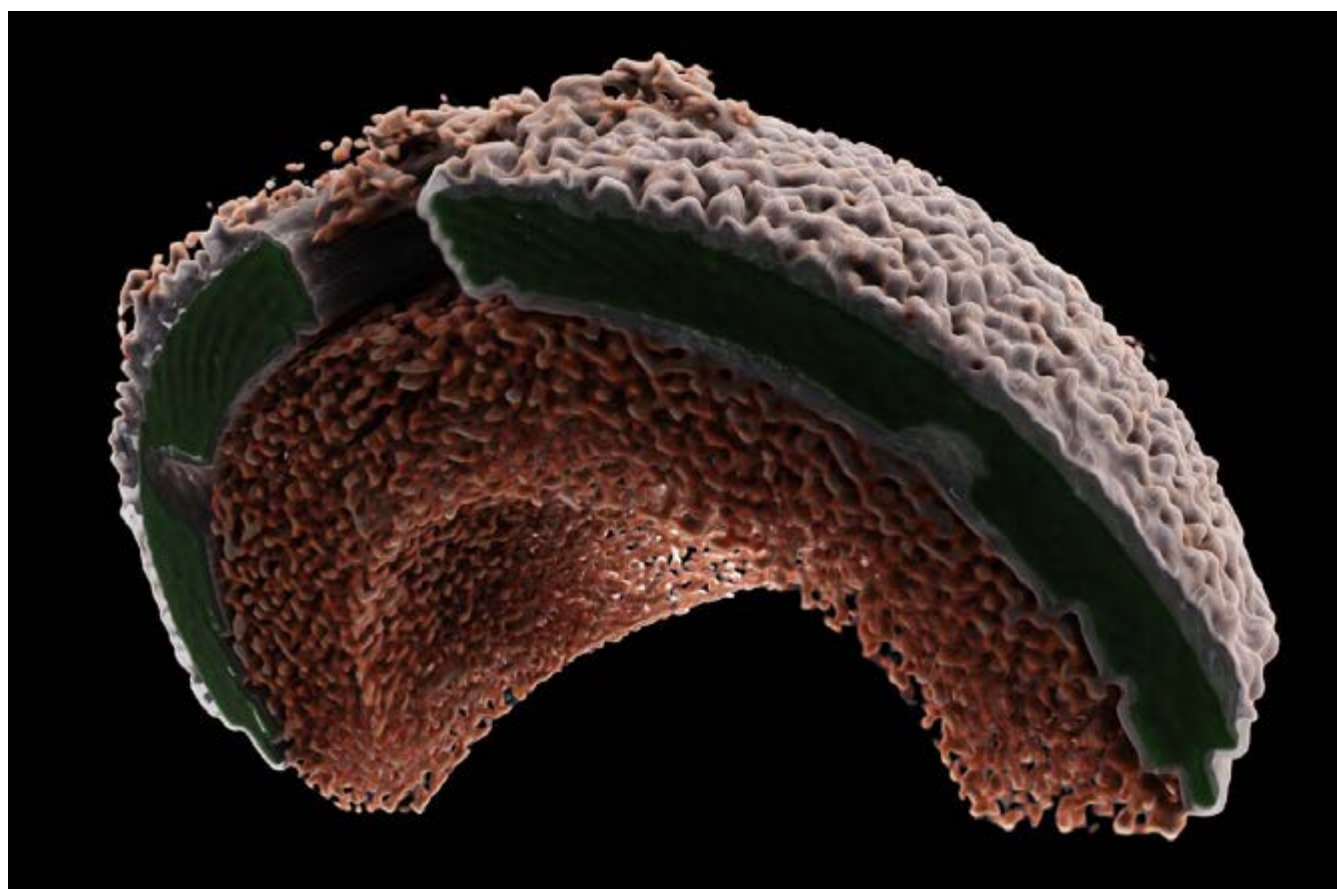


Unique photon counting detector CT inaugurated – a milestone for CT imaging

In August CMIV received the world's first clinical photon counting detector CT (PCD-CT) and on November 15, we finally inaugurated the NAEOTOM Alpha by Siemens Healthineers.

The X-ray photons are converted directly into electrical signals and then counted without information loss. This improves image sharpness and contrast, and the images include more relevant information. The new technique offers twice as sharp images at 40 % less dose and enables precise noninvasive examinations for more patients. This truly is a quantum leap for CT imaging.

The PCD-CT was inaugurated by Per-Olof Brehmer, Deputy Vice-Chancellor for Research at Linköping University, Mats Ulfendahl, Research Director at Region Östergötland, and Rolf Östlund, Director of Development at Region Östergötland.



High resolution images from CMIV's photon counting CT. The interface between bone and implant could be evaluated and could potentially help in the assessment of preoperative hip implant loosening. Mischa Woissetschläger, Jörg Schilcher, Anders Persson

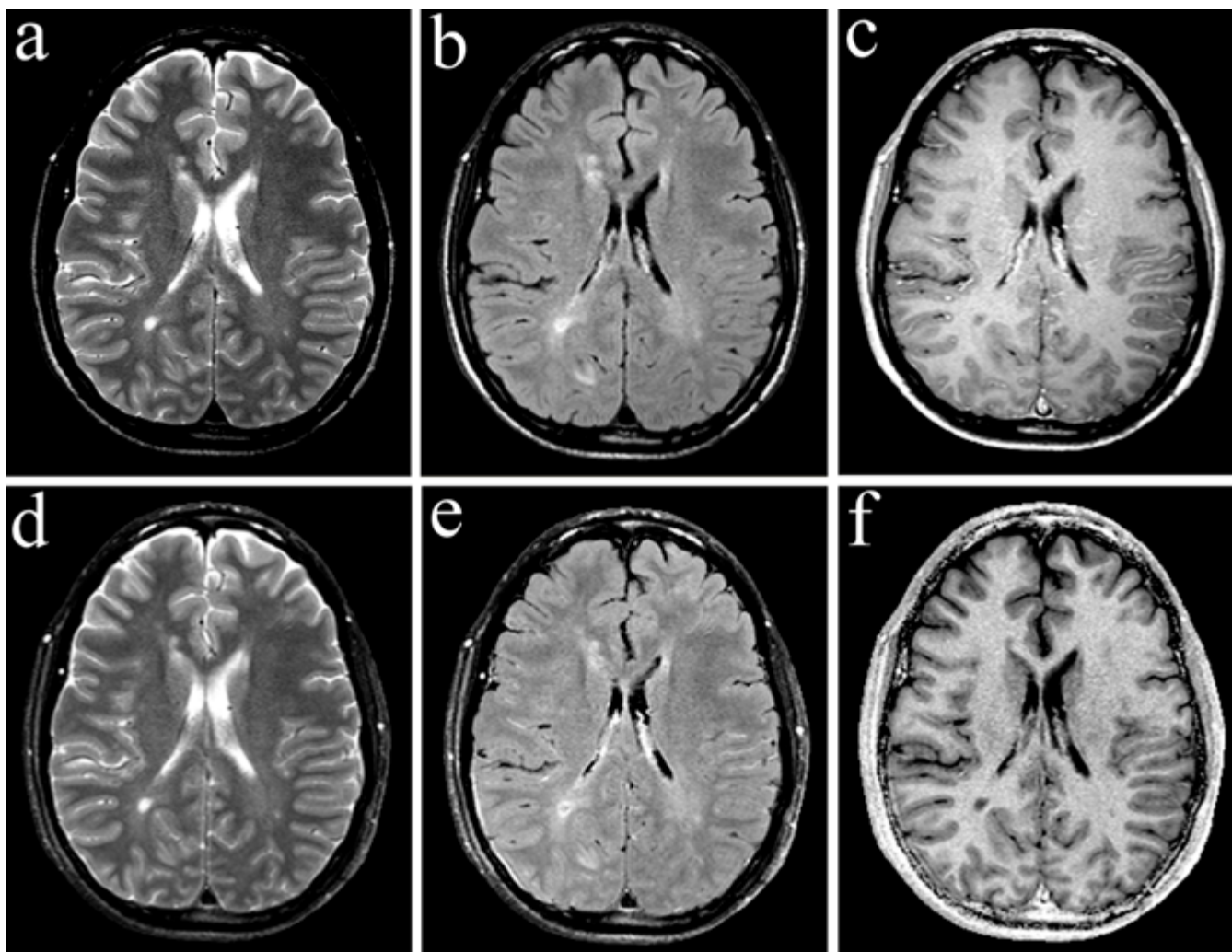
Article from CMIV is listed among the top 50 achievements since the first MRI in 1973

Physical and technical aspects of human magnetic resonance imaging: present status and 50 years historical review

This paper reviews the historical developments, current status and future prospects within MRI and an article from CMIV is listed among the top 50 achieve-

ments since the first MRI in 1973. It is the research Warntjes JB, Dahlqvist Leinhard O, West J, Lundberg, P. Rapid magnetic resonance quantification on the brain: op-

timization for clinical usage. *Magn Reson Med.* 2008;60:320–329 which has made it on the list.



Anders Persson

received the Erna Ebeling Award 2021

Congratulation Prof Anders Persson, who has been awarded the Erna Ebeling Award 2021.

The award is presented by the Board of the Swedish Medical Technology Association and the Swedish Society of Medicine with the motivation: “For outstanding research and development in the borderland between radiology, medical

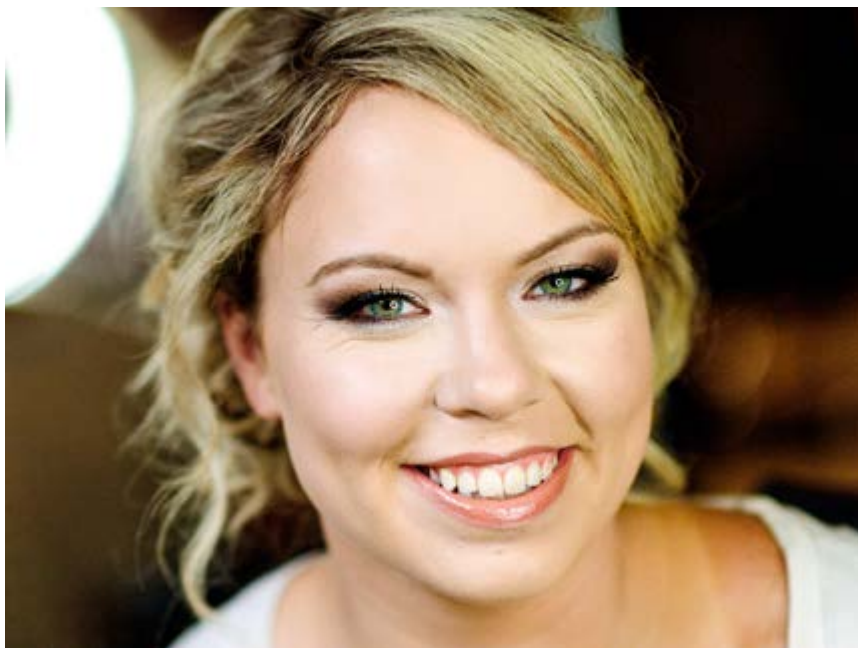
imaging and visualization with clinical applications in cardiology and post-mortem imaging, among other things. He has also initiated and run several collaborations with the medical technology industry and developed Center for Medical Image Science and Visualization at Linköping University.”



Great Achievements of Leah Mayo

Assistant professor Leah Mayo at CSAN received the Somerfeld-Ziskin Research Award for her outstanding research investigations in biological psychiatry.

The Somerfeld-Ziskind Award from the Society of Biological Psychiatry offers an annual award of 5000 dollars. She received the award for best published article in 2020 on her main research goal to improve clinical care for patients suffering from post-traumatic stress disorder (PTSD). Leah Mayo also was the winner of the Young Investigator Award by European Behavioural Pharmacology Society (EBPS) in the fall of 2020.



SEK 4.8 million from Swedish Research Council to Petter Dyverfeldt

The purpose of this project is to enable rapid quantification and visualization of turbulence in cardiovascular blood flow by developing a novel method termed magnetic resonance (MR) turbulence angiography. This will be achieved through rapid MR data acquisition and automated quantification and visu-

alization of turbulence in all cardiac chambers and major vessels. Successful accomplishment of this project will offer a new paradigm in the evaluation of several cardiovascular diseases by rapidly quantifying and visualizing turbulent blood flow.

CMIV part of BIGPICTURE

At the end of January, it was revealed that CMIV together with Sectra, Region Östergötland and other players engage in the new project BIGPICTURE led by the Innovative Medicine Initiative to construct a large-scale database of pathology images enabling development of AI methods. The 6-year, €70 million project will herald a new era in pathology.

CMIV is responsible for the technical infrastructure in collaboration with the SciLifeLab Bioinformatics platform NBIS and ELIXIR-SE and the Finnish ELIXIR node CSC.



AIDA Data Hub Has Become a SciLifeLab Facility

As of July 2021, the Data Hub of AIDA has been given the status of an official facility of SciLifeLab. This means that the long-term funding for the Data Hub has been secured, and that the AIDA community now has a direct connection to resources and expertise at SciLifeLab.

The AIDA Data Hub offers data sharing, policy support, and compute services for medical imaging AI, including the currently largest national AI research system for sensitive personal data. The Data Hub was started with seed funds from VINNOVA, with the ambition to establish a permanent setup elsewhere after the start-up phase.

In 2020, SciLifeLab announced a call for proposals about additional facilities, in which the AIDA Data Hub ended up being one of the few selected for inclusion. The AIDA Data Hub is part of the SciLifeLab Bioinformatics Platform (NBIS) and its BioImage Informatics facility, while remaining fully connected to all other AIDA activities, which reside in the Medtech4Health program.



*Håkan Gustafsson in our
Photon Counting Detector
CT NAEOTOM Alpha*





The CMIV Landscape

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, engineers, technicians and medical doctors could work close together with immediate access to the patients. A place where there were 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.

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 at the university provides health care with the opportunity of clinical benefits, while the industry gain from the research with e.g., spin-offs. The activities aim to combine different demands where the university strives for scientific publications in high quality journals and development of new products, and Region Östergötland expects the research and development to come to patient benefit. CMIV's organization, fully embedded in the university hospital, creates conditions to successfully meet these requirements. Results from basic research at the university can be utilized in clinical research which then can result in scientific publications, and improved patient care.

The CMIV research projects can be described as links in a sequential imaging chain. Projects move dynamically through the chain and researchers from different disciplines work together to reach the goal of patient benefit. Nowadays, the imaging chain perspective is complemented with additional research areas like artificial intelligence and precision medicine.

We are in the middle of a paradigm shift in healthcare. Focused research and development in all steps of the chain are still important to continue improving quality of care. However,

embracing new possibilities and letting the research grow in new dimensions is key to stay in the frontline of medical imaging. CMIV is now adapting its research to be in the forefront of this development. The advances in precision medicine are due to rapid development in a number of important areas that are groundbreaking by themselves. But their impact can also be greatly magnified if they are wisely combined. These areas include molecular biology, large-scale genetic sequencing and artificial intelligence.

Precision medicine can be defined as clinical, therapeutic and diagnostic methods for optimal disease management based on the patients' individual variations, often including a genetic profile. It provides more effective treatments, fewer adverse effects and increased survival. Examples of other advantages of precision medicine are increased possibilities to identify and thereby prevent or mitigate disease at an early stage, to make it easier for patients to manage their illness and shortening hospital stays.

The CMIV projects are not easily categorized as they move dynamically over research areas, always looking for new ideas from other fields. In an attempt to visualize the CMIV research areas we have created an overview table with the projects from the annual report and marked the main areas that the projects involve. The categories used are divided in three main research areas; imaging data source, biomedical research area and technical research area. The main research areas consist of a number of sub-areas.



Cardiovascular Magnetic Resonance group meeting with Tino Ebbers, Sophia Bäck, André Da Luz Moreira, Kajsa Tunedal, and Federica Viola on the screen.

IMAGING DATA SOURCE

The overall dominating data source at CMIV is magnetic resonance imaging (MRI). The method is versatile and allows great opportunities for project specific development. Another advantage is the use of volunteers not being restricted by radiation dose. In computed tomography (CT), the development of low dose CT has opened up for larger prospective studies and at the same time clinical examinations can be used for potent simulations. Since 2020, CMIV is one of the few clinical research centers in the world that has access to new photon-counting CT technology. The most recent photon-counting CT is approved for clinical use and has two X-ray tubes and two detectors and offers unimaginable possibilities.

CMIV has several exciting new studies in all of these fields. Another interesting field with an increasing contribution is microscopy, where the ongoing digitization of the clinical routine has opened up for new applications in image analysis and deep learning.

BIOMEDICAL RESEARCH AREA

CMIV has strong traditions in the fields of cardiovascular and neurology research. Other strong areas are musculoskeletal and gastrointestinal research. However, with new constellations forming, projects are less focused on individual organs and instead have a more holistic approach.

TECHNICAL RESEARCH AREA

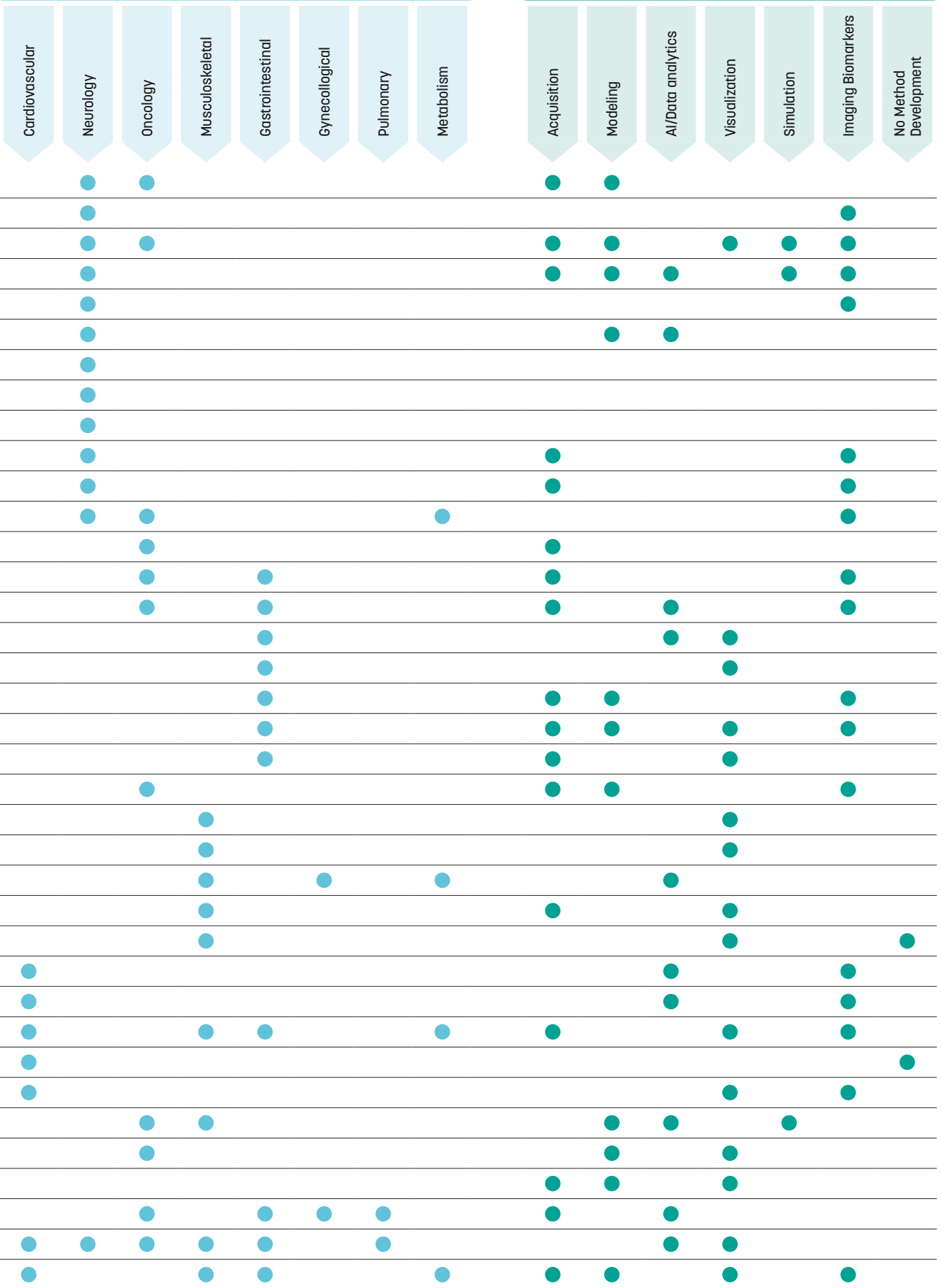
A foundational aspect of CMIV is that the research spans all the technical areas involved in the imaging chain. This type of cross-disciplinarity means that scientific efforts in one technology domain at CMIV is enriched by in-depth knowledge on the characteristics of preceding steps and on subsequent use of the results later in the chain. The overview shows that CMIV projects are fairly evenly distributed in terms of technical contribution, from data generation through acquisition and simulation to a wide range of analytics and visualization methods.

A SELECTION OF CMIV PROJECTS DEVIDED BY RESEARCH AREA

	IMAGING DATA SOURCE				
	Computed Tomography	Magnetic Resonance Imaging	Digital Microscopy	Ultrasound	Other
Statistical Analysis of NeuroImaging Data		●			
Pathophysiology Behind Prolonged Whiplash Associated Disorders		●			
High Resolution MR Quantification		●			
Image-Based Biomarkers of Brain Disorders		●			
Clinical Application of Synthetic MRI on Malignant Gliomas		●			
Localization of Seizure Onset Zone in Focal Epilepsy		●			
Emotion Regulation in PTSD		●			
The behavioral and neural mechanisms of alcohol choice preference		●			
Experiencing the self through touch		●			
Detection and Neurological Effects off Manganese		●			
SouthEast Sweden Neuroinflammation Cohort		●			
Investigating Neurological Disease Using Amino Proton Transfer Chemical Exchange Saturation Transfer		●			
Developing 3D qMRI		●			
Abdominal Synthetic MRI		●			
Photon Counting in Pancreatic Ductal AdenoCarcinoma (PhDAC)	●				
Semiautomatic Liver Volume Determination and Segmentation		●			
Optimizing Hepatobiliary Contrast in Liver Imaging		●			
Liver Function Evaluation		●			
Assessment of Hepatic Function in Health and Disease		●			
Evaluation of reconstruction methods in CT	●				
MR Mammography		●			
Evaluation of Photon Counting CT in Spinal Deformities	●				
CT-MOCAP: Visualization of Skeletal Joint Movement	●				
Health Effects of Resistance Training in Post-menopausal Women		●			
Bone Structure Analyses for Reducing Future Osteoporotic Fractures	●				
Post-Surgical Visualization of Tibial Plateau and Pilon Fractures	●				
Carotid MRI		●			●
Ascending Aortic Dilation		●			
SCAPIS-HEALTH		●			
Diffuse Myocardial Fibrosis		●			
Swedish CardioPulmonary bioImage Study (SCAPIS) in Linköping	●	●		●	
Tissue Classification Using DECT and MBIR	●				
Evaluation of New Brachytherapy Planning Methods	●	●		●	
CTTechIQ	●				
BigPicture			●		
AIDA	●	●	●	●	●
EPSONiP		●		●	

BIOMEDICAL RESEARCH AREA

TECHNICAL RESEARCH AREA



*Erik Tesselaar in the Photon
Counting Detector CT
with a wrist phantom.*





Flagship Projects

The 2021 flagship projects were selected by the CMIV scientific council in the autumn. The chosen projects complement each other in modalities, project stage and medical area and therefore well represent the broad and multi-disciplinary research at CMIV.

Advanced Quantitative MRI of the Brain

Neuroradiology is the part of radiology that focuses on the diagnosis and characterization of abnormalities of the central nervous system consisting primarily of the brain and the spinal cord. Magnetic resonance imaging (MRI) is a common modality in neuroradiology.

This project is focusing on Quantitative MRI of the brain. Quantitative MRI is a novel and promising technique for diagnose or prognose disease and to determine the choice of therapy, or to monitor the result of the chosen therapy.



Anders Tisell, PI



When talking about quantitative MRI (qMRI) we mean methods that measures the relaxation values. In contrast, to weighted images which are dependent on many more factors than relaxation such as patient size, scanner imperfections. This gives us measurable values and help the radiologist to understand if the suspected tumor for example really is a tumor, which can be hard to tell by just looking at the image. Anders Tisell, PI for this project and adjunct senior lecturer is involved in many of the qMRI research projects at CMIV.

Previously we have worked with a technique which was based on the two-dimensional technique of thick slices of the whole brain. This has now been developed into the three-dimensional technique we call QALAS, where the information is gathered as a volume with one-millimeter isotropic resolution of the whole brain.

After we have measured, we can still create weighted MR images by calculating them from the qMRI and this is called synthetic MRI.

From the qMRI we can also calculate the amount of myelin, which is the fatty insulating layer formed around nerves in the brain and spinal cord, Anders explains. The myelin helps speeding up the nerve impulse. Multipel Sclerosis (MS) breaks down the myelin and we have a technique to measure these damages or scarrings, so called MS lesions. We can see if the amount of myelin starts to decrease or remain stable. By following the patients, we can discover early signs of MS lesions so that the treatment might be changed, if necessary, Anders continues. With new drugs coming, we can help monitoring to see if they can maintain the amount of myelin.

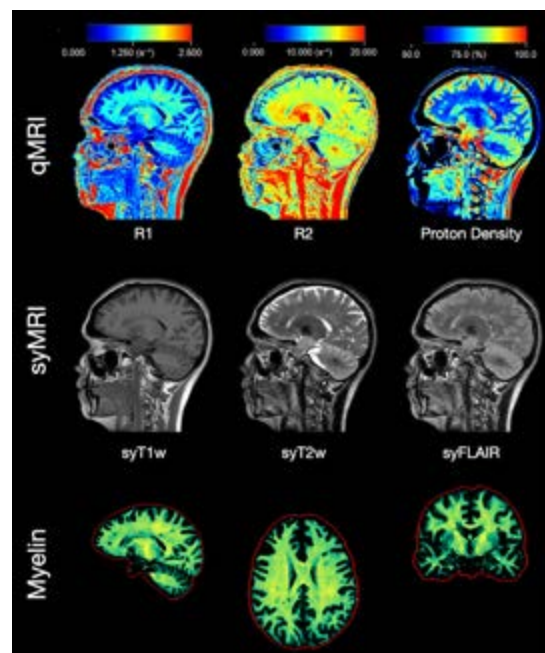
Another project also using the same technique with 3D QALAS is monitoring brain tumors.

The radiologist sees the tumor since the tumor loads contrast agents. By using the quantitative technique mentioned above, it is possible to see that outside the part of the tumor that the

radiologist sees we can see that there are more tumors. Tumors in the brain are often very aggressive and even if the neurosurgeon removes everything that we can see, we know that there is still tumor tissue left.

– With the new 3D-technique we get better resolution and hope that we in that way will be able to see where the tumor will continue to grow, that we will be able to detect the real tumor border, Anders continues.

Yet another example of how this technique is used is in radiation therapy, where patients who are in the middle of radiation therapy or who have finished it are followed. Due to the radiation that is given during therapy it looks as if there are contrast agents loaded. This is a reaction to radiation, so called pseudo progress. Due to this pseudo progress MRI is not performed one month after surgery but only after three months, when the pseudo progress is de-



Example images of a 33 years old MS patient. All images are calculated from a single 6 minute QALAS scan. In the top row quantitative parameter maps, in the middle row synthetic contrast images and in the bottom row the myelin volume.



Anders Tisell, Marcelo Pereira Martins, Anna Ljusberg and Peter Lundberg.

creased. With these patients you must wait even though the diagnosis is not so good, so it would be much more preferred if you did not have to wait.

– With the qMRI, both 2D and 3D, we hope to see already after one month if it is pseudo progress or tumor progress. We are right now evaluating this new technique, Anders says.

It is well known that radiation therapy causes tissue damages. Another aspect of the project is also to investigate these damages and see how the tissue is affected by radiation. If it is possible to see damaged tissue, there might be a possibility to change the dose plan and treat the tumor from another angle.

Still with the same the same technique there are ongoing research with Parkinson's disease which is a progressive nervous system disorder that effects movement. Today there are no MRI examination that can specifically diagnose Parkinson's disease. The symptoms starts gradually and by looking at the substantia nigra there are hopes of early detection of changes. Is there a difference between healthy volunteers and patients? If the project turns out well this examination method could be implemented clinically.

Patients suffering from hydrocephalus i.e., when there is excessive cerebrospinal fluid (CSF) in the brain which can cause gait difficulties and mild dementia, are often treated surgically by inserting a shunt to relieve pressure on the brain. There are problems with monitoring the pressure to find the optimal state in the ventricles. With QMRI it is possible to see CSF as well as white and gray matter and hopefully

also the ventricular volume to help deciding the optimal pressure state.

There is so much going on and still much to do, Anders conclude.

MRI **Neurology** **Oncology** **Metabolism** **Acquisition**
Imaging Biomarkers

Project information

PROJECT NAME

Advanced Quantitative MRI of the Brain

PROJECT LEADER

Anders Tisell, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS

Marcel Warntjes (CMIV), Peter Lundberg (CMIV, MSF), Ida Blystad (CMIV, Rtg), Charalampos Georgiopoulos (CMIV, Rtg), Maria Kristoffersen Widberg (Rtg), Johan Mellergård (Neurologen), Fredrik Lundin (Neurologen), Rafael Holmgren (NK), Angie Landgren Liu (Rtg), Anna Ljusberg (MSF), Frederik Testud (Siemens)

GRANTS

ALF

KEY PUBLICATIONS

Anders Tisell, Peter Lundberg, Marcel Warntjes, Frederik Testud. 3D Quantitative MRI of the Brain: Effects of B1 Inhomogeneity in 3D-QALAS. ISMRM; 2021.

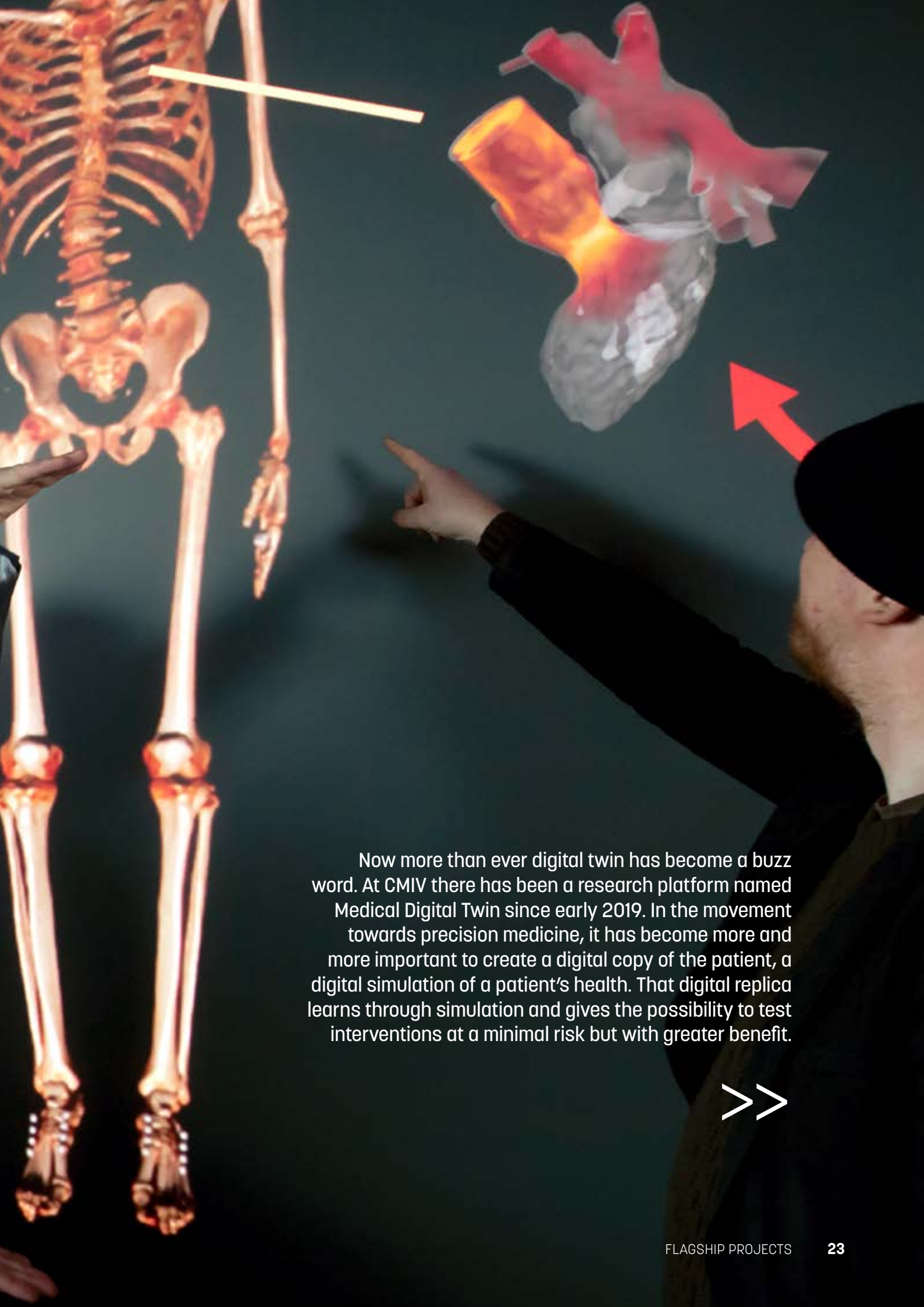
Blystad I, Warntjes M, Smedby O, Lundberg P, Larsson E. M, Tisell A. Quantitative MRI using relaxometry in malignant gliomas detects contrast enhancement in peritumoral oedema. Sci Rep 10, 17986 (2020). <https://doi.org/10.1038/s41598-020-75105-6>.

Håkansson I, Tisell A, Cassel P, Blennow K, Zetterberg H, Lundberg P, Dahle C, Vrethem M, Ernerudh J. Neurofilament levels, disease activity and brain volume during follow-up in multiple sclerosis. J Neuroinflammation. 2018 Jul 18;15(1):209.

Medical Digital Twin – MeDigiT



*Sophia Bäck,
Tino Ebbers, PI and
Gunnar Cedersund*



Now more than ever digital twin has become a buzz word. At CMIV there has been a research platform named Medical Digital Twin since early 2019. In the movement towards precision medicine, it has become more and more important to create a digital copy of the patient, a digital simulation of a patient's health. That digital replica learns through simulation and gives the possibility to test interventions at a minimal risk but with greater benefit.



“The body is a very complex system with many physiological interconnected networks that need to be simulated.”

Tino Ebbers

A prerequisite for being able to maintain cost-effectiveness and high qualitative healthcare is to make the treatment of patients more individualized. Advanced data driven techniques offer the possibility to measure and quantify the course of disease. However, it is difficult to make a diagnosis based on measurements as local ailments often affect the whole body. In addition, patients seldom have only one ailment but several at the same time. To be able to understand and use all these data, a tool is needed that can evaluate and visualize the entire patient's complex anatomy and physiology. A common solution for this in the industry is to create a digital twin, a replica in a computer. In the same way this is applied to medicine.

Thus, in a clinical environment it is possible to simulate different treatment scenarios by using a digital twin of a patient. This digital model can be used to optimize treatment but also to gain insight on how different treatments for

different diseases affect each other. In the development of medical digital twins, health care and MedTech companies need to work together. That cooperation is a prerequisite for moving forward.

Tino Ebbers, professor in physiological measurements, with special research interest in cardiovascular imaging with focus on assessment of blood flow dynamics and tissue characterization, is leading the MeDigiT platform. The goal is to enable the use of individual-specific digital models in healthcare to facilitate diagnoses, more individualized treatment of different illness and improved training of healthcare staff.

The platform consists of five demonstrator projects, Tino explains. One of the projects is a collaboration with Sectra and Region Östergötland and focuses on the use of time-resolved digital twins of the body's joints in teaching.

Another demonstrator is focusing on CM-IV's cutting edge research on imaging of the



André Da Luz Moreira, Sophia Bäck, Tino Ebbers, Gunnar Cedersund, Marie Waltersson and Kajsa Tunedal.



cardiovascular system. By simulating the heart flow based on examinations in the computed tomography (CT) scanner, individualized digital twins are tested for diagnosis and treatment evaluation in heart disease. The goal is to improve valve surgery and risk assessment of blood clot formation in atrial fibrillation.

The third demonstrator is a collaboration with Scandinavian Real Heart. This demonstrator strives to improve the design of medical implants as for example the artificial heart by using magnetic resonance imaging (MRI), conventional CT as well as the new photon counting detector CT (PCD-CT). The entire measuring equipment is huge for two reasons (see image above). One is that it is a heart with a motor in it and that motor cannot be in the MR scanner. The second is that to test a heart, you need to have the whole system around in order to simulate the vascular system. It must work with a certain pressure, Tino explains.

In the Whole-body demonstrator a SheDigiT and a HeDigiT are created. It also develops a platform to enable the creation of digital twins of patients with public diseases.

Last there is a new demonstrator of the whole-body composition digital twin, which is focusing on body composition measurements in cooperation with AMRA Medical.

The main objective with MeDigiT is to create and promote a network for the exchange of knowledge and experience between Linköping University, Region Östergötland and companies in medical visualization.

– The most important thing about the platform is that we create a network where we can learn from each other, Tino concludes.

Computed Tomography	MRI	Cardiovascular
Musculoskeletal	Metabolism	Modeling
AI/Data analytics	Visualization	Imaging Biomarkers

Project information

PROJECT NAME

Medical Digital Twin

PROJECT LEADER

Tino Ebbers, Department of Health, Medicine and Caring Sciences, Division of Diagnostic and Specialist Medicine

MAIN PROJECT PARTICIPANTS

Marie Waltersson, Anders Persson, Nils Dahlström, Faisal Zaman, André Da Luz Moreira, Federica Viola, Mariana Bustamante, Several participants from companies

GRANTS

Visual Sweden 2019-2022

KEY PUBLICATIONS

Lantz J, Bäck S, Carlhäll CJ, Bolger A, Persson A, Karlsson M, Ebbers T. Impact of prosthetic mitral valve orientation on the ventricular flow field: Comparison using patient-specific computational fluid dynamics. *Journal of Biomechanics* 116, 2021.

Cedersund G, Casas B, Bauer S, Kanebratt K, Huldt CW, Magnusson L. Insulin resistance and type 2 diabetes studied using a new combination of microphysiological systems and mathematical modelling. *DIABETOLOGIA* 64 (SUPPL 1), 190-191 2021.

Pieper IL, Sonntag SJ, Meyns B, Hadi H, Najjar A. Evaluation of the novel total artificial heart Realheart in a pilot human fitting study. *Artificial Organs*, 44 (2), p174-177, 2020.



Erik Tesselaar, PI

Musculoskeletal Imaging Using CT

Musculoskeletal imaging is an important part of the clinical diagnosis of diseases or structural damage in bones, joints, ligaments and tendons. This flagship is an umbrella project of several different research projects all involved in the new photon counting detector computed tomography (PCD-CT), which is especially well suited for musculoskeletal imaging. The enhanced resolution of the system and the capability of giving a very detailed image of the anatomy provides many opportunities for new research projects within this area.



“This new PCD-CT will have a direct impact on patient care, eventually leading to improved quality of life.”

Erik Tesselaar

Medical physicist Erik Tesselaar is principal investigator of the musculoskeletal imaging project using computed tomography (CT) and above all photon counting detector computed tomography (PCD-CT).

– The availability of the new PCD-CT at CMIV has created a massive interest to start new research projects, and many of the projects are still in a very early phase, Erik says. We know that the new system has a better performance than current CT scanners, but what we do not know how much better it is, and in which areas it adds the most value.

For musculoskeletal imaging there are two major advantages of PCD-CT. The first is the increased spatial resolution, which makes it possible to visualize smaller structures, and especially the microstructure on the inside of the bones called the trabecular bone, which is the porous and spongy bone tissue.

The second is the possibility to separate different photon energies. The ability of the detector to analyze the absorption of different photon energies in the body provides much more information about different materials in the body.

– Separating different materials in bone structures is very useful when looking at small fractures that cannot be distinguished on plain radiographs, Erik explains. With PCD-CT you can not only see smaller fractures, due to the

better resolution of the images, but it is actually possible to see ‘bone bruising’, which is the buildup of blood and fluid in and around the injured bone. We expect that the PCD-CT may offer a good alternative to magnetic resonance imaging in the diagnosis of these small fractures.

One of the sub-projects is specifically looking into osseointegration, which is the functional connection between bone and a load-bearing implant e.g., in orthopedic hip replacements. If a patient needs to replace the hip with an implant, it is important that the interface between the bone and the implant is stable. When the osseointegration fails the hip implant becomes loose and this can cause a lot of pain. It is hard to diagnose this condition, and we think that PCD-CT may offer a better way to evaluate the osseointegration.

For complicated fractures near joints more advanced imaging techniques are required and CT is the most used modality both for preoperative as well as postoperative planning to verify the result.

After surgery of a knee or an ankle there are often screws or plates attached to the bone and the metal causes artifacts making it hard to see the healing process. By using the PCD-CT the metal artifacts can be substantially reduced.

Yet another project is looking at osteoporosis, a disorder that results in fragile bones that easily break. Elderly people are sometimes screened for osteoporosis with Dual-energy X-ray absorptiometry, (DXA) by looking at the amount of bone mineral. The microstructure of the bone, the trabecular bone is very important when looking for the risk of future fractures. In this project the DXA measurements are compared with the images obtained with different CT scanners: dual energy CT, cone beam CT (CBCT) and the new PCD-CT.

In the last project Erik himself is involved. In this project the visualization of small bone structures in the wrist is compared between PCD-CT and the best conventional CT that we



Mårten Sandstedt, Nina Kämmerling, Eva Klintström, Ronald Booij and Simon Farnebo

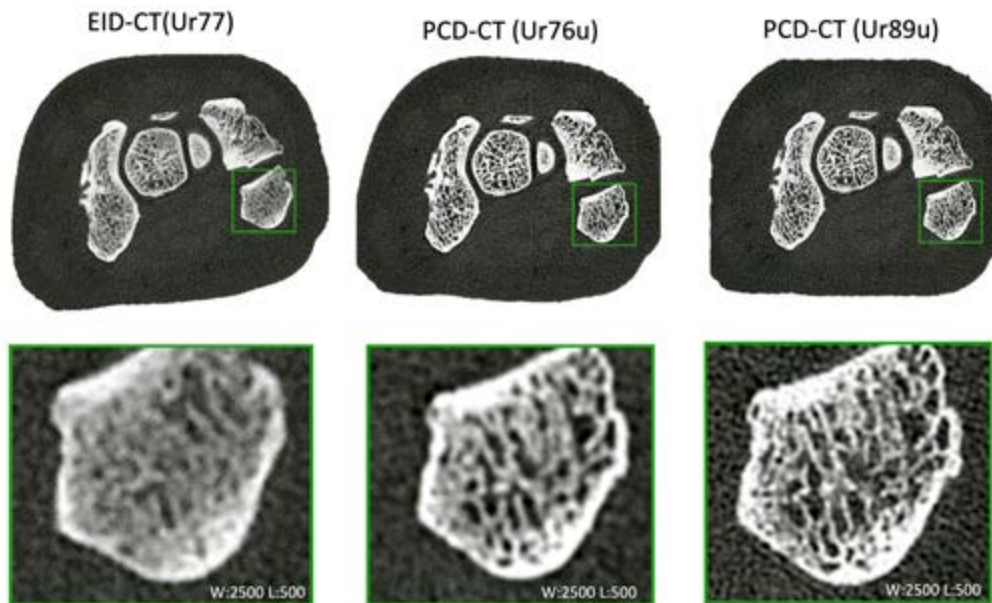


Figure 1. Axial slice of a wrist specimen with the distal part of the ulna (green boxes) magnified. Images on the left acquired by conventional, state-of-the-art CT, whereas the middle and right images are acquired using photon-counting detector CT using a medium and sharp reconstruction kernel, respectively.

currently have in Linköping, the Siemens Somatom Force.

– We scanned wrist specimens on both systems and asked five radiologists to evaluate the image quality by looking at the visualization of the bones, the trabecular bones, the nutritional channels in the bones and the amount of noise. It was very clear both in terms of spatial resolution and contrast-to-noise ratio that the PCD-CT was better for this imaging task, Erik explains.

The next step will be to study patients with traumatic wrist injuries. At Vrinnevi Hospital in Norrköping, all patients with a suspected fracture of the wrist are examined by using CBCT, which is a small CT scanner available in the emergency department. In the CBCT, fractures can be more accurately diagnosed since the resolution is much better than regular radiographs, but very small fractures in some of the bones of the wrist may still be missed due to the limited image quality. In this new study, we work together with the orthopedic surgeons in Norrköping. They will ask all patients examined in the CBCT to be examined in the PCD-CT at CMIV as well. We expect that with PCD-CT, we will see the same fractures much better and that we will detect fractures in other wrist bones that are not visible on the CBCT images.

– With this new technology we also hope that we will be able to track subtle signs of healing so that hand surgeons easier can decide on when the fracture is sufficiently healed so that the cast may be removed.

This new PCD-CT will have a direct impact on patient care, eventually leading to improved quality of life, Erik concludes.

Computed Tomography Musculoskeletal Acquisition
Modeling

Project information

PROJECT NAME

Musculoskeletal Imaging Using Computed Tomography

PROJECT LEADER

Erik Tesselaar, Department of Biomedical and Clinical Sciences, Division of Surgery, Orthopedics and Oncology

MAIN PROJECT PARTICIPANTS

Nina Kämmerling, Simon Farnebo, Märten Sandstedt, Eva Klintström, Lilian Henriksson, Anders Persson, Ronald Booj, Mischa Woisetschläger, Jörg Schilcher, Ludvig Vavruch, Seppo Koskinen, Ann-Sofi Björkman, Håkan Gauffin, Alexandr Malusek

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Indranil G, Klintström B, Klintström E Zhang X, Smedby Ö, Moreno R, Saha P. A comparative study of trabecular bone micro-structural measurements using different CT modalities *Physics in Medicine and Biology*, ISSN 0031-9155, E-ISSN 1361-6560, Vol. 65, nr 23 2020.
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Mattias Ekstedt, Nils Dahlström, Peter Lundberg, Bengt Norén and Patrik Nasr

A photograph of two men in a presentation room. The man on the left is older, with glasses, wearing a grey blazer over a striped shirt and a blue bow tie. The man on the right is younger, with a beard and glasses, wearing a red t-shirt. They are both looking at a large screen displaying a cross-sectional MRI scan of a human head. The screen also shows a small blue bar at the bottom with some icons and text. The background is dark, and the lighting is focused on the men and the screen.

Research Projects

The research within CMIV is based on innovations in medical image science and visualization. A common goal is to strengthen the interdisciplinary approach and enhance the possibilities of image-based diagnosis and treatment. At CMIV research is conducted within several medical 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.

Statistical Analysis of NeuroImaging Data

Functional magnetic resonance imaging (fMRI) is a popular tool for studying brain activity, as it can non-invasively image the human brain without any ionizing radiation. Similarly, diffusion MRI (dMRI) is a popular tool for studying structural brain connectivity, by for example measuring how easily water can travel along different directions. From a statistical perspective, analyzing fMRI and dMRI data is a challenging task for several reasons. One reason is that the noise has a complex spatio-temporal structure, which is virtually impossible to simulate in a computer. Another reason

is that there are several noise sources which distort the signal of interest, for example head motion, breathing and pulse. In this project we validate and improve existing statistical models for neuroimaging data, often using open data available through data sharing.

In our most recent work, we calculate brain activity maps for brain tumor patients, and use the activity maps as risk organs in Elekta's software Leksell GammaPlan. The result is a treatment plan that will still kill the tumor cells, but will avoid damaging important areas in the brain.

MRI **Neurology** **Modeling**
AI/Data analytics

Project information

PROJECT NAME

Statistical Analysis of NeuroImaging Data

PROJECT LEADER

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GRANTS

VR (2018 - 2021)

VINNOVA/ITEA3 ASSIST (2021 - 2024)

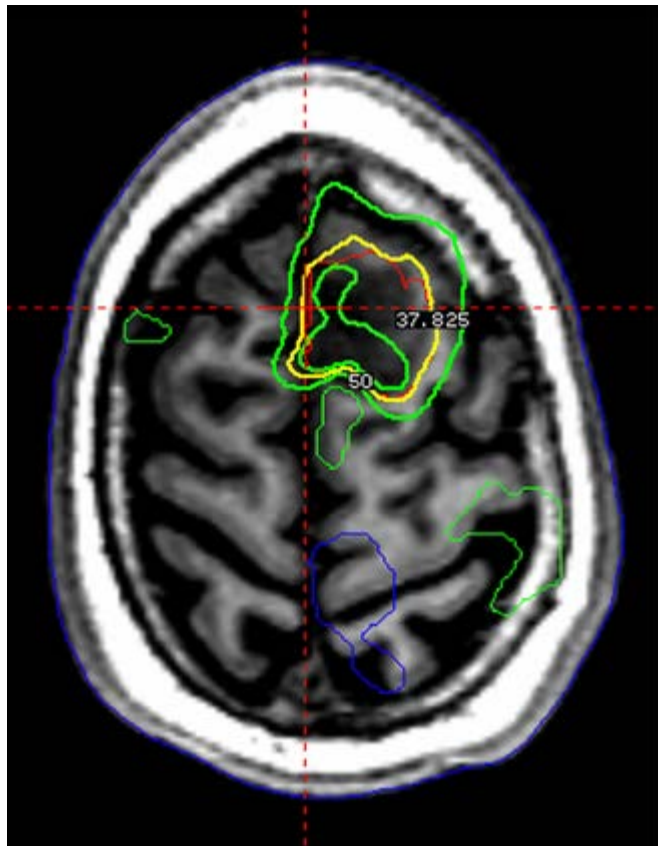
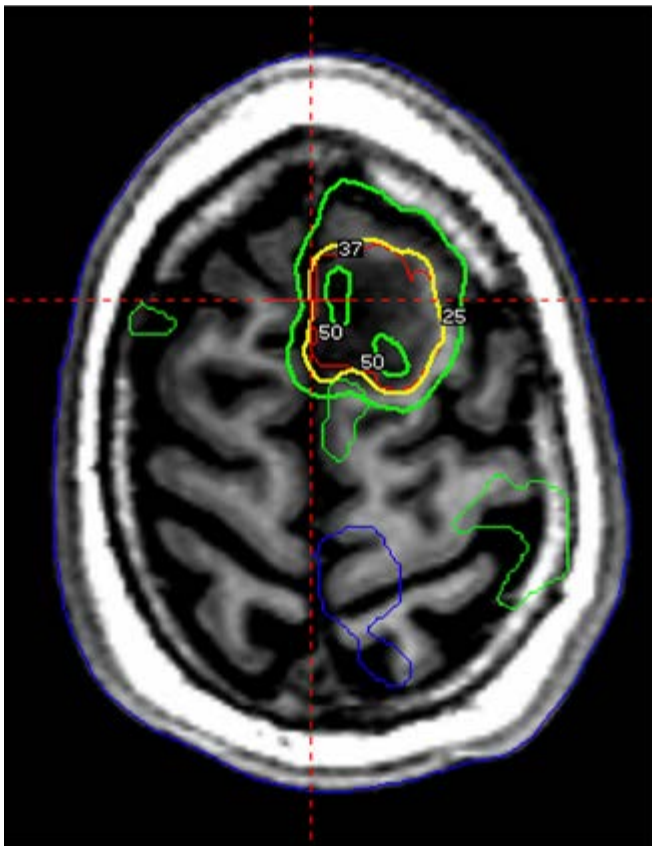
CENIIT (2018 - 2023)

KEY PUBLICATIONS

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Left: Treatment plan from Elekta's software Leksell GammaPlan, for a rather large brain tumor (marked by the red contour). Note that the gamma radiation will also affect the green area in the middle (representing brain activity in the supplementary motor area, SMA). Right: Treatment plan when using the brain activity maps as risk organs in the treatment plan optimization. The gamma radiation will now not be applied to the SMA, which is good for the patient.

Pathophysiology Behind Prolonged Whiplash Associated Disorders

There is insufficient knowledge of pathophysiological parameters to understand the mechanism behind prolonged Whiplash Associated Disorders (WAD) and yet unknown whether changes can be restored by rehabilitation or not. The aim of the project is to investigate imaging and molecular biomarkers, cervical kinaesthesia, postural sway and the association with pain, disability and other outcomes in individuals with longstanding WAD before and after a neck-specific intervention. Another purpose is to compare individuals with WAD with healthy controls. The participants are a sub-group (n=30) of individuals recruited from an ongoing randomized controlled study (RCT). Measurements in this experimental prospective study will be made at baseline (before intervention) and at 3 months follow-up (end

of physiotherapy intervention) and will include muscle structure and inflammation using magnetic resonance imaging (MRI), brain structure and function related to pain using functional MRI (fMRI), muscle function using ultrasonography, biomarkers using samples of blood and saliva, cervical kinaesthesia using the "Butterfly-test" and static balance test using an iPhone app. Association for other measures (self-reported and clinical measures) obtained in the RCT (e.g., background data, pain, disability, satisfaction with care, work ability, quality of life) may be investigated. Healthy volunteers matched for age and gender will be recruited as controls (n=30). The study results may contribute to the development of improved diagnostics and improved rehabilitation methods for WAD.

MRI **Neurology** **Imaging Biomarkers**

Project information

PROJECT NAME

Pathophysiology Behind Prolonged Whiplash Associated Disorders

PROJECT LEADER

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GRANTS

Swedish Research Council
VINNOVA
Region Östergötland

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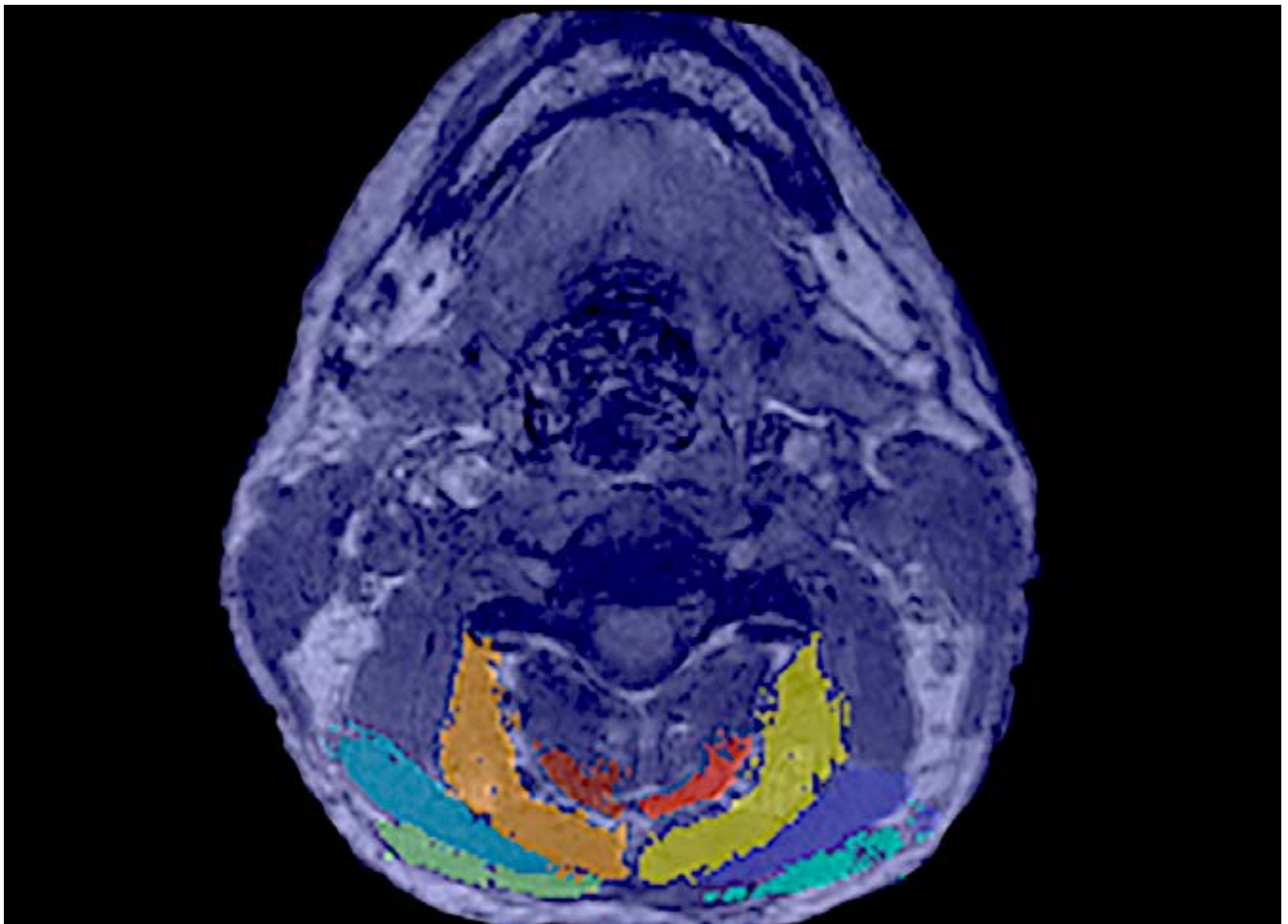


Figure: From superficial (closest to the skin) to deep (closest to the vertebrae) dorsal neck muscles: green= trapezius, blue/purple=splenius, yellow/orange Semispinalis capitis and cervicis, red= multifidus muscle.

High Resolution MR Quantification in 3D

In the regular clinical workflow MRI is typically used as a qualitative method, where images are subjectively interpreted by a radiologist. At CMIV a method was developed to actually measure physical properties instead, in order to provide numbers and statistics of a patient rather than user-dependent interpretation. This method, MDME, was based on a multi-slice TSE approach, meaning that relatively thick slices were acquired to show an image. Nowadays there is a great need for 3D approaches, where the same resolution is obtained in all directions, in order to visualize the patient in 3D. Therefore, a new sequence was developed, which can obtain high resolution in full 3D within an acceptable scan time. The scan time for the 3D sequence is 6-8 minutes, measuring the most important characteristics for MRI: the R1 relaxation rate ($1/T_1$), the R2 relaxation rate ($1/T_2$) and proton density PD.

For more familiar visualization, a range of conventional MR images can be recreated based on the R1, R2 and PD maps, an approach called synthetic MRI. The single quantification sequence can generate conventional contrasts such as T1W, T2W, FLAIR, but even Double IR and Phase-Sensitive IR. Moreover, being objective data, tissue can be recognized and assessed automatically. This means that a relatively short scan time is sufficient to reproduce a large part of a

normal MR examination and, additionally, to provide more objective means of patient follow-up. Examples of tissue recognition are brain volume measurement, myelin detection and GD-enhancement detection. These clinical parameters can be used for monitoring development and degeneration of the brain, for example in pediatrics, Multiple Sclerosis, hydrocephalus, cancer and dementia. Quantification also provides robust input to recognize pathologies automatically.

A spin-off company, SyntheticMR AB, was created to ensure an installable, safe product including the necessary regulatory requirements for several markets around the globe. The 3D sequence is now available on all major vendors and clinical evaluation has started. It has been shown that the quantitative values from Siemens, GE and Philips scanners are identical. Also, the image quality of the synthetic images greatly improved. Currently, clinical evaluation is in progress to fit this new method into the clinical workflow.

In the recent year the image quality, accuracy and precision of the 3D acquisition was greatly improved. Also, a verification was preformed to make sure that the measured values of R1, R2 and PD, and in turn the brain segmentation, were equal on all vendors. Fully functional prototypes now exist on Siemens, GE and Philips scanners.



Project information

PROJECT NAME

High Resolution MR Quantification in 3D

PROJECT LEADER

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MAIN PROJECT PARTICIPANTS

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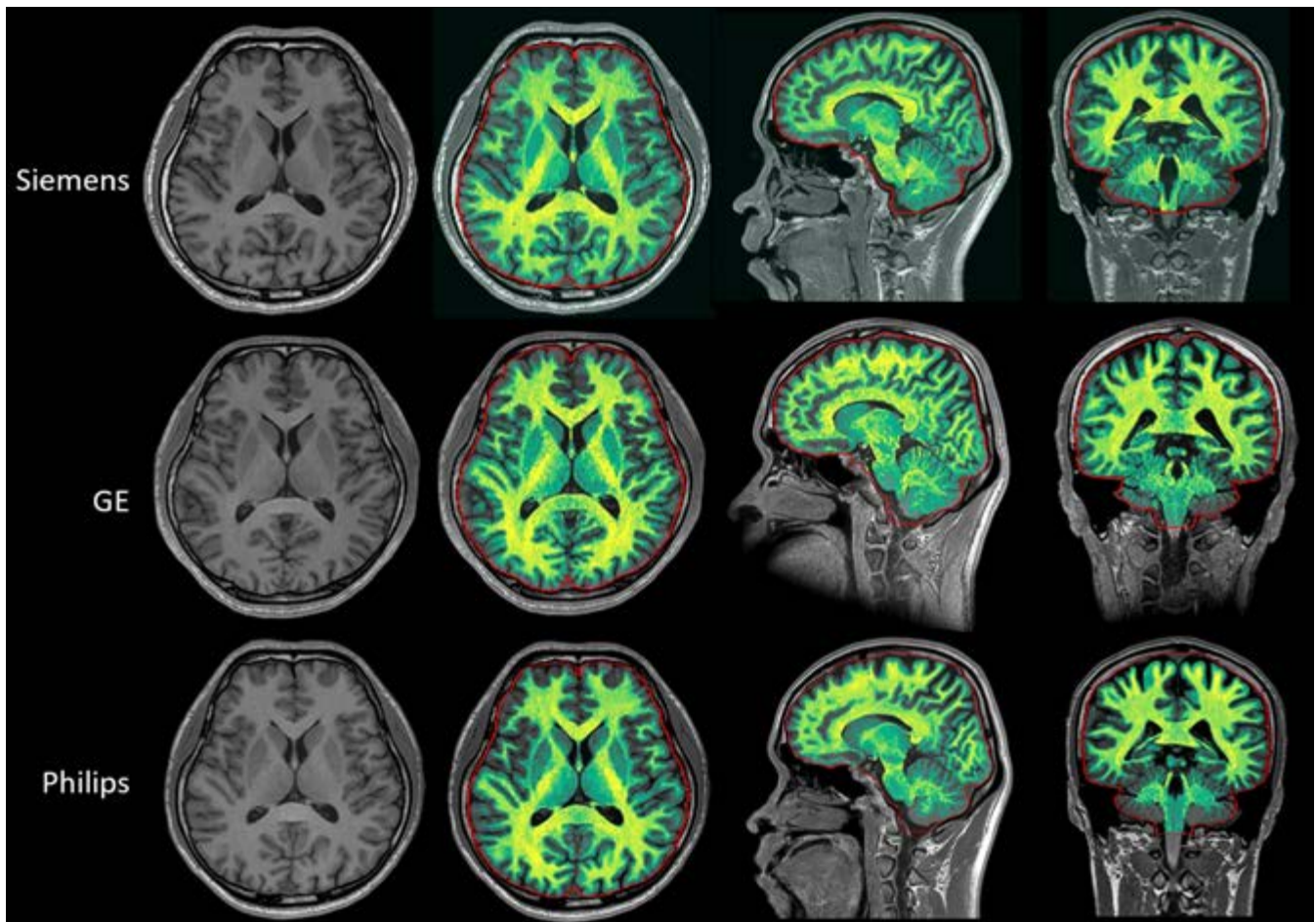


Fig.1. Example of the 3D MR quantification on various vendors. The sequence provides the physical properties R_1 , R_2 and PD , after which synthetic images such as the TIW on the left can be generated. Moreover, further modeling provides, for example, a measure for myelin partial volume (right), which is important to monitor in neurodegenerative diseases. MR quantification results in the removal of scanner imperfections, such that the data is identical for all vendors, leading to unification of MR imaging. The resolution of the 3D approach is 1.2 mm in all directions, obtained in 6 minutes acquisition time.

Image-Based Biomarkers of Brain Disorders (IBBB)

Functional MRI (fMRI) is a method for visualisation of brain activation. fMRI is widely applied in research and in the clinic, yet the biological mechanisms behind fMRI are largely unknown. We have only little knowledge about the relation between activated neuronal cells and the subsequent changes in blood oxygenation i.e., the neurovascular coupling underlying the blood oxygen level dependent (BOLD) response in fMRI.

This lack of knowledge can be overcome by mathematical modelling where different hypotheses describing e.g., excitatory and inhibitory neurons, are translated to mathematical equations (= models). These models are tested against multimodal data describing e.g., cerebral blood flow, oxygenation, and metabolism. If a model cannot explain data the hypothesis is rejected, if a model can explain the data the model is further investigated and tested against new experimental data. In this way, we can deepen our knowledge about mechanisms and obtain model-based biomarkers.

Our first model could reject the hypothesis of brain metabolism being the driving force behind the BOLD response. We have also shown that neural inhibition can explain so-called negative BOLD responses, thus providing a more complete explanation of fMRI data (Sten et al., 2017).

Recent research has been focused on explaining interactions between excitatory and inhibitory neurons, and their influence on the neurovascular coupling, including explanations of changes in vascular dynamics in response to an anesthetic agent (Sten et al., 2020). More recently, we have extended the quantitative model and included mechanisms in different neural cell types, cerebral oxygenation, metabolism, and vascular dynamics in different blood vessels, as well as a comprehensive model for the fMRI signal (Fig. 1). By this multi-dimensional model, we were able to explain several datasets from different experimental conditions (Sten, 2021). In addition, we have added a metabolic model by which we can explain time-dependent MRS data of glucose, lactate, aspartate, and glutamine in addition to BOLD response data (Sundqvist et al., submitted).

In summary, by our modelling approach we can firmly reject hypotheses that cannot explain data and we can obtain new knowledge about brain mechanisms. We can also explain pharmacologically induced brain responses. We are aiming to define model-based biomarkers of brain function, biomarkers that can express brain activation in terms of biological properties.

MRI	Neurology	Metabolism	Acquisition
Modeling	AI/Data analytics	Simulation	
Imaging Biomarkers			

Project information

PROJECT NAME

Image-Based Biomarkers of Brain Disorders (IBBB)

PROJECT LEADER

Maria Engström, Department of Health, Medicine, and Caring Sciences, Division of Diagnostics and Specialist Medicine/Radiological Sciences

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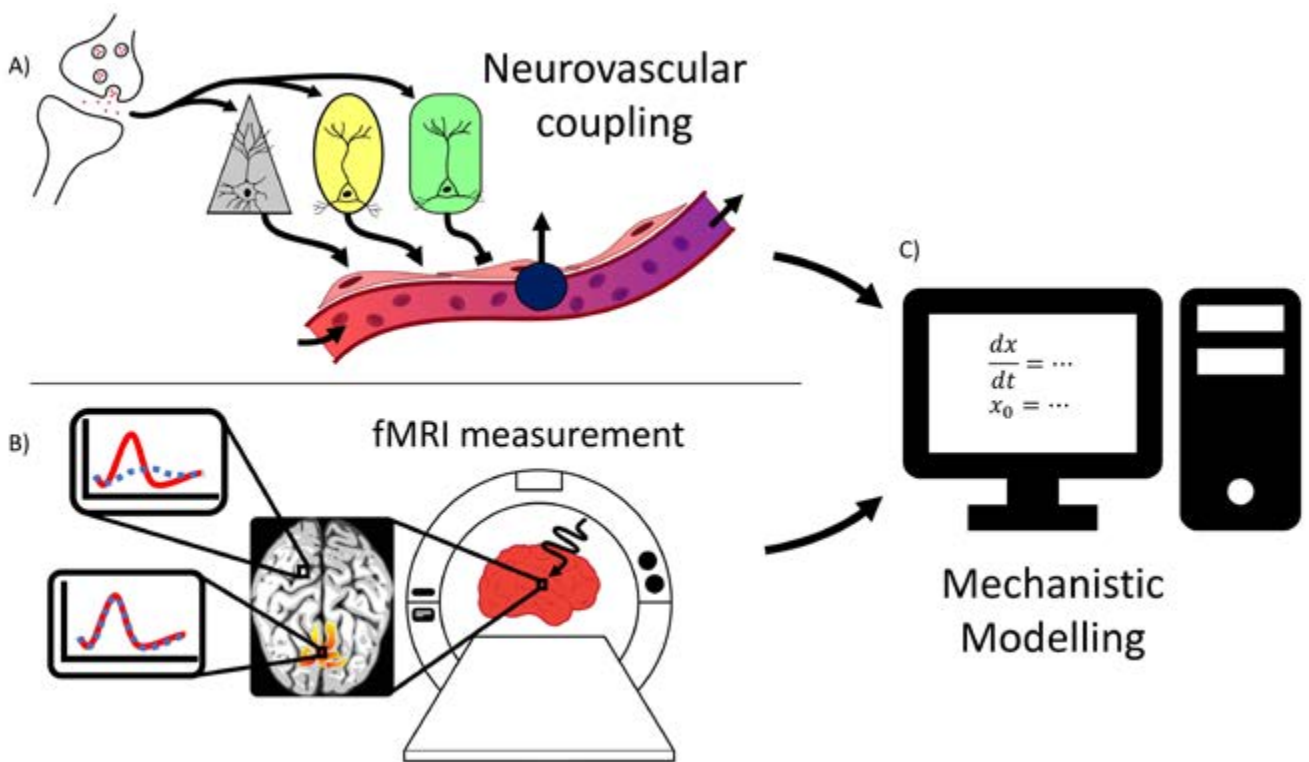
Swedish Research Council (2019-01-01 - 2022-12-31)
Swedish Brain Foundation (2021-07-01 - 2022-12-31)

KEY PUBLICATIONS

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Sebastian Sten. Mathematical modeling of neurovascular coupling. Linköping University Medical Dissertation No. 1742, 2020.



Schematic picture of the research approach. A) Hypotheses are formulated from multimodal data of the neurovascular coupling. B) Brain activation is measured by fMRI. C) The hypotheses are formulated as mathematical equations and fMRI measurements are used for hypothesis testing. Image courtesy Nicolas Sundqvist.

Clinical Application of Synthetic MRI on Malignant Gliomas

Conventional MR images are assessed visually by the radiologist to obtain a diagnosis or to evaluate treatment effects. New MR sequences can offer the possibility of quantitative assessment of physical properties of the tissue, which gives a more objective tool for evaluation. Synthetic MR is a quantitative MR sequence with a scan time of approximately 6 minutes, developed at CMIV. In this project the aim is to apply this sequence in different clinical settings, mainly in patients with primary brain tumors; malignant gliomas.

Patients with high-grade malignant gliomas (primary brain tumors) are treated with surgery, chemo- and radiotherapy and then followed with MRI-examinations to evaluate treatment response and to detect early signs of tumor recurrence. Due to their infiltrative nature, gliomas are difficult to treat and to assess. Surgery aims for maximum safe resection of the tumour, and complete removal of the contrast-enhancing portion is regarded as radical resection.

However, glioma infiltration extends beyond the visibly contrast enhancing border of the tumour, and these changes are not easily differentiated from the peritumoral oedema on conventional MR images. Using quantitative MR techniques, tumour infiltration can be analysed for diagnosis and prognosis, and during recent years, such new quantitative MRI sequences using relaxometry have been applied for brain tumour analysis in research. In this project, we follow patients with malignant gliomas from diagnosis during the follow-up after surgery and oncological treatment. If it is possible to find tumor specific quantitative values, it might be possible to distinguish tumor from healthy brain, and from treatment effects and thereby improving the diagnostic arsenal in these difficult cases. This would be of great significance for the radiologists as well as the neurosurgeon and oncologist in treatment planning, and of benefit for the patient.

MRI **Neurology** **Imaging Biomarkers**

Project information

PROJECT NAME

Clinical Application of Synthetic MRI on Malignant Gliomas

PROJECT LEADER

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MAIN PROJECT PARTICIPANTS

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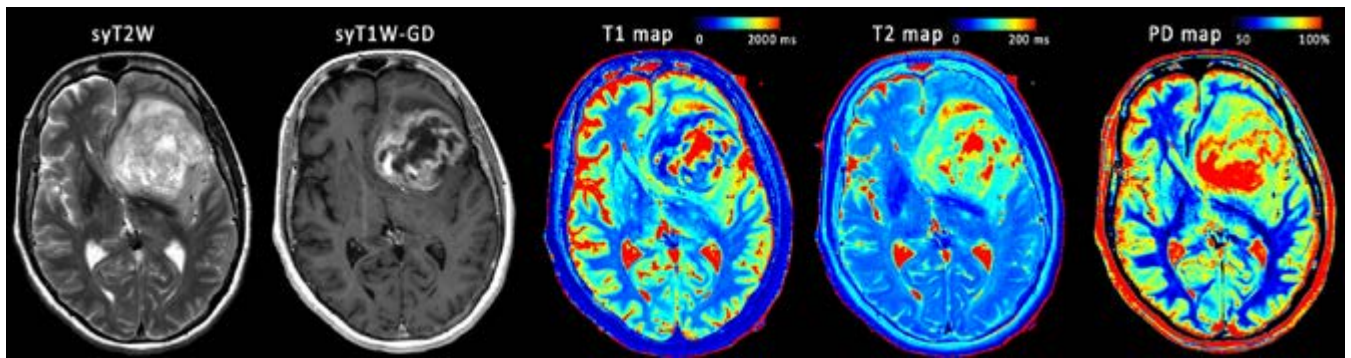
Medical Research Council of Southeast Sweden

KEY PUBLICATIONS

Blystad I, Warntjes JBM, Smedby Ö, Lundberg P, Larsson E-M, Tisell A. Quantitative MRI using relaxometry in malignant gliomas detects contrast enhancement in peritumoral oedema. *Sci Rep* 10, 17986 (2020). <https://doi.org/10.1038/s41598-020-75105-6>.

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Images and quantitative maps derived from the quantitative scan of one of the brain tumor patients. From left: synthetic T2W image, synthetic T1W image post-contrast agent injection, T1-, T2- and PD-maps.

Localization of Seizure Onset Zone in Focal Epilepsy

EEG-fMRI is a method that combines EEG (electroencephalogram) and fMRI (functional magnetic resonance imaging) to localize the epileptogenic zone in patients with medically refractory focal epilepsy who are candidates for epilepsy surgery. The method is in use in some epilepsy centers around the world but not in clinical practice in Sweden. The aim of this study is to implement the method in epilepsy surgery evaluation and to compare the results with other investigations.

Epilepsy is a disorder with uncontrolled electric activity in the cortex of the brain. In most people with epilepsy, the seizures are controlled by medication. About 30 % of patients continues to have seizures despite medication with one or more antiepileptic drugs. The disease is then defined as medically refractory and some of these patients are evaluated for epilepsy surgery. Epilepsy surgery is a treatment option that can cure patients with epilepsy. In most cases, a small part of the brain is resected. Before this operation, it is very important to define the area where the seizures starts, called the seizure onset zone. There are many different methods such as MRI (structural lesion), EEG (electrical activity), PET (metabolism) and SPECT (blood flow) used to localize this zone. Sometimes invasive methods like intracranial EEG must be used. Combined EEG-fMRI allow mapping of BOLD (blood oxygen level dependent) signal changes correlated to epileptiform discharges in the EEG. The electrical discharges in the cortex that is typical for epilepsy correlates to localized changes

in oxygen consumption and blood flow, which alters the BOLD-signal (the hemodynamic response function). The EEG defines the time for epileptiform discharges and fMRI is recorded continuously. Studies in other centers have concluded that this method can accurately localize the seizure onset zone. It is difficult to record EEG of good quality in the MR scanner because of artifacts induced by the magnetic and electromagnetic fields. Special equipment is necessary to be successful in recording a good quality EEG in the MR scanner. CMIV and The Department of Clinical Neurophysiology at the University Hospital in Linköping has the equipment for recording of EEG in the MR scanner.

Method: With an MR safe EEG cap, EEG is recorded with 64 electrodes during fMRI scanning (3T) for 30 minutes. Offline analysis of EEG to identify epileptiform discharges and timing of these events. Analysis of fMRI data with different hemodynamic response functions in relation to the events in EEG. This gives maps with the strongest BOLD changes.

Material: 20 adult patients with medically refractory focal epilepsy who are evaluated for epilepsy surgery are included in the study. The collection of data started in September 2019 and so far, 19 patients with epilepsy have been examined.

Results: The EEG has been examined and in seven patient there were sufficient amount epileptiform activity during scanning to analyze the correlation between epileptiform activity and BOLD-changes. Preliminary results from two patients are shown in figure 1 and 2.

MRI Neurology Modeling
AI/Data analytics

Project information

PROJECT NAME

Localization of Seizure Onset Zone in Focal Epilepsy

PROJECT LEADER

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MAIN PROJECT PARTICIPANTS

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GRANTS

Sinnescentrum, Region Östergötland Föreningen Margarethahemmet

KEY PUBLICATIONS

Pittau F, Dubeau F, Gotman J. Contribution of EEG/fMRI to the definition of the epileptic focus. *Neurology* 2012;78:1479-1487.
 Khoo HM, Hao Y, von Ellenrieder N et al. The hemodynamic response to interictal epileptic discharges localizes the seizure-onset zone. *Epilepsia* 2017;58(5):811-823.
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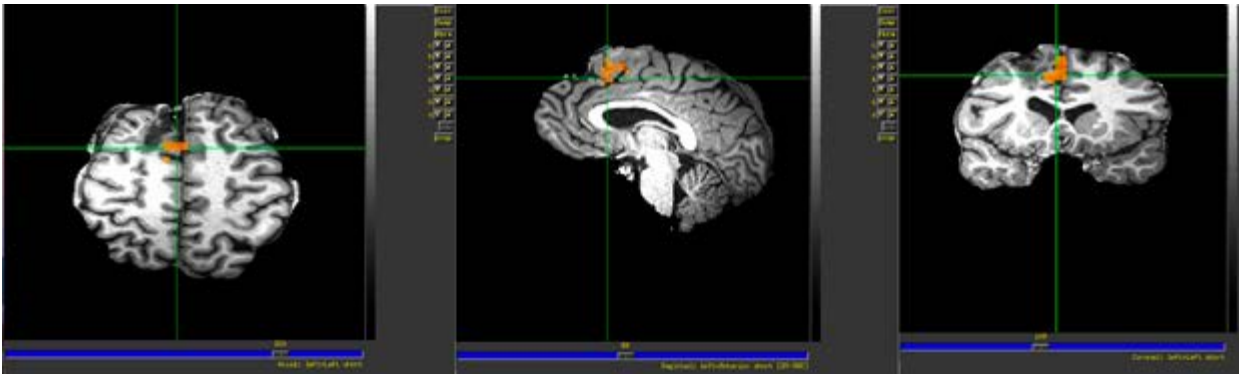


Figure 1. The most significant BOLD-changes correlated to epileptiform activity in a patient with epilepsy that was earlier operated for focal cortical dysplasia in the left frontal lobe.

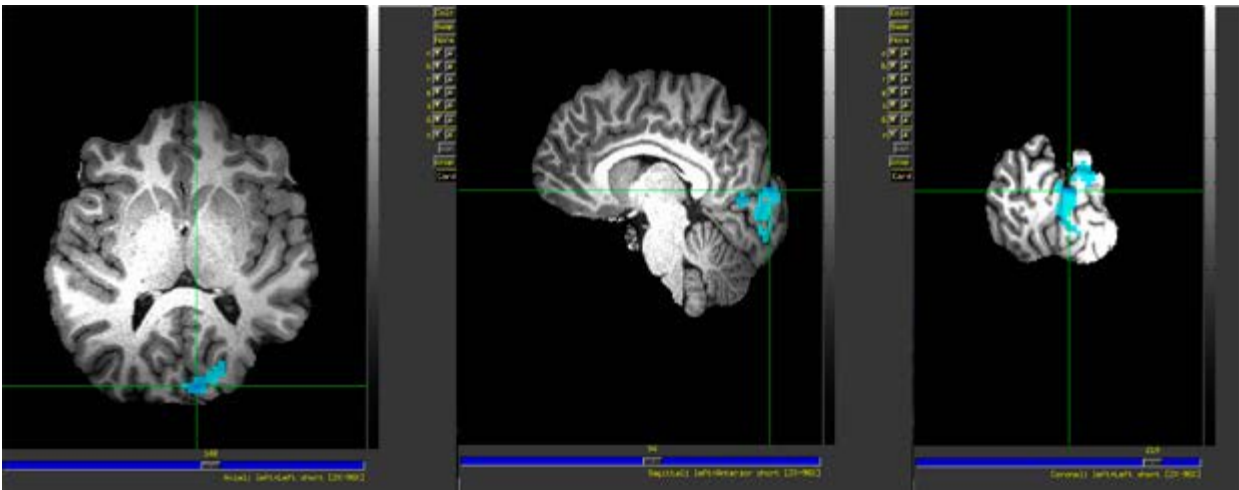


Figure 2. The most significant BOLD-changes correlated to epileptiform activity in a patient with epilepsy that was earlier operated for focal cortical dysplasia in the right occipital lobe.



Patient and nurses by the MR scanner.

Emotion Regulation in PTSD

Posttraumatic stress disorder (PTSD) is a debilitating condition that occurs in a subset of people after exposure to a life-threatening event or threat of serious bodily injury. The course of PTSD is chronic and often severe, with many patients taking decades to achieve remission, and remission is frequently incomplete. New, more effective treatments for PTSD are desperately needed. The goal of our current study is to meet this need by evaluating a novel treatment strategy for PTSD patients.

In this RCT, we are evaluating a novel endocannabinoid compound (JNJ-42165279) that elevates levels of the endocannabinoid anandamide (AEA), the body's own cannabis-like substance. Our goal is to use this compound together with internet-delivered cognitive behavioral therapy to improve treatment outcomes for PTSD patients. A total of 90 patients will be recruited and rand-

omized under double-blind conditions to receive JNJ-42165279 or placebo daily for a total of 12 weeks. Following the first 4 weeks of pharmacological treatment, patients will come in to complete an fMRI scan consisting of an emotion regulation task to assess emotional reactions and the ability to regulate them. Subsequently, patients will continue taking medication and also undergo an 8-week internet-delivered cognitive behavioral therapy. We will then determine whether the effect of JNJ-42165279 on neural indices of emotion regulation at 4 weeks of treatment is predictive of a reduction in symptoms following the 8-week cognitive behavioral therapy. Together, this study will provide new insights into the role of the endocannabinoid system in PTSD and may provide a completely novel treatment option for this patient population.

MRI **Neurology**

Project information

PROJECT NAME

Emotion Regulation in PTSD

PROJECT LEADER

Leah Mayo, CSAN

MAIN PROJECT PARTICIPANTS

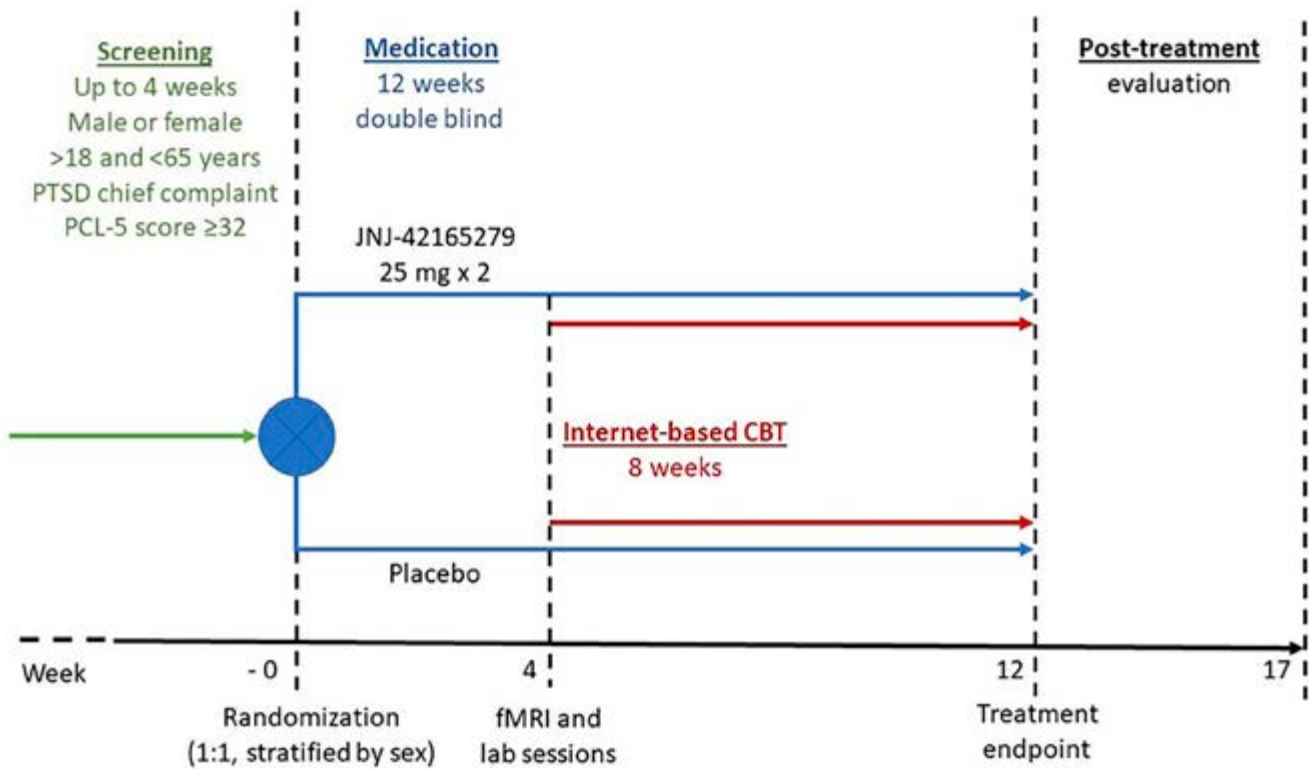
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GRANTS

Swedish Research Council (Vetenskapsrådet) Establishment Grant 2019-01887 (2020-2024)

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Study design

The Behavioral and Neural Mechanisms of Alcohol Choice Preference

Alcohol addiction has a deleterious impact on individuals and on society. Alcohol dependent patients often face interpersonal, economic and health issues. These issues strongly affect patients' quality of life and are themselves a major cause of relapse, setting up a vicious circle. Despite these negative consequences, alcohol dependent patients continue to consume alcohol and prioritize alcohol over healthy rewards, features that set alcoholism apart from recreational alcohol use. It is therefore important to characterize in humans the mechanisms behind the decision making that results in choosing alcohol at the expense of valuable alternative rewards.

Research in rodents has shown that the concurrent availability of alternative valuable rewards is a crucial determinant of drug related behaviors, such as drug seeking and taking. Our Center has identified in rodents that self-administration of alcohol is markedly reduced when a high value alternative reward (e.g. sweet solution) is concurrently present (Augier et al. 2018, Science). When the sweet solution was available, only 15% of rodents continued to choose alcohol, a percentage which is similar to human alcoholism rates. The phenotype of the alcohol-choosing rats was associated with decreased expression of γ -aminobutyric acid (GABA) transporter GAT-3 in the central nucleus of amygdala.

This project builds on the evidence in rodents reviewed above. It aims to characterize the behavioral and neural correlates of alcohol choice preference in humans using two paradigms in two populations of light and heavy social drinkers (N=60 in total). The first paradigm, the "Concurrent Choice Alcohol Food (CCAF)" task, modified from Hogarth et al. 2018, investigates the decision-making process behind choosing between two mutually exclusive alternative rewards presented concurrently (Figure 1). The second paradigm, the "Alcohol Food Incentive Delay (AFID) task", is specifically tailored to probe reward-related neural processes (Grodin et al., 2018, BC:CNNI). A secondary aim of this project is to investigate the mechanisms behind the interpersonal issues that people with alcohol addiction often face. Our Center has shown a negative bias in processing social situations in a population of adolescents who engage in nonsuicidal self-injury (NSSI), a problem behavior that is associated with increased risk of developing substance use disorders (Perini et al. 2019, EClinical Medicine). Building from these results, we will use the Online Game task to determine whether individuals who engage in heavy drinking might present a negative bias in perceiving social judgment from others.

MRI Neurology

Project information

PROJECT NAME

The Behavioral and Neural Mechanisms of Alcohol Choice Preference

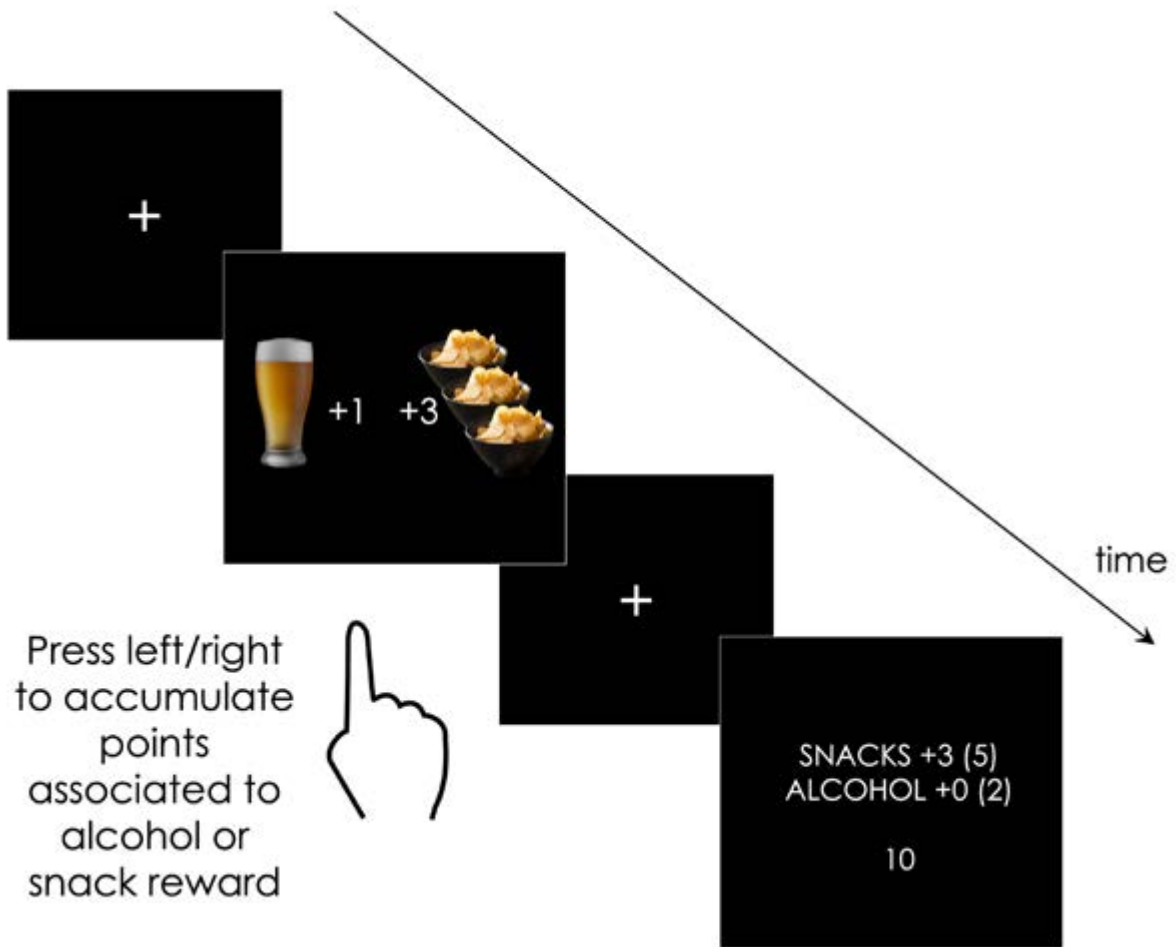
PROJECT LEADER

Markus Heilig, Department of Biomedical and Clinical Sciences, Center for Social and Affective Neuroscience

MAIN PROJECT PARTICIPANTS

Irene Perini, Hanna Karlsson, Sarah Gustavson, Oliwer Kenell

Concurrent Choice Alcohol Food (CCAF)



Concurrent Choice Alcohol Food (CCAF) design. In this task, participants are instructed to accumulate points associated with alcohol or snacks. The points can then later be redeemed at the end of the session, with the respective reward.

Experiencing the Self through Touch

Somatosensation and interoception are necessary for the establishment of the bodily self. To develop a functional bodily self, humans need to identify the boundaries of their body and differentiate "self" from "others". Disturbed tactile self-other-distinction might affect the establishment of the bodily self, and even of the higher-order self. Such dysfunctional self-processes constitute a core symptom in many psychiatric disorders, e.g. in schizophrenia.

Here, we study the neural mechanisms of bodily self-perception and its dysfunction, focusing on three questions:

I) Using the novel method of simultaneous functional imaging of the cortex and the spinal cord: How do the spinal cord and the cortex interact to differentiate between self and other?

II) Using ketamine to induce transient dissociative symptoms during functional imaging of healthy participants: Does a reduction in the experienced boundary of the bodily self alter tactile self-other-distinction?

III) Using functional imaging and somatosensory evoked potentials: Is self-other-distinction reduced in patients with schizophrenia? If so, can signs of this be found at the spinal cord level and does the reduction relate to dysfunctional self-processes?

This project lays the groundwork for the development of novel interventions for treating the symptom domain of the bodily self, which is affected in many psychiatric disorders, and substantially enhances our understanding of the sense of self.

MRI **Neurology** **Imaging Biomarkers**

Project information

PROJECT NAME

Experiencing the Self through Touch

PROJECT LEADER

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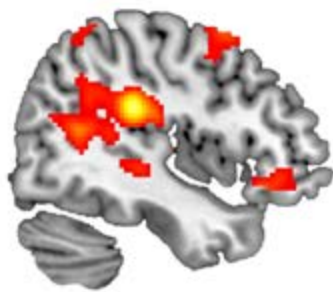
Vetenskapsrådet startbidrag
Åke Wiberg stiftelse
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KEY PUBLICATIONS

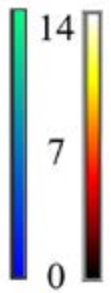
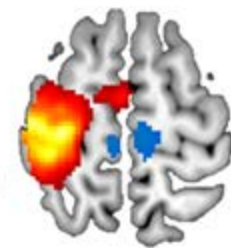
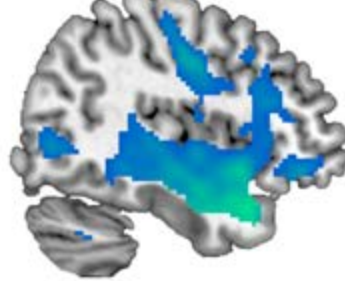
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A) Other-touch



B) Self-touch



Detection and Neurological Effects of Manganese

Manganese (Mn) is a metal that occurs naturally in our environment. It is an essential substance that is part of several important enzyme systems for example it participates in body energy conversion and also protects against free radicals. Among the general population the food is the main source of exposure to manganese.

In working environment, exposure to manganese-containing dust and smoke occur mainly during welding, but also within the steel and smelting industry. Via inhalation of dust and smoke, manganese can be deposited in the respiratory tract where some is taken up and transported further into the body.

Manganese can pass the barriers that protect the brain and accumulate in specific areas of the brain, e.g. the basal ganglia. Welders examined with MRI have previously shown accumulation of manganese in the brain. When exposure is terminated, manganese is only gradually excreted and the concentration in the body is returned to natural equilibrium.

Workers that in their profession are exposed to high levels of manganese in the air (> 1 mg/m³) during a long period risk to be subject to manganism, a serious condition which is very similar to Parkinson's disease. Several studies have shown potentially harmful effects on the central nervous system such as influence on motor and cognitive func-

tions, increased tremor and an increased frequency of neuropsychiatric symptoms among groups of manganese exposed workers at significantly lower exposure levels than 1 mg/m³.

In many welding methods the air exposure is at levels where negative effects on the central nervous system have been demonstrated and there are indications that these effects may persist even when the exposure ceases. Compared to smelters, welders have much more manganese accumulated in the basal ganglia and thalamus and greater influence on neurological transmitter substances. This is despite the fact that traditional exposure measures such as the manganese concentration in air were 10 times lower for welders. The exposure form of manganese (particle size, and the chemical compound) therefore seems to have great significance for which areas of the brain are affected.

This project aims to investigate the effects of manganese accumulation primarily in the subcortical tissues and the cognitive effects thereof, in the brains of welders with certain types of occupational exposure. The protocol involves quantitative MR including spectral editing for detecting neurotransmitters, diffusion measurements and resting state fMRI. The complete project also involves a large range of occupational measurements including blood panels.

MRI **Neurology** **Acquisition**
Imaging Biomarkers

Project information

PROJECT NAME

Detection and Neurological Effects of Manganese (Mn) in the Brain of Welders and Other Subjects (MANGAN)

PROJECT LEADER

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GRANTS

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Welding in progress.

SouthEast Sweden Neuroinflammation Cohort

Multiple Sclerosis (MS) is a chronic autoimmune disease in the central nervous system (CNS). MS often appears in young adulthood and lead to lifelong consequences for the individual, family and society.

This complex disease has both inflammatory and degenerative features even at early stages and the clinical picture may vary substantially between patients and over time. A well-known aspect of the disease is that it develops long before symptoms show and it is likely that the brain initially has a better capacity to compensate for pathological changes than in later disease stages. Accordingly, early treatment has shown to be crucial for long-term prognosis.

There are an increasing number of immunomodulatory treatments available for inflammatory active MS, but guidelines on how these potent therapies should be used are often lacking as are data on long-term outcome and side-effects of these drugs.

Taken together, there is consequently a need for reliable non-invasive methods to describe MS pathology in more detail and to develop and evaluate novel imaging biomarkers for prognosticating the disease course and monitoring treatment.

MS brain lesions cannot be detected by conventional non-quantitative MR. This advocate a shift from conventional MRI to the use of more advanced MR-methods including quantitative MRI methods (qMRI). qMRI can be used for volume determination of grey and white matter, cerebrospinal fluid (CSF) and automatic lesion measurements in MS. Such accurate measures are critical when determining the overall atrophy of the brain. More specifically, qMRI can be used to create myelin concentrations maps that may be useful in determining the level of disease progression, at a regional or global level. We have developed a suitable mathematical model for mapping myelin, based on our time-efficient qMRI-technique.

The MR methods used in this project are combined with extended blood and CSF profiles for determining tissue degradation products and immunological parameters. A better definition of pathogenic mechanisms may characterize subtypes of MS and identify new targets for both prediction and treatment.

MRI **Neurology** **Acquisition**
Imaging Biomarkers

Project information

PROJECT NAME

SouthEast Sweden Neuroinflammation Cohort (SESNIC)

PROJECT LEADER

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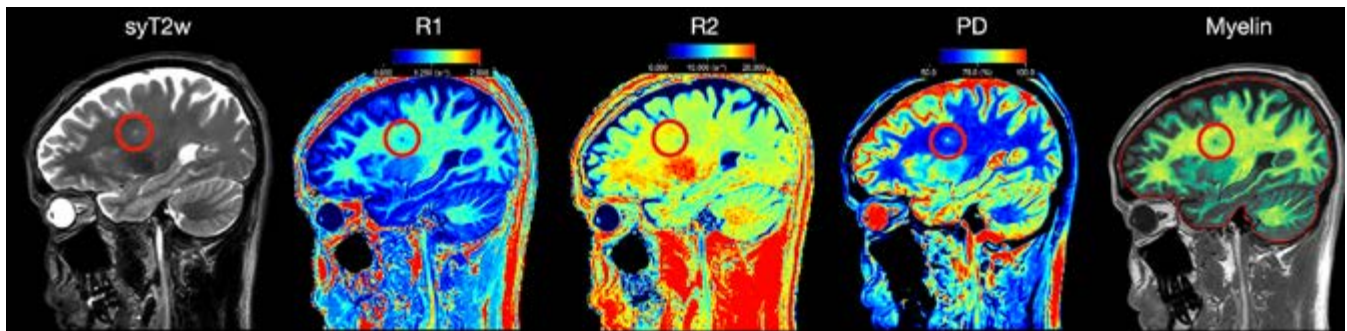
Swedish Research Council
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QALAS images of a 33 years old MS patient. In the red circle a lesion showing low myelin content. All images are calculated from a single acquisition of 6 min

Quantitative MRI on Brain Tumors

Standard treatment for a high-grade brain tumor glioblastoma consists of radical surgical resection, followed by adjuvant radiation- and chemotherapy with temozolomide. Despite this, tumor recurrence is expected in these patients, and the median survival is therefore only 15 months. Moreover, up to 30% of the patients develop 'pseudoprogression' due to a treatment-related effect from chemo- and radiation therapy that mimics tumor recurrence on conventional MRI.

Pseudoprogression is often correlated with an effective treatment response and confirms that the planned adjuvant chemotherapy should be continued. In contrast, true tumor progression requires a change in therapy. Histopathological analysis is the gold standard for correct diagnosis. However, this will require a biopsy of the suspected lesion, which increases both morbidity and mortality, apart from increased healthcare costs for the treatment. Thus, the need for a reliable non-invasive imaging method for distinguishing pseudoprogression from tumor progression is essential.

One promising novel method is 'Chemical Exchange Saturation Transfer' (CEST) imaging, a new MRI contrast approach in which natural compounds containing exchangeable protons are selectively saturated.

CEST is a merge of MR-Spectroscopy (MRS) and MRI (Imaging), whereas quantitative MRI (qMRI) is a pure imaging technique. Following frequency specific saturation, selective saturation of magnetization is transferred, and subsequently detected indirectly via the water signal with a greatly enhanced sensitivity. This indirect and amplified detection of a tumor associated molecular species can be used to increase spatial, or temporal resolution of the imaging experiment. Thus, 'Amide Proton Transfer-CEST' (APT-CEST) can potentially be used as an imaging biomarker for distinguishing pseudoprogression from true progression in glioma patients. The aim of this project is therefore to determine if APT-CEST, separately, or in combination with qMRI, is able to distinguish tumor recurrence from pseudoprogression.

MRI | Neurology | Oncology | Metabolism
Acquisition | Imaging Biomarkers

Project information

PROJECT NAME

Investigating Neurological Disease Using Amino Proton Transfer Chemical Exchange Saturation Transfer (indCEST)

PROJECT LEADER

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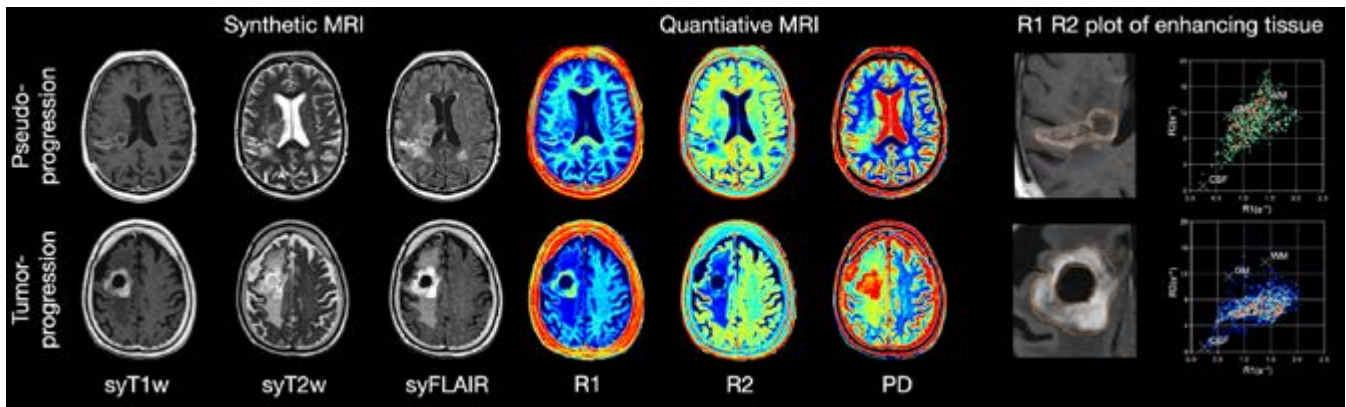
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Jan B. M. Warntjes, Ida Blystad, Anders Tisell, EM Larsson. Synthesizing a Contrast-Enhancement Map in Patients with High-Grade Gliomas Based on a Postcontrast MR Imaging Quantification Only. 2018 *AJNR*.



Images calculated for the 6 minutes qMRI examination. In the top row data from of a patient with pseudoprogression, in the bottom row data from a patient with tumor-progression.

Developing 3D qMRI

Conventional MRI-examinations relies on the neuroradiologist ability to recognise subtle patterns by visual assessment. A new approach is qMRI. The underlying contrast mechanism in MR are quantitatively measured by relaxometry, using qMRI, in contrast to the conventional use which just results in image grey-scale image contrast.

Previously the 2D qMRI method QRAPMASTER was implemented on CMIV and is now clinical available for all vendors worldwide. We have so far showed that qMRI can potentially detect tumor infiltration invisible on conventional MRI. We have also shown that MR-contrast agent uptake can quantitatively be measured using qMRI images post-GD potentially giving higher sensitivity of infiltrating tumor

In this project, the aims were to further develop the qMRI method and implement a 3D qMRI method QALAS (3D-QuAntification using an interleaved Look-locker Acquisition Sequence with T2 preparation pulse) on the Siemens MR systems.

A 3D qMRI method with a whole brain coverage and isotropic resolution will enable us to analyse the brain images in the three anatomical planes (axial, coronal, sagittal), as well as providing greater detail of the tissue structure due to the higher resolution. This will hopefully enable a better delineation of the tumor before surgery and provide quantitative tissue information which can help the neuroradiologist, neurooncologist, and neurosurgeon in the treatment decisions of these difficult cases.

MRI **Neurology** **Acquisition**

Project information

PROJECT NAME

Implementing QALAS on Siemens

PROJECT LEADER

Anders Tisell, Department of Medical and Health Sciences, Division of Radiological Sciences

MAIN PROJECT PARTICIPANTS

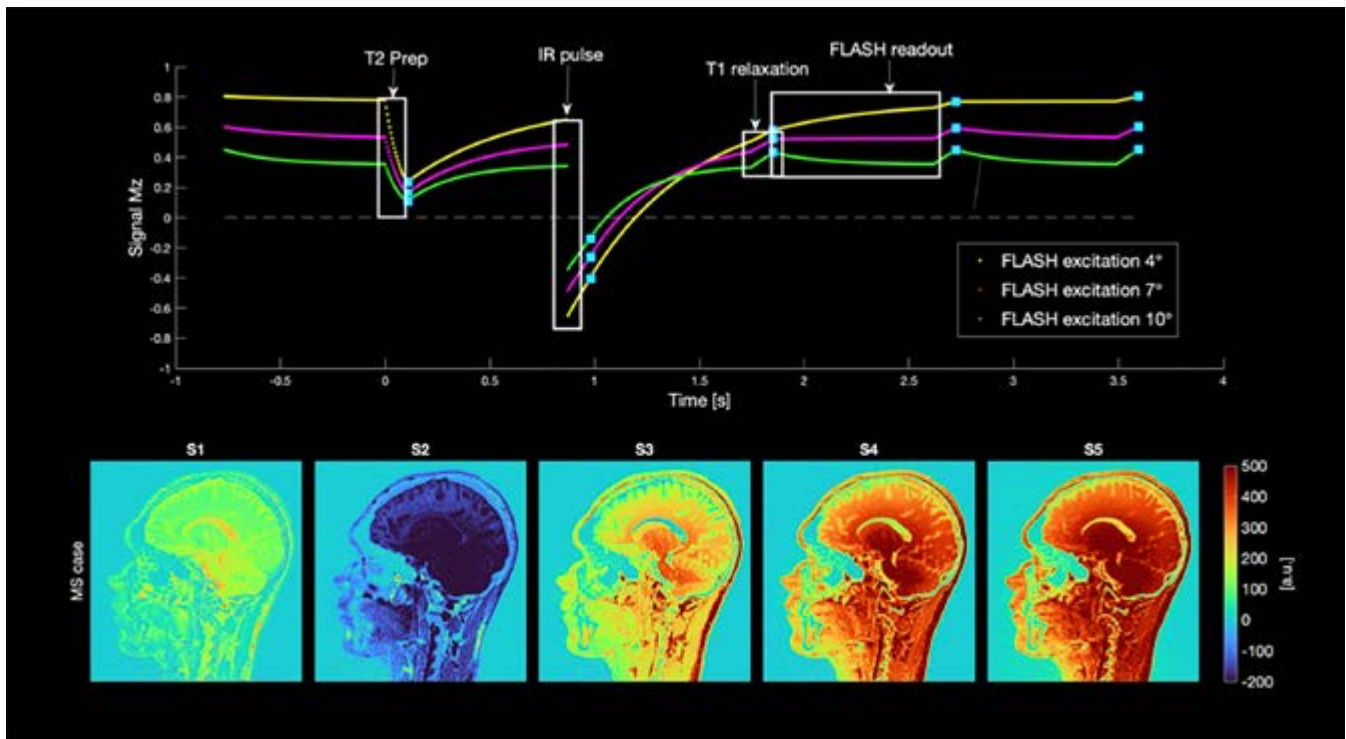
Peter Lundberg, Frederik Testud, Marcel Wraantjes

GRANTS

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KEY PUBLICATIONS

Anders Tisell, Peter Lundberg, Marcel Wraantjes, Frederik Testud. 3D Quantitative MRI of the Brain: Effects of B1 Inhomogeneity in 3D-QALAS. ISMRM; 2021.



QALAS sequence model and data: (top panel) the signal model for the QALAS sequence is shown with $M = 1$, describing the effect of different flip angles (different colours), and the corresponding measured data. (bottom) QALAS data from an MS patient showing the signal maps for the individual dynamics.

Abdominal Synthetic MRI

Synthetic MRI is a new method for producing MRI images, where T1, T2 and PD weighted images can be calculated from a single MRI acquisition, instead of 3 different acquisitions as made today. The method also provides the opportunity to quantify T1, T2 and PD relaxation times, which are tissue-specific parameters, which can theoretically be used to distinguish different tissues in the body. With this technology, it is thus possible to differentiate quantitatively between tissues (tissue characterization) and pathology (healthy or diseased tissue).

In this project we want to investigate whether synthetic MRI can increase the detection ability for certain cancers within the abdomen; whether synthetic MRI can be used to increase the confidence of treatment results after various chemotherapies and local treatments (RF and TACE treatments), and whether synthetic MRI can increase the ability to distinguish between scar tissue and cancer tissue.

Hypothesis: Quantitative MRI scans provide added value in the detection, follow-up, treatment planning and evaluation of cancers and other diseases within the abdomen and the rest of the body.

Method: A quantitative sequence of 7 minutes will be added to standard clinical examinations (MR cervix, MR prostate and MR rectum).

In the MRI rectum follow up, we will also plan for another MRI examination including a quantitative sequence just before surgery.

The quantitative information from tumour and plain tissue will be correlated with different clinical parameters, as well as probability assessments of tumor disease (i.e. PI-RADS, Li-RADS).

Knowledge gains: If the quantitative information from synthetic MRI sequences is stable and reliable, this information can possibly be used in radiation planning, prediction of treatment results, detection and segmentation of MRI images and more secure separation of healthy from pathological tissue.

MRI **Oncology** **Gastrointestinal**
Acquisition **Imaging Biomarkers**

Project information

PROJECT NAME

Implementation of Synthetic MRI in the Abdomen

PROJECT LEADER

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MAIN PROJECT PARTICIPANTS

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GRANTS

LFoU
Forsknings- och stipendieförvaltningen

KEY PUBLICATIONS

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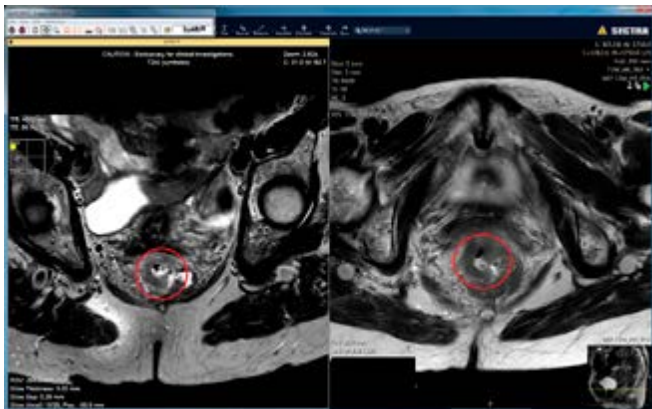


Image 1: Comparison of image quality of T2 weighted images obtained by the original MR sequence (to the right) and the synthetic T2 weighted image with the same TR and TE as the clinical sequence (to the left). The circle shows the rectal cancer.

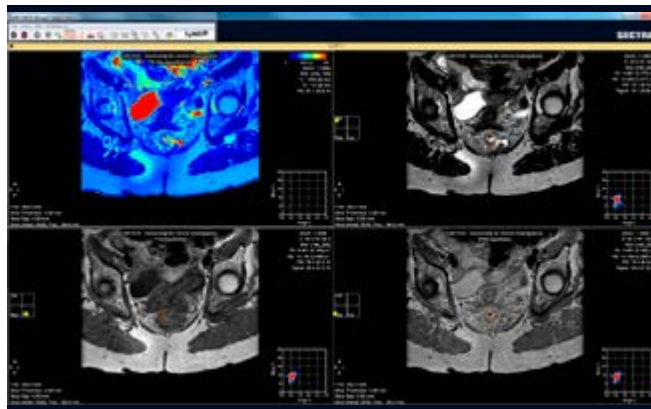


Image 2: Synthetic MRI acquisition of a rectal cancer with a quantitative T2 map (upper left), T2 weighted images (upper right), T1 weighted images (lower left) and PD weighted images (lower right). The tumour was outlined with a freehand ROI tool. The quantitative information of these ROIs is shown as R1/R2 plots.



Image 3: Comparison of image quality of T2 weighted images obtained by the original MR sequence (to the left) and the synthetic T2 weighted image with the same TR and TE as the clinical sequence (to the right). The circle shows the prostate cancer (PI-RADS 5).



Image 4: Synthetic MRI acquisition of a prostate cancer with a quantitative T2 map (upper left), T2 weighted images (upper right), T1 weighted images (lower left) and PD weighted images (lower right). The tumour was outlined with a freehand ROI tool. The quantitative information of these ROIs is shown as R1/R2 plots.

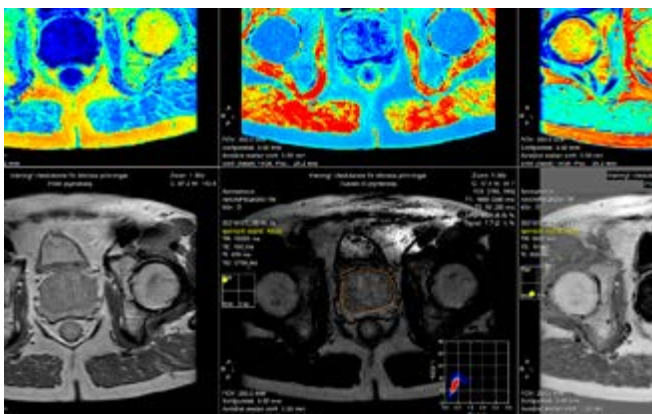


Image 5: Segmentet transitional zone of a prostate in T2 weighted images (developed from a synthetic MRI scan) with the R1 and R2 values in the insert diagram, as well as the color mapped quantitative images from the synthetic scan.

PhDAC

Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal malignancies, and is expected to be the second most common cause of cancer related death within short. Approximately 50 % of the newly diagnosed patients present with metastasized disease and locoregional disease, respectively. The latter group can be further divided into resectable, borderline resectable and locally advanced PDAC depending mainly on extent of tumour vessel involvement (e.g. coeliac trunk, superior mesenteric artery and hepatic artery). The assessment of these parameters is today done with CT images taken at different contrast phases with conventional CT machines. The

restricted resolution of today's CT machines makes the evaluation of certain parameters, as for example the involvement of vessel structures uncertain. In this project we want to evaluate if the increased resolution of the Naeotom photon counting CT might be able to increase the reliability of overgrowth information and by that enhance the selection process for surgical or oncological therapy. We will also study if the increased quantitative information from the Naeotom CT together with radiomics information and AI information might be used as an imaging biomarker for the prediction of possible therapy outcomes.

Computed Tomography	Oncology
Gastrointestinal	Acquisition
AI/Data analytics	Imaging Biomarkers

Project information

PROJECT NAME

Photon Counting in Pancreatic Ductal AdenoCarcinoma

PROJECT LEADER

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MAIN PROJECT PARTICIPANTS

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GRANTS

RFoU (2022)

KEY PUBLICATIONS

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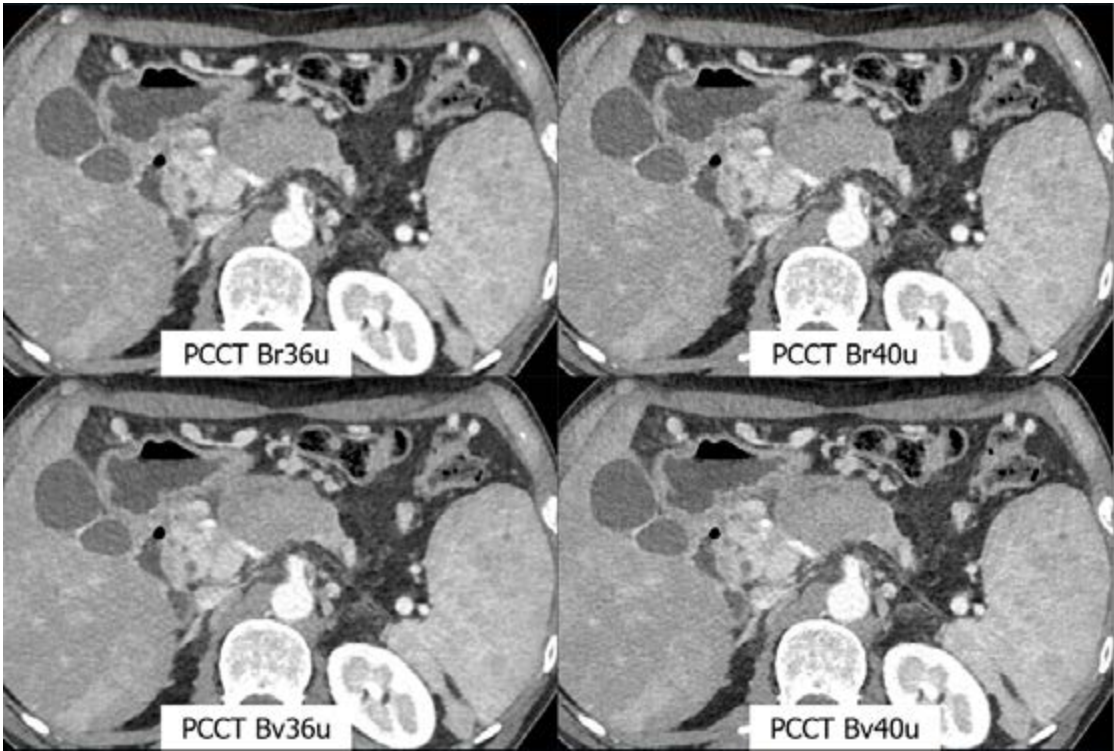


Figure 1. Reconstructions of a pancreatic tumor with a photon counting CT at different kernels.

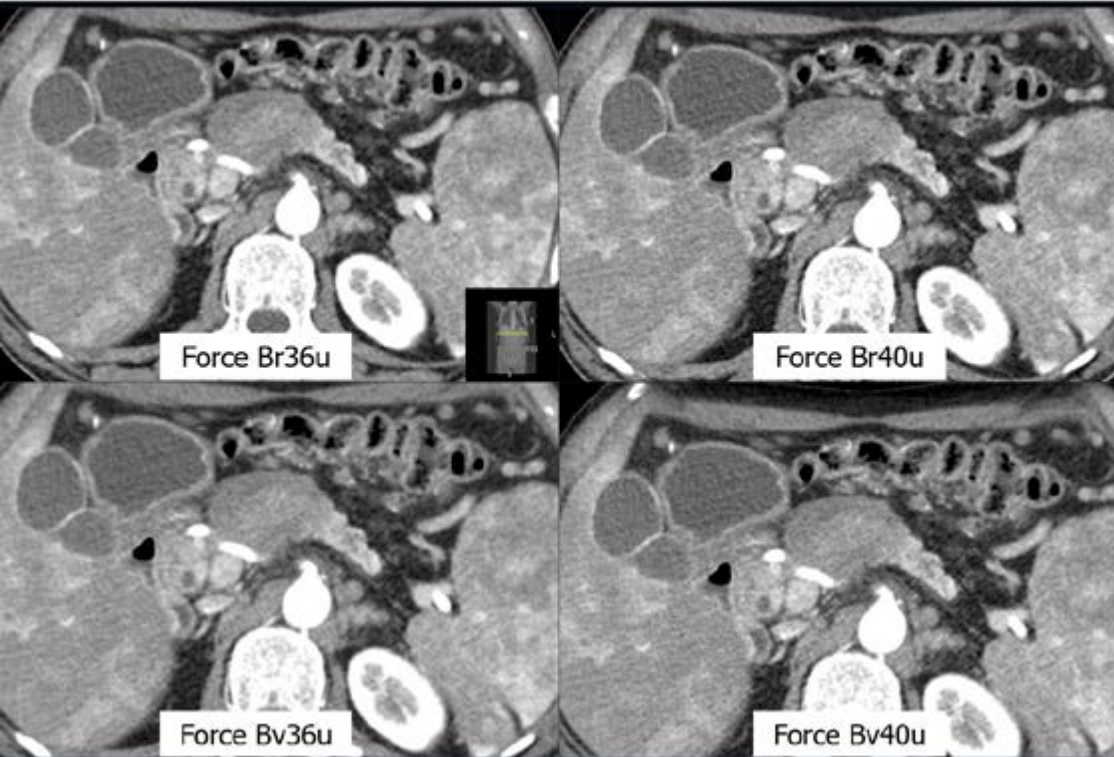


Figure 2. Reconstructions of a pancreatic tumor with a regular CT machine (Siemens Somatom Force) at different kernels.

Semiautomatic Liver Volume Determination and Segmentation

A common trait of diffuse liver diseases is that they may lead to the formation of fibrosis, inflammation and ultimately, cirrhosis. Since the liver can regenerate and thus compensate for some damage, liver diseases are often not discovered until at a late stage when there is a loss of liver function. At this stage liver transplantation may be the only available treatment. Patients with malignant liver tumors are increasingly surgically treated, removing the part(s) of the liver with tumors. Measuring the expected liver volume that remains after resection has become standard procedure. To improve treatment planning, adding an evaluation of liver function to the liver volume measurements is desired.

Magnetic resonance imaging (MRI) offers a noninvasive method to monitor liver function using liver specific contrast agents. In developing system biology models for describing liver function, it is important to estimate the total liver volume and preferably also liver segment volumes. Although tools for liver segmentation using datasets from computed tomography have become easily available, useful applications aimed at MRI datasets are lacking. A sub-project within the Liver Function Evaluation project was formed to evaluate available software to measure 3D volumes of late hepatobiliary phase datasets from examinations of patients with diffuse liver disease.

The first objective of this study is to compare the measured total liver volumes from several semi-automatic liver segmentation tools and a fully automatic application (developed in-house), with manual, detailed segmentation in a separate software environment serving as “ground truth”.

Preliminary results show that a fully automatic segmentation is feasible and has a precision that is sufficient for clinical use. Both semi-automatic applications were found accurate but have quite different user interfaces, sometimes complicating the measurement task.

Another objective is to provide the total liver measurements needed for modeling the individual liver function estimates in quantitative MRI studies (e.g., LIFE and HIFI), and also introduce the means for segment-based liver function modeling.

In 2016 the in-house application was extended to include segmentation of the liver into the classical Couinaud segments, producing 3D masks defining the shape and volume of each segment. This feature is currently not readily available for MRI datasets in clinical segmentation or surgery planning applications, which rely on CT studies. The measurement of liver segmental volumes will permit segmental liver function assessment in the NILB, LIFE and HIFI studies. In 2018, the project began further exploration and testing of new algorithms for automatic segmentation.

MRI **Gastrointestinal** **AI/Data analytics**
Visualization

Project information

PROJECT NAME

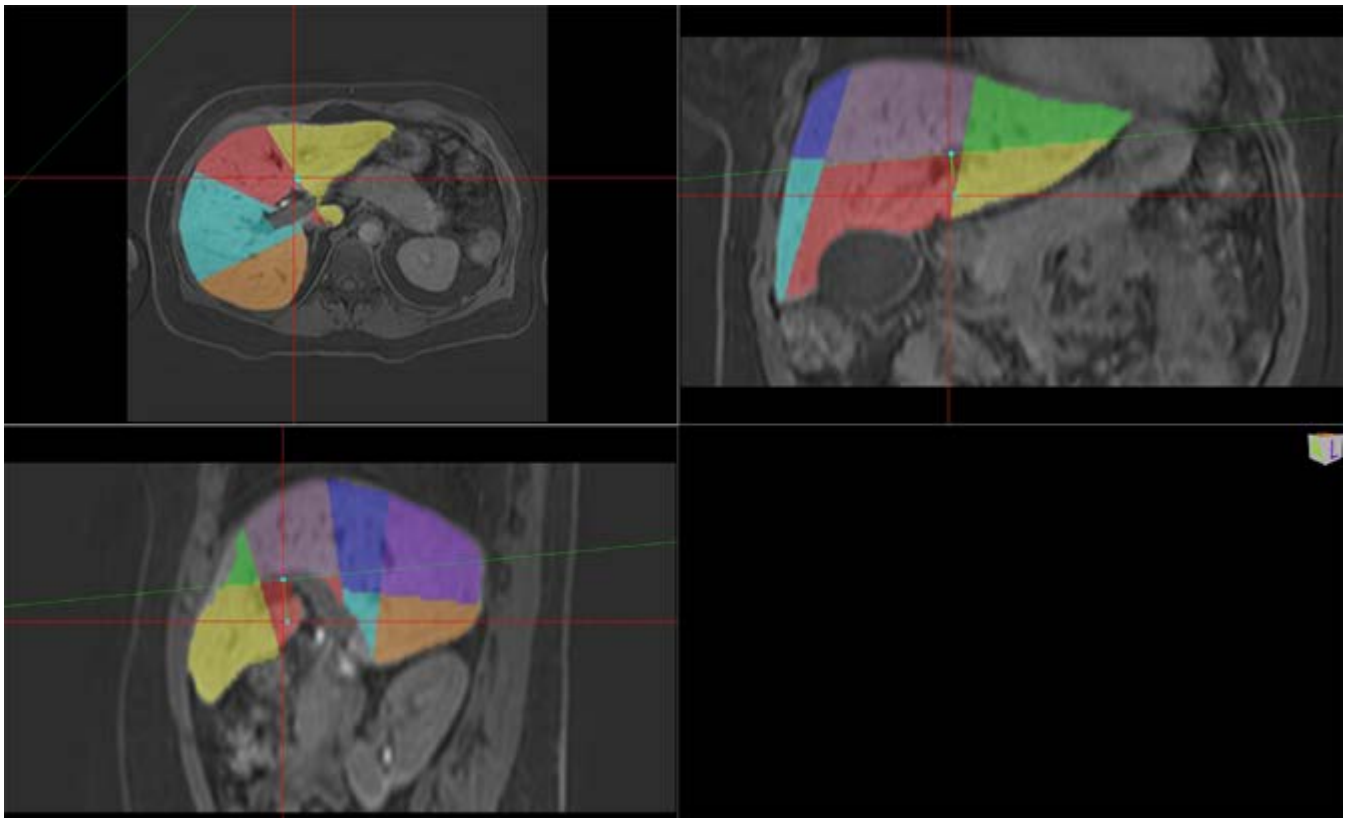
Semiautomatic Liver Volume Determination and Segmentation

PROJECT LEADER

Nils Dahlström, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine, Unit of Radiological Sciences

MAIN PROJECT PARTICIPANTS

Mikael Forsgren, Chunliang Wang, Amir Razavi, Markus Karlsson, Peter Lundberg



Sample view of liver segmentation into Couinaud segments using one of the software applications studied, MiaLite 2.0 (research software developed by Chunliang Wang, CMIV)

Optimizing Hepatobiliary MRI in Metastatic Liver Disease

Colorectal cancer is the third most common form of cancer worldwide. Though mortality has been relatively stable in the last decade, significant improvements have been achieved in terms of long-term survival. Key to improved survival is the detection of metastatic disease as early and completely as possible. In colorectal cancer, the by far most common site of metastatic disease is the liver, and the best method to detect metastases in this organ is MRI with hepatobiliary contrast media. However, the complexity of the examination, long scanning times, challenging interpretation and overall high costs involved have severely limited the use of this modality in cancer patients and restricted it mainly to radiology departments of major hospitals or university hospitals.

We aim to show that a shortened version of the regular MRI protocol with liver specific contrast can preserve the same level of sensitivity for metastases as the complete protocol while greatly reducing complexity and scanning times. In-camera time is reduced from 60–75 minutes to 12–15 minutes and most of the technical challenges in acquisition will be eliminated. This will enable more patients to be evaluated with MR without the need for more equipment. It will also open the examination for acquisition at minor hospitals that normally would

refrain from using the more complex protocol, further increasing capacity.

As the shortened protocol is focused on detection (sensitivity) rather than differential diagnosis (specificity), a drop in specificity is expected and will be measured. However, in real life, clinical decision making happens always in the context of all available examinations, including priors, patient history and clinical data.

It is the aim of the next part of the project to study how a shortened protocol will affect the clinical decision making and treatment process of cancer patients. The patients will be presented in a simulated multidisciplinary team meeting, using all relevant clinical data and prior examinations. It will evaluate if clinical management of the patient will actually differ when using either a complete or a shortened protocol and if implementation of such a protocol can have a negative effect on patient treatment in form of e.g., unnecessary delays and additional imaging.

Finally, economic impact of using a more expensive contrast media – the only monetary factor as of now that cannot be reduced – will be evaluated. In the last part, we will study if large scale introduction of such a method would be a financially viable and sustainable option for the public health service.

MRI **Gastrointestinal** **Visualization**

Project information

PROJECT NAME

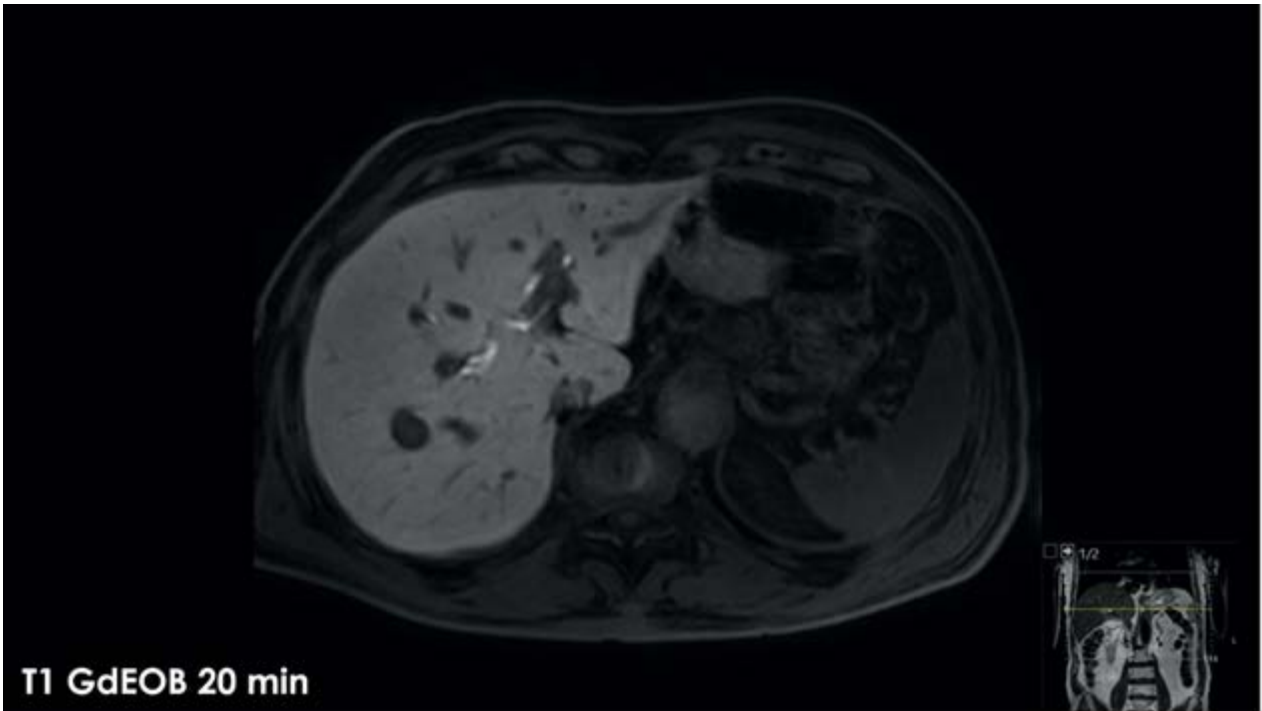
LIVERMET

PROJECT LEADER

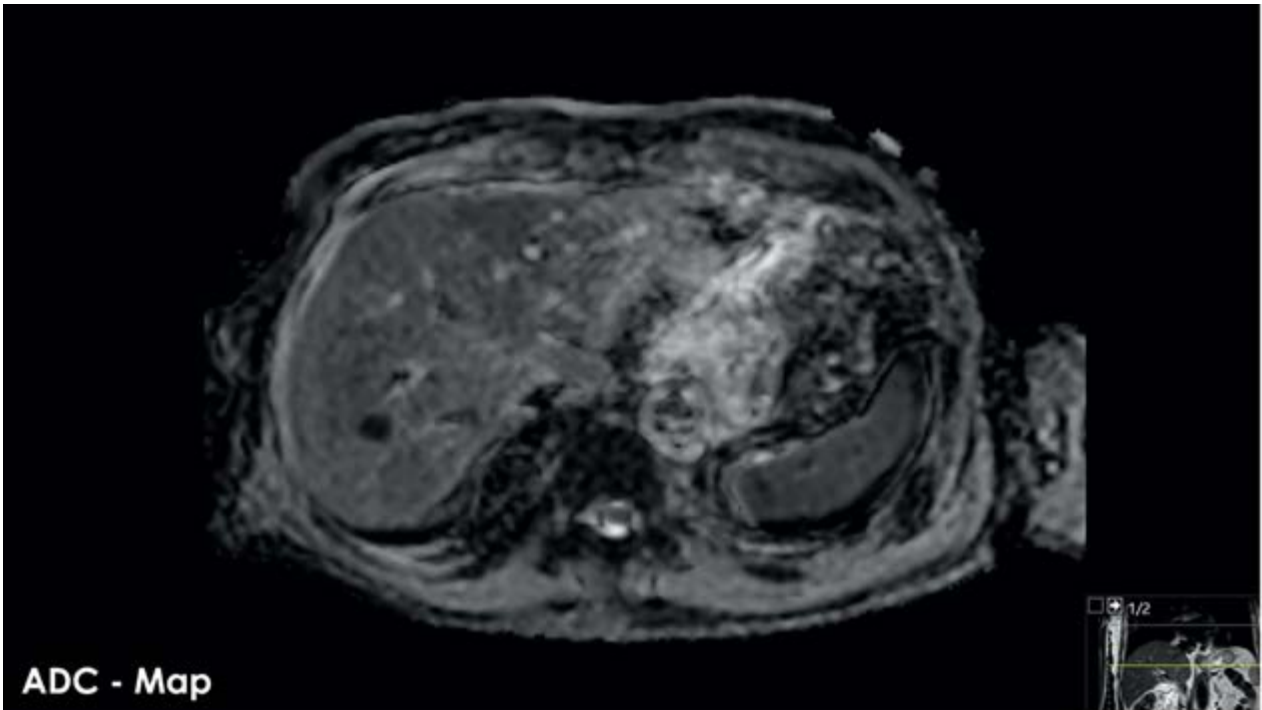
Nils Dahlström, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine, Unit of Radiological Sciences

MAIN PROJECT PARTICIPANTS

Wolf Bartholomä, Peter Lundberg, Per Sandström, Mischa Woisetschläger, Lars Valter, Johan Kihlberg, Martin Henriksson, Anders Persson, Bergthor Björnsson



Figur 1A metastasis from colorectal cancer is seen here in the right liver lobe in a T1-weighted image acquired 20 minutes after i.v. injection of the liver-specific contrast agent Gd-EOB-DTPA (Primovist®, Eovist®). Normal liver tissue and biliary ducts have high signal (light grey and white), whereas the metastasis has very low signal (black or dark grey) since it has no uptake of the contrast agent.



A metastasis from colorectal cancer is seen here in the right liver lobe in an Apparent Diffusion Coefficient (ADC) map as a round area homogenously markedly darker than the normal liver tissue.

Liver Function Evaluation

The liver is an important organ involved in vital processes as metabolism and removal of toxins. The western way of life is putting a high strain on the organ and liver diseases are consequently increasing. Liver Function Evaluation is a clinical research project that with the help of magnetic resonance (MR) will develop new methods for diagnosing liver disease. The new technology is expected to result in better treatment of diffuse liver diseases and safer liver surgery.

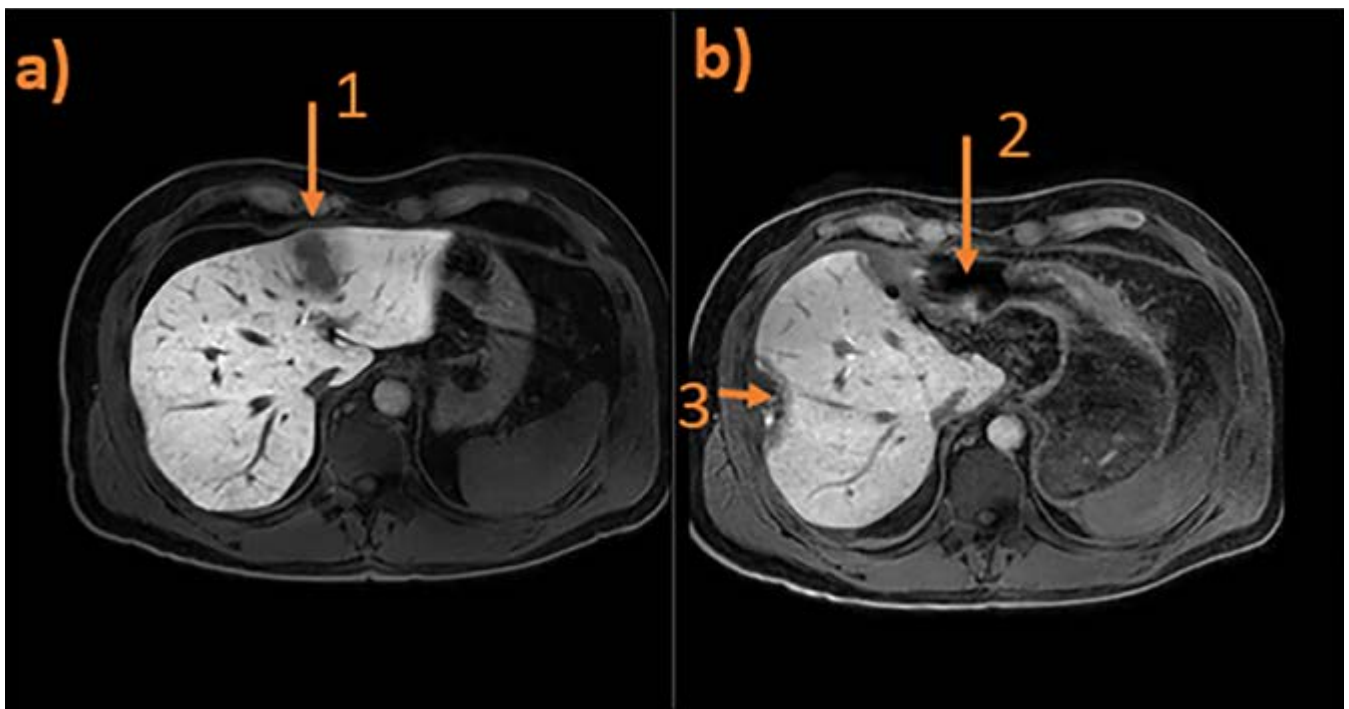
Many malignant liver diseases are diagnosed when they are in an advanced

stage and the liver may be seriously damaged. At that time, surgery or liver transplantation is often the only curable treatment option. In order for the patient to survive a liver tumor operation, 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 sized 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 be surgical candidates.

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



Example of DCE-MRI images 20 minutes after bolus gadoxetateinjection for both pre- and post resectivesurgery, for the same patient. a) Pre-surgery image, with visible metastasis at 1). b) Post-surgery image. Resection of the left liver lobule is shown at 2), and a small local resection at 3). Also, at 3) a small accumulation of gadoxetate I seen due to biliary leakage. [Simonsson, unpublished]

status as a whole compared to 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.

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. In this project multimodal methods for analyzing the liver is developed.

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 its normal elasticity. During MR mechanical 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 regions.

MRI **Gastrointestinal** **Acquisition** **Modeling** **Imaging Biomarkers**

Project information

PROJECT NAME

Liver Function Evaluation

PROJECT LEADER

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

MAIN PROJECT PARTICIPANTS

Christian Simonsson, Wolf Bartholomä, Stergios Kechagias, Mattias Ekstedt, Per Sandström, Olof Dahlqvist Leinhard, Nils Dahlström, Mikael Forsgren, Markus Karlsson, Patrik Nasr, Johan Kihlberg, Marcel Warntjes, Gunnar Cedersund, Bengt Norén, Torkel Brismar, Martin Henriksson

GRANTS

Swedish Research Council
VINNOVA
Swedish Research Council (VR/NT)
ALF (2019 - 2022)

KEY PUBLICATIONS

Karlsson M, Ekstedt M, Dahlström N, Norén B, Forsgren MF, Ignatova S, Dahlqvist Leinhard O, Kechagias S, Lundberg P (2019). Liver R2* is affected by both iron and fat: A dual biopsy-validated study of chronic liver disease. *J Magn Reson Imaging*. 2019 Jan 13. doi: 10.1002/jmri.26601.

Nasr P, Forsgren MF, Ignatova S, Dahlström N, Cedersund G, Leinhard OD, Norén B, Ekstedt M, Lundberg P, Kechagias S (2017). Using a 3% Proton Density Fat Fraction as a Cut-Off Value Increases Sensitivity of Detection of Hepatic Steatosis, Based on Results From Histopathology Analysis. *Gastroenterology*. 2017 Jul;153(1):53-55. e7. doi: 10.1053/j.gastro.2017.03.005. Epub 2017 Mar 9.

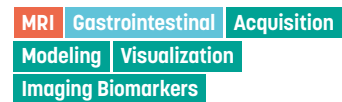
Homeyer A, Nasr P, Engel C, Kechagias S, Lundberg P, Ekstedt M, Kost H, Weiss N, Palmer T, Hahn HK, Treanor D, Lundström C (2017). Automated quantification of steatosis: agreement with stereological point counting. *Diagn Pathol*. 2017 Nov 13;12(1):80. doi: 10.1186/s13000-017-0671-y.

Assessment of Hepatic Function in Health and Disease

The long-term purpose of this project is to achieve the procedural means for a thorough understanding of the complex both short time-scale and long-time-scale events involved in liver disease, especially early stages, and to devise a both comprehensive and non-invasive method for their quantification. Major aims of the project are to allow the early detection of liver inflammation and fibrosis as proxies for chronic liver disease, and also to be able to understand the underpinnings of the consequences of fibrosis and fat storage on up-stream events including portal hypertension. Portal hypertension is clinically highly significant and early signs are therefore of importance. Quantitative measurement of hepatic blood flow would be useful to the understanding of disease progression in the cirrhotic liver, particularly the early development of fibrosis and inflam-

mation, since the development of liver fibrosis and lipid accumulation constrict the blood flow to the liver.

The project is divided into two separate phases, the first being a developmental phase involving different protocols and healthy research subjects, and the second clinical patients. The research will in the early phase mainly focus on the challenges of developing, implementing and validating the technologies for measurements of dynamic characteristics of disease including restrictions of flow. Four-dimensional flow (4D-Flow) MRI is an emerging method for quantitative evaluation of hemodynamics of in the liver and abdomen, however, it is limited to be used in clinical setting due to the long acquisition time. Compressed sensing (CS) is a method for image acquisition acceleration that is gaining in popularity in abdominal imaging.



Project information

PROJECT NAME

Comprehensive Assessment of Hepatic Function in Health and Disease, Techniques for early disease detection and tissue characterization

PROJECT LEADER

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

MAIN PROJECT PARTICIPANTS

Stergios Kechagias, Mattias Ekstedt, Nils Dahlström, Markus Karlsson, Bengt Norén, Jens Tellman, Christian Simonsson, Frederik Testude, Ralph Sinkus, Marcel Warntjes, Magnus Borga

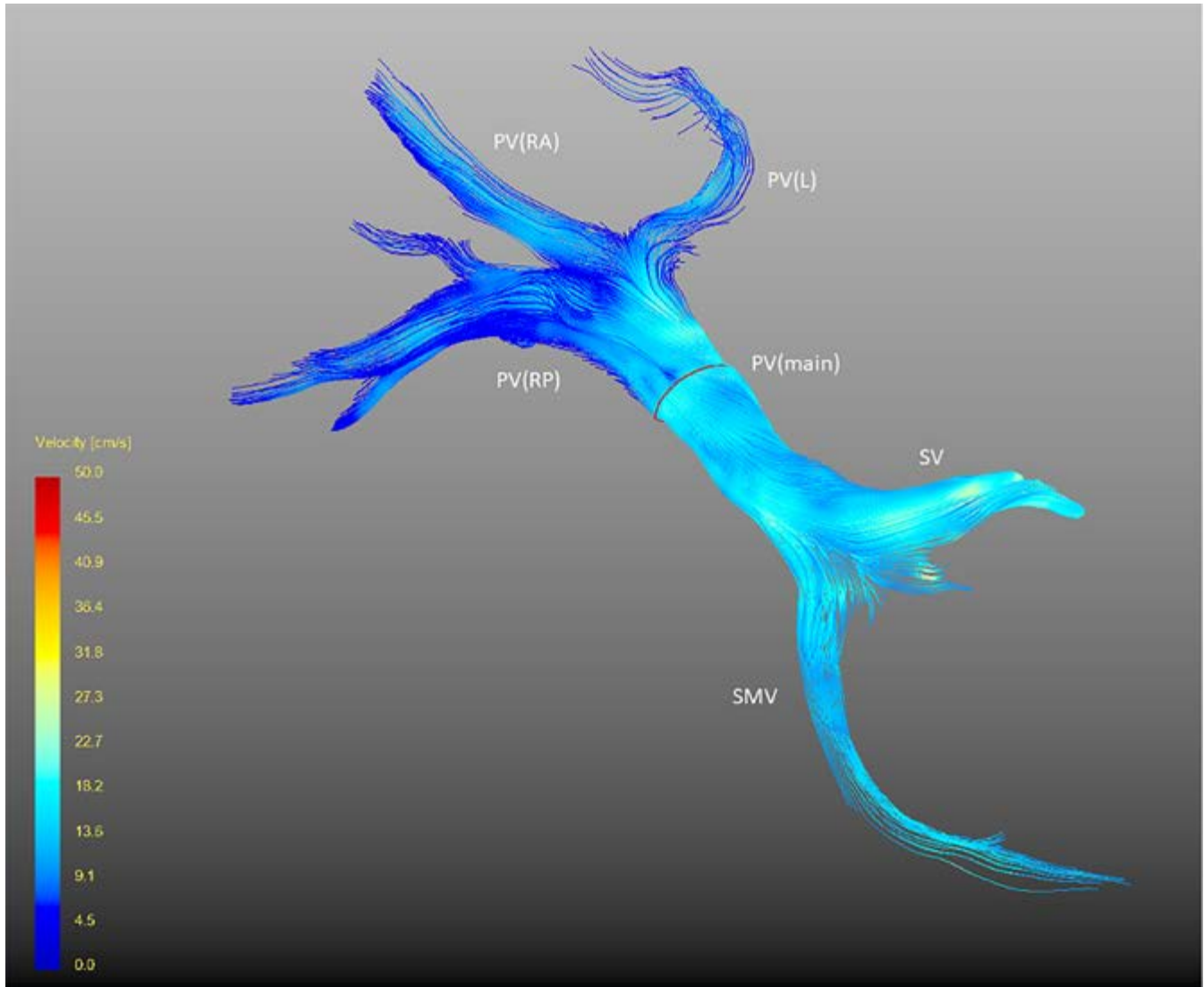
GRANTS

Swedish Research Council (VR/NT) (2021–2024/2025 etc)
ALF (2019–2022)

KEY PUBLICATIONS

Forsgren MF, Nasr P, Karlsson M, Dahlström N, Noren B, Ignatova S, Sinkus R, Cedersund G, Dahlqvist Leinhard O, Ekstedt M, Kechagias S, Lundberg P (2020). Biomarkers of liver fibrosis: prospective comparison of multimodal magnetic resonance, serum algorithms and transient elastography. *Scan J Gastroenterology*, <https://doi.org/10.1080/00365521.2020.1786599>.

Karlsson M, Tellman J, Testud F, Jin N, Dahlström N, Lundberg P (2020). Feasibility of 4D-Flow MRI of the Liver using Pencil Beam Navigator for Respiratory Gating and Compressed Sensing, ISMRM (Paris, France).



MR-measurements of blood flow in the portal system at 3 T using 4D-flow MRI streamlines visualization. The Portal Vein transports blood from the gastrointestinal tract, the spleen and the pancreas and consists of the Main Portal Vein, here denoted PV(main), which inside the liver divides into the following major branches: PV(RA): Right Anterior branch, PV(RP): Right Posterior branch and PV(L): Left branch. The two major tributaries to the Main Portal Vein are the Superior Mesenteric Vein (SMV) and the Splenic Vein (SV), seen in the lower right corner. Colour signifies the local blood velocity, here showing a lowering of the velocity as the blood travels from the SMV and SV into the liver. [Tellman, unpublished]

Evaluation of Reconstruction Methods in CT

In all diagnostic x-ray examinations ionizing radiation, it is imminent to produce images of good diagnostic quality while simultaneously keeping the radiation dose to human organs as low as reasonably achievable (ALARA principle) to minimise detrimental radiation effects. Abdominal and thoracic Computed Tomography (CT), are common examinations and irradiate radiosensitive tissues in humans.

Image quality in CT is related to the radiation exposure. A reduced exposure can increase the image noise and hence may reduce the image quality and visibility of anatomical structures as well as pathology. Therefore, reductions in patient exposure need to be evaluated carefully without impairment in diagnostic accuracy. New technology presents a wide range of noise and dose reduction strategies, the latest being iterative image reconstruction (IR). The aim of this project is to evaluate the performance and dose reduction potential of advanced modeled iterative reconstruction (AD-

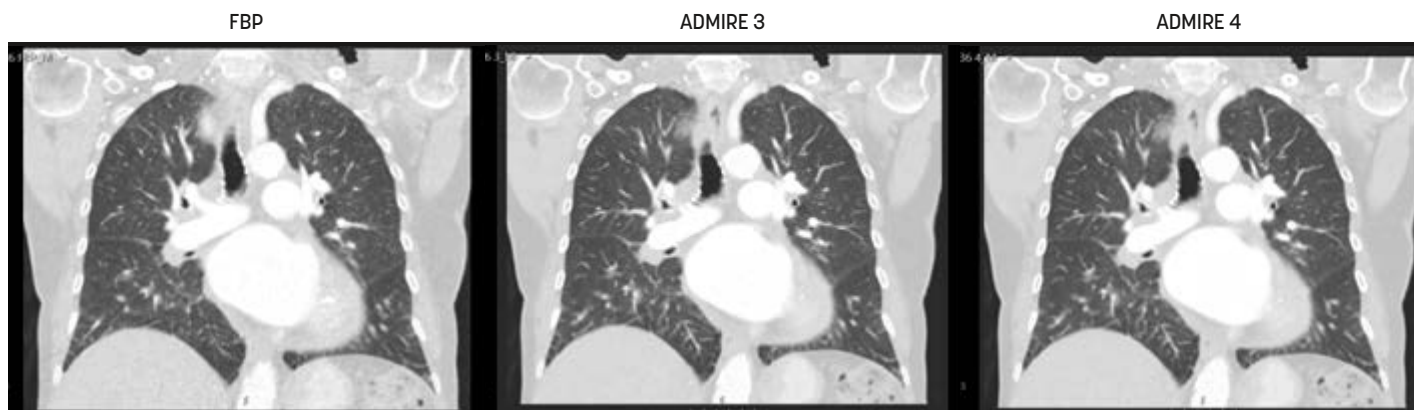
MIRE); a model-based reconstruction algorithm used by radiology departments in Region Östergötland.

In prospective visual grading experiments, radiologists evaluated the clinical image quality by comparing images of the same patient, simultaneously exposed to different doses using a novel technique with two x-ray tubes, to determine the potential dose reductions without compromising image quality. Established European guidelines on image quality criteria were used and the responses from the evaluation by experienced radiologists were analysed statistically with ordinal logistic regression models. This allows computation of potential patient dose reduction from the regression's coefficients of the statistical model.

Current published literature was reviewed to assess the performance of ADMIRE in abdominal CT (Kataria et al. 2021). The review highlighted a variety of methodologies can be used to assess image quality and to estimate potential

dose reduction in studies performed in human subjects or phantoms. Objective quantitative measurements in anthropomorphic phantoms do, to some extent, support our results from the qualitative subjective assessment by radiologist, but subtle changes in noise texture due to the reconstruction algorithm indicate that phantom measurements alone are not sufficient, but need to be complemented with evaluations in human subjects. Substantial dose reductions are possible with ADMIRE, however, for optimisation of clinical protocols visual grading studies performed on human subjects should be considered as the "in vivo" assessment task is more complex compared to lesion assessments in phantoms.

Our experimental design has been successful, and the novel statistical analysis is presently being used to optimise thoracic CT protocols. The imaging data from CT Thorax examinations (Figure 1) is under evaluation by radiologists and preliminary results will be available in the first quarter of 2022. Another

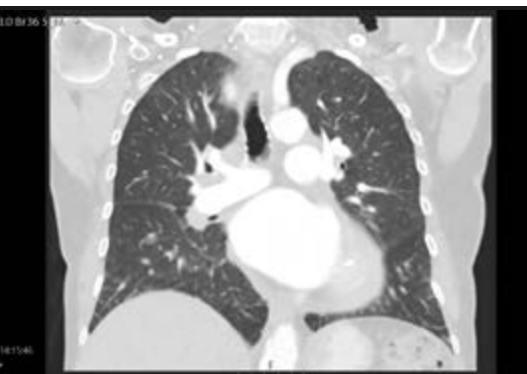


Patient images from a Thoracic CT examination using reconstruction algorithms Filtered Back Projection (FBP) and iterative reconstruction (ADMIRE) strengths 3, 4 and 5.

ongoing study explores the possibility of a learning curve for image quality produced by ADMIRE over time. Do radiologists' adapt to the image quality produced by the higher strength of ADMIRE when evaluating image quality over time? To study the change in radiologist evaluation of image quality over time, a reanalysis of the data from two studies (Kataria et al, 2018, 2020) were performed. Preliminary results suggest that radiologists increasingly dislike the image quality produced by the higher strength of the algorithm over time.

The important conclusion is that the model-based reconstruction algorithm, ADMIRE improved image quality in abdominal CT allowing for significant dose reductions (30%) which have been implemented clinically. Potential dose reduction can be estimated using ordinal regression models as they also allow for simultaneous analysis of several parameters.

ADMIRE 5



Computed Tomography | Gastrointestinal | Acquisition | Visualization

Project information

PROJECT NAME

Visual grading evaluation of reconstruction methods in Computed Tomography for improved patient safety

PROJECT LEADER

Bharti Kataria, Department of Radiology, Department of Health, Medicine and Caring Sciences

MAIN PROJECT PARTICIPANTS

Michael Sandborg, Anders Persson, Örjan Smedby and Jonas Nilsson Althen

GRANTS

ALF (2017, 2018, 2021)
FoU (2017 - 2021)
Patientsäkerhetsforskning (2018 - 2019)
RFoU (2017 - 2021)

KEY PUBLICATIONS

Kataria B, Nilsson Althén J, Smedby Ö, Persson A, Sökjer H, Sandborg M. Image quality and potential dose reduction using advanced modeled iterative reconstruction (ADMIRE) in abdominal CT – A review. *Radiation Protection Dosimetry* (2021), pp. 1-11, doi:10.1093/rpd/ncab020

Kataria B, Nilsson Althén J, Smedby Ö, Persson A, Sökjer H, Sandborg M. Assessment of image quality in abdominal CT: Effect of model-based iterative reconstruction, multi-planar reconstruction and slice thickness on potential dose reduction. *European Journal of Radiology* 122 (2020) 108703.

Kataria B. Visual grading evaluation of reconstruction methods and dose optimisation in abdominal Computed Tomography. Thesis Linköping University No 1683, 2019.

Kataria B, Nilsson Althén J, Smedby Ö, Persson A, Sökjer H, Sandborg M. Assessment of image quality in abdominal CT: potential dose reduction with model-based iterative reconstruction. *European Radiology* 2018; 28: 2464-2473.

MR-Mammography

Breast cancer is the most common form of cancer in women with a life-time risk of over 12%. A major risk factor for breast cancer is breast density. Women with dense breasts have been shown to have a four- to six-fold increased risk of developing breast cancer.

Dense breast tissue contains higher amounts of stroma, including collagen, and less fat tissue. Conflicting results regarding a difference in the amounts of epithelial cells have been reported, although it varies only between 1-6% and the proliferation of these cells is also very low. Hence, the underlying biological mechanism(s) of a higher breast cancer risk of dense breast tissue is to date unexplored.

In addition to dense breast tissue, exposure to sex steroids such as estradiol is an established risk factor for breast cancer. An inflammatory microenvironment has also been associated with increased risk of cancer and a reduced risk of breast cancer has been reported in women who regularly use anti-inflammatory drugs.

Despite the wide use of mammography as a general screening tool for breast cancer, this method has a painfully high false-negative rate (about 10-25%).

Today, there is growing interest in using Magnetic Resonance (MR) for breast cancer screening, in particular in the younger population as the higher density of the younger breast can obscure underlying lesions in mammography. The absence of ionizing radiation also makes MR a particularly interesting tool for clinical research on breast cancer risk factors.

In order to perform studies involving MR and MR-based risk assessment and diagnosis, a clinically useful MR protocol has recently been developed. The protocol has been developed, implemented at CMIV and used in a pilot study on 40 female subjects. Furthermore, methods for quantifying clinically relevant parameters from the MR data have been explored.

The aims of BREASA are to further validate a comprehensive MR protocol, and also to investigate the clinical relevance for the derived MR-based parameters in a cohort of subjects that are treated using an anti-inflammatory agent. Will the treatment affect the levels of inflammatory biomarkers, and will it affect the quantitative assessment of stroma, associated imaging biomarkers and the tissue? The ultimate long-term end-point is whether the treatment will reduce the risk for breast cancer.

MRI **Oncology** **Acquisition** **Modeling**
Imaging Biomarkers

Project information

PROJECT NAME

MR-Mammography 3.0 (BREASA): Pharmacological Prevention of Breast Cancer Monitored Using a Novel Comprehensive Magnetic Resonance-Based Protocol

PROJECT LEADER

Peter Lundberg, Radiation Physics, Department of Health, Medicine and Caring Sciences

MAIN PROJECT PARTICIPANTS

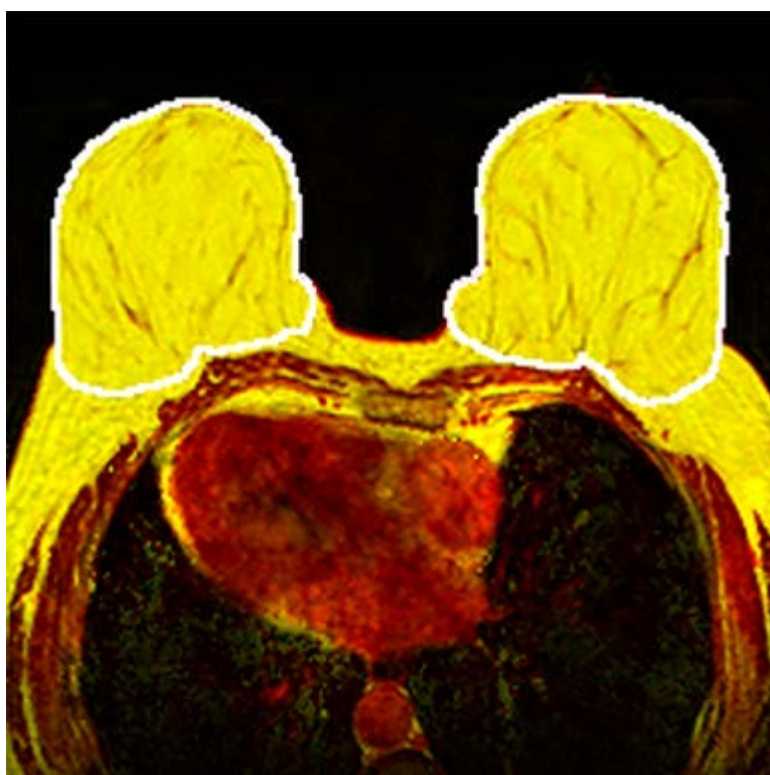
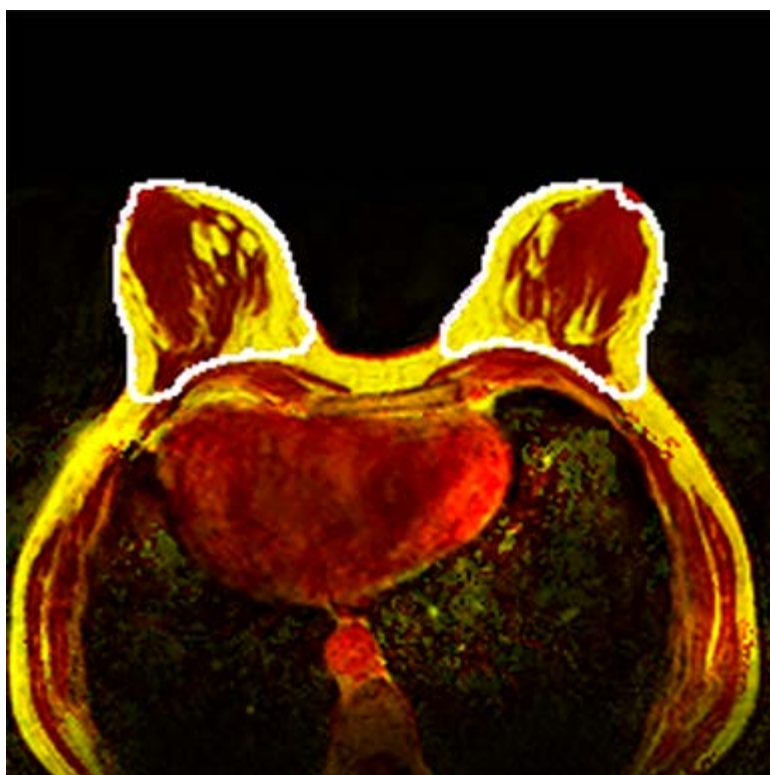
Charlotta Dabrosin, Anette Karlsson, Ieva Tomkeviciene, Mikael Forsgren, Johan Kihlberg, Maria Kristoffersen Wiberg, Magnus Borga, Marcel Warntjes, Olof Dahlqvist Leinhard, Pantelis Gialias, Anna Rzepecka

GRANTS

LiU-Cancer
Cancerfonden

KEY PUBLICATIONS

Abrahamsson A, Rzepecka A, Romu T, Borga M, Dahlqvist Leinhard O, Lundberg P, Kihlberg J, Dabrosin C. Dense breast tissue in postmenopausal women is associated with a pro-inflammatory microenvironment in vivo, *Oncoimmunology*, 5(10), 2016.



MR-quantification of lean tissue fraction in postmenopausal women attending the regular mammography screening program. The images are representative for dense (above) and non-dense (below) breasts.

Evaluation of Photon Counting CT in Spinal Deformities

Scoliosis is a three-dimensional deformity affecting the spine in both the coronal, sagittal and axial plane. Patients with scoliosis are usually adolescent or younger. The magnitude of the deformity increases as the patient grows. Different treatment options are available depending on the severity of the deformity ranging from conservative treatment to bracing and corrective surgery. Patients with scoliosis are subjected to many radiological examinations during the period of follow up. In case corrective surgery is required the patient is subjected to additional examinations. At our department,

these examinations include low-dose CT scans pre- and postoperatively. Consequently, patients with scoliosis receive considerable additional radiation exposure compared to peers.

Photon counting CT is a novel modality with promising properties regarding image resolution and reduced radiation dosage.

To further reduce the radiation exposure to patients with scoliosis and also possibly obtain additional radiological information, the aim of this project is to investigate the viability of photon counting CT in the assessment of scoliosis.

Computed Tomography Musculoskeletal
Visualization

Project information

PROJECT NAME

Evaluation of Photon Counting CT in Spinal Deformities

PROJECT LEADER

Ludvig Vavruch, Department of Orthopaedic Surgery, Region Östergötland

MAIN PROJECT PARTICIPANTS

Håkan Gustafsson, Lilian Henriksson, Michael Sandborg



Example of scoliosis.

Visualization of Skeletal Joint Movement

There are many tools available for the orthopedic doctor to help with the diagnoses, treatment, and overall care of their patients. Often imaging, like for example computerized tomography (CT) or magnetic resonance imaging (MRI), can assist in understanding the underlying cause of the problems. However, orthopedic problems most often involve issues related to a restriction or pain during movement. Standard CT or MRI merely show a static image of the skeletal or soft tissues. In some cases, these still images are not sufficient to understand the clinical problem presented by the patient. Currently, there are systems that can show movement of the skeletal and soft tissues during a short time frame. One method is 4D CT. With this method, a 3D image is taken over time (the 4th dimension). However, there are some major drawbacks with these systems. For example, the high levels of radiation, limited period and movement range of motion. It would be of incredible added benefit if, by some means, we could combine standard clinical imaging with the well-established motion capture methodology. The capture of whole body movements has been done as long back

as the 1980's both in the scientific field as well as in the movie making industry. There are different systems that can be used but in general, multiple cameras are used to track predetermined points (markers) on the subject's body. Using this method, many clinically relevant daily activities can be measured without any restrictions.

In the current project we are aiming to combine the standard CT images taken as part of the standard clinical care and combining that with the information from the motion capture system. By combining these two applications we could generate a visualization of the patients' skeleton movements while performing daily clinically relevant movements.

In addition to optimizing and simplifying the methodology, we need to focus on minimizing errors. For example, the errors introduced because our skin moves relative to our bones (soft tissue artifacts). Up to now these artifacts prohibit an acceptable visualization of skeletal motion. Further work has to be done improving programming. Our plan is to use a constrained model. The hip joint location is "locked" in the biomechanical model.

Computed Tomography Musculoskeletal
Visualization

Project information

PROJECT NAME

CT-MOCAP: A novel method to visualize joint movement by means of combining computed tomography with motion capture

PROJECT LEADER

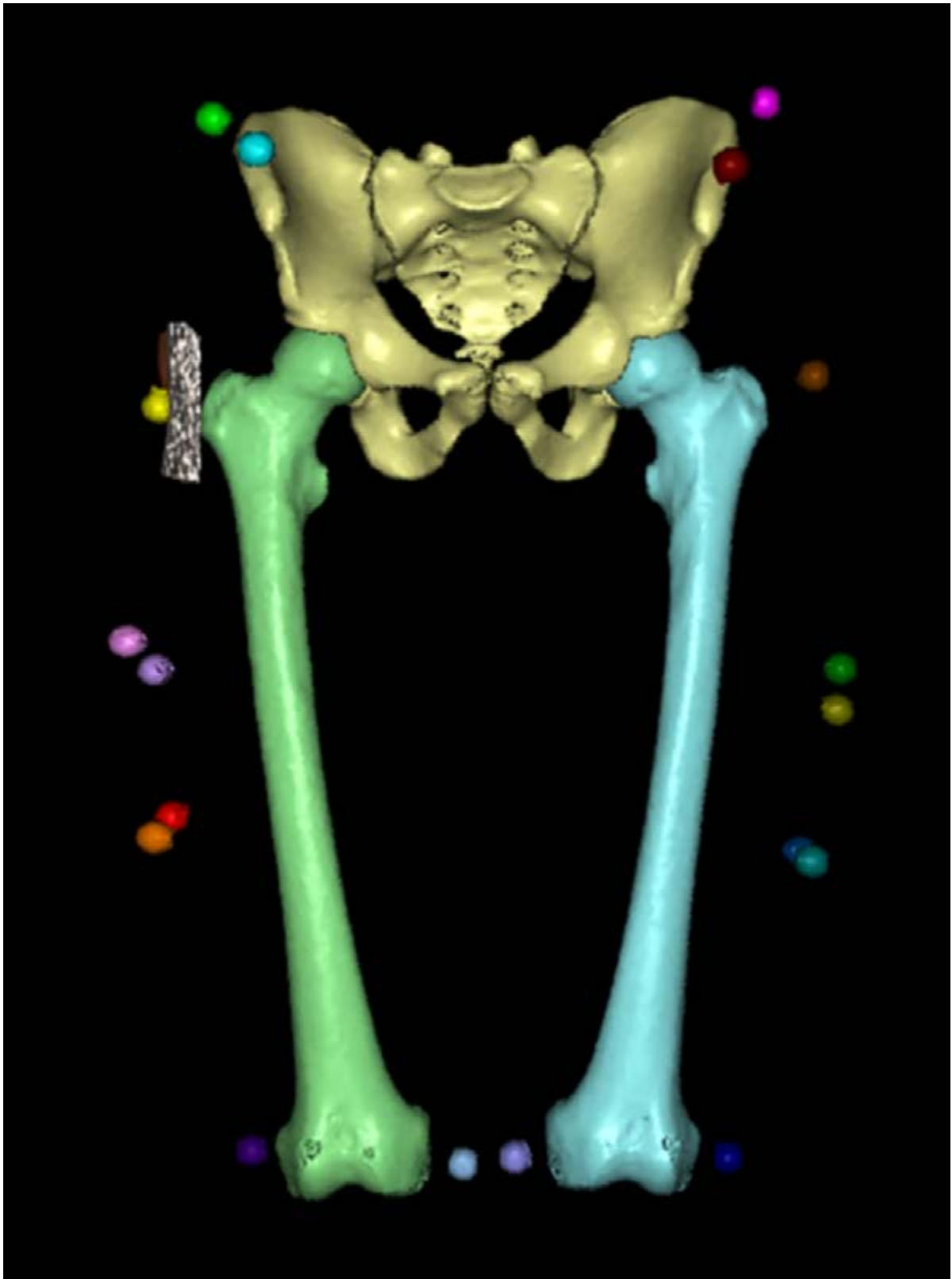
Hans Tropp, Department of Biomedical and Clinical Sciences, Division of Surgery, Orthopedics and Oncology

MAIN PROJECT PARTICIPANTS

Marcus Malmqvist, Daphne Wezenberg

GRANTS

FORSS (2021/22)



Pelvis and hip visualized by CT. Passive markers are seen on the segments.

Health Effects of Resistance Training in Postmenopausal Women

After menopause most women will suffer from hot flushes and sweating which may be very disturbing and may persist for > 5-7 years (median) up to life-long. These hot flushes have been suggested to be a separate riskfactor for cardiovascular disease. Furthermore, the hormonal changes related to menopause increase bone loss, affect lipoprotein metabolism negatively, and have impact on neuronal tissue with increased risk for neurodegeneration. Hormone therapy with estrogen combined with a progestogen is helpful but may not be used by all women due to contraindications or side effects.

Based on the mechanisms behind the hot flushes, stemming from the thermoregulatory center in the brain (hypothalamus) we have tried to treat the hot flushes with 15 weeks of resistance training. About 60 women were included in a randomized controlled trial and were after randomization either treated

with 60 min/day, 3 days/week supervised resistance training or asked to keep low physical activity in a control group. They all answered questionnaires, blood samples were drawn, and they were asked to undergo MRI at baseline, after 15 weeks intervention and after another 24 months.

This far we have found that the hot flushes decreased to about half after the 15 weeks intervention, that quality of life was significantly increased, that muscle strength and muscle volume increased, lipoprotein metabolism changed to a more beneficial profile and that markers of inflammation decreased. Measurements of telomer length, changes in fat distribution, change from white to brown fat are underway. One PhD student has been graduated with projects from this study, another three are working with projects based on the study and still another Ph student will be involved within a few months.

MRI Musculoskeletal Gynecological
Metabolism AI/Data analytics

Project information

PROJECT NAME

Health Effects of Resistance Training in Postmenopausal Women

PROJECT LEADER

Mats Hammar, Department of Biomedical and Clinical Sciences, Children's and Women's Health

MAIN PROJECT PARTICIPANTS

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GRANTS

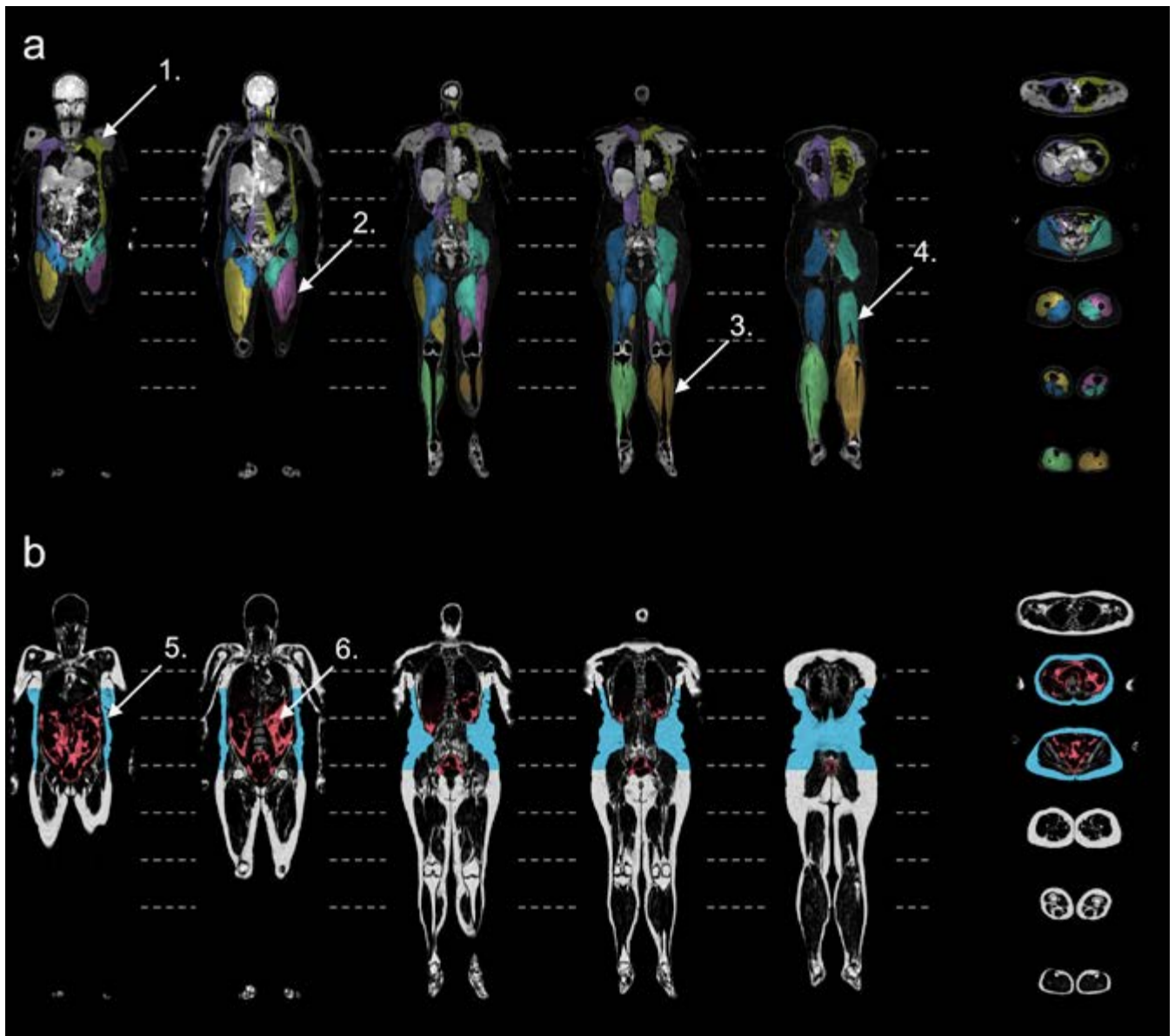
Swedish Research Council

KEY PUBLICATIONS

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Ward LJ, Nilsson S, Hammar M, Lindh-Åstrand L, Berin E, Lindblom H, Spetz Holm AC, Rubér M, Li W. Resistance training decreases plasma levels of adipokines in postmenopausal women. *Sci Rep*. 2020 Nov 16;10(1):19837. doi: 10.1038/s41598-020-76901-w.

West J, Romu T, Thorell S, Lindblom H, Berin E, Holm AS, Åstrand LL, Karlsson A, Borga M, Hammar M, Leinhard OD. Precision of MRI-based body composition measurements of postmenopausal women. *PLoS One*. 2018 Feb 7;13(2):e0192495. doi: 10.1371/journal.pone.0192495. eCollection 2018.



Whole-body magnetic resonance images showing a middle-aged woman. The top row shows segmentation of muscles, and the lower row shows segmentation of fat deposits. The difference between subcutaneous fat and visceral fat is visualized as red and blue (West J. et al. <https://doi.org/10.1371/journal.pone.0192495.g001> CC BY 4.0)

Bone Structure Analyses for Reducing Future Osteoporotic Fractures

Patients suffering from osteoporosis have an increased risk of fractures. When studying osteoporosis, the amount of calcium in bone is measured. This bone mineral density (BMD) is lower in osteoporotic bone. Research have shown that bone microstructure, seems to be more important for its strength than the reduced calcium content. The internal bone microstructure consists of a network of thin bone structures called trabeculae. This network of trabeculae can be measured by different parameters like their thicknesses, number, free ends and distance between them. Earlier, the 3D microstructure of humans could be studied only by microscopy and by mi-

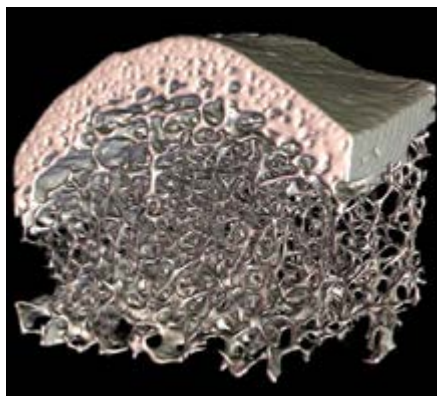
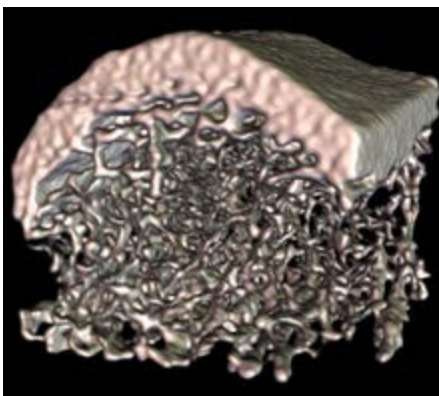
cro-computed tomography (micro-CT) of specimens removed from the body.

This project aims to study this 3D structure in living humans, by using methods available in a radiological department, in particular different types of CT methods. Since the trabeculae often are less than 0.1 mm thick, the limited resolution of the radiological methods may be a problem. We have focused on examinations on CT devices with possibilities of imaging at high resolution and on developing new image processing techniques for as accurate measurements as possible using these image data sets.

Data from dental cone beam CT (CBCT) shows very strong correlations

for bone microstructure when compared to micro-CT and results from the research are published in a number of publications. Most recently, a manuscript in collaboration with University of Iowa was published in the journal *Medical Physics*.

Another CT device with high resolution is photon-counting detector (PCD) CT. This is a very novel technique available only in 2-3 radiology departments around the world. One of the devices is installed on CMIV. This technique is very promising since it allows high resolution of central body parts like the hip and vertebrae where osteoporotic fractures are common. All other devices, so far, have



3D images from a bone specimen, PCDCT micro-CT, a foto, CBCT, MSCT

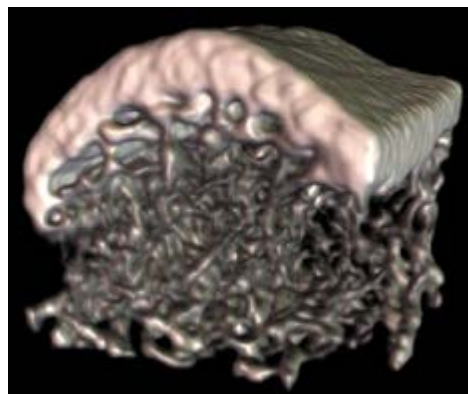
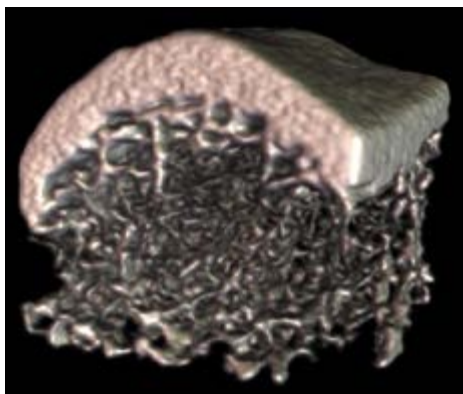
been able to image bone microstructure only in the peripheral skeleton like wrist and forearm. Studies on bone microstructure on this PCD-CT device have started just recently and show promising results.

A clinical study on patients visiting the Department of Endocrinology at Linköping University for osteoporosis examinations is ongoing. CBCT data of forearm and mandible is compared to dual energy X-ray absorptiometry (DXA) data.

On the segmented CT-data sets, we also analyse bone strength by finite element modeling (FEM), a computational method that requires long time even

on very fast computers. Our segmented data, presented in previous studies, correlates well with results from FEM analyses.

In the future, we hope that our methods will be useful in particular in early detection of osteoporosis. With better tools to measure the structure of the 3D bone network, it will be possible to diagnose osteoporosis at an earlier stage. We hope for a diagnosis already at the time for the first fracture, which will result in reducing the number of future painful fractures.



Computed Tomography | Musculoskeletal
Acquisition | Visualization

Project information

PROJECT NAME

Bone microstructure and strength derived from imaging data from different CT devices: relation to osteoporosis and fractures

PROJECT LEADER

Eva Klintström, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS

Örjan Smedby, Rodrigo Moreno, Benjamin Klintström, Mischa Woisetschlager

KEY PUBLICATIONS

Klintström E, Smedby Ö, Moreno M, Brismar TB. Trabecular bone structure parameters from 3D image processing of clinical multi-slice and cone-beam computed tomography data. *Skeletal Radiology*, 2014 Vol. 43, nr 2, s. 197-204.
Klintström E, Klintström B, Pahr D, Brismar TB, Smedby Ö, Moreno M. Direct Estimation of Human Trabecular Bone Stiffness Using Cone-Beam Computed Tomography. *PLoS ONE*, Vol. 11, nr 8 2016.
Klintström E. Image Analysis for Trabecular Bone Properties on Cone-Beam CT Data. Linköping: Linköping University Electronic Press; 2017. Linköping University Medical Dissertations, 1594. 2017.

Post-Surgical Visualization of Tibial Plateau and Pilon Fractures

Bone fractures are common and often require surgical treatment with plate and screws (called orthopedic hardware) as well as long-term follow-up. Plain radiographs are the cornerstone of imaging. However, complex fractures near joints often require a more advanced imaging technology, such as computed tomography (CT) to visualize fracture morphology and to verify or exclude possible joint involvement. Therefore, in these complex and often complicated fractures, CT is the imaging method of choice for both primary diagnosis and preoperative planning. Postoperative CT is often performed to ensure and verify the operative results. In the case of intra-articular fractures, it is of utmost importance to restore the joint surface geometry. However, orthopedic hardware may degrade the CT image quality substantially, or even make this important evaluation impossible. To overcome these problems, the novel photon-counting CT (PCT) will be used in this project. It is a novel imaging method, which is not yet in full clinical use. There are only a few of these in the world for research use, of which one is at the CMIV. The unique thing about the PCT is that the detector

counts the exact number of incoming X-ray photons and their energy individually compared to the current conventional CT. The photon-counting detector has several important improvements compared to conventional CTs. First, it provides better resolution so that smaller structures can be seen, the lack of noise make images clearer and crisper, the radiation dose is decreased, and lastly, the metal artifacts have the potential to be reduced substantially. Moreover, even major improvements in imaging of soft-tissues, such as muscles, ligaments, and cartilage are expected.

In our project we are going to evaluate the reduction of artifacts caused by orthopedic hardware in patients with lower extremity fractures near the major joints, such as the knee and ankle.

The capabilities and advantages of this machine are obvious. As this is one of very few machines of that kind in the world and with the research environment provided by the CMIV we possess an ideal position to bring the musculoskeletal imaging into the future. This will have a direct impact on patient care, eventually leading to improved quality of life.

Computed Tomography Musculoskeletal
Visualization No Method Development

Project information

PROJECT NAME

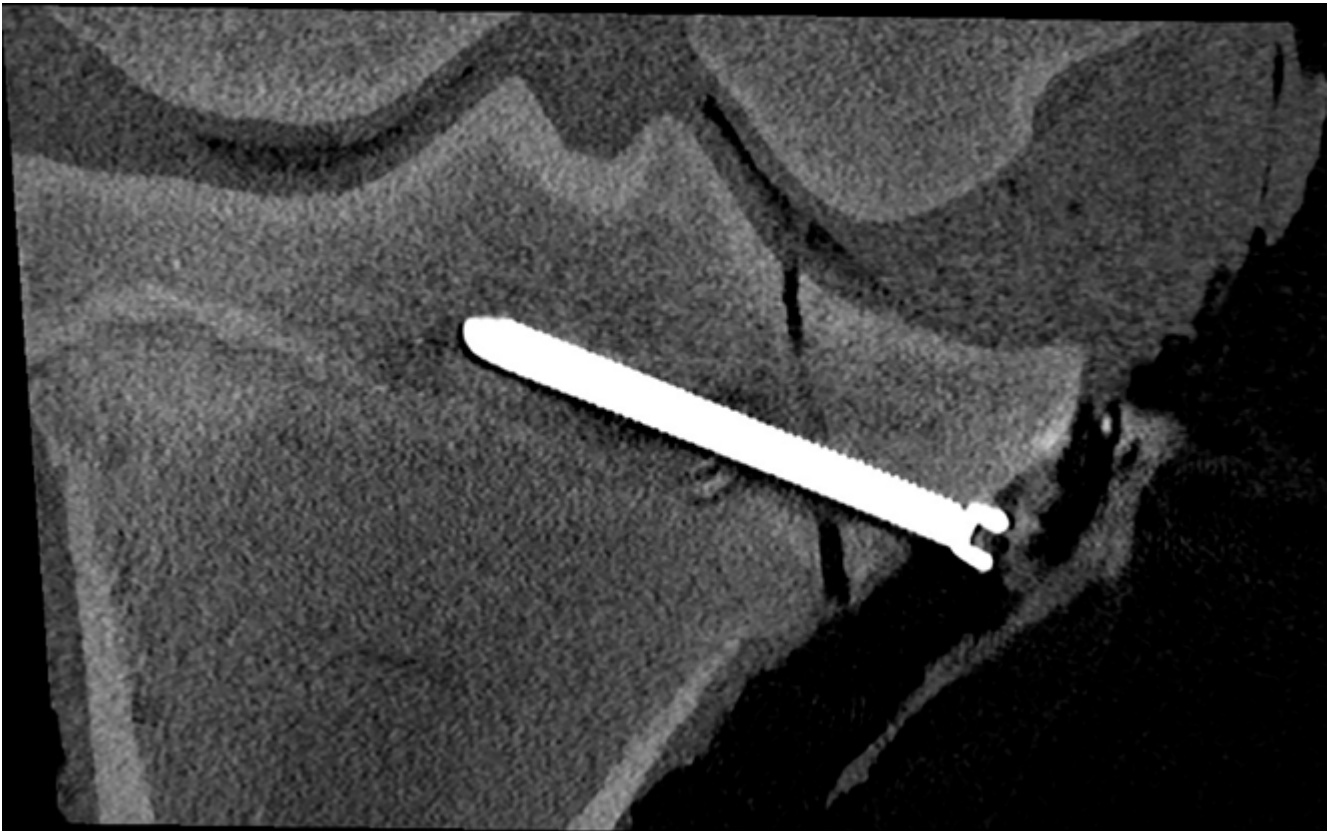
Post-Surgical Visualization of Tibial Plateau and Pilon Fractures

PROJECT LEADER

Seppo K. Koskinen, Department of Health, Medicine and Caring Sciences, Diagnostics and Specialist Medicine

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An image from the PCT showing the knee of a cow with a metal screw crossing a fracture line and almost no metal artifacts.

Carotid MRI

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. These thickened areas are called atherosclerotic plaques.

Strokes resulting from blood clots that migrate to the brain from plaques in the carotid arteries cause 2.5% of all deaths. Today, plaques that cause more than 70% constriction of the carotid in stroke patients are removed surgically to avoid future strokes. However, size does not tell the whole story. In addition to size, the composition of the plaque is a major determinant of rupture risk. Plaques with a large amount of fat and blood are considered hallmarks of vulnerable plaque phenotypes that are more prone to rupture. Furthermore, the blood flow around the plaque also is an important factor for the risk of thrombotic complications. Disturbed blood flow may erode the plaque surface and lead to thrombotic events even in patients with

stable plaque phenotypes. Unfortunately, current clinical tools are insensitive to these effects. Consequently, there is a clear and urgent need to improve carotid plaque assessment in order to more accurately assess risk of progression and rupture in patients as well as to improve risk management in patients with carotid plaques.

In this project we aim to improve carotid plaque risk assessment both for better assessment of overall cardiovascular risk and for better decision support in which patients will benefit from surgery.

We have recently developed tools for automated visualization and quantification of carotid plaque composition and hemodynamic effects on the vessel wall by combining advanced quantitative magnetic resonance imaging methods with novel image analysis. We are now applying these novel methods to patients with carotid atherosclerotic plaques so as to increase our understanding carotid atherosclerotic disease and its relationship to disturbed blood flow.



Project information

PROJECT NAME

Carotid MRI

PROJECT LEADERS

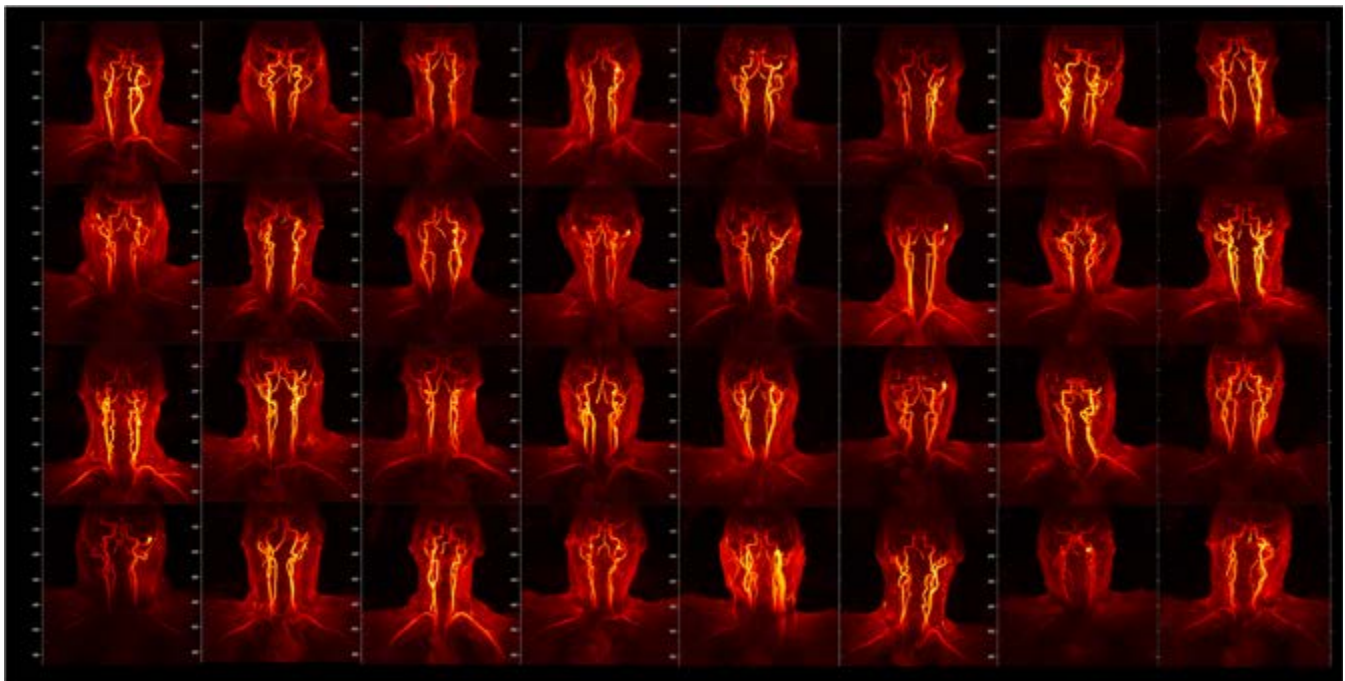
Petter Dyverfeldt, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine
Ebo de Muinck, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS

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GRANTS

ALF Grant, Region Östergötland
Henry and Ella Margareta Ståhl Foundation
Hälsöfonden, Linköping University and
Region Östergötland
Swedish Research Council



Challenge! Here you see overview images of the carotid arteries in 24 individuals. 23 of these individuals are between 50-64 years old and one of these individuals is 25 years old. Can you find the 25 year old? Hint: Increased tortuosity (twistedness) is a hallmark of vascular ageing, but young individuals have straight blood vessels.

Ascending Aortic Dilation

Background: Aneurysmal dilation of the ascending aorta (AscAo) is a silent, asymptomatic, disease that is often not detected until a fatal dissection or rupture occurs. While almost certainly multifactorial, basic vessel dimensions are the primary measurement used clinically to risk-stratify patients. But dimensions do not tell the whole story. We and others have previously leveraged the unique assessment of hemodynamics afforded by cardiac magnetic resonance (CMR) imaging to explore the role of abnormal hemodynamics in AscAo dilation. As a result of those previous studies, hemodynamics is increasingly believed to contribute to disease progression in AscAo dilation. However, studies on patient cohorts that are representative of the broader population are needed to further elucidate the role of hemodynamics and circulating biomarkers in AscAo dilation.

Purpose and hypotheses: The overall purpose of this project is to identify novel markers of mild to moderate AscAo dilation and growth with the unique assessment of hemodynamics afforded by cardiac magnetic resonance (CMR) imaging.

We hypothesize that:

– Hypothesis 1. Patients with mild to moderate AscAo dilation are characterized by altered AscAo hemodynamics when compared to matched controls

– Hypothesis 2. Circulating markers of pathological processes in the vessel wall are a) different in patients with mild to moderate AscAo dilation when compared to matched controls and b) related to abnormal hemodynamics in patients with AscAo dilation

– Hypothesis 3. Growth of AscAo dilation occurs in regions with abnormal hemodynamics

Method: We will investigate our hypotheses by using CMR to comprehensively map AscAo hemodynamics in a unique cohort of individuals with and without mild to moderate AA dilation and analyze plasma samples in the two groups. Progression of AscAo dilation will be monitored on an annual basis and used to establish relationships between abnormal hemodynamics and growth.

Significance: AscAo diameter is a blunt and insufficient measure to appropriately risk-stratify AscAo dilation. Successful accomplishment of this study of a well-defined population-based cohort of individuals with mild to moderate AscAo dilation will contribute to a greater understanding of the role of altered hemodynamics and circulating biomarkers in AscAo dilation. This may facilitate development of best practices and effective clinical guidelines, and in so doing, optimize clinical outcomes for patients with AscAo dilation.

MRI Cardiovascular AI/Data analytics
Imaging Biomarkers

Project information

PROJECT NAME

Novel markers and risk factors for ascending aortic dilation using advanced hemodynamics imaging and circulating biomarkers

PROJECT LEADER

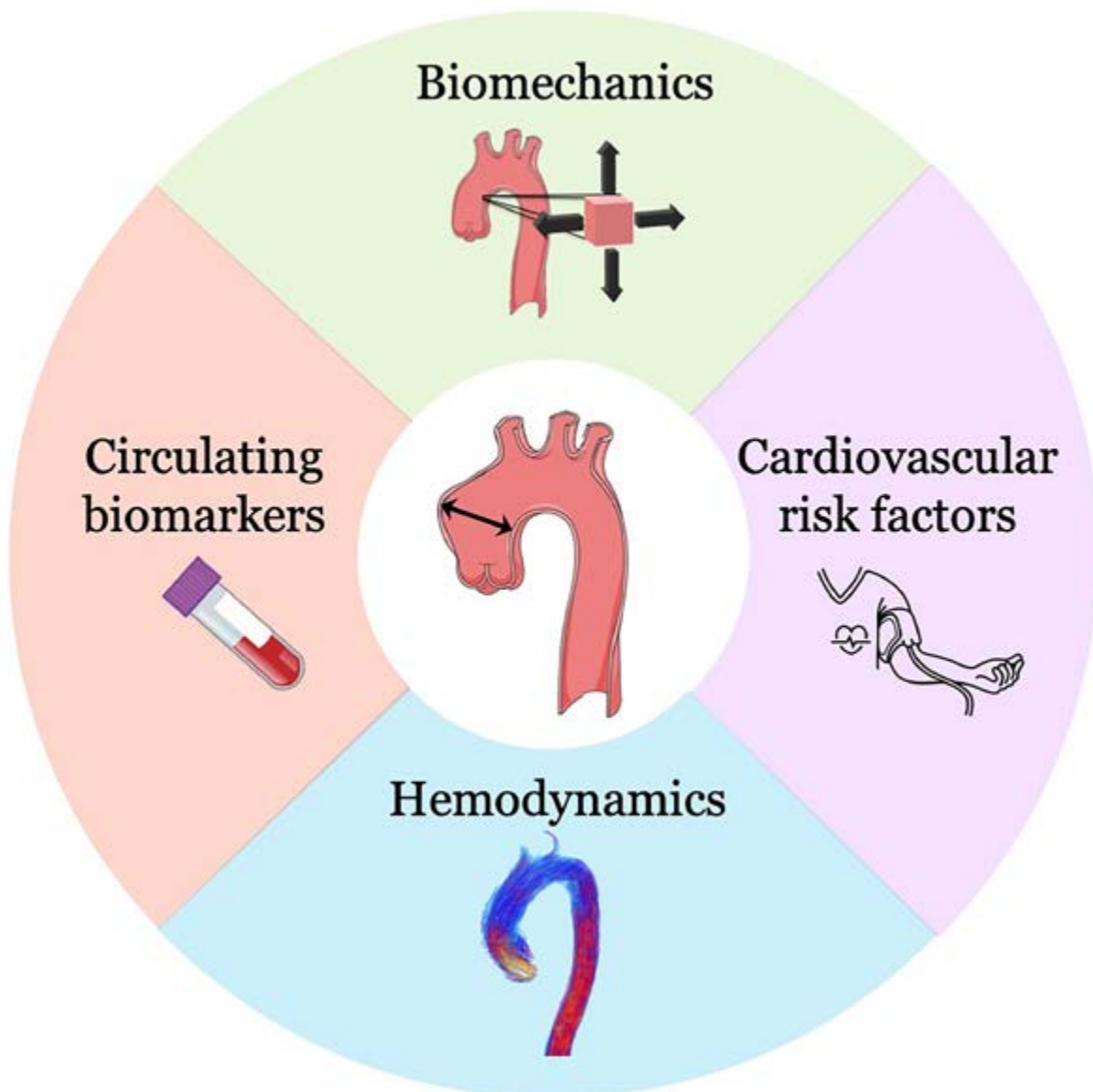
Petter Dyverfeldt, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS

Chiara Trenti, Filip Hammareus, Lena Jonasson, Eva Swahn, Jan Engvall

GRANTS

ALF Grant, Region Östergötland, Linköping University Strategic Research Area in Circulation and Cardiovascular Metabolic Risk Factors
Medical Faculty at Linköping University



Project overview. Improved characterization and risk-stratification of mild-to-moderate ascending aortic (AA) dilation will be achieved by a thorough analysis of cardiovascular risk factors and a comprehensive investigation the potential role of several novel hemodynamics, biomechanics and circulating markers in a unique cohort of individuals with mild to moderate AA dilation and age- and sex-matched controls. Annual follow-up measurements of AA diameter will provide data on growth rates and allow us to explore novel predictors of growth.

Scapis-HEALTH

Swedish Cardio Pulmonary bioImage Study (SCAPIS), is a large-scale national population study initiated by The Swedish Heart and Lung Foundation and supported by the Wallenberg Foundation. The study is lead by a national research group in collaboration with the University Hospitals in Sweden.

SCAPIS is aiming for improved diagnosis and treatment of cardiovascular and lung disease. In total 30 000 healthy individuals in the age of 50-64 years will be examined in the study. Of these 5000 will be examined in Linköping. The participants' lungs and cardiovascular system are examined with computed tomography and ultrasound. All the collected data will be saved in a knowledge bank, which will be a national resource used for research.

The overall aim of the HEart-Adipose tissue-Liver TrusT (HEALTH) project is to establish a relationship between cardiovascular disease, liver disease and ectopic fat storage in a cohort with Type 2 Diabetes Mellitus (T2DM), something that has never been done previously.

We hypothesize that advanced MRI-based measurements of the heart, liver and body composition in combination will relate stronger to adverse cardiac

remodeling, cardiovascular events, and metabolic disease compared to individual measurements.

At CMIV in Linköping we intend to study the relationship between measurements with highly advanced MR methods on heart (e.g., myocardial deformation / fibrosis/fat, blood flow), liver status (e.g., fibrosis, liver fat, iron), ectopic fat infiltration (visceral, intramuscular and pancreatic), and body composition (total abdominal fat tissue, occurrence of brown fat, and fat-free muscle volume). We will also study how such MRI-based measurements, individually and in various combinations, can relate to adverse heart remodeling, cardiovascular events and metabolic disease.

It would also be of great value to supplement with a longitudinal follow-up of the same research subjects after 3-4 years to study how long-term changes in the estimated MRI-based measurements relate to adverse cardiac remodeling, cardiovascular events, and metabolic disease.

The study subjects were recruited from the SCAPIS cohort. In total 46 persons with T2DM (as reported in SCAPIS forms) and 46 matched control subjects without T2DM.

MRI	Cardiovascular	Musculoskeletal
Gastrointestinal	Metabolism	Acquisition
AI/Data analytics	Imaging Biomarkers	

Project information

PROJECT NAME

Scapis-HEALTH

PROJECT LEADER

Carl-Johan Carlhäll, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS

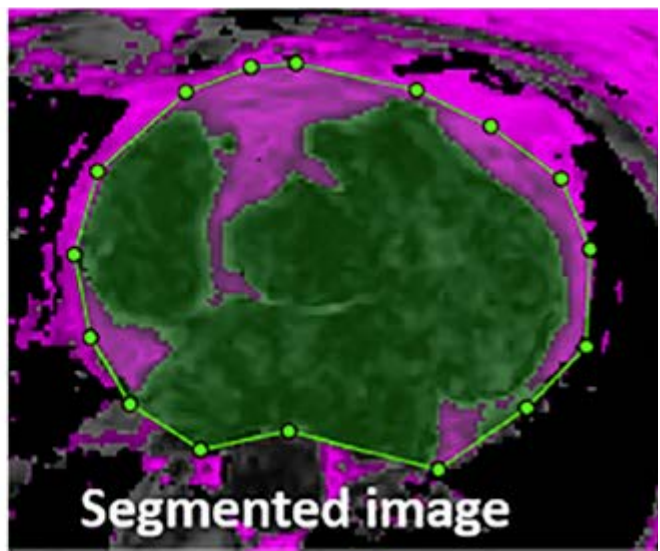
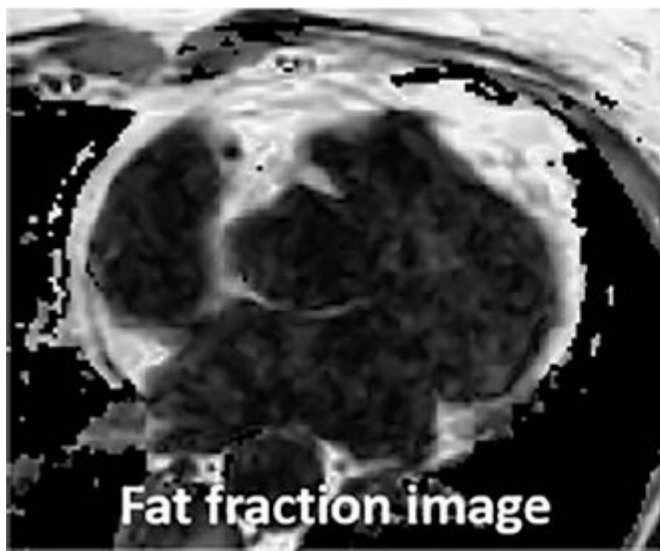
Peter Lundberg, Tino Ebberts, Olof Leinhard, Jan Engvall, Carl Johan Östgren, Eva Swahn, Mattias Ekstedt

GRANTS

KAW
Swedish Heart and Lung Foundation
Swedish Research Council

KEY PUBLICATIONS

Bergström G, Berglund G, Blomberg A, Brandberg J, Engström G, Engvall J, Eriksson M, de Faire U, Flinck A, Hansson MG, Hedblad B, Hjelmgren O, Jansson C, Jernberg T, Johnsson Å, Johansson L, Lind L, Löfdahl CG, Mellander O, Östgren CJ, Persson A, Sandström A, Schmidt C, Söderberg S, Sundström J, Toren K, Waldenström A, Wedel H, Vikgren J, Fagerberg B, Rosengren A. The Swedish CArdioPulmonary BIomage Study (SCAPIS): objectives and design. *J Intern Med.* 2015 Dec;278(6):645-59. doi: 10.1111/joim.12384.



Cardiac fat images in transversal view from a 3D Dixon sequence, showing the fat fraction image (left) and the segmented image (right) where the fat is color coded (purple) and the epicardial border outlined (green).

Diffuse Myocardial Fibrosis

Approximately 1 800 aortic valve implantations are performed every year in Sweden, the majority due to aortic valve stenosis. Symptoms and/or impairment of left ventricular function are indications for surgery. However, symptoms and ventricular dysfunction occur late in the natural history of aortic valve stenosis. Irreversible impairment of left ventricular function (LVF) is believed to be related to diffuse myocardial fibrosis, which develops during disease progression as the heart compensates and develops hypertrophy. Regional fibrosis is known to cause impaired LVF after myocardial infarction, but data are scarce on how diffuse fibrosis affects cardiac performance and aerobic exercise capacity.

The overall purpose of the project is to improve patient management by generating knowledge on how diffuse myocardial fibrosis affects cardiac function and physical capacity over time, and how fibrosis is affected by surgical intervention. The specific hypotheses for the present project are that cardiac magnetic resonance imaging (CMR) gives a valid representation of diffuse myocardial fibrosis and compared to endomyocardial biopsy, fibrosis has a prognostic value for post-operative heart function and aerobic exercise capacity.

The preliminary results showed that our novel automated assessment support for diastolic function proved to be consistent for the analysis of a larger group of patients with aortic stenosis pre- and postoperatively. The algorithm is freely available for researchers and clinicians on-line (<https://liu.se/en/research/left-ventricular-diastolicfunction-decision-support>).

Analyses of a subgroup of CMR examinations pre- and postoperatively indicate that changes in myocardial relaxation times and thus changes in tissue characteristics can be observed already within the first 3 months after aortic valve implantation. The significant changes from preoperative examinations to the follow up may be interpreted as a reduction of interstitial fibrosis in the left ventricular wall.

This study has a unique design, where we adapt and develop new technology (both for research purposes and clinical use) within echocardiography, cardiopulmonary exercise testing and CMR. We also perform myocardial biopsy in the same patients, making it possible to gain new insights into the functional consequences of fibrosis, the effects of valve surgery, and ultimately, optimize pre- and post-operative treatment for patients with aortic stenosis.

MRI Cardiovascular
No Method Development

Project information

PROJECT NAME

Diffuse Myocardial Fibrosis: Functional Consequences for Cardiac and Overall Function in Patients with Aortic Stenosis

PROJECT LEADER

Éva Tamás, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

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GRANTS

The Swedish Heart-Lung Foundation
ALF
Region Östergötland

KEY PUBLICATIONS

Tamás É, Nylander E. Decision support for assessment of left ventricular diastolic function. *Physiol Rep*. 2018 Aug;6(16): e13815. doi: 10.14814/phy2.13815.

Kvernby S, Warntjes M, Carlhall C, Engvall J, Ebbers T. Clinical feasibility of 3D-QALAS - Single breath-hold 3D myocardial T1- and T2-mapping. *Magn Reson Imaging*. 2017 May;38:13-20. doi: 10.1016/j.mri.2016.12.014. Epub 2016 Dec 18. PMID: 2799874.

Kvernby S, Rönnerfalk M, Warntjes M, Carlhall C, Nylander E, Engvall J, Tamás É and Ebbers T. Longitudinal changes in myocardial T1 and T2 relaxation times related to diffuse myocardial fibrosis in aortic stenosis; before and after aortic valve replacement. *J Magn Reson Imaging*. 2018 Feb 23. doi: 10.1002/jmri.25980. [Epub ahead of print] PMID: 29473982.

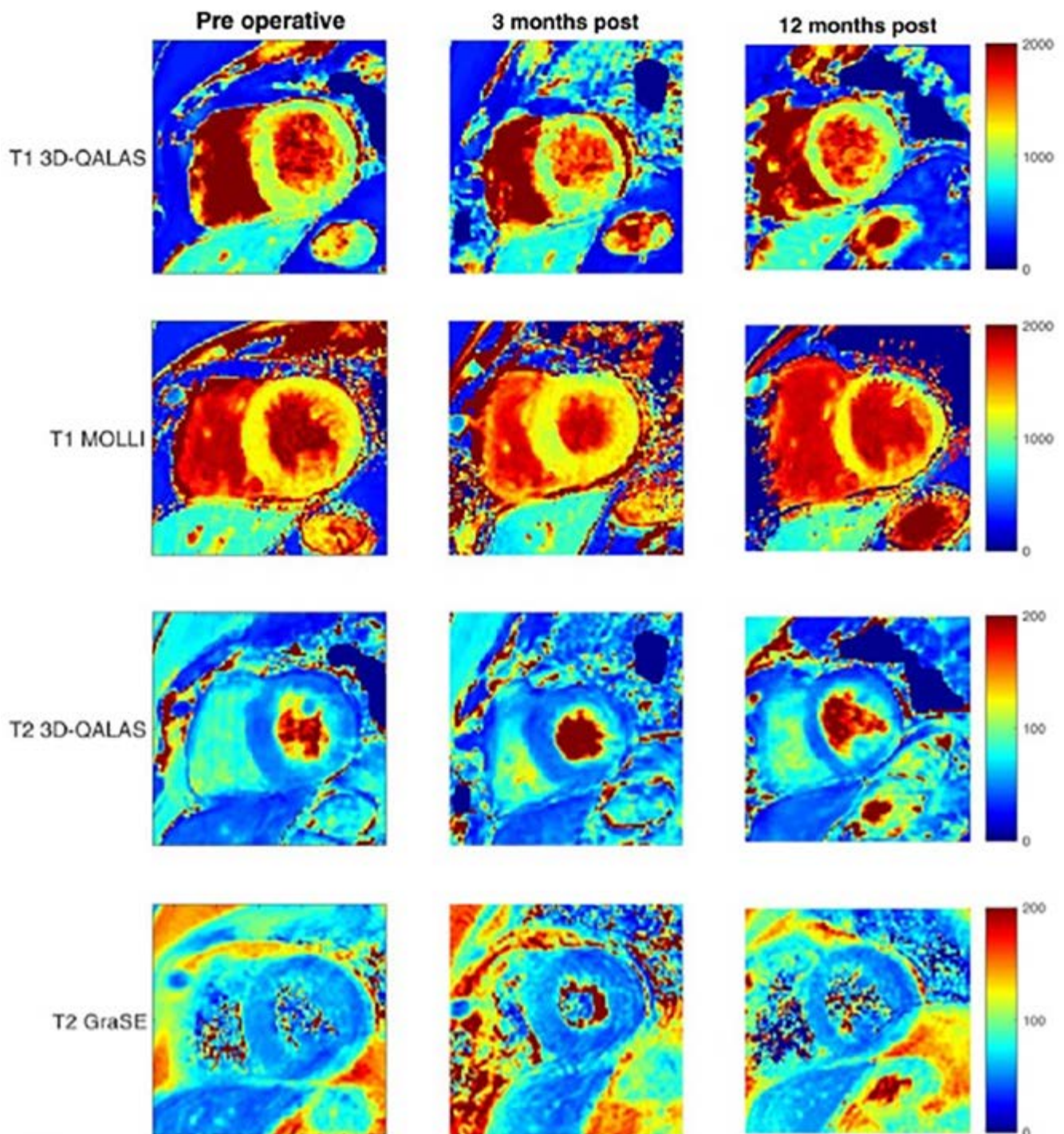


Illustration of mid-ventricular maps with 3D-QALAS, MOLLI and GraSE in a patient with severe aortic stenosis. The T1 and T2 relaxation times maps are acquired at three different time points: before, 3 and 12 months after surgery.

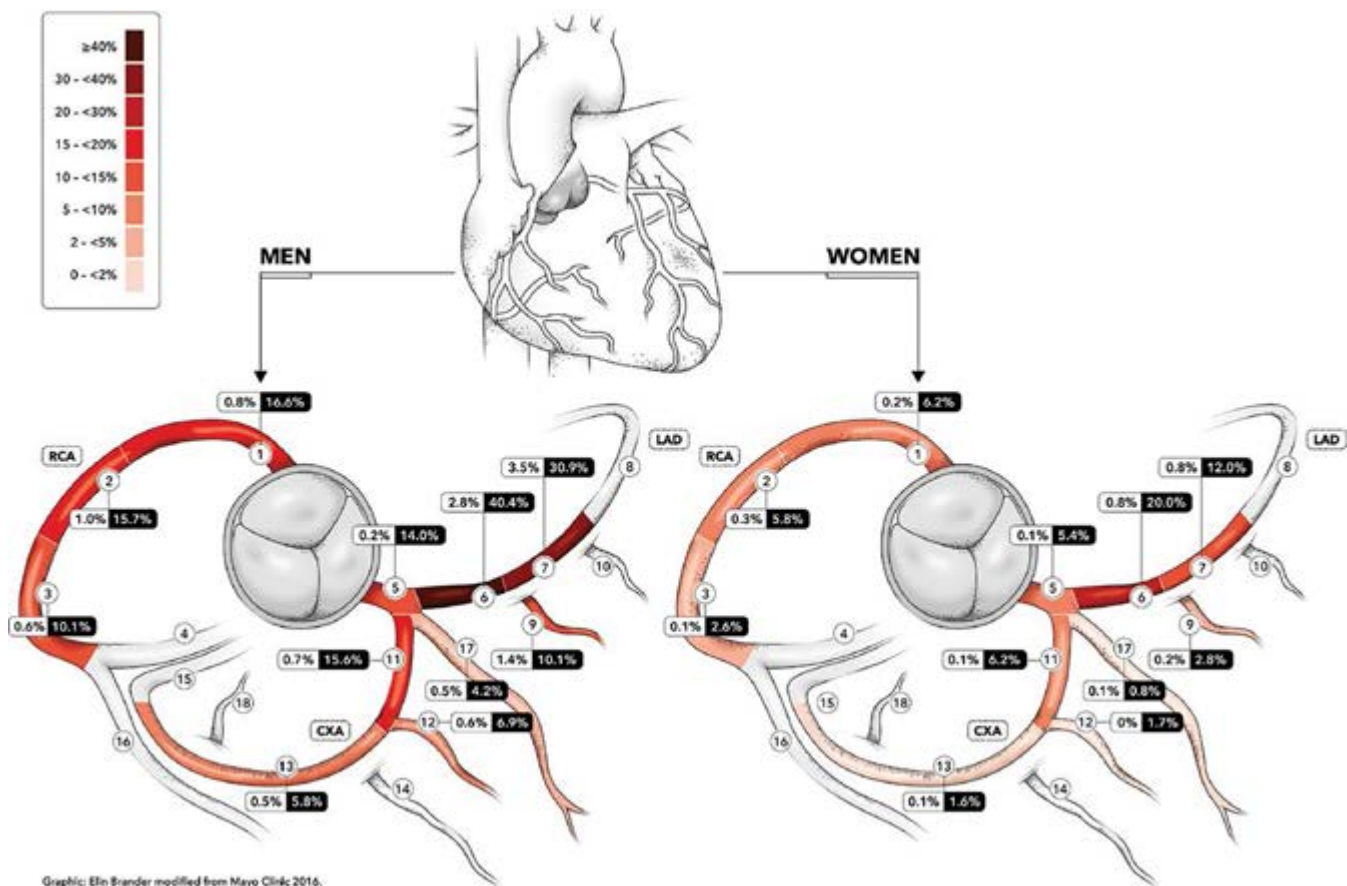
Swedish CARDioPulmonary bioImage Study (SCAPIS) in Linköping

SCAPIS is a collaborative project between six Swedish universities. We randomly invited 30,000 individuals from the general population living in six Swedish university cities (Gothenburg, Linköping, Malmö/Lund, Stockholm, Umeå and Uppsala), aged 50–64 years.

In Linköping we included 5058 study participants during 2015 and 2018 with a participation rate of 58%.

In addition to determining the traditional cardiovascular risk factors, the participants underwent extensive imaging, including non-contrast and con-

trast-enhanced computed tomography (CT) coronary angiography; CT scanning of the abdomen for the quantification of visceral and subcutaneous adipose tissue, liver fat; and ultrasound analysis for carotid artery atherosclerosis.



Distribution of coronary computed tomography angiography-detected atherosclerosis. Frequency of atherosclerosis in the 18 most proximal coronary segments in men (n=12 444) and women (n=12 738) in the SCAPIS cohort. The heat map refers to the frequency of any form of coronary computed tomography angiography-detected atherosclerosis. The numbers within boxes indicate the frequency of different degrees of vessel stenosis (white box, ≥50% stenosis; black box, any form of coronary computed tomography angiography-detected atherosclerosis). *Circulation*. 2021;144(12):916-929

In addition to the core study protocol, we have in SCAPIS-Linköping added several optional investigations as home blood pressure recordings (7 days), measuring stress exposure by cortisol levels in hair, echocardiography, microcirculatory function by integrated laser Doppler flowmetry and diffuse reflectance spectroscopy in a fiberoptic probe for skin, and determination of pulse wave velocity as a surrogate marker for arterial stiffness.

In a recent publication we showed that calcification in the coronary arteries was present in 39.5% and carotid plaque in 56.0%. In men, coronary artery calcium score (CACs) >0 ranged from 40.7% to 65.9% and presence of carotid plaques from 54.5% to 72.8% in the age group 50-54 and 60-65 years, respectively. In women, the corresponding difference was from 17.1% to 38.9% and from 41.0% to 58.4%.

At national level we are currently planning for a physical follow-up and a re-examination of the SCAPIS cohort. The re-examination will most likely start in the beginning of 2024 and broadly follow the baseline protocol and include a fasting blood samples for both immediate analysis and stored in a bio-bank for later analyses, anthropometry, blood pressure, accelerometry, dynamic spirometry and imaging of heart (including coronary arteries), lungs and fat depots with computed tomography.

Thus, we are investigating the prerequisites for performing a re-investigation of the SCAPIS cohort at Linköping University Hospital starting in 2024.

Computed Tomography MRI Ultrasound Cardiovascular Visualization
Imaging Biomarkers

Project information

PROJECT NAME

Swedish CardioPulmonary bioImage Study (SCAPIS) in Linköping

PROJECT LEADER

Carl Johan Östgren Department of Health, Medicine and Caring Sciences, Division of Prevention, Rehabilitation and Community Medicine

MAIN PROJECT PARTICIPANTS

Carl Johan Carlhäll, Jan Engvall, Eva Swahn, Petter Dyverfeldt, Anders Persson, Lena Jonasson, Märten Sandstedt, Elin Good, Fredrik Nyström, Tomas Faresjö, Tomas Lindahl, Tomas Strömberg

KEY PUBLICATIONS

Bergström G, Persson M, Adiels M, Björnson E, Bonander C, Ahlström H, Alfredsson J, Angerås O, Berglund G, Blomberg A, Brandberg J, Börjesson M, Cederlund K, de Faire U, Duvernoy O, Ekblom Ö, Engström G, Engvall JE, Fagman E, Eriksson M, Erlinge D, Fagerberg B, Flinck A, Gonçalves I, Hagström E, Hjelmgren O, Lind L, Lindberg E, Lindqvist P, Ljungberg J, Magnusson M, Mannila M, Markstad H, Mohammad MA, Nyström FH, Ostenfeld E, Persson A, Rosengren A, Sandström A, Sjölander A, Sköld MC, Sundström J, Swahn E, Söderberg S, Torén K, Östgren CJ, Jernberg T. Prevalence of Subclinical Coronary Artery Atherosclerosis in the General Population. *Circulation*. 2021 Sep 21;144(12):916-929. doi: 10.1161/CIRCULATIONAHA.121.055340. Epub 2021 Sep 20.

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Östgren CJ, Söderberg S, Festin K, Angerås O, Bergström G, Blomberg A, Brandberg J, Cederlund K, Eliasson M, Engström G, Erlinge D, Fagman E, Hagström E, Lind L, Mannila M, Nilsson U, Oldgren J, Ostenfeld E, Persson A, Persson J, Persson M, Rosengren A, Sundström J, Swahn E, Engvall JE, Jernberg T. Systematic Coronary Risk Evaluation estimated risk and prevalent subclinical atherosclerosis in coronary and carotid arteries: A population-based cohort analysis from the Swedish Cardiopulmonary BioImage Study. *Eur J Prev Cardiol*. 2021 Apr 23;28(3):250-259. doi: 10.1177/2047487320909300.

Tissue Classification Using DECT and MBIR

Today's computed tomography (CT) images are affected by inaccuracies and artifacts caused by the use of polyenergetic photon beams. Despite active research in this field, even the most advanced image reconstruction algorithms still do not provide quantitatively accurate CT numbers. We have developed a dual-energy iterative image reconstruction algorithm (DIRA) which improves the accuracy of CT numbers by modeling the material composition of the imaged object. The improvement can be seen when compared to both the Monoenergetic Plus and Alvarez-Macovski based reconstructions, see Figures 1 and 2.

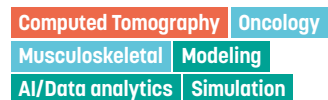
In DIRA, image pixels of patients are typically classified into the bone and soft tissue. Bone pixels carry information about percentages of compact bone and a mixture of red and yellow bone marrow. Soft tissue pixels carry information about percentages of water, protein, and lipid. Other organ-specific classification schemes are possible.

The estimated material composition can be used for improved medical diagnosis and treatment. For instance, DIRA can be used for the determination of calcium content in the prostate gland. Such information is useful for radiation treatment planning in brachytherapy with low-energy photons; a high calcium content in the prostate changes the spatial distribution of absorbed dose since

the dose strongly depends on the tissue's atomic number. DIRA is also useful in proton radiation therapy since the position of the dose maximum is sensitive to the material composition of the patient tissues.

DIRA is a proof-of-concept code for testing various data processing approaches. For instance, we developed a method for the segmentation of bones using a deep learning algorithm (González Sánchez et al, 2020) (Figure 3) and we work on deep learning methods for the segmentation of other tissues and the determination of elemental composition. To compare the performance of DIRA with clinically used algorithms, we enhance DIRA (Magnusson et al 2019) so that it can work with data produced by CT scanners using energy integrating detectors and energy-resolving photon-counting detectors. In the latter case, DIRA is being extended to work with multi-energy CT data.

The advanced algorithms used in DIRA are time demanding. To shorten the reconstruction time, we develop a deep learning algorithm capable of mimicking the performance of DIRA. Such an algorithm would perform the image reconstruction and determination of the elemental composition of tissues in a fraction of time only. In this effort, DIRA is used for the generation of training data for this algorithm.



Project information

PROJECT NAME

TCDECT - Tissue Classification using Dual Energy CT and Iterative Reconstruction

PROJECT LEADER

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MAIN PROJECT PARTICIPANTS

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GRANTS

VR-NT (2017 - 2020)
Cancerfonden
(2013 - 2015, 2016 - 2018, 2019 - 2021)
Patientsäkerhetsforskning, Region Östergötland (2018 - 2019)

KEY PUBLICATIONS

Magnusson M, Sandborg M, Alm Carlsson G, Henriksson L, Carlsson Tedgren Å and Malusek A [2021]. Accuracy of CT Numbers Obtained by Dira and Monoenergetic Plus Algorithms in Dual-Energy Computed Tomography Radiat Prot Dosimetry, Vol. 195, No. 3-4, pp. 212-217.
Gonzalez Sanchez J C, Magnusson M, Sandborg M, Carlsson Tedgren Å and Malusek A [2020]. Segmentation of bones in medical dual-energy computed tomography volumes using the 3D U-Net Phys Med 69 241-7.
Magnusson M, Björnfor M, Carlsson Tedgren Å, Alm Carlsson G, Sandborg M and Malusek A [2019]. DIRA-3D—a model-based iterative algorithm for accurate dual-energy dual-source 3D helical CT Biomedical Physics & Engineering Express 5 065005.

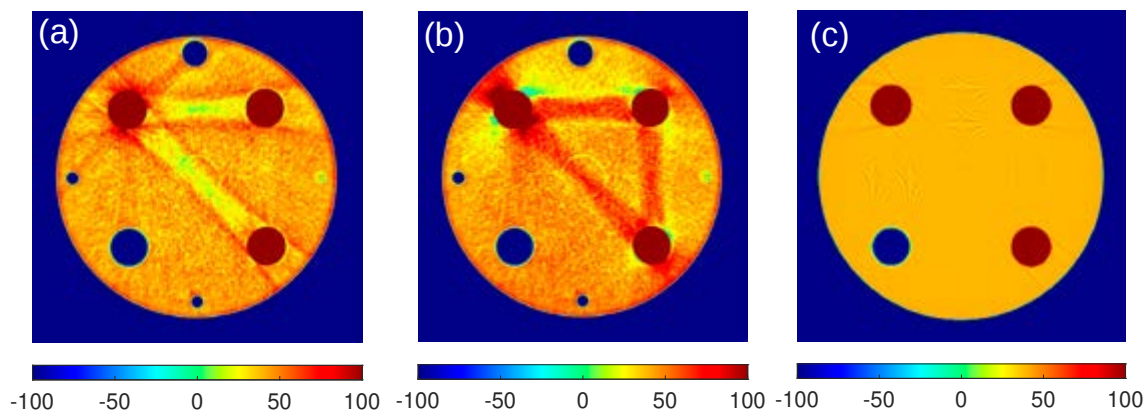


Figure 1. Images of a cylindrical PMMA phantom containing aluminium, low density polyethylene, and Teflon inserts reconstructed at 40 keV using Monoenergetic Plus (a) without and (b) with iBHC, and (c) DIRA. The range of CT numbers has been adjusted to emphasize the beam hardening artifact. Taken from (Magnusson et al 2021) under CC BY.

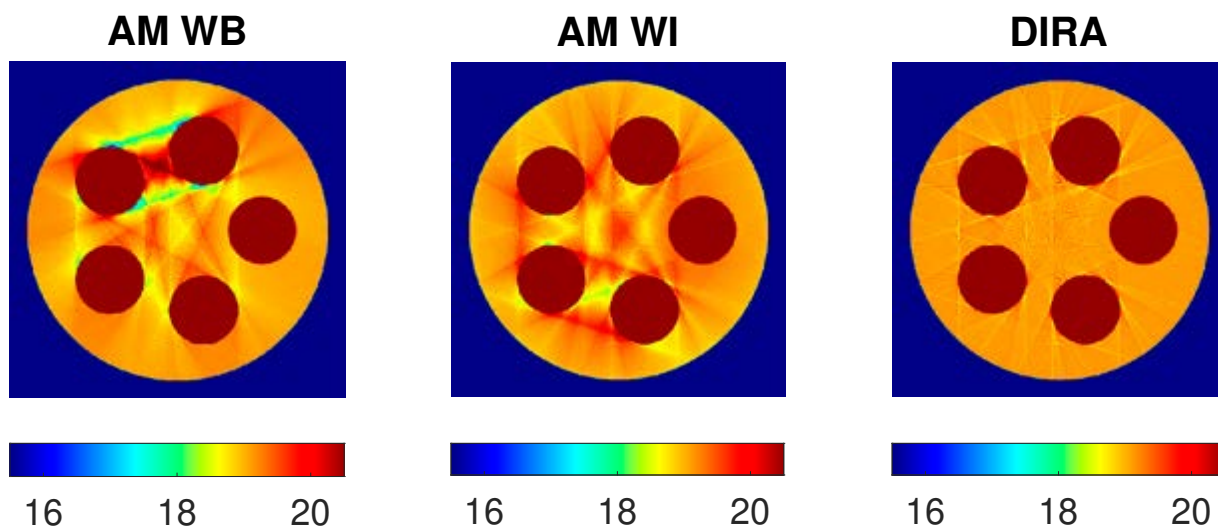


Figure 2. Images of a cylindrical protein phantom containing water, bone and iodine solution inserts reconstructed at 50 keV by the Alvarez-Macovski method using (a) the (water, bone) and (b) (water, iodine) doublets. (c) A reconstruction by DIRA using the (lipid, protein, water) triplet in the protein region, (water, bone) doublet in the bone region, and (iodine, water) doublet in the iodine region. Taken from Magnusson et al, doi.org/10.1093/rpd/ncab097 under CC BY.

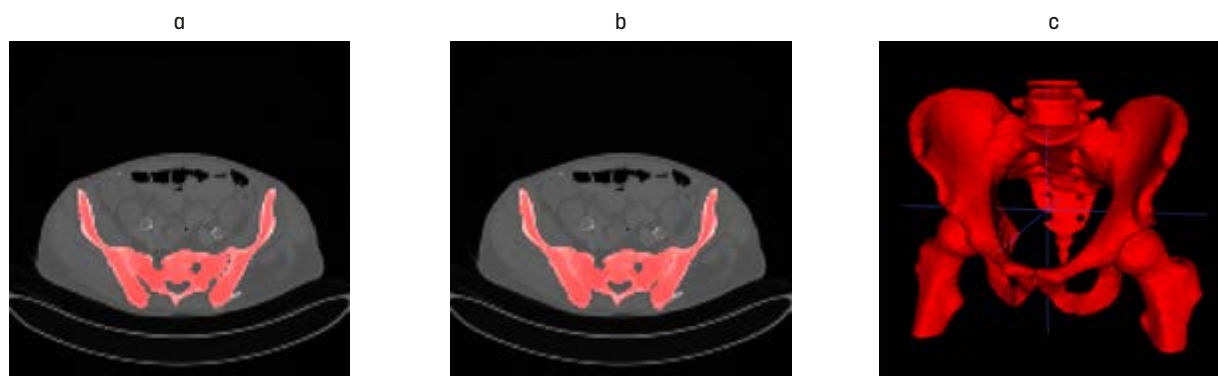


Figure 3. Segmentation of pelvic bones via the 3D U-Net architecture. (a) Ground truth. (b) Prediction of our algorithm. (c) 3D view of the prediction. Taken from (González Sánchez et al, 2020) under CC BY.

Evaluation of New Brachytherapy Planning Methods

High dose rate brachytherapy is a form of radiation therapy commonly used as a boost to external beam radiation therapy in treating prostate and cervical cancer. A small (dimensions of mm) sealed radioactive source of the isotope ^{192}Ir , emitting photons at an average energy of 350 keV is used. Brachytherapy is sometimes called interior radiation therapy. Invasively inserted catheters or anatomy shaped applicators are inserted and provides the possible positions to place the source in the patient. Advantages over external beam radiotherapy is the capacity to better conform the dose to the treatment volume (the target), lower dose to healthy tissue and less problem with organ motion (as the catheters move with the target). Three-dimensional (3D) imaging with ultrasound, magnetic resonance or computed tomography is used to assist catheter placement and to delineate the volume to be treated (the target) and the nearby healthy organs at risk. The dwelling time of the single ^{192}Ir source is varied dependent on location in the patient to create the final dose distribution. Treatment planning amounts to decide source positions and source dwelling times in a way that yields best compromise between high dose to the target volume and doses to organs at risk low enough to limit the risk for severe side effects. Manual methods or methods based

on mathematical optimization are used. Benefits of the latter is that it goes faster (of advantage in brachytherapy as the patient awaits treatment in anesthesia), is more consistent and less dependent on staff experience. Our group works on developing improved methods and models for automated brachytherapy treatment planning based on mathematical optimization and the aim of this project is to evaluate and further develop them in clinical context. Automated treatment planning is prone to yield uneven distribution of dwelling times, giving rise to regions with high dose, often resolved by manual fine-tuning. Currently we work on evaluating an in-house developed adjustment tool, developed to improve clinical treatment plans upon spatial properties (Morén et al 2019). A paired observer study is under setup, to validate the performance of the adjustment tool against original clinical approved prostate treatment plans. Observers are radiation oncologists experienced with prostate brachytherapy from three Swedish hospitals. Visual grading methods with origin in radiology will be used, to our knowledge such methods have not before been investigated in grading radiotherapy treatment plans.

Computed Tomography MRI Ultrasound
Oncology Modeling Visualization

Project information

PROJECT NAME

CT BTP – Dosimetric evaluation and development of new methods for automated brachytherapy treatment planning

PROJECT LEADER

Åsa Carlsson Tedgren, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine Main Project Participants

MAIN PROJECT PARTICIPANTS

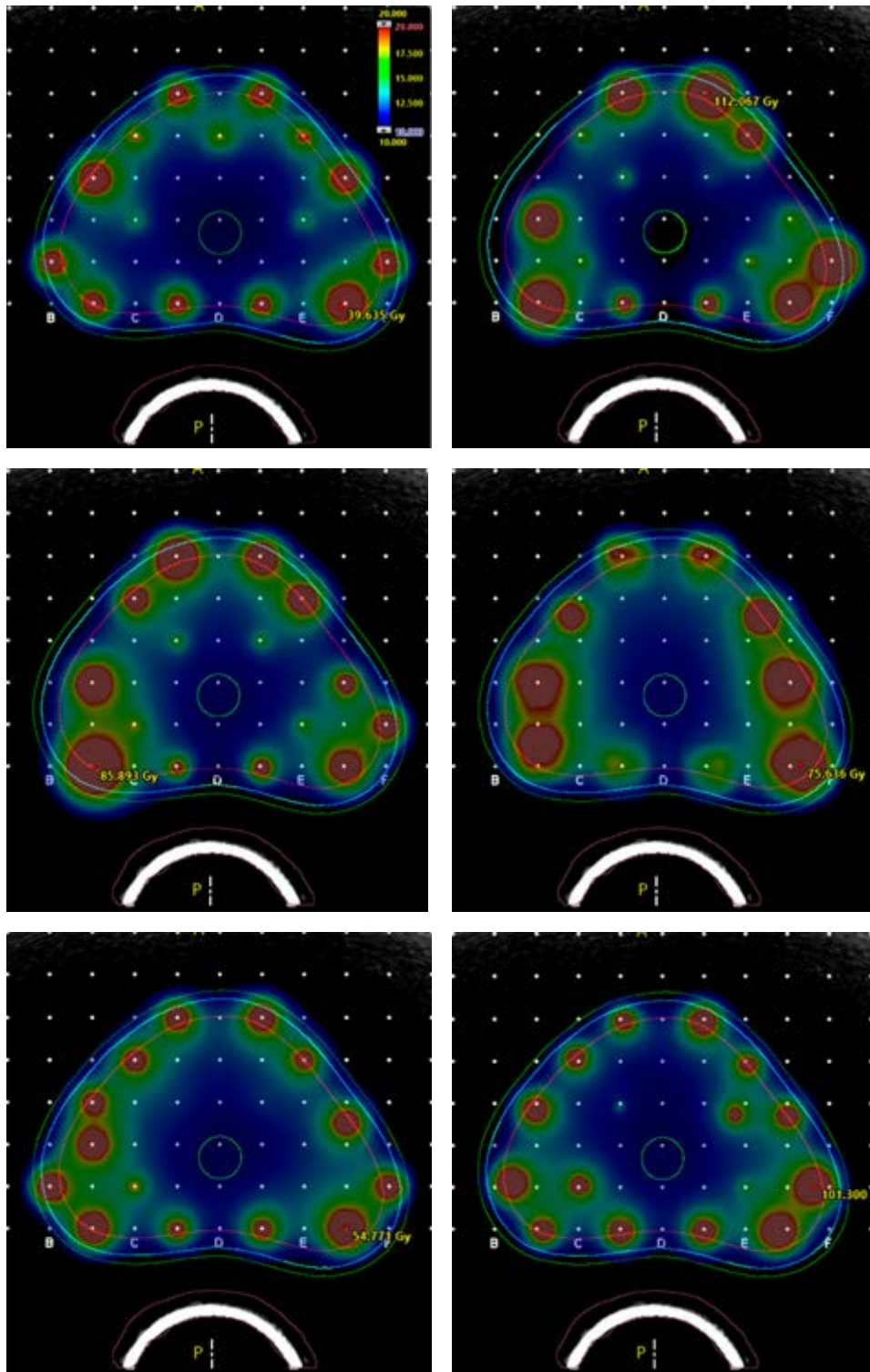
Frida Dohlmär, Michael Sandborg, Björn Morén, Torbjörn Larsson

GRANTS

VR-NT (2020 - 2023)
Cancerfonden (2019 - 2021)
LiU Cancer (2020 - 2021, 2021 - 2022)
Region Östergötland "student till docent" (2021 - 2022)

KEY PUBLICATIONS

Dohlmär F, Johansson S, Larsson T, Sandborg M and Carlsson Tedgren Å [2021]. An audit of high dose-rate prostate brachytherapy treatment planning at six Swedish clinics J of Contemp Brachyther 13 59-71.
Morén B, Larsson T and Carlsson Tedgren Å [2021]. Optimization in treatment planning of high dose-rate brachytherapy – Review and analysis of mathematical models Med Phys 48 2057-82.
Morén B, Larsson T and Carlsson Tedgren Å [2019]. A mathematical optimization model for spatial adjustments of dose distributions in high dose-rate brachytherapy Phys Med Biol 64 225012.



A dosimetric audit of prostate brachytherapy treatment planning has been conducted to study differences in approach [Dohlmair et al 2021]. The six Swedish clinics performing prostate brachytherapy planned a treatment on the same "patient" (a phantom with contoured prostate (the target), urethra and rectum). One slice from the resulting 3D treatment plans with the dose in color wash is shown here. All plans fulfilled dosimetric constraints. Taken from Dohlmair et al (2021) under CC BY.

Comparison of CT Technical Image Quality of Using PCCT and EID

The clinical use of computed tomography (CT) increases steadily which favors the patient since CT is a quick and non-invasive examination. Previously we have evaluated the benefits of using two energies of the X ray beam to more reliably separate human tissues for more accurate patient dose delivery in proton radiotherapy. We have also explored the positive effects on image quality of using advanced image reconstruction methods by reducing the noise in the images and hence enabling significant reductions in patient exposure to minimize radiation risk.

The introduction of new types of CT photon counting detectors (PCD) have many advantages, such as potentially sharper images and less image noise. We have explored the noise properties of a prototype CT scanner from Siemens

Healthineers (SOMATOM Count Plus) and compared it to a CT scanner with conventional energy integrating detectors (SOMATOM Force).

Quantitative measurement of the noise properties (noise power spectrum, Elgström et al. 2021) provides valuable support to explain the findings from surveys of clinical image quality when images are assessed by radiologists. The use of so-called model observers, where a computer algorithm mimics the radiologists, minimizes the bias found with human observers.

With the 2021 new clinically released photon counting CT system with a strong focus on research, we aim to further explore the noise advantages of using photon counting detector in clinical patient trials to further improve patient safety.

Computed Tomography Acquisition
Modeling Visualization

Project information

PROJECT NAME

Comparison of CT technical image quality of using photon counting and energy integrating detection

PROJECT LEADER

Michael Sandborg, Medical Radiation Physics, Department of Medicine, Health and Caring Sciences

MAIN PROJECT PARTICIPANTS

Michael Sandborg, Henrik Elgström, Jonas Nilsson Althén, Alexandr Malusek, Erik Tesselaar, Yuting Wang, Erik Nordström, Nils Dahlström

GRANTS

RFoU (2021)

KEY PUBLICATIONS

Henrik Elgström, Jonas Nilsson Althén and Michael Sandborg. Preliminary assessment of noise properties of a prototype photon counting CT. Oral presentation at NACP symposium 11-13 April 2021.

Erik Nordström. Image Quality and Radiation Dose of Photon-Counting Computed Tomography Compared to Conventional Computed Tomography. Fördjupningsarbete Läkarpogrammet, Kurs 8 Linköpings Universitet. Supervised by Nils Dahlström.

Yuting Wang. An application of channelized Hotelling observer for optimization of CT scanning protocols. Master thesis Uppsala University and Linköping University (work in progress) Supervised by Alexandr Malusek.

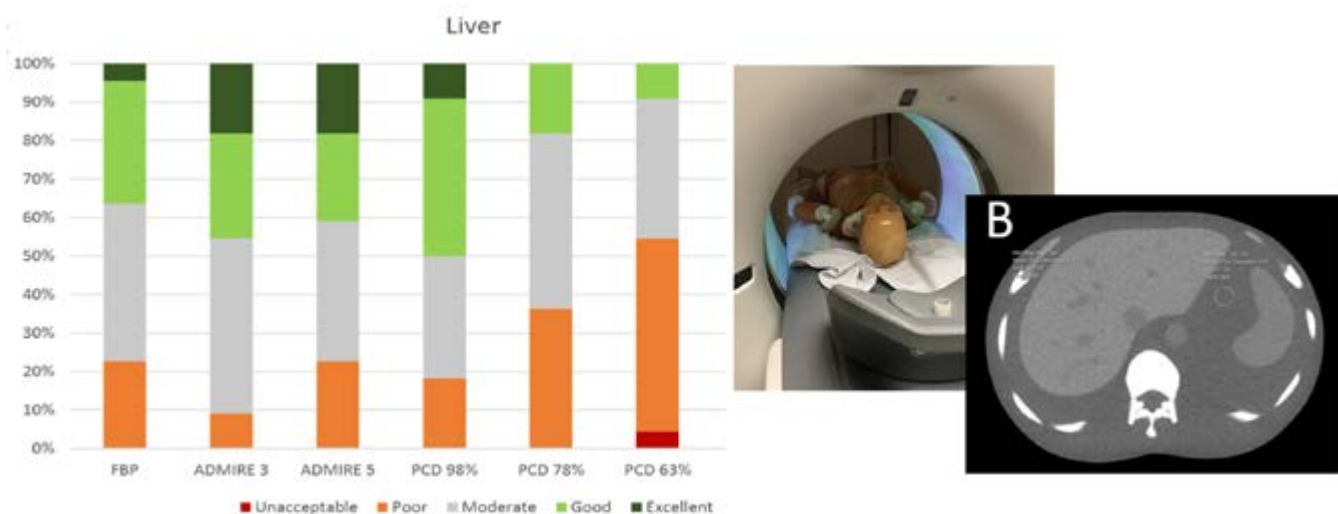


Figure 1 (Nordström 2021) shows the results of 11 radiologist combined perception of how well the liver is visualized in an anthropomorphic phantom. The results show that the prototype CT-scanner (PCD) was significantly better when compared to the traditional scanner with image reconstruction using filtered back projection, FBP, at the same patient dose. However, using model-based iterative image reconstruction (ADMIRE 3 and 5) with the conventional CT scanner, improved visualization of the liver.

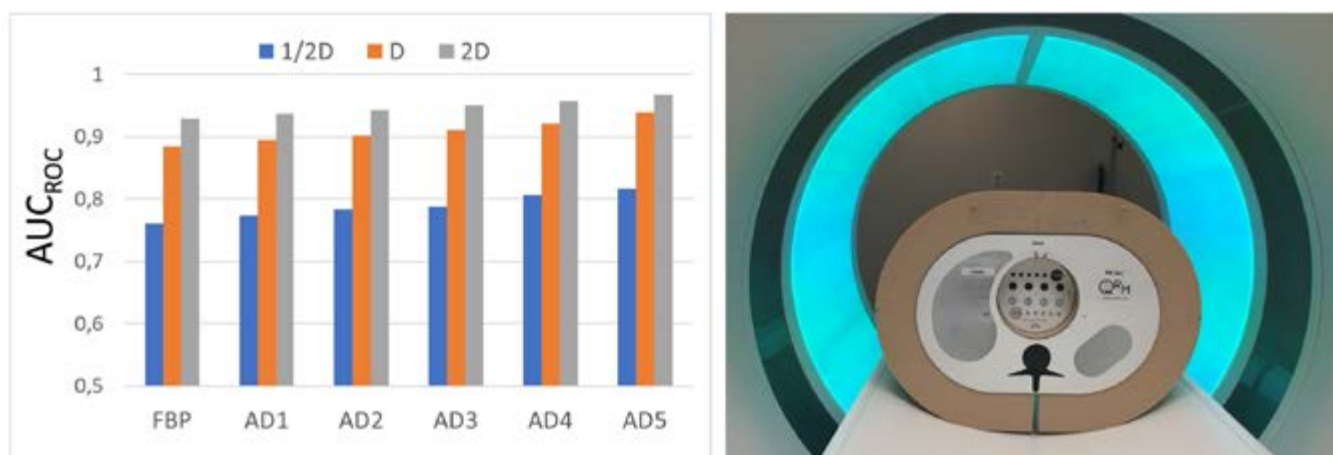


Figure 2 (Wang 2021) shows the detectability of low-contrast details (lesions) in a semi-anthropomorphic phantom using a model observer (computer algorithm). The area under the Receiver Operating Characteristic curve, AUCROC is a measure of lesion detectability. The detectability increases (AUCROC closer to 1) with increasing patient dose, D (D/2, D and 2D) and with iterative reconstruction strength AD1 to AD5. By reliably tuning the model observer AUCROC to radiologist's evaluation would enable quick, and systematic assessment of lesion detectability in CT.

BIGPICTURE

To take AI development in pathology to the next level, a European consortium combining leading European research centres, hospitals as well as major pharmaceutical industries, is going to develop the world's biggest repository for sharing of pathology data. The 6-year, €70 million project called BIGPICTURE, will herald a new era in pathology.

Center for Image Science and Visualization (CMIV) at Linköping University engages heavily in BIGPICTURE. CMIV is responsible for the technical infrastructure in collaboration with the SciLifeLab Bioinformatics platform NBIS and ELIXIR-SE and the Finnish ELIXIR node CSC.

The project partly builds on experiences from the CMIV-hosted AIDA Data Hub. The CMIV efforts include close collaboration with BIGPICTURE partners Region Östergötland and Sectra.

To allow the fast development of AI in pathology, the BIGPICTURE project aims to create the first European, ethical and GDPR-compliant (General Data Protection Regulation), quality-con-

trolled platform, in which both large-scale data and AI algorithms will coexist.

The BIGPICTURE platform will be developed in a sustainable and inclusive way by connecting communities of pathologists, researchers, AI developers, patients, and industry parties.

The project is divided into four main aspects that concern the large-scale collection of data. First, an infrastructure (hardware and software) must be created to store, share and process millions of images that can be gigabytes each.

Second, legal and ethical constraints must be put in place to ensure adequate usage of data while fully respecting patient's privacy and data confidentiality. Then, an initial set of 3 million digital slides from humans and laboratory animals will be collected and stored into the repository to provide data for the development of pathology AI tools. Finally, functionalities that aid the use of the database as well as the processing of images for diagnostic and research purposes will be developed.

Digital Microscopy	Oncology
Gastrointestinal	Gynecological
Pulmonary	Acquisition AI/Data analytics

Project information

PROJECT NAME

BIGPICTURE

PROJECT LEADER

Joel Hedlund, Department of Science and Technology, Media and Information Technology

MAIN PROJECT PARTICIPANTS

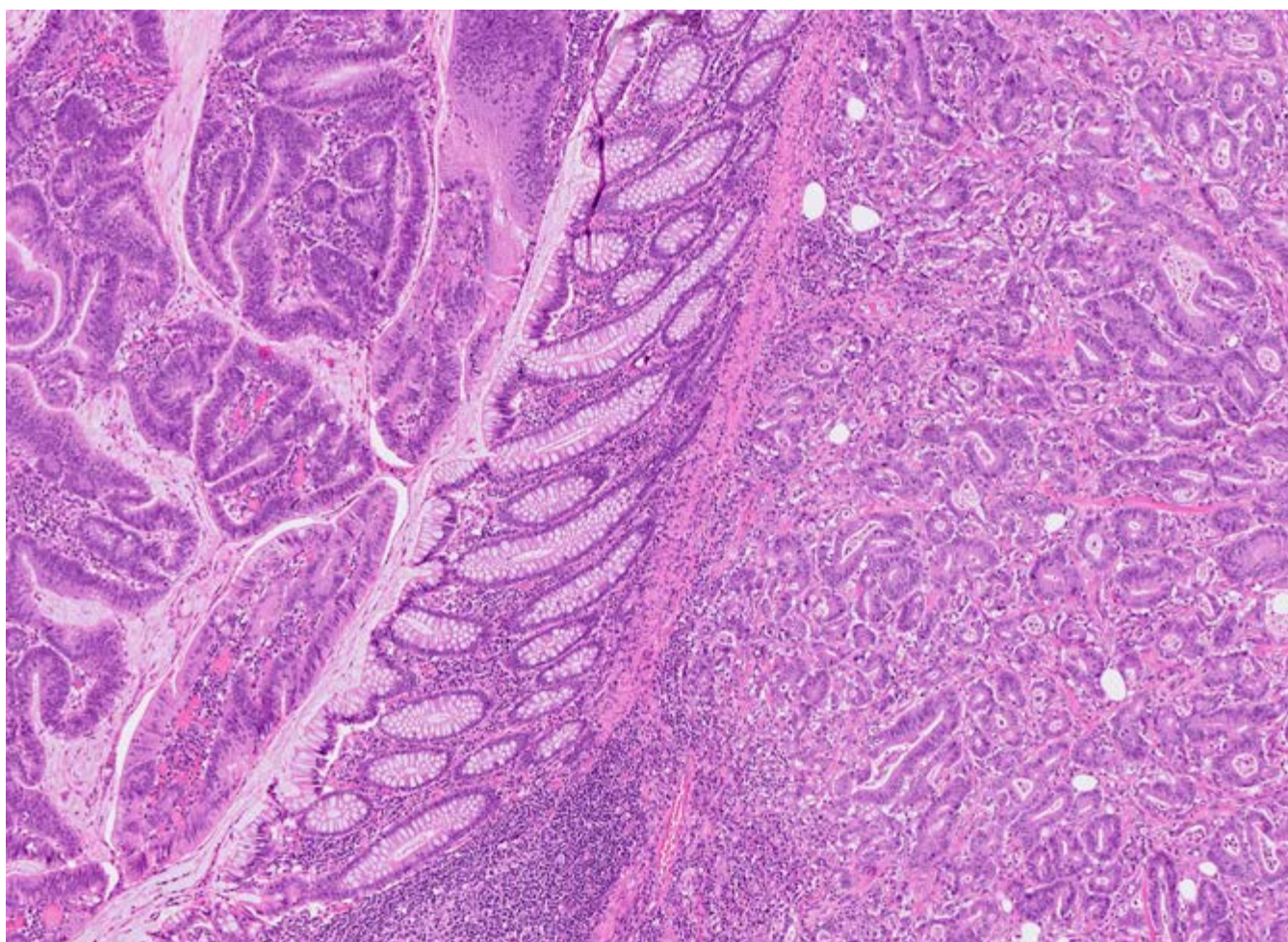
Shreyas Shivakumara, Caroline Bivik Stadler, Claes Lundström, Jeroen van der Laak, Darren Treanor, Anna Bodén, Håkan Gustafsson

GRANTS

Innovative Medicines Initiative (Horizon2020, EFPIA)



This project has received funding from the Innovative Medicines Initiative 2 Joint Undertaking under grant agreement No 945358. This Joint Undertaking receives support from the European Union's Horizon 2020 research and innovation program and EFPIA (www.imi.europa.eu). This communication reflects the consortium's view. Neither IMI nor the European Union or EFPIA are responsible for any use that may be made of the information contained therein.



Digital image of a tissue sample of colon cancer from the BIGPICTURE predecessor AIDA Data Hub.

AIDA

Analytic Imaging Diagnostic Arena (AIDA) is a national arena for research and innovation in medical image analysis. AIDA is a cross-disciplinary collaboration aiming for largescale use of Artificial Intelligence (AI) in healthcare. Here, academia, healthcare and industry meet to translate technical advances in AI technology into patient benefit in the form of clinically useful tools. CMIV is the host and physical meeting place of AIDA but aims to assist all Swedish actors in this domain.

The technical development within AI has been extremely strong in recent years. Modern AI is a toolbox that fits perfectly into the healthcare vision of “precision medicine”, the fully tailored treatment for each patient. Very few modern AI solutions have yet, however, reached actual use in imaging diagnostics. The reason is that the step from experiments to clinical routine entails many challenges. Even the most powerful algorithms need to be carefully placed in a context of workflow and interaction innovations to be useful.

AIDA’s objective is to develop AI-based decision support solutions for imaging diagnostics that reach all the way to clinical use. An underpinning fundamental insight is that this complex challenge requires both interdisciplinary and cross-sectoral collaboration.

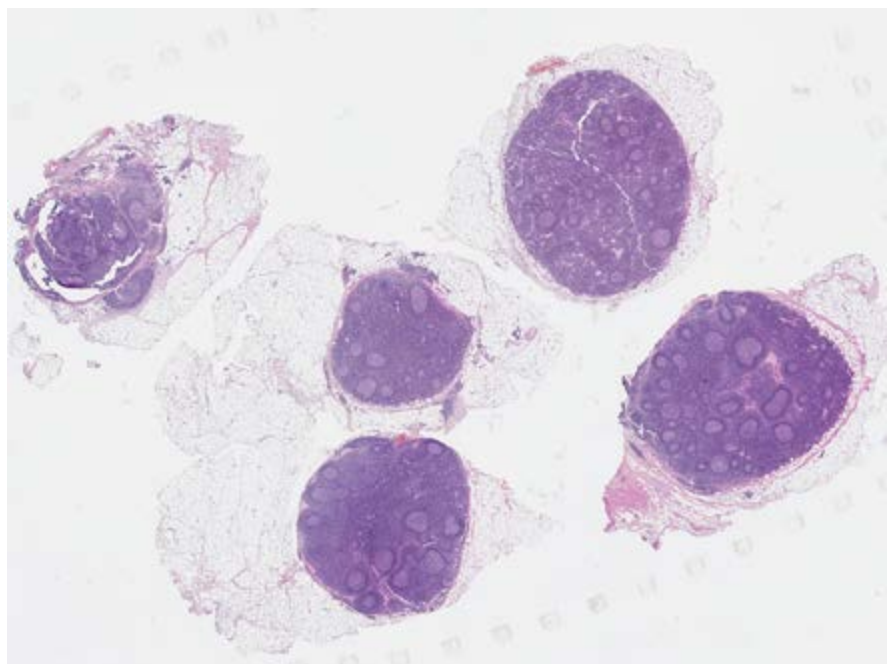
AIDA activities can be divided into three areas. Most resources are used for projects developing AI-based decision support solutions. These are run by research groups in industry and academia across Sweden, in collaboration with healthcare providers. The second area

is clinical competence development, to give healthcare the right knowledge base to drive the AI development in the most effective direction. AIDA offers clinical fellowships where care provider employees carry out an individual project as continued education. AIDA also regularly organizes AI courses for physicians.

A third area was started in 2021, an incubator for validation platforms. The challenge targeted is the ability of

Swedish healthcare to validate existing AI products. The platforms developed within the incubator will provide ready-to-use curated datasets and methods for high-quality validation.

The AIDA operations are supported by the core AIDA environment at CMIV. There is a tailor-made technology platform for efficient AI development, with the flagship resource being the heavy-load computational system DGX-



An example from the LNC02 data set, showing a whole slide pathology image with colon lymph nodes. The LNC0 and LNC02 data sets are one of the biggest shared histology data sets in the world.

2 shared between the groups across the country. AIDA also hosts a data hub with clinically relevant data available for AI research, currently over 5 TB and growing. Perhaps even more important is the meeting place aspect of the core environment, where workshops and meet-ups are frequently organized, providing valuable knowledge and exchanges.

AIDA is an initiative within the Strategic innovation program Medtech-4Health, jointly supported by VINNOVA, Formas and the Swedish Energy Agency. The AIDA Data Hub is from July 2021 a part of the BioImage Informatics Facility within SciLifeLab.

Computed Tomography	MRI	Digital Microscopy	Ultrasound	Other	Cardiovascular
Neurology	Oncology	Musculoskeletal	Gastrointestinal	Gynecological	Pulmonary
AI/Data analytics	Visualization				

Project information

PROJECT NAME

Analytic Imaging Diagnostic Arena

PROJECT LEADER

Claes Lundström, Department of Science and Technology, Media and Information Technology

MAIN PROJECT PARTICIPANTS

Caroline Bivik Stadler, Joel Hedlund, Catrin Nejdeby, Håkan Gustafsson, Maria Kvist, Jonas Unger, Gabriel Eilertsen, Shreyas Shivakumara, Betül Eren Keskin, Marie Waltersson, Darren Treanor, Petter Dyverfeldt, Evren Özarslan, Anders Eklund, Tino Ebberts, Martin Lindvall, Karin Stacke

GRANTS

VINNOVA Medtech4Health, SciLifeLab VINNOVA Innovation environments in precision health

KEY PUBLICATIONS

Jakub Olczak, John Pavlopoulos, Jasper Prijs, Frank FA Ijzema, Job N Doornberg, Claes Lundström, Joel Hedlund, Max Gordon. Presenting artificial intelligence, deep learning, and machine learning studies to clinicians and healthcare stakeholders: an introductory reference with a guideline and a Clinical AI Research (CAIR) checklist proposal. *Acta orthopaedica* (2021).

Joel Hedlund, Anders Eklund, Claes Lundström. Key insights in the AIDA community policy on sharing of clinical imaging data for research in Sweden. *Nature Scientific Data* (2020).

Caroline Bivik Stadler, Martin Lindvall, Claes Lundström, Anna Bodén, Karin Lindman, Jeronimo Rose, Darren Treanor, Johan Blomma, Karin Stacke, Nicolas Pinchaud, Martin Hedlund, Filip Landgren, Mischa Woissetschläger, Daniel Forsberg. Proactive Construction of an Annotated Imaging Database for Artificial Intelligence Training. *Journal of Digital Imaging* (2020).



AIDA Data Hub has facilitated legal and ethical data sharing with researchers in 22 countries across five continents.

EPSONIP

In EPSONiP (Evaluate Prevalence and Severity of Non-Alcoholic Fatty Liver Disease in Primary Care) the latest magnetic resonance imaging (MRI) techniques are used to investigate 400 patients with diabetes type 2. The patients are identified in primary care ensuring a representative selection of typical Swedish diabetes patients. The MR technique can measure body composition and map fat content in different adipose tissue throughout the body, such as intra-abdominal and gluteal. Moreover, we can with great detail measure fat content within several internal organs, such as the liver.

Fatty liver is the most common liver disease worldwide. One in five have fatty liver with a risk of developing diabetes, cardiovascular disease, and severe liver disease. Fatty liver is the fastest growing indication for liver transplantation in Sweden. There is a strong link between diabetes and fatty liver, but it is not known how many diabetes patients that

are affected. Even though fatty liver is very common, only a minority develop severe liver disease.

Fatty liver is closely related to the metabolic syndrome and share several risk factors for developing cardiovascular disease. This project will investigate fat infiltration in the heart as well as measurement of cardiac function using MR imaging. Through EPSONiP we will gain a unique insight into the relationship between fat distribution and development of liver and cardiovascular disease in diabetic patients.

Recruitment is ongoing and we have currently included 150 individuals, whereof 120 individuals have completed all parts of the study protocol. A sub study within the EPSONIP, EPSONIP-SLEEP, has started with the aim to study sleep patterns in patients with type 2 diabetes with and without fatty liver disease.

MRI	Digital Microscopy	Cardiovascular
Musculoskeletal	Gastrointestinal	
Metabolism	Acquisition	Modeling
Visualization	Imaging Biomarkers	

Project information

PROJECT NAME

Evaluating Prevalence and Severity Of NAFLD In Primary care

PROJECT LEADER

Mattias Ekstedt, Department of Medical and Health Sciences, Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS

Joakim Alfredsson, Martin Bergam, Carl-Johan Carlhäll, Gunnar Cedersund, Tino Ebbers, Nils Dahlström, Martin Henriksson, Fredrik Iredahl, Stergios Kechagias, Peter Lundberg, Patrik Nasr, Karin Rådholm, Christian Simonsson

GRANTS

ALF-Grant
Mag-tarmfonden
Rut och Rikard Juhlin

KEY PUBLICATIONS

Nasr P, Iredahl F, Dahlström N, Rådholm K, Henriksson P, Cedersund G, Dahlqvist Leinhard O, Ebbers T, Alfredsson J, Carlhäll CJ, Lundberg P, Kechagias S, Ekstedt M. Evaluating the prevalence and severity of NAFLD in primary care: the EPSONIP study protocol. *BMC Gastroenterol.* 2021 Apr 20;21(1):180. doi: 10.1186/s12876-021-01763-z. PMID: 33879084; PMCID: PMC8056630.

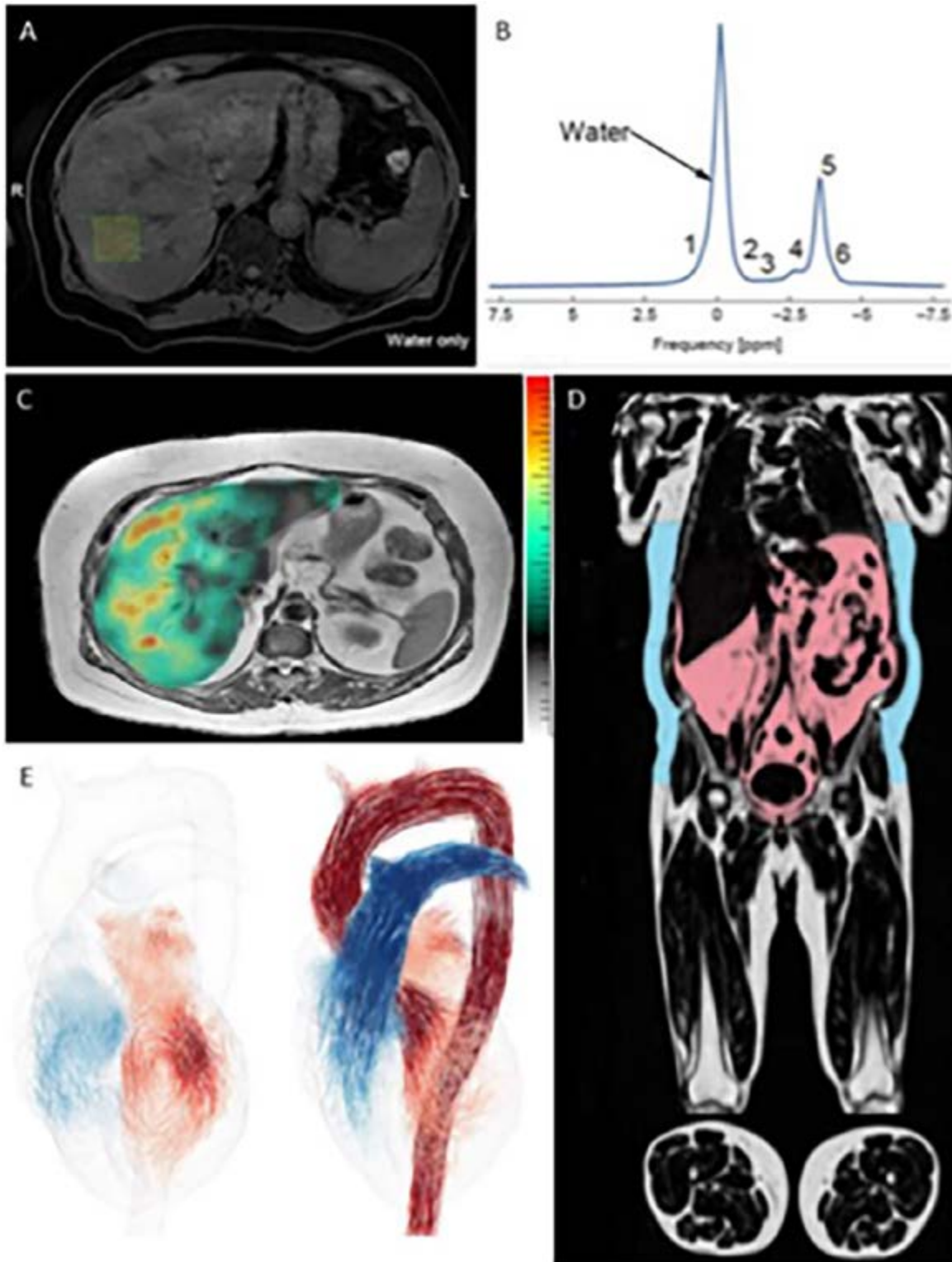


Image A shows the representative water MR image with 547 the placement of a proton magnetic resonance spectroscopy (^1H -MRS) voxel in the right hepatic lobe. Image B shows in vivo ^1H -MRS spectrum for water and fat. Image C shows MRE for a cirrhotic NAFLD patient. Image D shows a whole-body water-fat separated imaging for quantification visceral and subcutaneous adipose tissue volume. And image E shows a 4D flow image of a healthy heart.

*Sandra Fornell, Anders Persson,
Maria Kvist, Mona Cederholm
and Marcelo Pereira Martins*





CMIV Post-Distance Mode

At last we were able to return to work and meet again after a long period of distance work.

At the end of September, the scientific council together with the CMIV research school and the management group had an internal conference in Vadstena.

Nothing beats the actual physical meeting even though the meeting through teams and zoom now has turned into being the new normal and has proven to work much better than expected at first.

It was great to finally being able to meet again and to have fruitful discussions together, sitting in the same room. CMIV is the mix of people. That is what makes us unique, the twin-

ning in the research school with PhD students with both technical and medical background and the pairing of supervisors.

Our new chairman and vice chairman of the research school, Sophia Bäck and Milda Pocevičiūtė have done an excellent work engaging the PhD students. They all presented their PhD projects to the scientific council and the management group with a short pitch, which was a very good way to present.

The research school then had some team-building activities together outside in the beautiful surroundings of Vadstena.



Chiara Trenti, Deneb Boito, Ann-Sofi Björkman and Milda Pocevičiūtė



Marie Waltersson, Caroline Bivik Stadler, Håkan Gustafsson and Catrin Nejdeby



Gustav Magnusson, David Abramian and Kajsa Tunedal



Sophia Bäck, Sofia Jarkman, Robin Kämpe and Iulian Emil Tampu



David Abramian and Gustav Magnusson



*Milda Pocivičiūtė and
Chiara Trenti*



Why be a part of CMIV Research School?

Read about what two of our PhD students think about our research school.



Sophia Bäck, Milda Pocevičiūtė, Ann-Sofi Björkman and Chiara Trenti



Ann-Sofi Björkman and Chiara Trenti

In 2020, the scientific council took the decision to reorganize the research school and let the PhD students take a bigger responsibility on how to develop the research school. Sophia Bäck and Milda Pocevičiūtė were appointed chairman and vice chairman and in 2021 they started their new part time job. It was not such an easy task since we were in distance mood, but they have succeeded in tightening the group and carry through distance PhD student seminars.

Now when we are back at CMIV again, it is very pleasing to see how the group has grown and that there are many activities adjacent to the seminars with pizza evenings and film events.

Master in Biomedical engineering Sophia and Milda interviewed Chiara Trenti, from Italy and Ann-Sofi Björkman, radiologist from Linköping on how they see on the research school. Both of them were enrolled in the research school during the pandemic in 2020.

What research are you doing in your PhD?

Chiara Trenti: In my PhD, I use 4D flow cardiovascular magnetic resonance imaging to assess hemodynamics and biomechanics of healthy and diseased aorta.

Ann-Sofi Björkman: My research is about improving musculoskeletal imaging using a new type of CT, the photon counting detector CT.

How do you benefit from being a member of the CMIV research school?

Chiara Trenti: My research benefits from it in several ways. I am using CMIV's infrastructure (CMIV scanner, CMIV network). But CMIV is also a place where I meet people from other fields. We have monthly meetings with PhD students from the research school, where we present our research and listen to other's presentations. It is a good opportunity to train your presenting skills and get inspiration from other research fields.

Ann-Sofi Björkman: It gives me contact with other researchers in CMIV, provides an opportunity to present my research as well as to listen to presentations about research done by others.

One key concept of the CMIV research school is that every student has a technical and a medical supervisor

Since you have a technical background, how does your medical supervisor support you in your research?

Chiara Trenti: My medical supervisor helped me to keep my research more clinically relevant. For example, I created visualizations of aortic blood flow, and my supervisor gave me some feedback on what can be interesting and what can be understandable in the clinic.

Since you have a medical background, how does your technical supervisor support you in your research?

Ann-Sofi Björkman: My technical supervisor helps me with concepts that relate to physics concerning the new CT machine that we are studying.

Would you recommend other students to join the CMIV research school? If so, why?

Chiara Trenti: I would definitely recommend other students to join CMIV research school! It is really important for a PhD to be part of a community. It is great to share ideas, experiences. It helps you to learn to explain your research to people that are not from your same field.

Ann-Sofi Björkman: I recommend being part of the CMIV research school for several reasons. First of all, it provides a platform for meeting other PhD students. Secondly, it gives insights into the CMIV environment by providing news of what's going on. Finally, CMIV research school gives the PhD students the means to interact with the CMIV scientific council which has an important strategic position.

*PhD Student Seminar with
Milda Pocevičiūtė, David
Abramian, Iulian Emil
Tampu, Sophia Bäck, Kajsa
Tunedal, Deneb Boito and
Gustav Magnusson*

End diastole

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The CMIV Research School

The CMIV Research School offers a doctoral program with both medical and technological entries and a coherent research education. A basic principle for our doctoral program is the translational approach where we encourage projects to have a close connection to the clinic. Currently there are around 30 PhD students admitted to the research school. Here a selection of them presents their research.

fMRI Methods for Brain Tumour Treatment

Functional magnetic resonance imaging (fMRI) is an MRI modality used to reveal the location of brain activity when a subject performs a certain task. Its use has revealed a lot about functional localization in the brain, but its application is generally limited to the gray matter, one of the two main tissue types of the brain. Gray matter is found in the outer layers of the brain, and is where brain processing takes place. However, the brain is also composed of white matter, which constitutes around 50% of the brain mass, and serves to connect gray matter regions. This tissue has until recently been neglected in fMRI studies, due to questions about the mechanism by which the relevant signals are generated in this tissue, as well as the weakness of these signals in comparison to those generated

in gray matter. Nevertheless, the developing consensus is that these signals are meaningful, so the attention has to shift to the development of methods to address their weakness.

In our work we developed an improved method for detecting these signals that relies on knowledge of their spatial shape in white matter. Because white matter is made of long axonal strands, it has a very directed structure, and recent studies have shown that the fMRI signal in white matter follows this structure. To incorporate this knowledge into a standard fMRI processing pipeline, we devised a novel filtering approach informed by diffusion-weighted MRI, a modality that encodes the direction of the neuronal axons at every point in the brain. We evaluated our fil-

tering approach on carefully constructed simulated data, as well as on real fMRI data from 100 subjects. Our results show that our method is capable of detecting very subtle activations that conventional methods cannot detect.

Recent advances in the study of fMRI in white matter can provide new ways of characterizing the brain and diagnosing diseases. Our work incorporates several of these advances, and we believe it can be helpful in reaching this goal.

PROJECT INFORMATION

Project

Methods for Analyzing fMRI d' Data - with Applications to Brain Tumour Treatment

Supervisors

Anders Eklund, Evren Özarslan, Ida Blystad, Hamid Behjat

Short CV

Master of Science in Electrical Engineering (double degree studies), Lund University, Lund, Sweden 2017
 Master of Science in Telecommunications Engineering, Technical University of Madrid, Madrid, Spain 2017
 Bachelor's Degree in Telecommunications Engineering, Technical University of Madrid, Madrid, Spain 2015

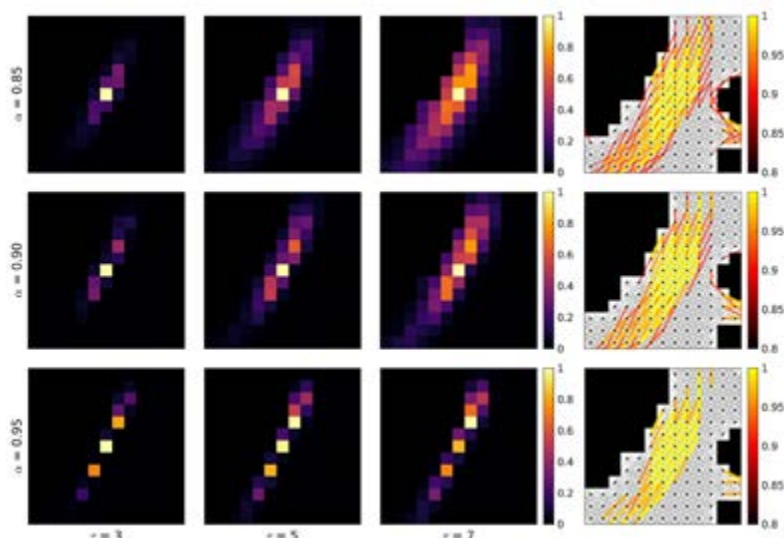


Figure 1: Illustration of the range of shapes that filters can take with the proposed method. While conventional fMRI analyses rely on isotropic (i.e., round) filters, our approach enables the definition of very slender filters that closely follow the orientation of neuronal axons.

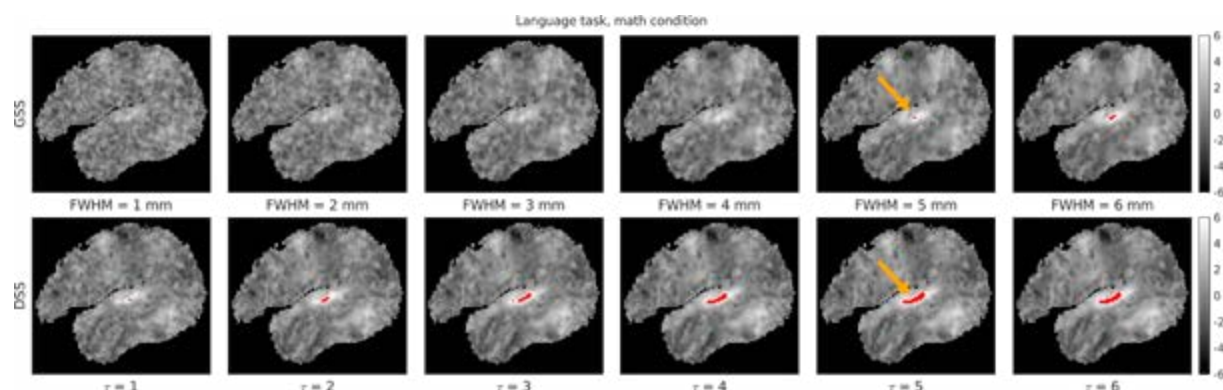


Figure 2: Example group white matter activations with conventional methods (top) and the proposed method (bottom). Conventional methods are less capable of detecting activity in white matter, while the proposed method is capable of finding sizeable and subtle detections over a range of filter sizes. In this figure, our method detects a thin elongated activation, which goes mostly undetected by the conventional approach.

Prediction of posthepatectomy liver failure with hepatobiliary MRI

■ Posthepatectomy liver failure (PHLF) describes a life-threatening condition that occurs after part of the liver has been removed surgically. In these patients, the liver remnant is insufficient to sustain adequate liver function, resulting in liver failure.

To ensure sufficient liver function post hepatectomy, various methods have been and still are used to help assess preoperative liver function and estimate the minimum size of the remnant liver, such as CT volumetry or indocyanine green (ICG) test. Yet, even using these criteria recent studies indicate that the incidence of post hepatic liver failure is around 20% with a mortality rate of 1.7%. Clearly, there still is a need for a more accurate predictor of post hepatectomy liver function.

Several studies have reported that liver function can be predicted using MRI with liver specific contrast – both in patients with colorectal metastases (that usually have an otherwise healthy liver),

as well as patients with hepatocellular cancer and biliary cancer (that usually have diffuse liver disease (HCC) or very heterogenous liver parenchyma due to biliary disease (biliary cancer). These studies have been, however, quite limited in the number of patients that have been studied, with the number of patients examined averaging around 70 individuals.

Our PHLF study, internally called LIFE2, is a retrospective Nordic multi-center study where CMIV and Linköping University Hospital are cooperating with hospitals in Stockholm, Göteborg, Uppsala, Copenhagen, Oslo and Helsinki to examine the predictability of posthepatic liver failure in patients that have received resective liver surgery. We are using both the established HUI index model of function prediction as well our own dynamic liver function model developed in house at CMIV to analyze if we can better predict PHLF. To achieve this, we have registered in excess of 280 patients with the aim to verify whether it

is possible to preoperatively predict post hepatic liver failure in patients stemming from a large and diverse group of patients more reflective of a typical patient population in a national liver center. This can help optimizing liver surgery and preoperative planning to help further reduce live threatening complications caused by posthepatectomy liver failure.

PROJECT INFORMATION

Project

Optimizing hepatobiliary MRI in metastatic liver disease (Livermet)
Prediction of posthepatectomy liver failure with hepatobiliary MRI (Life2)

Supervisors

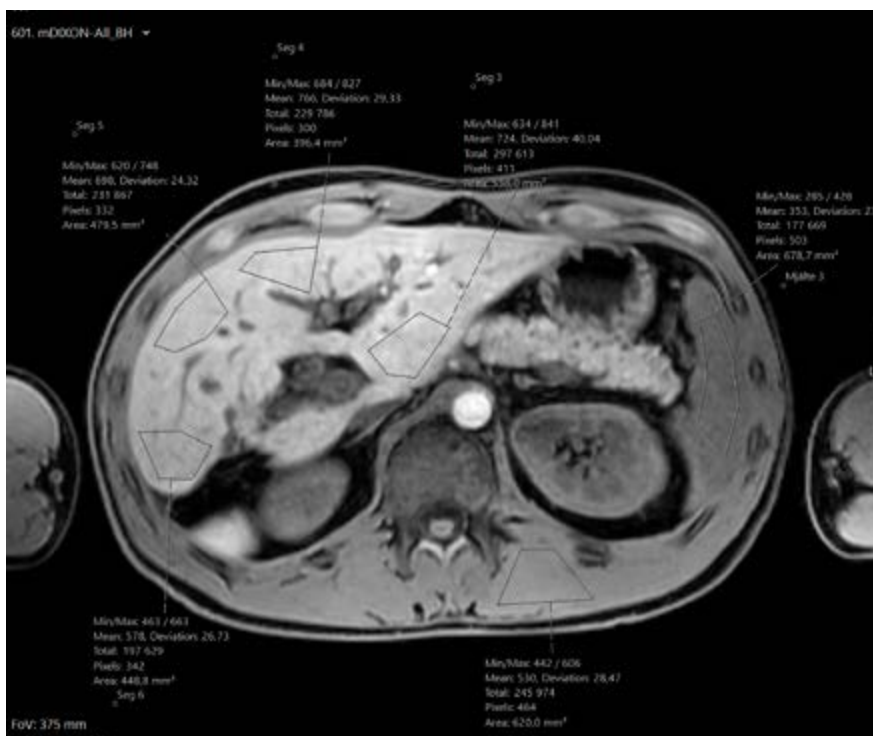
Peter Lundberg, Nils Dahlström, Miska Woisetschläger, Per Sandström

Short CV

Medical degree, Medical School, Justus-Liebig University, Gießen, Germany, 2002

Radiologist, Department of Radiology, University Hospital, Linköping, Sweden, 2010

Consultant Radiologist, Department of Radiology, University Hospital, Linköping, Sweden 2014-present
European Diploma in Radiology, 2016
ESGAR Certificate of Excellence in Abdominal Radiology, Level II, 2021



Typical ROI distribution for assessment of liver function in LIFE 2 study.

Neural Tissue Composition via Diffusion MRI

Diffusion MRI is an imaging technique that allows the study of heterogeneous media by probing the random motion of water molecules in the scanned specimen. Its non-invasive character makes it a powerful tool for characterizing the brain microstructure without the use of ionizing radiation. Diffusion MRI's potential as a tool for exploring the brain architecture both in terms of neural connections and local structure has been proven over the years. Many models and methods have been proposed to estimate meaningful parameters from diffusion sensitized images. Recent advances in diffusion encoding lead to the development of new methods able to resolve microscopic features of the scanned specimen otherwise unachievable using conventional acquisition schemes. Ideally, such features can provide new insights especially in cases where the neural microstructure is altered due to different diseases. One such framework maps the

brain microstructure at the sub-voxel scale as a collection of small separate domains. By using this approach it is possible to obtain parameters that provide a description of the neural tissue at the cellular scale. However, the results obtained with commonly employed implementation of this method yield mathematically unacceptable results and are susceptible to noise. We therefore developed an estimation framework in which positivity constraints are enforced, providing increased reliability and robustness. The Figure shows an example of how the results obtained with the proposed estimation framework retain a higher degree of information compared to the current implementation when less and less data are available. We envision the deployment of the developed framework to facilitate the translation of this method into clinical practice, where acquisition time is a major limitation.

PROJECT INFORMATION

Project

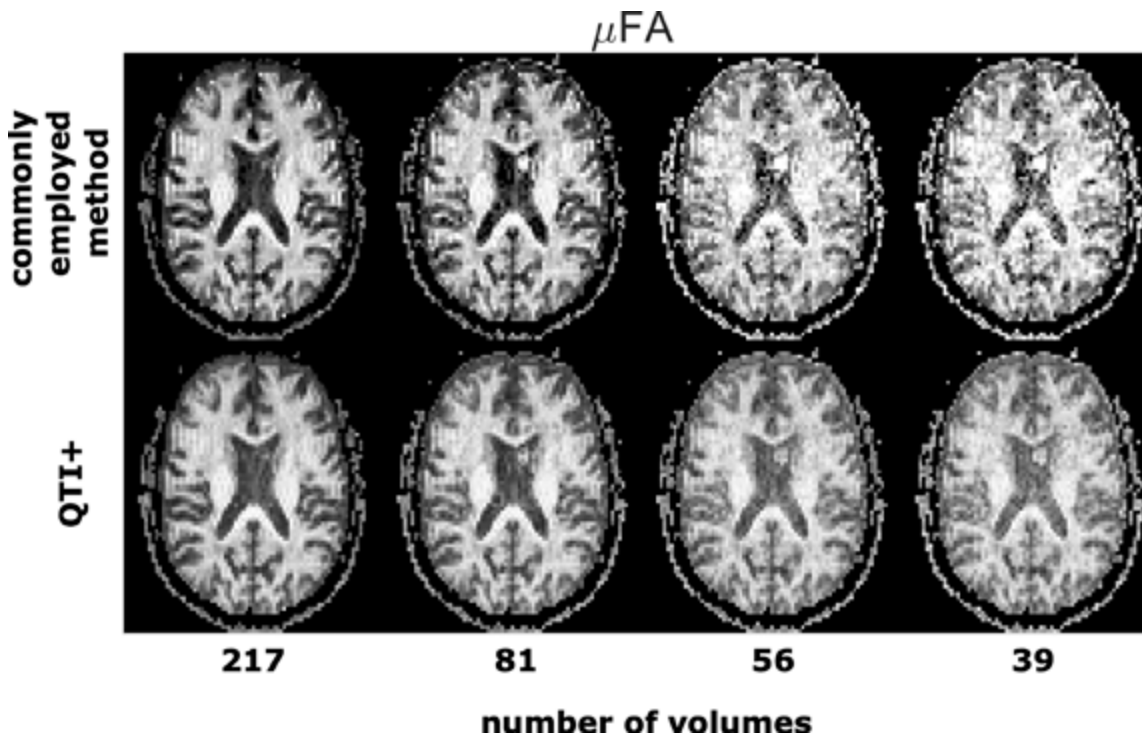
Diffusion MRI with general gradient waveforms (DGGW)

Supervisors

Evren Özarslan, Ida Blystad, Anders Eklund, Magnus Herberthson

Short CV

Master's Degree in Biomedical Engineering, 2018, Linköping University
Bachelor's Degree in Biomedical Engineering, 2015, University of Padova



The figure shows a comparison between microscopic fractional anisotropy maps estimated using the commonly employed and the developed methods (QTI+) on progressively fewer numbers of volumes.

Cardiac Blood Flow During Atrial Fibrillation Therapy

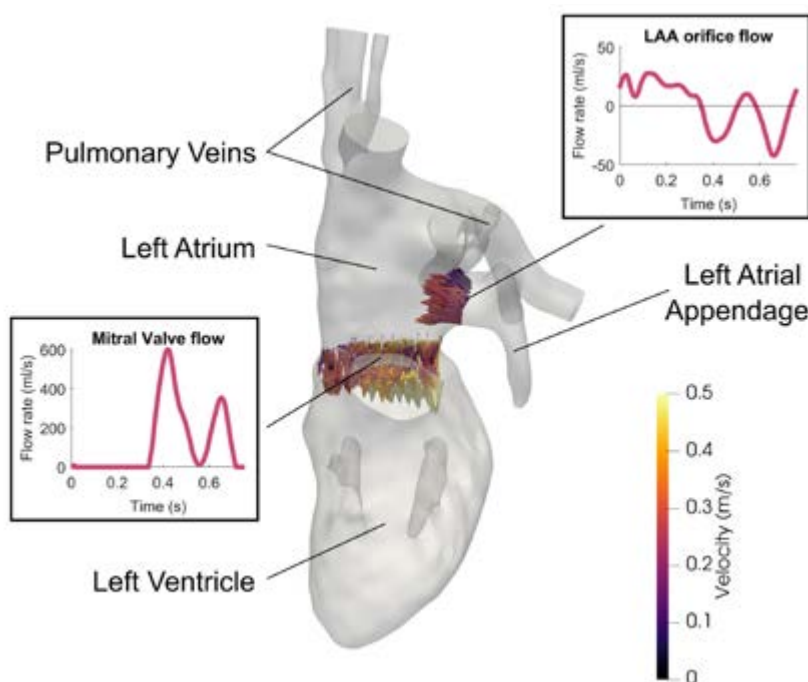
■ Atrial fibrillation (AF) is a very common disease of the heart. It is characterized by an irregular contraction of the atria of the heart. This changed motion can lead to blood coagulation, which can cause stroke. In this project, we want to understand how the motion of the left atrium influences the blood flow and how the blood flow is changed in patients with atrial fibrillation.

We focus especially on a structure in the left atrium called left atrial appendage (LAA). The shape of left atrial appendage differs between people, but there are also differences in the contraction patterns.

There are two techniques to measure the geometry and motion of the heart

in people: Computed tomography (CT) and magnetic resonance imaging (MRI). With MRI it is possible to directly measure the blood velocity in the heart (4D flow MRI), however the resolution of the images is relatively low, and it is difficult to measure low speeds. CT on the other hand produces images with a high resolution but does not provide direct velocity information and it exposes the patient to radiation. With the use of modern computers, we can calculate the velocity of blood inside the heart based on the high-resolution CT images. This way, we can also calculate the blood flow in regions where the blood speed is low and the risk for blood coagulation is high.

In the current stage of the project, we focus on improving the preprocessing of the data and decreasing the computation time, in order to be able to apply the technique in a larger cohort of patients. We developed a technique to calculate the flow through the mitral valve and the LAA orifice based on time resolved CT and compared it to 4D flow MRI. In the future, we will apply this technique to patients with atrial fibrillation to investigate the relation of the flow field and blood markers related to higher blood coagulation. This information might lead to improved patient selection and therapy of atrial fibrillation.



Geometry of the left heart at late diastolic filling with flow rate through mitral valve and LAA orifice derived from time resolved CT

PROJECT INFORMATION

Project

Simulation of time-resolved, three-dimensional cardiac blood flow from Computed Tomography (4D flow CT)

Supervisors

Tino Ebbers, Carl-Johann Carlhäll, Matts Karlsson, Anders Persson

Short CV

Chair of CMIV research school, January-December 2021
 PhD student Linköping University, Since November 2019
 Research engineer at Linköping University, August 2018–October 2019
 Master of Science, Mechanical Engineering, RWTH Aachen, Germany October, 2016–June 2018
 Bachelor of Science, Mechanical Engineering, RWTH Aachen, Germany, October 2012–September 2016

¹⁸FDG Uptake in Carotid Plaques Using PET/MRI

Background: Death in cardiovascular disease is often caused by the rupture of atherosclerotic plaques resulting in a heart attack or stroke. Plaques with a high content of fat and blood (caused by bleedings inside plaque) are known to be especially vulnerable and it is also known that inflammation is a process that accelerates the plaque towards rupture.

However, no-one has previously assessed the quantitative relationships between plaque inflammation and plaque components like fat and blood.

Aim: Since this is not previously done, we wanted to explore a new method for investigating the quantitative relationship between fat and blood inside carotid plaques and inflammation

in the same plaques. To this end we used a simultaneous whole-body PET/MRI scanner that has the possibility to generate both MRI and PET images at the same time. This current study is a pilot study.

Methods: Twelve patients with high-grade carotid artery stenosis were enrolled in the study. The extent of fat and blood was quantified from a previously validated but new quantitative magnetic resonance imaging (MRI) technique, in a stand-alone MRI scanner. PET/MRI was used to measure ¹⁸F-FDG uptake (a measure for inflammation) in the plaques alongside T1W sequences for anatomical bearings. The different images were then synchronized to generate localized plaque data both for inflammation and for plaque components.

Results and conclusion: It was possible to access reliable and quantitative data from the carotid plaques using our method. The plaques were heterogeneous with respect to their volumes and composition. The results we received did not indicate any linear relationships between FDG, fat and blood. However, this pilot study was not powered for statistically significant correlations and for a thorough analysis of the interdependence of these plaque characteristics a larger and adequately powered study would need to be done.

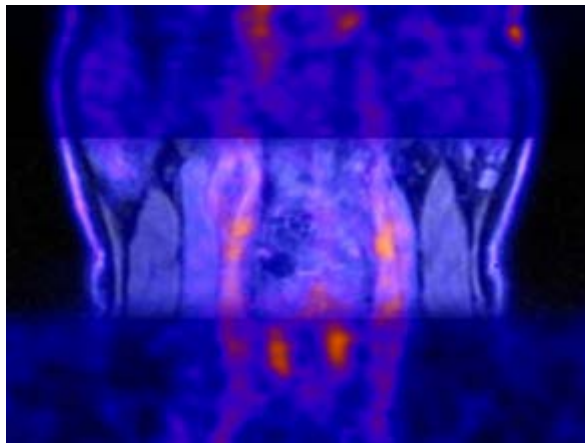


Image 1. Fusion image of PET and T1W sequences from the simultaneous whole-body PET/MRI scanner. Neck region with the carotid arteries from a coronal plane is shown.

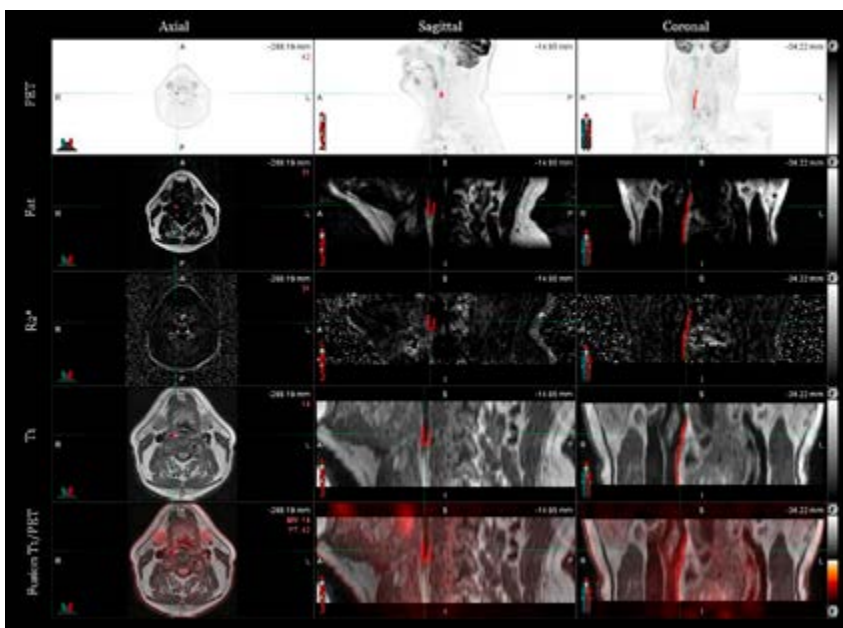


Image 2. The figure illustrates the segmentation and fusion methodology applied in the current study. Segmented carotid plaque is shown in red. Axial, coronal and sagittal planes are automatically aligned for PET, fat, R2* and T1W images.

PROJECT INFORMATION

Project

CARMA-PET Study

Supervisors

Ebo de Muinck, Petter Dyverfeldt

Short CV

Degree of Master of Science in Medicine. Medical School, Linköping University, 2012.

Resident physician in cardiology and internal medicine, Department of Cardiology, Region Östergötland, 2015-present.

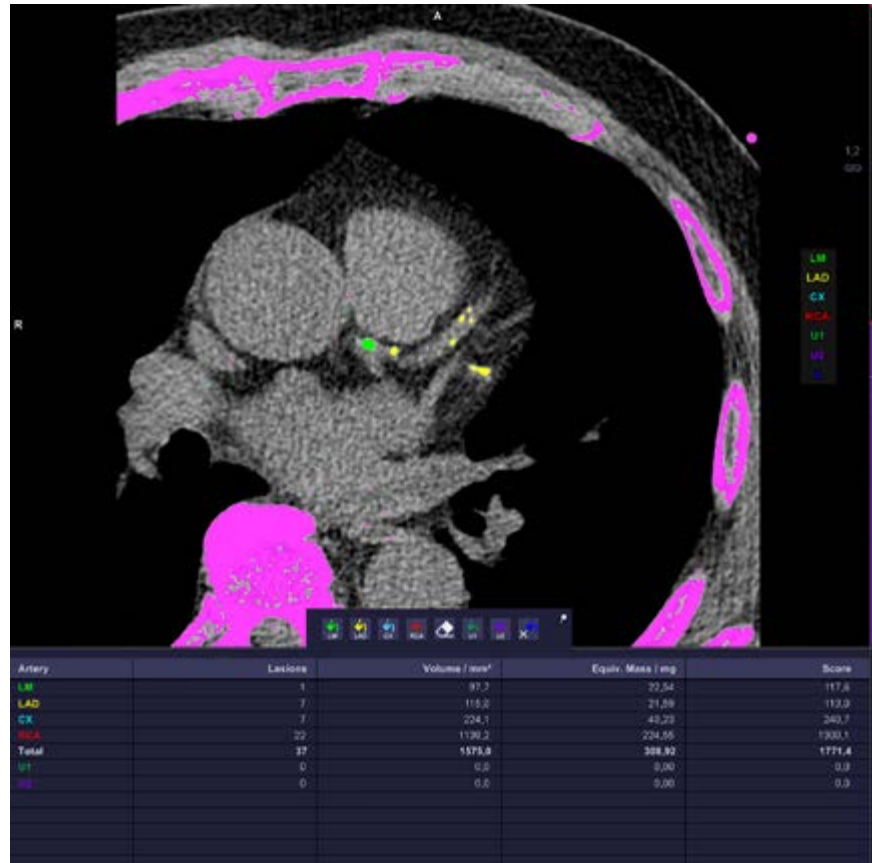
Coronary Computed Tomography: Stenosis Evaluation and Calcium Score

■ A healthy coronary artery wall does not contain calcifications. If calcifications are present this is a specific sign of coronary artery disease (CAD). The extent of coronary artery calcifications (CAC) has also shown to be proportional to the degree of CAD. The amount of CAC can be measured with calcium scoring computed tomography (CSCT) which is an ECG triggered examination of the heart. The CAC evaluation is usually done using semiautomatic software. It is a task which is not considered to be particularly difficult but still needs to be performed by a specialized radiologist.

The Swedish cardio pulmonary bioimage study (SCAPIS) is a unique study within the cardiopulmonary field that includes 30000 randomly chosen research subjects in the age group 50-64 years of age. The study is a collaboration between the Universities in Gothenburg, Lund, Linköping, Uppsala, Umeå and Karolinska institutet in Stockholm. It is also a collaboration between the university hospitals in the same cities. A pilot project was conducted in 2012 and data inclusion of study baseline examinations carried on from 2013 to 2018.

These baseline examinations include a number of tests e.g. computed tomography (CT) of the heart. SCAPIS data have resulted in a database located at Gothenburg University which can be used for studies of population diseases such as cardiovascular disease in order to gain better understanding of disease mechanisms as well as preventive measures and treatments.

International guidelines are advocating CSCT for an improved CAD risk estimation for individuals without symptoms but with an intermediate risk based on their traditional CAD risk evaluation. This means that we are probably going to see an increased use of CSCT. An automated evaluation of the CAC extent would therefore be of use in order to unburden the radiologist and to increase efficiency thus contributing to improved health economy. Recently published



Semi-automatic evaluation of coronary artery calcifications (CAC). All pixels in the image with an attenuation value above 130 HU are automatically segmented by the software. The reader selects and marks pixels representing CAC and the results are presented as per vessel and total Agatston score.

studies have shown excellent results for automatic evaluation e.g. lung cancer in CT images using artificial intelligence (AI) base software.

This aim of this project is to use about 5000 CSCT examinations performed within the SCAPIS study in Linköping to evaluate the precision of an AI-software for CAC scoring compared to conventional semi-automatic evaluation. The agreement and correlation between the AS, number of calcifications and the placement of the calcifications will be evaluated.

PROJECT INFORMATION

Project

AI evaluation of calcium score in SCAPIS CT images

Supervisors

Anders Persson, Jan Engvall, Tino Ebberts, Mischa Woisetschlager

Short CV

Radiology nurse, 2005
M.Sc. medical science, 2013
CT Research nurse, 2015

Deep Learning as an Aid for the Pathologist in Cancer Diagnostics

■ Clinical pathology is essential for diagnosing cancer. Today, demands on pathology increases with more requests of parameters, and at the same time there is a shortage of pathologists. The introduction of digital pathology opens opportunities of novel workflows and potentially enhanced diagnostics. Digital pathology means that histopathological glass slides are scanned with a high-resolution glass slide scanner, and the pathologist analyses the slides directly on a computer screen instead of using a microscope. The pathology department in Linköping have been scanning all the histopathological glass slides since 2011, making over 2 million digital slides stored in the digital archive. To fully reach the potential of digitized pathology, the next step is introduction of image analysis, that potentially could lead to more efficient and accurate diagnostics. Today computational pathology research groups develop image analysis tools based on machine learning algorithms and so called deep convolutional neural networks, also called deep learning. Deep learning image analysis studies have been performed on digitized histopathology cases, for example for detecting prostate cancer and lymph node metastases. But still, not many algorithms have reached the pathologist clinical praxis.

In this project we aim to develop and evaluate algorithm-based tools to aid pathologists in diagnosing and staging cancer. Important questions are: How accurate are algorithms at detecting cancer cells on digitized histopathology material? How can we transfer image analysis algorithms to clinical settings?

We initially focus on evaluating an algorithm for detecting lymph node metastases in breast cancer cases. The algorithm is developed and trained by the Computational Pathology group at Radboud University medical center in Nijmegen in the Netherlands. An important step is to be able to transfer or generalize an algorithm to material from another setting. A large dataset of digitized histopathological slides of axillary

lymph nodes from breast cancer cases was during 2019 collected, anonymized, and transferred from the clinical digital archive to a research environment similar to the clinical working environment (AIDA PACS) and published on the AIDA Datahub. Lymph nodes with metastases were detailed annotated by a pathologist (resident) with correlation to an immunohistochemical stain that indicates breast cancer cells. The performance of the algorithm on the clinical material without retraining or adjustment will be evaluated, and the result also analyzed by a pathologist. Further steps will be to evaluate the clinical usability of the algorithm.

PROJECT INFORMATION

Project

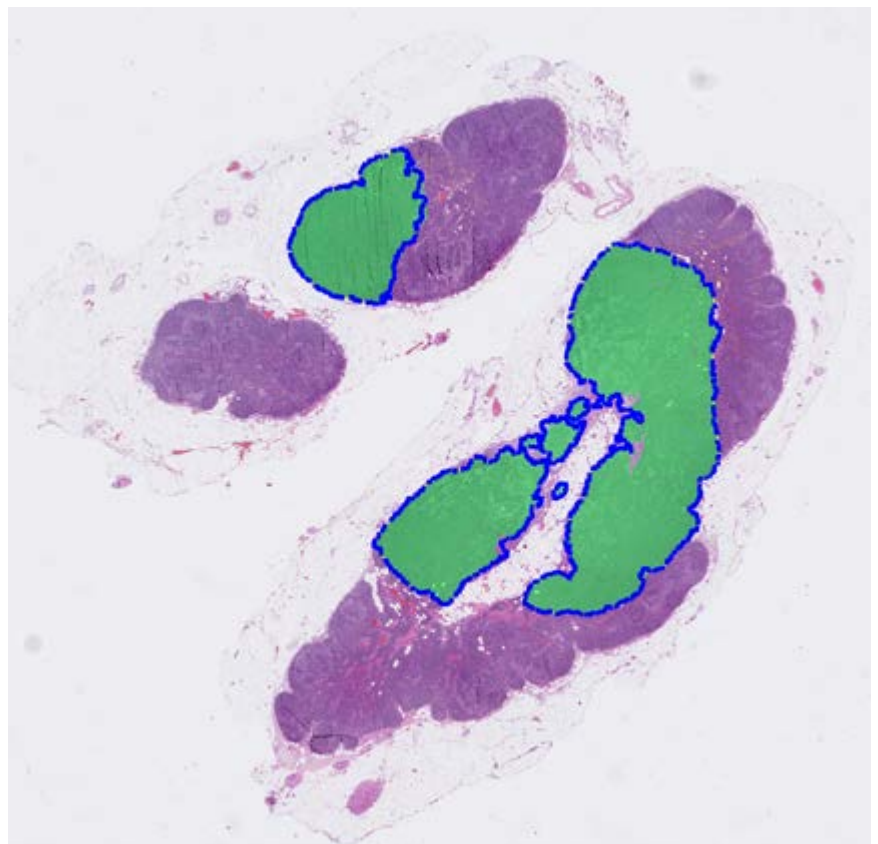
Deep Learning as an Aid for the Pathologist in Cancer Diagnostics

Supervisors

Jeroen van der Laak, Darren Treanor, Claes Lundström

Short CV

Residency in Clinical Pathology, Linköping University Hospital, 2016-present
Medical degree, Lund University, 2013



Example of lymph node with breast cancer metastasis with corresponding algorithm prediction (blue lines) and ground truth annotation (green area).

Deep Learning Applied to Large and Small Multimodal Datasets in Psychiatry

■ Among all medical conditions, major depressive disorder (MDD) is a world leader in terms of years of productive life lost due to illness. This loss of productive life is due to a higher risk of suicide for people suffering from depression, but it is also caused by depression's negative effect on work and family relations. Scientists have for a long time tried to understand the underlying brain mechanisms of depression and have made important advances. There are, however, still no good objective biomarkers that can determine if someone has depression or predict whether a patient could benefit from a specific treatment. In this project we want to develop deep learning methods that could help us address these challenges. Our plan is to apply a deep learning algorithm to a large, open repository of structural and functional neuroimaging data from depressed and never-depressed persons. This deep learning algorithm can detect patterns that are often undetectable when using more traditional "mass univariate" methods. The algorithm will first be trained and tested using only anatomical data, and next on the neural functional data and, finally, on a combined anatomical plus functional dataset. We can then compare what kind(s) of data result in the best performance of the deep learning network

in terms of distinguishing healthy from depressed persons. Provided that one or more modalities of neuroimaging data are useful in distinguishing depressed from never-depressed categories, we can advance the theoretical neuroscience of MDD by determining which neural features most inform accurate categorization of disordered and non-disordered subjects. What region or brain function allows us to tell the difference between a healthy and depressed individual? A question like this can be addressed by using a different kind of deep learning network: A network that produces artificial brains. Specifically, this generative network will be trained to translate from a healthy brain to a depressed brain. Then, by subtracting the fake depressed brain from the real healthy brain we will be able to tell what the deep learning network changed in the healthy brain in order to make it look depressed. By applying the same kind of approach, we could, for example, find the neural differences between depressed people who respond well to a specific treatment and others who did not respond to this treatment.

Applying techniques such as those presented here could strongly advance personalized medicine in psychiatry.

PROJECT INFORMATION

Project

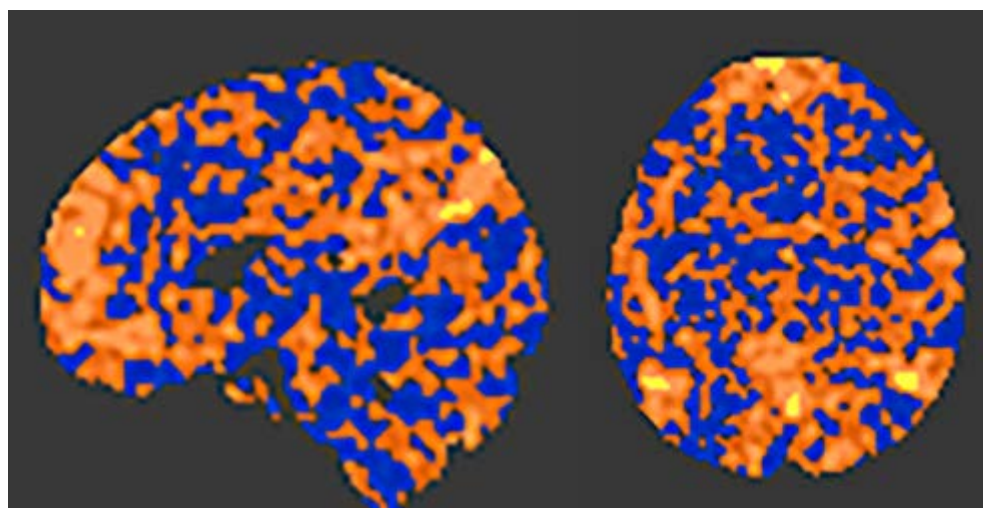
Deep Learning Applied to Large and Small Multimodal Datasets in Psychiatry

Supervisors

Markus Heilig, Anders Eklund, Paul Hamilton

Short CV

Center for Medical Image Science and Visualization (CMIV) and Affective Neuroscience, Part time employee, Linköping University, Research Engineer, 1/2019-present
 Center for Social and Affective Neuroscience (CSAN), Linköping University, Research Engineer, 3/2015-present
 Department of Medical Radiation Physics, Lund University, Stipend worker, 7/2014-3/2015
 Radio Therapy Center, Linköping University Hospital, Medical assistant, summers of 2013-2014
 Master of Science (M.Sc) Medical Physics, Lund University, 9/2009-6/2014, Licensed Medical Physicist, Leg. Sjukhusfysiker
 High School/Gymnasium: Science and Healthcare, Birgittaskolan, Linköping 2005-2008
 Member of the CMIV board as Student representative



The image shows one of the top 25 components from a group independent component analysis. High values (red) are highly correlated with the posterior node of the default mode network. Multiple networks like these will be fed into a convolutional neural network, and compete in classifying depressed individuals from healthy controls.

Verifiable AI-Assistance for Biomarker Quantification

Cell-based biomarker quantification through immunohistochemistry (IHC) assays has important prognostic and predictive uses in routine diagnostics. Recent advancements in image analysis have made automated quantification a viable alternative to the current practice of manual scoring. While automated scoring of thousands of cells can increase reproducibility and scalability, it offers challenges when manual oversight is needed. For instance, verifying automated outputs for thousands of individual cells might prove more time-consuming than standard manual scoring protocols.

This project explores visualizations and interactions that enhance manual oversight and control in automated scenarios. User studies involving pathologists are currently evaluating several potential strategies for reducing the verification and correction effort. These include systematic spatial sampling, unsupervised clustering of similar decisions, and interactive machine learning.

The results aim to inform how we might use imperfect AI efficiently and confidently in future routine diagnostics.

PROJECT INFORMATION

Project

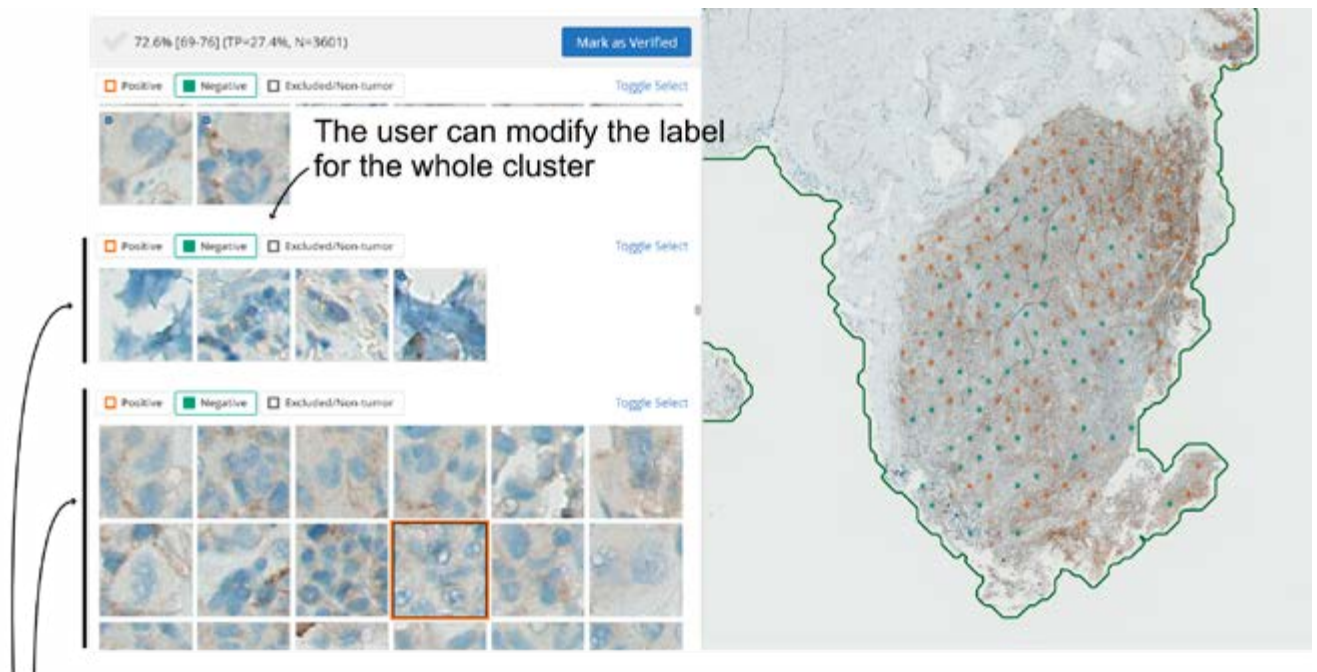
Verifiable AI-assistance for cell-based biomarker quantification

Supervisors

Jonas Löwgren, Claes Lundström, Darren Treanor

Short CV

Cognitive Science, LiU, 2012
Senior Software Engineer at Sectra AB



Similar patches within the same label are grouped

Prototype for AI-assisted PD-L1 biomarker quantification. Cells are systematically sampled for verification and correction (right). Further simplifying the workload, the user can work with batches of visually similar cells (left).

Cerebralvascular Reactivity Studies

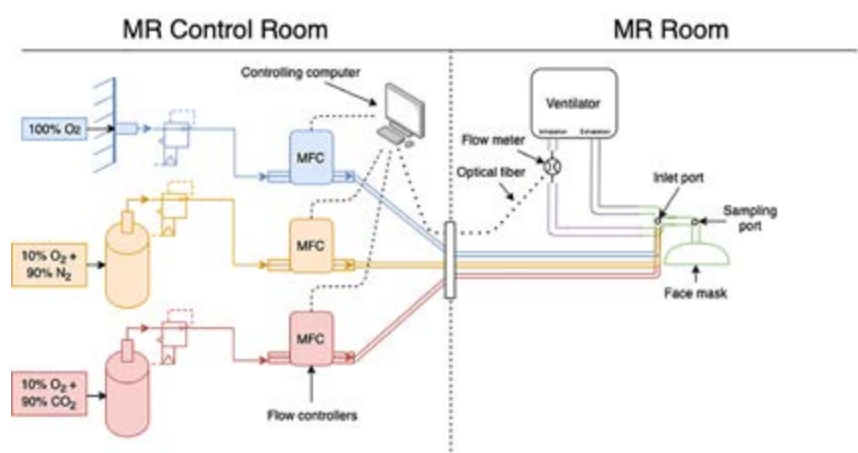
■ We are looking at the possibility to probe the health of blood vessel in the brain of Subarachnoid Hemorrhage (SAH) in a technique called Cerebrovascular Reactivity (CVR). The idea is to stimulate the blood vessel and measure the corresponding change in blood flow. The hope is that this reactivity measurement can be used to earlier assess the risk for secondary complication for this patient group, such as delayed ischemia.

To stimulate the blood vessel, small amount carbon dioxide is introduced through inhalation. The blood vessels have built in mechanism to sense the amount of carbon dioxide in circulation and, if functioning properly, will dilate as a response. The corresponding change in blood flow is measured in a MR-camera where the patient is laying during the full exam. Maps of the cerebrovascular reactivity can then be constructed from the measured blood flow and information about the stimulus.

Our current focus is the technical aspect of building the necessary equipment. What is different from CVR-experiment done elsewhere is that our solution needs to work together with a ventilator. We hope to soon start testing our equipment on healthy volunteers before moving on to the target patient group. The final goal of project is to evaluate the CVR-technique and its diagnostic power for SAH-patients.



Illustration of our CVR setup outside of the MRI camera. The patient is breathing by assistant of the ventilator shown in the middle of the image. The two gas tubes shown in the left portion of the image contains carbon dioxide and nitrogen, respectively. By mixing the flow from these two gas tubes, plus an additional flow of oxygen from the hospital wall outlet (not shown), into the ventilator gas stream, the content of the inhaled gas by the patient can be controlled. By this method, a precise carbon dioxide stimulus can be administered to the patient. If then the blood flow response is measured inside an MR-camera (not shown), CVR-maps can be constructed.



A schematic sketch of the CVR system. To the left, three different sources of gas are shown, oxygen from the hospital wall outlet, nitrogen from a gas tube and carbon dioxide from a gas tube. The flows of these gases are controlled three by mass flow controllers (MFC) which is in turn is controlled by a computer. The flows from the MFCs are guided into MR Room where the ventilator is located and added to the ventilator gas stream to the patient. By measuring the flow from the ventilator, the computer calculates the necessary flow for the three MFCs to achieve the desired gas content in the inhaled gas. The inhaled gas is continuously sampled through the sampling port at the face mask, right part of image, to make sure the system is working as intended.

PROJECT INFORMATION

Project

Magnetic Resonance Imaging Studies on Cerebrovascular Reactivity

Supervisors

María Engström, Anders Tisell,
Charalampos Gergiopoulos, Gunnar
Cedersund

Short CV

Bachelor and master's degree in
engineering physics from Chalmers
University
Research assistant at Gothenburg
University
Research engineer at Linköping University

The Pathomechanism of Idiopathic Scoliosis

■ Scoliosis is a disorder of the spine characterized by a deformity in three dimensions. While some forms of scoliosis have a known origin, e.g., due to neuromuscular disease or congenital defects, the cause of idiopathic scoliosis remains unknown. Potential factors for disease and deformity progression includes genetics, the musculoskeletal system, the hormonal system and the connective tissues. An established driver for deformity is the so called Heuter-Volkman principle which states that compression forces inhibit skeletal growth and tensile forces stimulate skeletal growth.

The treatment of idiopathic scoliosis varies depending on curve severity. A mild curve may be observed and if there is progression corset treatment may be an option. If the curve progress further, it may be necessary to surgically correct the deformity. The result of physiotherapy is currently conflicting and is under further evaluation in controlled studies.

To increase the understanding on he both the pathogenesis of idiopathic

scoliosis and the effects of the above treatment methods we want to study the deformity using visualization techniques and biomechanical modelling. To our help we have radiology including computed tomography as well as a motion lab with an optical motion tracking system. Here we use a 10-camera system which registers reflective markers placed on anatomical landmarks on the skin of the patient. This gives us plenty of information on joint kinematics and can be combined with force plates to measure the forces on the ground exerted by the patient. Combining this with biomechanical modeling we can investigate the compressive and shear forces acting on the separate spinal segments during movement, physiotherapy, corset treatment or before and after surgery. Understanding these forces that are acting on the spine may elucidate the pathomechanism of idiopathic scoliosis and clarify the effects of our treatment methods.

We have also developed a novel method, “CT-mocap” which essentially is

a fusion of optical motion tracking and computed tomography. This allows us to visualize the patient’s own skeletal system during actual movement. We have applied this method to the hip and knee joint and we are currently working on optimizing the method in order to apply it to the spine.

PROJECT INFORMATION

Project

Idiopathic scoliosis - pathomechanism and morphology

Supervisors

Hans Tropp, Ludvig Vavruch, Jörg Schilicher, Allan Abbott, Stefan Lindholm

Short CV

Medical School, Linköpings University, 2014 - 2019
Assistant Physician, Linköping University Hospital, 2020-present



Figure 1: Pictured above is a 3D CT scan of the pelvis, femora and tracking markers, each segmented individually. Here shown using specific Unity software to allow for visualization of previously tracked movements.



Figure 2: A 3D CT reconstruction of a scoliotic curve showing the deformity in the frontal, sagittal and axial plane.

Brain Tumours in Children: Clinical Applications of Novel Magnetic Resonance Biomarkers

■ This research seeks to validate new techniques (including qMRI and APT-CEST) for more precise imaging of CNS tumour diagnosis in children and young adolescents (0–18 years of age). Thus, we will have to introduce and implement novel means of detecting and visualizing MR-contrast-enhancing mechanisms based on tumour-associated molecular parameters. One method, APT-CEST (APT-Chemical Exchange Saturation Transfer), enables us to determine tumour-specific chemical exchange in tumour and adjacent affected tissues. Other techniques are microdiffusion, to depict tissue alterations, and a qMRI method (QALAS) developed at Center for medical image science and visualization (CMIV) here in Linköping, synthetic MR, which can quantitate imaging biomarkers such as degree of myelination (and changes thereof). The ultimate aim of this project is to expand our capability for early detection of brain tumours in the pediatric population and to define the tumour's spatial extension into the brain parenchyma by the imple-

mentations and application of procedures that are not currently available in conventional clinical MR examinations. It is essential to be able to determine the spatial relationship between the lesion and adjacent functional tissue for adequate planning of treatment, using these methods we believe that we will be able to achieve this.

We also try to correlate the q MR measurements (QALAS) and functional MR to assessments by the clinical multidisciplinary pediatric CNS tumour team, which conducts standard evaluation including educational performance, physiotherapist and neuropsychological testing. This includes comparison of the 2-year and 5-year MR imaging post-treatment control. Moreover, we have initiated a collaboration with the Swedish Childhood Tumor Bank (Barn-tumörbanken, BTB). BTB is a national biobank for pediatric tumors in Sweden that collects and distributes material for research. The biobank includes approximately 500 histology whole slides from pediatric brain tumors.

PROJECT INFORMATION

Project

Brain Tumours in Children: Clinical Applications of Novel Magnetic Resonance Biomarkers (Brain tumor grading using multimodal images and artificial intelligence)

Supervisors

Peter Lundberg, Jan Hillman, Ida Blystad, Ulf Samuelsson

Short CV

Pediatric oncologist and the head of critical clinical care of pediatric CNS-tumours in 'Sydöstra sjukvårdsregionen' and PhD Student Medical Radiophysics, Linköping University and Center for Medical Image Science and Visualization (CMIV) Research School
Allocation NBCNS Clinical Fellow, 2020 June
Specialist in Pediatric Oncology and Hematology, Linköping University Hospital, 2019 August 30
Specialist in Pediatrics, Linköping University Hospital, 2015 May 21
Doctor of Medicine, Linköping University Hospital /Motala Hospital, 2009 June 26
Bachelor of medicine and surgery, Lund University, Sweden, 2007 June 8

XAI Applied to Histopathology Image Analysis

■ Introduction of digital pathology enabled research in Artificial Intelligence (AI) assistance tools for a pathologist. There have been several studies showing that the diagnoses done by pathologists tend to be biased: different doctors provide different assessments of the same patient. Therefore, AI tools combined with a pathologist's expertise could result in a more reliable diagnosis as well as a better-chosen treatment. However, bringing these tools to hospitals has additional challenges. The algorithms should not only have high performance (high accuracy of predictions) but also be transparent, understandable and reliable from a physician's point of view.

This project focuses on the issue of understandability, transparency and reliability of the AI tools that are developed for assisting the work of pathologists. In order to do this, the methods of explainable AI (XAI) and uncertainty estimation

are explored with the aim to apply them in AI solutions for digital pathology. What is Explainable AI? It is an active research field that aims to provide means of understanding the reasoning behind the predictions, inner workings as well as the limitations of an AI algorithm. For example, in tumour diagnosis, it would provide an insight into why a whole slide image (WSI) has been labelled as containing a "benign tumour". The methods achieve this by creating a heatmap on the original image, generating synthetic visualisations or providing some other scores.

Another important aspect of XAI is understanding the limitations of an AI tool. This is crucial for a safe deployment these tools to clinical practice. What happens if an AI algorithm encounters some data samples that are significantly different from what it has seen so far? Can we catch when the algorithm is making

a wrong prediction? In our projects, we are using uncertainty and out-of-distribution detection to develop methods for capturing and understanding situations when AI predictions are unreliable.

PROJECT INFORMATION

Project

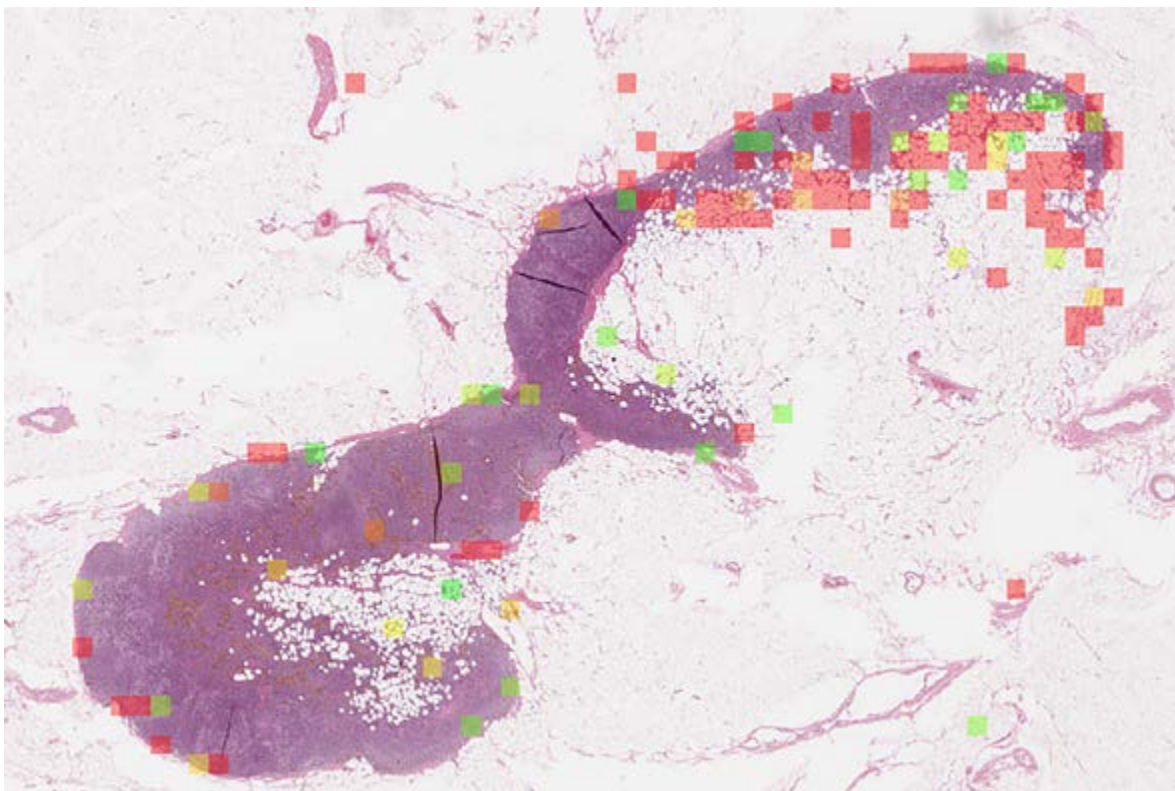
Explainable AI Applied to Histopathology Image Analysis

Supervisors

Claes Lundström, Gabriel Eilertsen and Stina Garvin

Short CV

Lancaster University, BSc Hons. Financial Mathematics, 2011-2014
Linköping University, MSc Statistics and Machine Learning, 2017-2019
Linköping University, PhD candidate, 2019-now



H&E stained section of lymph node with breast cancer metastasis. The green, yellow, and red squares indicate the level of uncertainty of an AI algorithm (green for least uncertain, red - most uncertain). This can be used in clinical practice to skip the predictions from the most uncertain regions as they are least reliable.

Segmentation of Brain Tumor Structure Using MRI and Deep Learning

Medical images are common sources of information used every day by clinicians to design and follow-up treatment planning. In research, medical images are used, for example, to investigate efficient ways for diagnosing diseases and design tools to help clinicians in their daily work. The use of deep learning for medical image analysis expands the frontier of what applications can be developed that exploit the information contained in the image data even more and automatize certain tasks to assist clinicians.

One clinical scenario where medical images are necessary is during diagnostic procedure of a brain tumor. Using magnetic resonance imaging (MRI), clinicians can visualize the tumor structure inside the patient's brain. From these images the tumor border and substructures are identified and used for treatment planning, i.e., radiotherapy and surgery.

Unfortunately, the manual annotation of the tumor is a time-consuming task, affected by the experience of each clinician and by what is visible in the images.

In this project, deep learning-based methods for brain tumor segmentation are explored with the purpose of overcoming the limitations of manual annotation and improving the current available deep-learning methods. Context-aware strategies are currently an emerging topic in deep learning applications, to allow models to use information from the surrounding context. To investigate the concept, the impact of anatomical contextual information on segmentation accuracy is tested, where white matter, gray matter and cerebrospinal fluid masks or probability maps are added to the model input during training [1]. Another approach is to provide the model with more data originating from different MR acquisi-

tion modalities, such as quantitative MR. By using different combinations of input data, we study the impact of the different modalities on model performance.

PROJECT INFORMATION

Project

Brain tumor segmentation using magnetic resonance images (MRI)

Supervisors

Anders Eklund, Neda Haj-Hosseini, Evren Özarslan, Oliver Gimm, Ida Blystad

Short CV

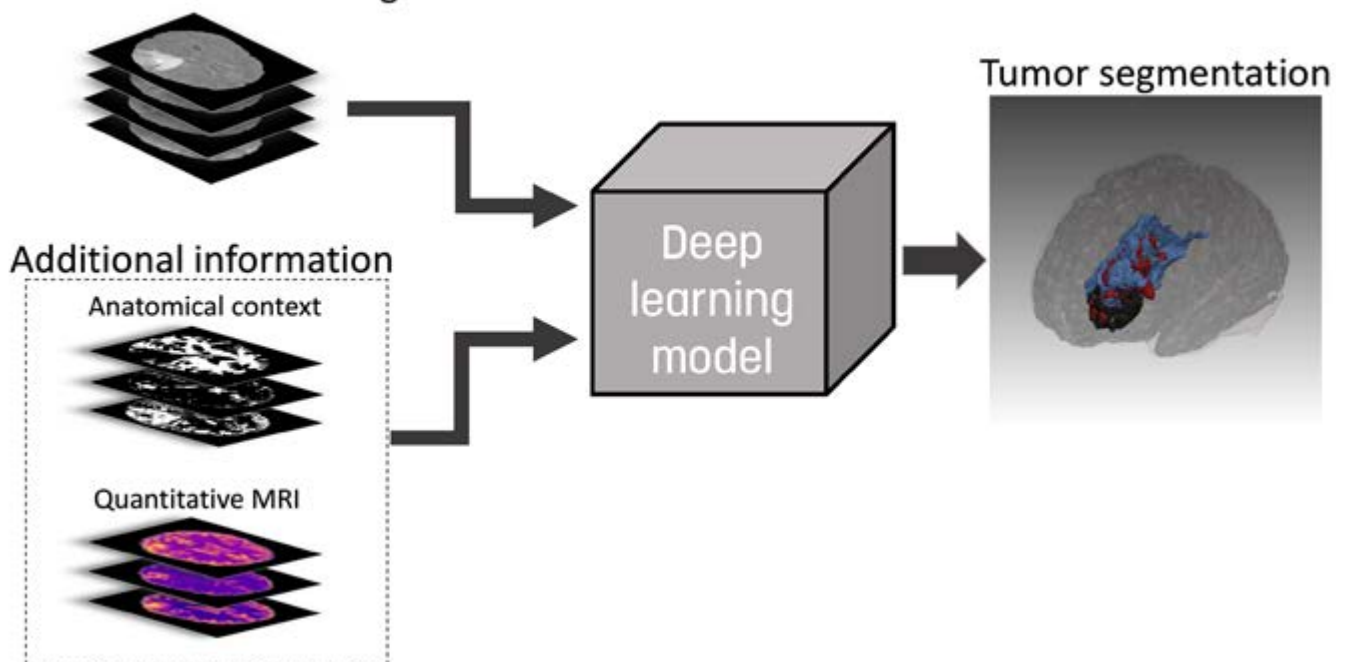
Bachelor's in biomedical engineering from the University of Padova (2013-2016).

Master of Science in Biomedical Engineering from Linköping University (2017-2019).

Research Engineer at the Department of Biomedical Engineering at Linköping University (2019 -2020).

[1] Tampu IE, Haj-Hosseini N, Eklund A. Does Anatomical Contextual Information Improve 3D U-Net- Based Brain Tumor Segmentation? *Diagnostics*. 2021; 11(7):1159.

Conventional MR images



Brain tumor segmentation pipeline. In addition to conventional MR images, other information can be used to train the model for segmenting the tumor. For example, anatomical contextual information and quantitative MR data.

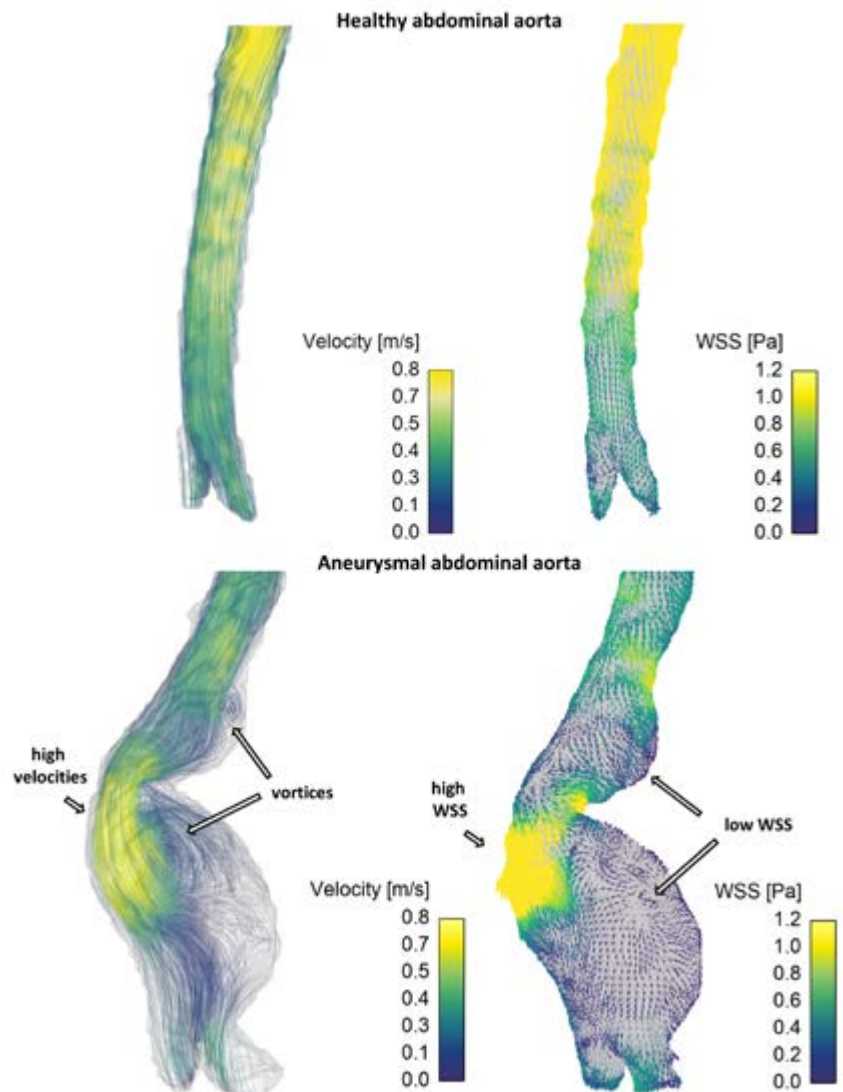
Nonsize Factors in Aortic Dilatation

■ Aneurysmal dilatation of the aorta is an asymptomatic disease that is often not detected until a fatal dissection or rupture occurs. Current guidelines traditionally depend on diameter based criteria for stratification towards surgical intervention. However, size alone is not a sufficient predictor for complications. For example, the majority of patients with ascending aorta dissection present with an aneurysm diameter of < 5.5 cm and thus do not fall within the current guidelines for elective aneurysm surgery¹. We lack scientific understanding and clinical tools to properly manage individuals with aortic dilatation.

The main objective of this project is to investigate if aorta dilatation is related to alterations in aortic wall properties or blood flow. We want to achieve this aim by means of advanced cardiovascular magnetic resonance (CMR) imaging. By improving our understanding of aortic dilatation and exploring new measures to discriminate between cases and controls, this project may lead to new ways to improve risk stratification for subjects with aortic dilatation.

In a first study, we investigated the altered hemodynamics in patients with abdominal aortic aneurysm. 18 patients and 23 age- and sex-matched controls with abdominal aortic diameters ≥ 3.5 cm and < 3.5 cm, respectively, were recruited from a screening program at our institution. The selected cohort has undergone a defined CMR imaging protocol, including time-resolved three-dimensional phase-contrast magnetic resonance imaging with three-directional velocity encoding (4D flow CMR), an advanced CMR technique that allows for quantification of blood flow. 4D Flow CMR images were properly processed in order to compute wall shear stress (WSS), which represent the friction force of blood on the aortic wall.

Patients with dilated abdominal aorta experienced significantly low velocities and WSS in the abdominal infrarenal aorta compared to controls. Peak systolic streamlines highlight the presence of altered swirling flow, which results in low and oscillating WSS vectors (Figure). Future studies will focus on correlating locations of low and oscillating WSS with aneurysm growth and rupture.



Peak systolic velocities, represented as streamlines (right), and wall shear stress (WSS), as vectors (left), for a healthy control (upper row) and a patient with abdominal aortic aneurysm (bottom row). Due to the expansion of the vessel, velocities are reduced inside the aneurysm and the altered flow generates vortices, resulting in low and non-uniformly oriented WSS at the vessel wall.

PROJECT INFORMATION

Project

Novel Assessment of Aortic Function in Health and Disease

Supervisors

Petter Dyverfeldt, Lena Jonasson, Tino Ebbers

Short CV

Master's degree in biomedical engineering - Biomechanics and Biomaterials, Politecnico di Milano University, Milan, Italy

Bachelor's degree in biomedical engineering, Politecnico di Milano University, Milan, Italy

A Cardiovascular Model for Blood Pressure Regulation

High blood pressure, or hypertension, is one of the most common health issues today with 22% of all adults worldwide affected and it is twice as common in patients with type 2 diabetes (T2D). In Europe, hypertension is defined as systolic blood pressure above 140 mmHg or diastolic blood pressure above 90 mmHg. Blood pressure and blood flow dynamics, together called hemodynamics, are tightly interconnected, and a high blood pressure requires the heart to work harder to pump blood through the body. Uncontrolled hypertension is a risk factor for cardiovascular diseases such as coronary artery disease, heart failure, and renal failure.

The basic causes of hypertension, such as hemodynamic changes due to increased blood volume and aortic and vascular stiffness, are known. Nonetheless, hypertension treatment is usually based on a trial- and error approach including lifestyle changes and testing of various anti-hypertensive drugs. There is a need

for a deeper understanding of the changes in hemodynamics during hypertension and especially during T2D. Detailed hemodynamic data can be acquired with non-invasive measurements such as 3D imaging of blood flow over time, four-dimensional magnetic resonance imaging (4D Flow MRI). However, 4D Flow MRI cannot directly measure blood pressure or aortic stiffness.

In this project, we combine 4D flow data with a cardiovascular model (Figure 1) to extract information that otherwise is hard to measure non-invasively. Such a cardiovascular model that can describe person-specific hemodynamics in healthy individuals was previously developed in the group. The model is now further developed to investigate blood flow dynamics in hypertensive and non-hypertensive individuals, and T2D patients and controls. This allows for assessment of model-derived hemodynamic parameters such as the contraction and relaxation of the left ventricle, which are

compared between the groups. The study can bring new insights into the hemodynamic mechanisms behind hypertension in patients with or without T2D and may provide a new clinical tool for the assessment of personalized hemodynamics.

PROJECT INFORMATION

Project

A cardiovascular mechanistic avatar for blood pressure regulation

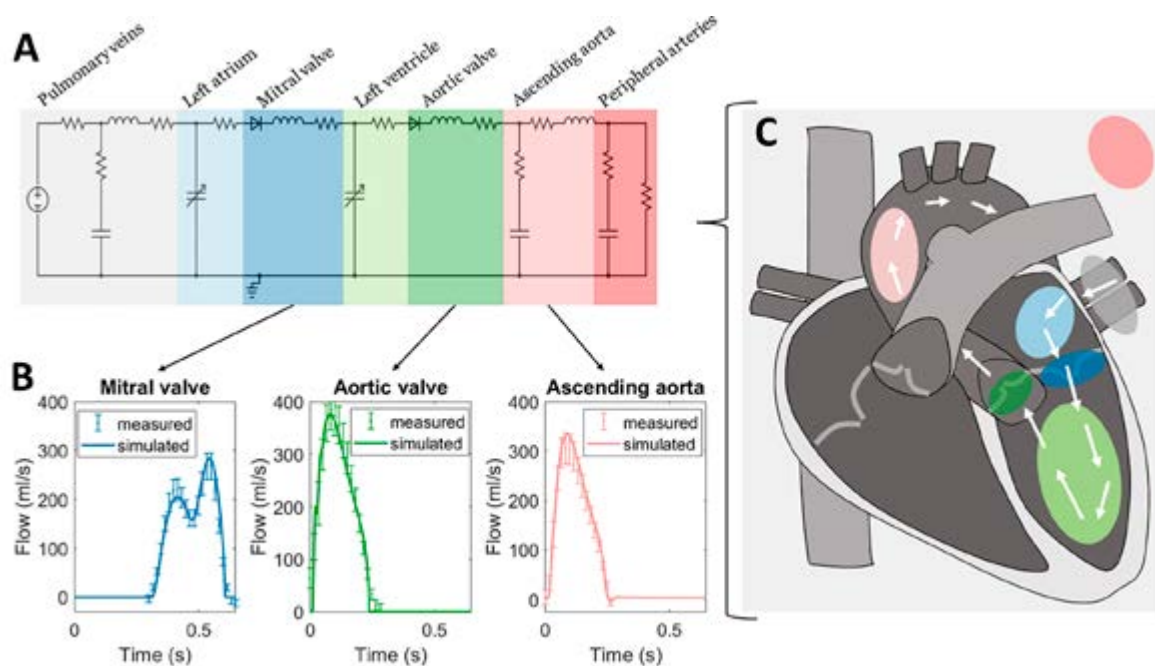
Supervisors

Gunnar Cedersund, Tino Ebbers, Carl-Johan Carlhäll

Short CV

PhD student Linköping University, since February 2020

M.Sc. in Engineering Biology, Linköping University, 2021



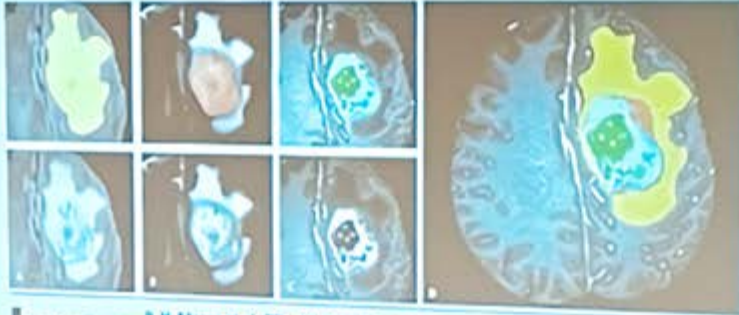
A) The mathematical model of the cardiovascular system. B) Personalized model simulations of blood flow in the mitral valve, aortic valve and ascending aorta show good agreement with 4D flow MRI measurements. C) Each part of the model corresponds to a part in the heart and cardiovascular system (color coded).

PhD student Marco Domenico Cirillo is defending his thesis on the day of his dissertation.



Gliomas

ED (yellow), NET (red), NCR (green), ET (azure)



li.u
LUND
UNIVERSITY

B. H. Menze et al., "The Multimodal Brain Tumor Image Segmentation Benchmark (BRATS)," in *IEEE Transactions on Medical Imaging*, vol. 34, no. 10, pp. 1993-2024, 2015.

Dissertations

During 2021 two of the CMIV PhD students have finished their studies and defended their theses. The PhD students and the research school are an important part of CMIV and we are proud to present their theses here.



PhD student Martin Lindvall is nailing his thesis to the public to scrutinize three weeks before his public defense.

Designing with Machine Learning in Digital Pathology: Augmenting Medical Specialists through Interaction Design

■ Advancements in machine learning (ML) have dramatically increased artificial intelligence (AI) capabilities for medical diagnostic tasks. Recent research has shown that AI adequately trained can make assessments on par with experts when, for instance, grading and detecting cancers. However, several challenges remain for translating those AI capabilities into usable tools fit for routine workflows in clinical practice. This thesis explores how human-centred design methods might resolve some of those challenges.

One challenge is to make AI-assisted decision making better than either human or AI acting alone. While some predictive models might consistently perform above human experts, many are less than perfect, regularly failing in unexpected ways or delivering mediocre performances, leading to time-consuming human verification. The thesis shows that user interface design can make AI-assisted decision making efficient if guided by an understanding of the specific task, the human expert, and AI imperfections.

Another challenge is that ML-derived models typically learn from input-output examples. The implication for software design methods is that responsibility is shifted from programmers expressing logical statements towards medical professionals providing annotated data. The thesis makes several contributions concerning this novel machine teaching aspect, including designing and evaluating an efficient annotation tool, seven datasets, and identifying success factors for continuous learning in deployed products.

A path along deep learning for medical image analysis With focus on burn wounds and brain tumors

■ The number of medical images that clinicians need to review on a daily basis has increased dramatically during the last decades. Since the number of clinicians has not increased as much, it is necessary to develop tools which can help doctors to work more efficiently. Deep learning is the last trend in the medical imaging field, as methods based on deep learning often outperform more traditional analysis methods. However, in medical imaging a general problem for deep learning is to obtain large, annotated datasets for training the deep networks.

This thesis presents how deep learning can be used for two medical problems: assessment of burn wounds and brain tumors. The first papers present

methods for analyzing 2D burn wound images; to estimate how large the burn wound is (through image segmentation) and to classify how deep a burn wound is (image classification). The last papers present methods for analyzing 3D magnetic resonance imaging (MRI) volumes containing brain tumors; to estimate how large the different parts of the tumor are (image segmentation).

Since medical imaging datasets are often rather small, image augmentation is necessary to artificially increase the size of the dataset and, at the same time, the performance of a convolutional neural network. Traditional augmentation techniques simply apply operations such as rotation, scaling and elastic deformations to generate new similar images, but

it is often not clear what type of augmentation that is best for a certain problem. Generative adversarial networks (GANs), on the other hand, can generate completely new images by learning the high dimensional data distribution of images and sampling from it (which can be seen as advanced augmentation). GANs can also be trained to generate images of type B from images of type A, which can be used for image segmentation.

The conclusion of this thesis is that deep learning is a powerful technology that doctors can benefit from, to assess injuries and diseases more accurately and more quickly. In the end, this can lead to better healthcare for the patients.

*Martin Norling de Brun
and Tobias Ekholm in
the 4K projector room*

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

CT 1 – Siemens Healthineers NAE-OTOM Alpha. This is a first-generation dual source CT scanner with photon counting technology. The photon counting detectors have 4 main advantages compared to conventional (scintillator based) CT detectors. The pixels of the detectors are much smaller than before without radiation dose penalty. This leads to images with spatial resolution at a new level. Each photon's energy is measured and therefore images are created without electronic noise. The energy information of the photons can be used for advanced spectral applications, such as k-edge imaging. Moreover, the detector is more sensitive for low-energy photons, which makes it possible to reduce the radiation dose and contrast media dosage drastically.

CT 2 – Siemens Healthineers SOMATOM Force. This CT 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 SOMATOM 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. 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

MR 1 – The Siemens 3.0T Prisma has a 60 cm bore and gradients with 80mT/m and 200 T/m/s simultaneously, which facilitate fMRI and DTI studies in a 64 receive channels head coil. The coil

concept also offers high coil density using parallel transmit technology called TimTX TrueShape for cardiac, abdominal and musculoskeletal examinations.

MR 2 – The Philips Ingenia 3.0T has a 70 cm bore. It is equipped with Xtend gradient system (up to 45mT/m and 200 T/m/s) and two parallel RF transmission channels (Multitransmit 4D), which adapt the 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 fiber-optic cable.

MR 3 – The Philips Achieva 1.5T has a 60 cm bore and is equipped with Nova Dual gradients (up to 66 mT/m and 160 T/m/s), and the latest software release and upgraded to dStream resulting in up to 40 % higher SNR, and a dynamic range that exceeds 185 dB.



Advanced fMRI research is possible using video glasses with built-in eye-sight correction as well as eye-tracking, and it is also possible to combine these measurements with simultaneous multichannel MR-EEG. Other specialty equipment includes several MR-elastography (MRE) systems for both 1.5 T and 3 T, based on both electrodynamic and gravitational transducers. Our MRE-capability is best in class and can be used to quantify changes of the biomechanical properties of pathologies, as is caused by fibrosis and inflammation. We have also access to a unique installation of multinuclear MR spectroscopy, allowing us to investigate both static and dynamic energy metabolism in tissues. The latter is highly facilitated by our MR-compatible MR-ergometers for quantitative cardiac and muscle research.

A full research agreement with Philips Medical Systems and Siemens Healthineers allows all possible clinical as well as critical technical research applications.

DIGITAL PATHOLOGY AND ANNOTATION

For histo-pathology CMIV has a glass scanner from Hamamatsu. The Nano-zoomer 2.0HT convert glass slides into high-resolution digital data by highspeed

scanning and has a capacity of scanning up to 210 glasses automatically. In addition, three workstations with touch screens are installed for annotation work.

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. 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 90 persons. The theatre is built around Barco dp4k-30L 6P Laser projector (21 000 lumens light output), with 4K resolution (4 096 Å-2 160). The Barco Laser 3D has a native 6-primary color-3D system. The system uses a Barco E2 Image processor, 4K Native 12 bits/color 3D input/output. The computer to screen connections are run by the Lightware mx-33R Digital Crosspoint matrix. The Wirecast 7.3 Recorder system allows recording and

online streaming. During 2018 Wranne was upgraded to an advanced Zoom room enabling remote meetings and education. In addition to the theatre there is also a 55" Sectra visualization table and a wall mounted 85" Sectra visualization monitor with ten fingers multi-touch. 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.

COMPUTING AND STORAGE

CMIV has its own server facilities hosting servers for secure handling of sensitive data, research calculations, analysis and NAS backup. In 2019 an HP Tetralith supercomputer and a new data storage unit of 660 TB were installed.

CMIV is the host for the AIDA infrastructure, where the flagship is the DGX-2 system from Nvidia with 16 high-end GPUs available for all AIDA partners across Sweden to use for AI training. The service has been validated secure enough for processing sensitive personal data. Thanks to the good collaboration with Region Östergötland, the DGX-2 system was installed in the hospital's server hall at the end of 2020 for increased technical and physical security.





Mats Jonsson and Mirjana Vukusic are preparing a patient for an MR elastography exam in the 3T MR scanner

Organization

CMIV is governed by its Board of Directors, with representatives from academia, healthcare 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

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Marie Waltersson	Research Coordinator
Marcel Warntjes	Senior Staff Scientist

*Anders Persson and Håkan
Gustafsson by the Photon
Counting Detector CT*





Publications

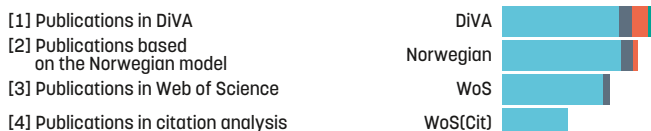
The CMIV research efforts lead to a steady stream of scientific publications. An overview of the 2021 production is given in the following pages. As papers from CMIV researchers may be primarily registered under other affiliations the listing is not complete, but still shows a good representation of CMIV. The CMIV researchers have presented their work at conferences all over the world during the year, however, conference abstracts are not included in this list unless published as a conference paper.

Bibliometric Analysis

Basis for analysis, 2017-2021

The analysis is based on sources [1]–[4], listed below. Different sources are used for different parts of the analysis. A criterion for inclusion is that publications have been registered in DiVA for the time period covered in the analysis. Publication types that are included in the analysis are:

- Refereed journal articles and reviews
- Scholarly book chapters
- Scholarly books
- Refereed conference publications



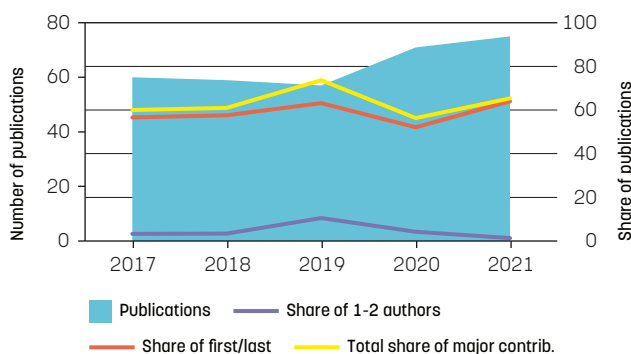
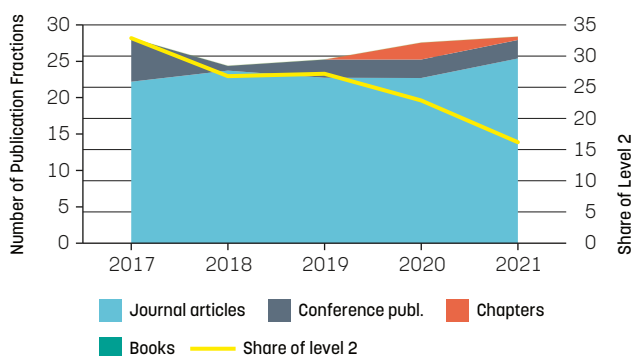
- [1] Publications in DiVA according to the selection stated above.
- [2] Publications in [1] included in the Norwegian model.
- [3] Publications in [2] indexed in Web of Science.
- [4] Publications in [3] where we have access to normalized citation data.

At each new section of the analysis, the symbol in the top right corner will mark the selection being used.

Norwegian model, 2017-2021

Publications published in journals and by publishers in the Norwegian list	Number of publications	Number of publication fractions	Share of level 2
Journal articles	287	116,8	29%
Conference publications	27	14,2	0%
Chapters	6	2,8	6%
Books	0	0,0	0%

Share of level 2, total: 25%



Publication fraction refers to the share of a publication originating from the department. For example, if two out of four authors are affiliated with the department, the fraction is 0.5.

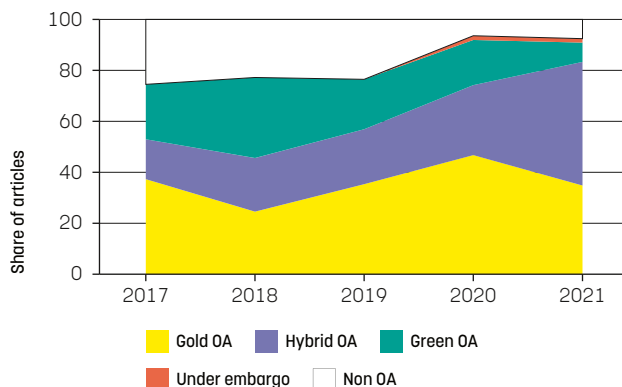
In the Norwegian model, the included publication channels are divided into two levels – 1 (scientific) and 2 (scientific and leading in its field of research). Level 2 publication channels comprise a maximum of 20 percent of channels in their research field.

Share of level 2 refers to the share of fractionalized publications in level 2 journals/publishers. At a higher aggregate level, the expected share is 20 percent.

Open access, 2017-2021

Share of open access publications (incl. OA after an embargo period):

Journal articles	84%
Conference publications	44%
Chapters	33%

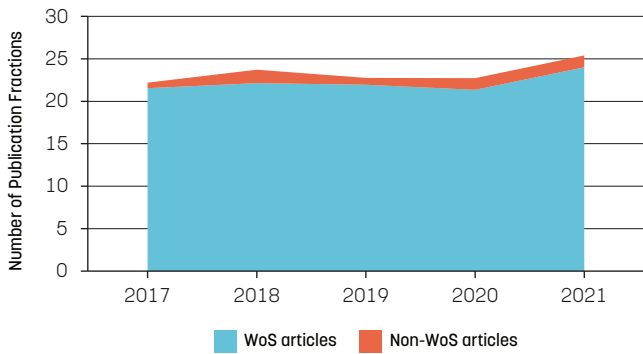


Open Access (OA) publications have been identified with the help of data from Unpaywall (unpaywall.org). The diagram shows articles according to Open Access type. OA data for articles has been supplemented with data from our own customized algorithm. Gold Open Access is defined as articles published in journals openly accessible in their entirety. Hybrid Open Access is defined as openly accessible articles published in subscription-based journals. Green Open Access is defined as the accepted version of articles published in online repositories.

Coverage in Web of Science, 2017-2021

	Number of publications	Number of publication fractions
Journal articles and conference publications *	289	119,6
Coverage		
Journal articles: 95%		
Conference publications: 55%		

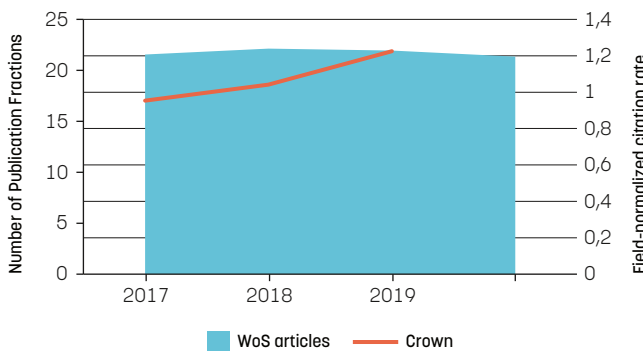
*Articles, reviews, letters, proceedings papers in WoS.



The analysis is based upon Clarivate Analytics Web of Science. For a citation analysis to be relevant and reliable, a sufficient basis is required. To give an indication of the coverage of journal articles in the database, the number of publications/fractions in the database is displayed. All citation indicators are fractionalized, i.e. the number of authors affiliated with the department is taken into account. Self-citations are excluded.

Citation analysis, 2017-2019		
	Number of publications	Number of publication fractions
Journal articles *	134	57,0
Results, field-normalized		
Field-normalized citation rate (crown): 1,06		
Share of highly cited articles (top 10 %): 15 %		
Share of uncited articles: 0 %		
Field-normalized journal citation rate (journal crown): 1,07		
Ranking of Journal Impact Factor (JIF), average: 0,67		

*Articles, reviews and letters in WoS.

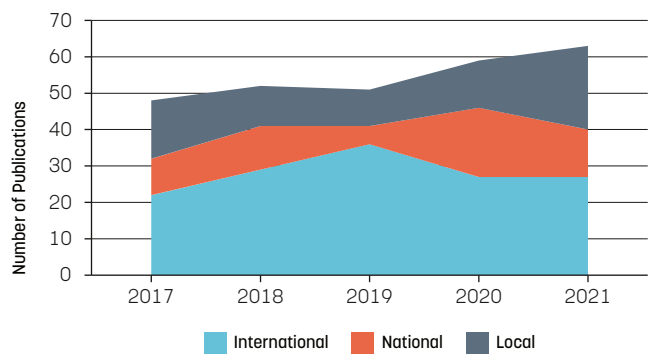


When publication fractions are less than 10, the citation indicators are not displayed. If the basis is small, individual items can have a high impact on averages.

- Field-normalized citation rate (Crown): a measure of impact of articles included in the analysis that provides a comparison with the international average for the same subject area, year and type of article, where 1 is the global average. Field normalized rate of citation is fractionalized, i.e. the number of authors affiliated with the department is taken into account. Self-citations are excluded. The average field normalized citation rate for universities in Sweden during 2016-2019 was 1.12, according to basic funding allocation data from 2021 from the Swedish Research Council.
- Share of highly cited articles (top 10 percent): share of publications in the top 10 percent of the most highly cited publications in the research subject within the time period, i.e. publications with high impact.

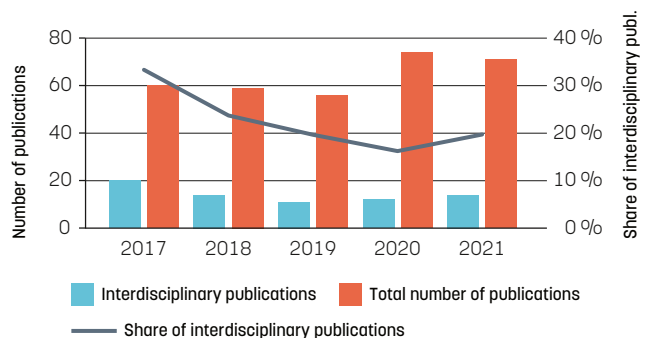
- Share of uncited articles: indicates how citations are distributed, i.e. if citations are evenly distributed among articles, or if a small number of articles account for the majority of citations.
- Field-normalized journal citation rate (Journal crown): A measure of impact of the journals chosen for publication. It provides a comparison for the average number of citations for the journals chosen for publication with the global average number of citations for journals in the same field. I.e, a value of 0.9 means that the chosen journals for publication are on average cited 10% less than journals in the same field(s).
- SNIP: normalized journal indicator based on data from Scopus.

Co-authorship – geographical, 2017-2021	
Share of articles with international co-authorship	52 %
Share of articles with national co-authorship	22 %
Share of articles with local co-authorship	27 %



Share of publications in WoS where department authors have co-authored with international, national or local collaborators (academic as well as non-academic). Local co-authors refers to other LiU authors. This category also includes single authors. International collaborations are also displayed, since studies have shown a higher citation rate for publications that are products of such collaborations. According to the Leiden ranking for 2020, the share of international collaborations for LiU was 56.7 percent during 2015-2018, which is low compared to other universities in Sweden.

Publications with interdisciplinary authorship	
Number	71
Share	22 %



CMIV affiliated researchers are written in bold.

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DISSERTATIONS

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Annual accounts

During 2021 CMIV had a turnover of more than 57 million.
The financial result for CMIV in 2021 was SEK 815 thousand.

During the fiscal year 2021 CMIV had several ongoing grant research projects and also received some new funding. AIDA – Analytic Imaging Diagnostics Arena continued its work, being funded by VINNOVA. Ten projects funded by AIDA together with one clinical fellowship and three clinical evaluation projects started during 2021.

Genomic Medicine Sweden funded a research project concerning Synthetic dataset for experimental research and clinical business development on broad panels (GMC Sydöst),

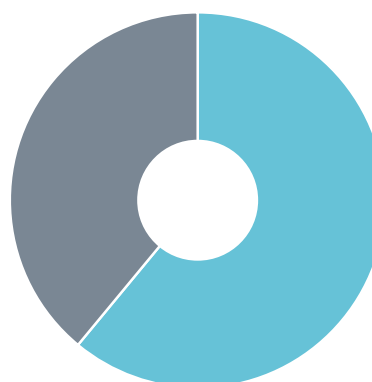
SciLifeLab started funding of AIDA data hub and VINNOVA started funding an Incubator for national platforms for systematic clinical validation of AI within imaging.

Research projects SCAPIS (Swedish Heart-Lung Foundation), MeDigiT (Visual Sweden) and SCAPIS-AI platform (VINNOVA) continued during 2021. Both the Faculty of Medicine and Health Sciences and the Faculty of Science and Engineering continued to support CMIV's work within the Digital pathology area.

ECONOMIC SUMMARY	2017	2018	2019	2020	2021
Total revenue	48,165	52,059	56,266	55,007	57,384
EXPENSES					
Staff expenses	-15,772	-16,711	-20,390	-22,480	-23,660
Cost of premises	-6,472	-6,657	-5,752	-6,647	-6,474
Misc. Operating expenses	-16,765	-18,704	-18,848	-17,928	-19,551
Depreciation expenses	-7,819	-8,129	-8,440	-7,848	-6,878
Financial expenses	-36	-151	-126	-11	-4
Total expenses	-46,864	-50,051	-53,556	-54,913	-56,568
Result of operations	1,300	2,008	2,710	95	815

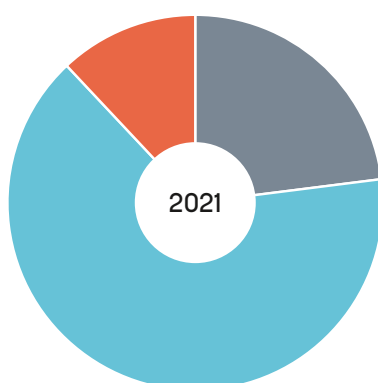
Research Funding at CMIV 2010-2021

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

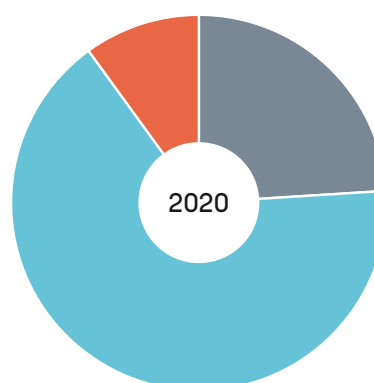


External funds: kSEK 140,408
Industrial funds: kSEK 89,102

CT Research and Clinic (%)

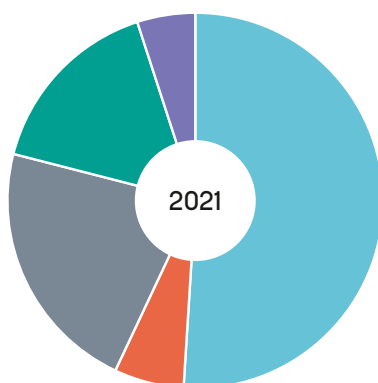


Research, 23
Clinic, 65
Special exams only at CMIV CT, 12

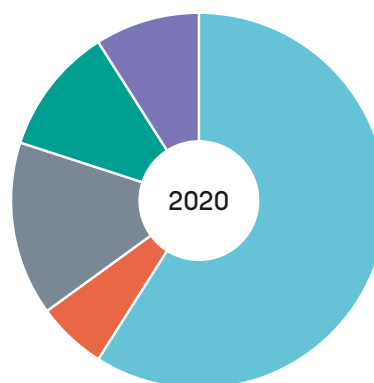


Research, 24
Clinic, 66
Special exams only at CMIV CT, 10

Distribution on Research on the MR Scanners (%)



Neuro, 51
Gastro, full body, 16
Musculoskeletal, 6
Development, 5
Cardiovascular, 22



Neuro, 59
Gastro, full body, 11
Musculoskeletal, 6
Development, 9
Cardiovascular, 15



*High resolution Photon count
CT image of the wrist to the
left and elbow to the right.
Ronald Booij, Erasmus MC
University Rotterdam/ CMIV
Linköping University.*



