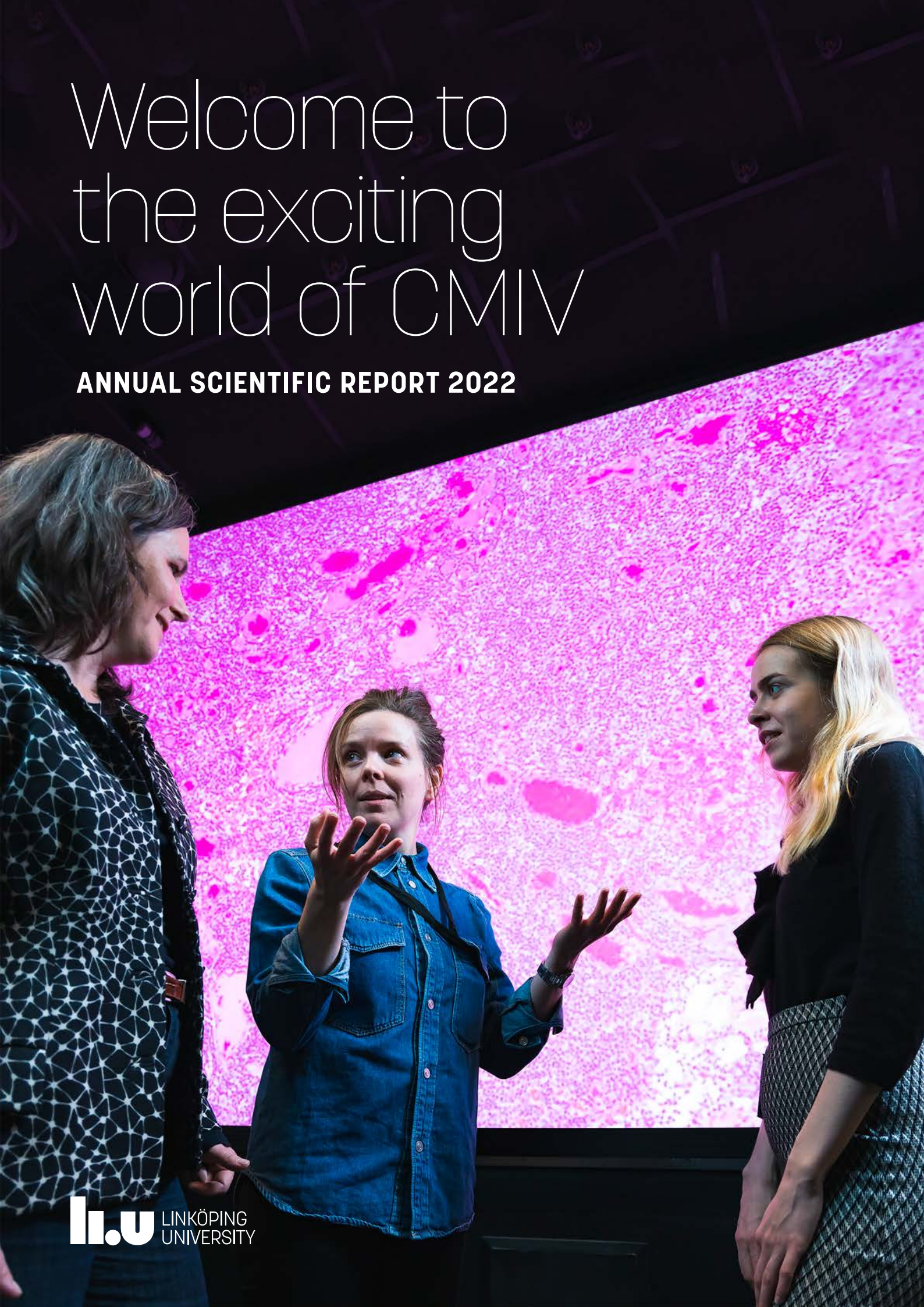
Welcome to the exciting world of CMIV

ANNUAL SCIENTIFIC REPORT 2022



LINKÖPING UNIVERSITY

The image shows Blood flow structures in the heart computed from CT images, Siemens Force, by Jonas Lantz, CMIV.

Project Leader CMIV: Maria Kvist

Production: LiU-Tryck

Graphic design: Tomas Hägg, LiU-Tryck

Photography: CMIV, Emma Busk Winquist, Thor Balkhed

Cover Image: PhD students discussing a pathology image in Wranne theater. Anna Bodén, pathologist, Sofia Jarkman, pathologist, and Milda Pocevičiūtė, MSc Statistics and Machine Learning.

Print: LiU-Tryck, March 2023

Fonts: Korolev, Miller, Paper: Galerie Art Silk

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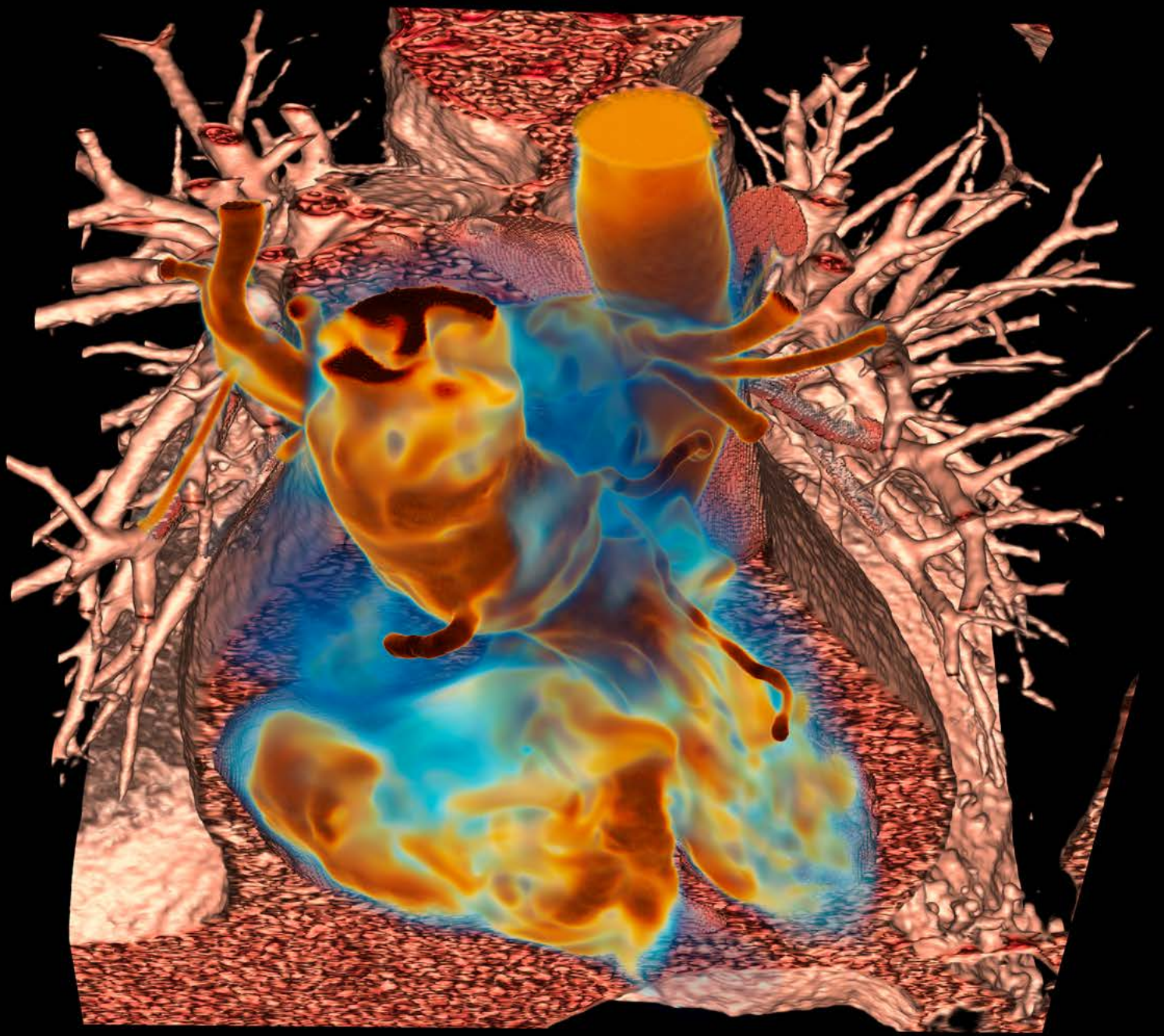

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30 YEAR MEMBER

We are glad that we now are more active at CMIV than ever before. We are running out of office space and our famous coffee room is overcrowded. The coffee machine's counter has reached the maximum number with more than 10,000 cups.

Since last year's inauguration of the world's first photon-counting computed tomography scanner (PCCT), it is now used daily in the clinical routine. The proportion of clinical research studies continues to increase, although the growing national shortage of radiology nurses is challenging. Thanks to the good cooperation with CMIV's neighbor the radiology department at the university hospital, the amount of active ongoing research projects has now increased to exceed 140. Among these the scientific council has elected the three flagship projects of 2022. 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 "Next generation imaging in Atrial Fibrillation" is the first multicenter study on MRI in Sweden. The second project "Epistemology and Post-Covid Syndrome – an Interdisciplinary Study" are looking into the symptoms of fatigue in relation to post-covid following in the swells of the pandemic and the third flagship project "AIDA Incubator for AI Validation Platforms (AIDA-VAI)" is about validating AI tools before implementing them into clinical workflow.

The board of directors is now working on developing future strategies for CMIV's expansion, which will likely be focused on data-driven imaging where you combine micro-macro data, from cells to the whole body, where the goal is increased patient benefit through improved health for the individual patient.

All in all, 2022 has been an exceptional yet demanding year. Many new research projects were initiated, 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

Håkan Gustafsson in our Photon Counting Detector CT NAEOTOM Alpha.

Highlights

As always, it has been an intensive year and a lot of things have happened. A selection of the greatest achievements is presented here.

The photon-counting CT now in clinical use

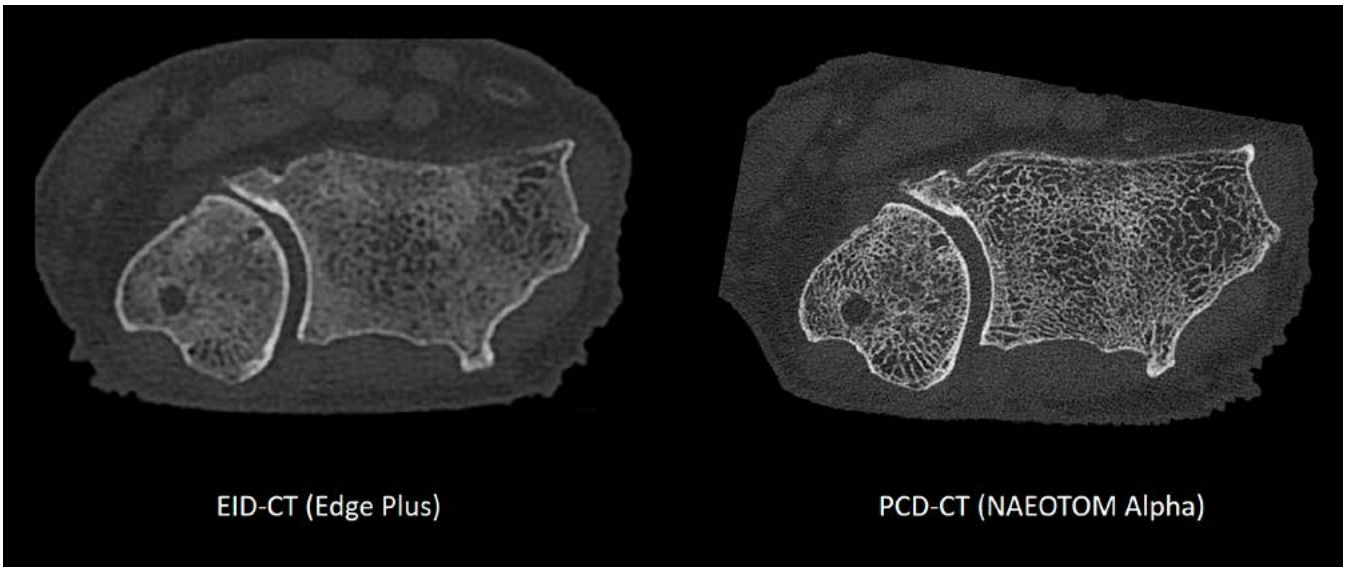
Our prototype photon counting CT Count Plus was replaced with the new Siemens Healthineer's NAEOTOM Alpha in November 2021. Since the inauguration it has now been fully incorporated into the clinical routine and is used, among other things, in examinations where narrowing's in the patient's coronary arteries are suspected. Our research has shown that the radiation dose and the amount of contrast agent can be halved when examining coronary vessels compared to conventional CT. The technique is also very good for examining other vessels in the body.

Musculoskeletal patients are routinely examined today with our photon counter. Our research has already given rise to several publications. Most recent publication "Assessment of visibility of bone structures in the wrist using normal and half dose with photon-counting detector CT" by Ronald Booij, et al. has been published in the European Journal of Radiology in December.

It has also been shown that the radiation dose can be further reduced compared to conventional CT, when examining severely obese patients without the image quality being negatively affected.

Overall, photon counting CT offers several advantages over traditional CT in terms of improved image quality, reduced radiation exposure, and improved quantification of materials and tissue properties.

Madeleine Edvinsson, Lilian Henriksson, Anders Persson and Susann Skoog.



CT scan of the same wrist with a conventional integration detector CT (left) and a new CT with photon-counting detectors. This new scanner can produce images of the wrist twice as sharp and with at least half the radiation dose of normal CT.

Lilian Henriksson and Madeleine Edvinsson at the Photon Counting Detector CT NAEOTOM Alpha.

Professor McCollough *finally became honorary doctor*

On May 21, Professor Cynthia H. McCollough finally was awarded an honorary doctorate for her great achievements and initiatives in medical image sciences.

She was awarded the honorary doctorate in the spring of 2020 but due to the pandemic she first now was able to travel to Sweden for the promotion.

Professor McCollough is director of Mayo Clinic´s CT Clinical Innovation Center in Rochester, Minnesota and her research interests resolve around the technology of CT imaging and its many clinical applications.

Mona Cederholm – *awarded employee of the year*

Mona Cederholm is assistant nurse and in charge of the booking of all research at the MR and CT scanners at CMIV. She has been working at the hospital for over 40 years. Due to her great effort, we have been able to optimize the use of our modalities, so that we get the maximum amount of research that will then benefit patients. She treats all researchers with great friendliness and has a lot of knowledge about the various investigation methods of the research performed. Her goal is always to help and make it as good as possible for both patients and coworkers. It is a huge puzzle that she puts together daily to make everything work in the best possible way.

Her extraordinary work was awarded Employee of the Year at the national radiology conference in Gothenburg in 2022.

Chiara Trenti
– winning the Potchen Basic Science Award

We are very proud over Chiara Trenti, PhD student at CMIV with research focus on the aorta dilatation, who in August received the Potchen Basic Science Award for outstanding oral presentation at the 34th annual MR Angiography Conference in Los Angeles. The title of the winning oral presentation was: 'Flow Displacement and Wall Shear Stress in Individuals with Mild-to-Moderate Aortic Dilation and Tricuspid Aortic Valves'.

Chiara has returned to CMIV after spending six months as a visiting researcher at Stephenson Cardiac Imaging Center, a clinical MRI center inside Alberta's Children Hospital affiliated with the University of Calgary.

SEK 10.8 million to three CMIV researchers

The Swedish Research Council is the largest governmental research funding body in Sweden and distributes almost SEK 8 billion every year to support Swedish research.

The three CMIV researchers Maria Engström, Tino Ebbers and Evren Özarslan received project grants within Natural and Engineering Sciences.

Professor Maria Engström received grants to her projects *Development of new mathematical models for determination of image biomarkers of cerebral function from fMRI data.*

Professor Tino Ebbers received grants for his project *Predicting thrombotic risk in atrial fibrillation using imaging, modelling and simulation.*

Professor Evren Özarslan received grants for his project *Novel diffusion MRI as a probe of brain structure and function.*

Swedish Research Council

Bigpicture receives its first datasets

In June, the Bigpicture data repository received its first three datasets, consisting of whole-slide pathology images and associated clinical metadata, from Region Östergötland, Medical University of Vienna, and University Medical Center Utrecht. The data that is amassed will enable development of groundbreaking AI tools for clinical diagnostics and drug development. CMIV is responsible for the Bigpicture repository infrastructure, in collaboration with the ELIXIR nodes in Sweden and Finland, at the SciLifeLab Bioinformatics platform (NBIS) and at CSC. The 6-year, €70 million project will herald a new era in pathology.

bigpicture

Mischa Woisetschläger and Erik Tesselaar.

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, artificial intelligence and precision medicine are integrated parts of the imaging chain.

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.

Meeting with the Cardiovascular Magnetic Resonance group.

IMAGING DATA SOURCE

The overall dominating data source at CMIV traditionally has been 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. While MRI still is a major data source, data from digital pathology and photon counting CT are rapidly increasing. The researchers' need to combine data from different data sources places great demands on infrastructure for data storage and access to computing power.

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 DIVIDED BY RESEARCH AREA

	IMAGING DATA SOURCE				
	Computed Tomography	Magnetic Resonance Imaging	Digital Microscopy	Ultrasound	Other
Photon Counting in Pancreatic Ductal Adenocarcinoma	●				
Abdominal Synthetic MRI		●			
Evaluation of Reconstruction Methods in CT	●				
Liver Function Evaluation		●			
Assessment of Hepatic Function in Health and Disease		●			
Neuroplasticity in Irritable Bowel Syndrome		●			
MR-Mammography		●			
Artificial Intelligence in Breast Cancer Screening					●
Advanced CT of the Hand and Wrist	●				
Accurate Trial on Acute Rotator Cuff Tears		●		●	
PHARAOH	●				
Bone Analysis for Reducing Osteoporotic Fractures	●				
Health Effects of Resistance Training in Postmenopausal Women		●			
The NACOX-study	●	●			
Swedish CArdioPulmonary bioImage Study (SCAPIS) in Linköping	●	●		●	
Carotid MRI		●			●
Ascending Aortic Dilation		●			
4D Flow MRI		●			
4D Flow CT	●				
Digital nuclear cardiology and AI in the diagnosis of myocardial ischemia					●
Computational integrated diagnostics panorama for liver cancer	●	●	●		●
AIDA	●	●	●	●	●
Bigpicture			●		
Comparison of CT Technical Image Quality of Using PCCT and EID	●				
Tissue Classification Using DECT and MBIR	●				
Evaluation of New Brachytherapy Planning Methods	●	●		●	
AIMPLANT		●			
Improved diagnosis of pediatric brain tumours using AI-based digital pathology			●		
EPSONIP		●	●		
MeDigiT	●	●			
Experiencing the Self through Touch		●			
Pathophysiology Behind Prolonged Whiplash Associated Disorders		●			
Image-Based Biomarkers of Brain Disorders (IBBB)		●			
High Resolution MR Quantification in 3D		●			●
The Behavioral and Neural Mechanisms of Alcohol Choice Preference		●			
ASSIST		●			
Detection and Neurological Effects of Manganese		●			
Localization of Seizure Onset Zone in Focal Epilepsy		●			
Quantitative MRI on Brain Tumors		●			
SESNIC		●			
Developing 3D qMRI		●			


BIOMEDICAL RESEARCH AREA
TECHNICAL RESEARCH AREA
Cardiovascular
Neurology
Oncology
Musculoskeletal
Gastrointestinal
Gynecological
Pulmonary
Metabolism
Acquisition
Modeling
AI/Data analytics
Visualization
Simulation
Imaging Biomarkers
No Method Development

Håkan Gustafsson, Catrin Nejdeby and Claes Lundström in the corridor outside of CMIV.

Flagship Projects

The 2022 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.

Carl-Johan Carlhäll, PI, Jennie Kemppi and Andreas Bussman.

Next Generation Imaging in Atrial Fibrillation

Cardiovascular disease is the most common cause of death in Sweden as well as in the rest of the world. Thanks to research, people suffering from heart disease in Sweden live on average 12-15 years longer today than thirty years ago. Major research achievements throughout the years have led to better treatment methods and care. One area that needs more research is atrial fibrillation. After coronary artery disease this is most probably the next public heart disease.

>>

"This project is the first large multicenter trial in Sweden using cardiac MRI."

Carl-Johan Carlhäll

When it comes to heart disease, the big culprit is of course coronary artery disease. A lot of diagnostics have been done there. What many consider to be the next major public disease is atrial fibrillation, a disease without the good treatment that coronary artery disease has.

Carl-Johan Carlhäll, professor in clinical physiology is principal investigator (PI) of the project that are looking thoroughly into atrial fibrillation by using magnetic resonance imaging (MRI).

What is atrial fibrillation?

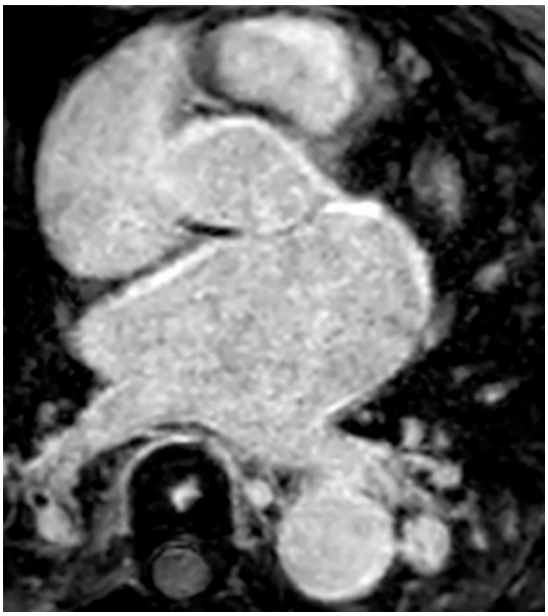
- The heart has two ventricles and two atria, where the atria contracts synchronously. When the atria lose their contracting ability and just stand and fibrillate then it is very dangerous. For one thing, blood clots can form because there is a lot of blood that remains in the atrium and the blood flow becomes slower. These blood clots can then cause a stroke or settle elsewhere in the body. Atrial fibrillation can also cause heart failure because the atrium does not help in the pumping work, Carl-Johan explains.

In Linköping, at CMIV, there are two projects running on advanced imaging in atrial fibrillation. One of them is part of a giant clinical research project called ABC-AF (Age, Biomarkers, Clinical history, which is a scoring system for stroke and bleeding and AF being Atrial Fibrillation), which is run by Uppsala University and the goal is to include 6.500 patients, where the intent is to compare traditional management strategies with newer strategies, e.g., based on blood test markers.

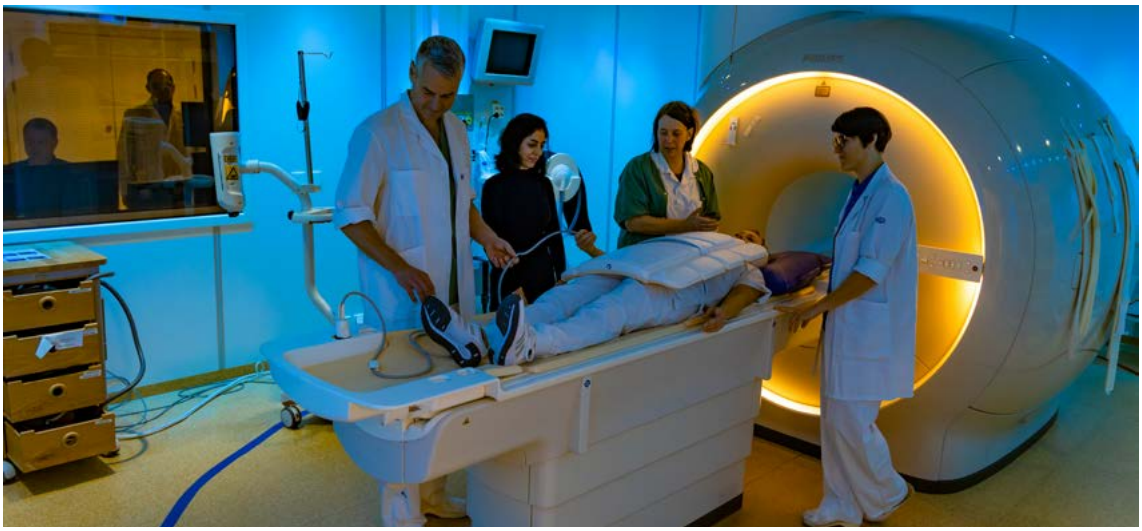
Carl-Johan is PI for the ABC-AF MRI substudy. The aim of this sub-study is to investigate function and tissue characteristics of the heart in patients with different types of atrial fibrillation. This is the first time that a national multicenter study with cardiac MRI is being conducted. Part of this is to try to build an infrastructure in Sweden to enable more multicenter studies on cardiac MRI. Apart from Linköping, Lund, Uppsala, Gothenburg, Örebro and Stockholm is participating in this study as well. Due to the pandemic the period of inclusion of patients is prolonged until the summer of 2024.

There are different types of atrial fibrillation depending on how far the patient has come in the disease process. The patients who have just begun experiencing atrial fibrillation are in the paroxysmal stage. The next stage is the persistent, where patients have had symptoms for up to a year. The last stage is the permanent, where the cardiologists have no more treatments to offer. These patients are often older and are given blood thinning medicine to avoid blood clots.

The other research project is dealing with patients coming to the university to undergo cardiac ablation. There is electricity in the heart and if you have some tissue that does not work properly there could be a spark causing the atria to fibrillate instead of pumping. Cardiac ablation is used to correct heart rhythm problems.



Late gadolinium enhancement (LGE) image of the left atrium.



Lars Karlsson, Marjan Firouznia, Caroline Kindesjö Nätt, Iulia Skoda.

The procedure is done by burning an area in the atrium causing scarring. The scarring blocks the electrical signals and removes the arrhythmia tendency.

– It is hard to obtain really good results by ablations and many patients have to come back, some patients even many times. This is why this research project is important, Carl-Johan says.

– We are now mapping to try to look more closely at fibrosis, which is a well-known substrate for arrhythmia, and with MRI we can then try to map how much fibrosis there is and try to map where exactly. By doing so we hope to help those who perform the cardiac ablations and partly help them identify and choose patients who respond to the ablation treatment, partly make sure that they ablate an appropriate area of the heart. This cannot be done with any other modality but MRI, Carl-Johan continues.

– We are a bit curious about and hope that in the long run we can do this with photon counting detector computed tomography, as well.

Atrial fibrillation has become a public disease and as the population ages, the number of patients with atrial fibrillation is increasing all the time. Due to this atrial fibrillation is a priority area for the Swedish Heart Lung Foundation since it affects so many people and costs the healthcare system enormous amount of money.

– The primary goal of this research is to map different types of atrial fibrillation with imaging to see tissue characteristics such as fibrosis and also fat. Hopefully this will be indicative of treatment so that patients can be better selected for better outcomes, Carl-Johan concludes.

MRI Cardiovascular Imaging Biomarkers

Project information

PROJECT NAME

(FFAA) ABC-AF MR-substudy

PROJECT LEADER

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

MAIN PROJECT PARTICIPANTS

Lars Karlsson, Iulia Skoda, Marjan Firouznia, Sara Gifting, Caroline Nätt Kindesjö, Christer Holm, Henrik Ekman, Andreas Bussman, Adelina Millberg, Jennie Kemppi, Mona Cederholm, Ellen Ostenfelt, Håkan Arheden, Jonas Oldgren.

GRANTS

Heart Lung Foundation (2021-2023)
Forskar ALF (2023-2025)

KEY PUBLICATIONS

Skoda I, Henningsson M, Stenberg S, Sundin J, Carlhäll CJ. Simultaneous assessment of left atrial fibrosis and epicardial adipose tissue using 3D late gadolinium enhanced Dixon MRI. J Magn Reson Imaging 2022.

Henningsson M, Carlhäll CJ. Inflow artifact reduction using an adaptive flip-angle navigator restore pulse for late gadolinium enhancement of the left atrium. Magn Reson Med 2020;84(6):3308-3315.

Charitakis E, Karlsson L, Papageorgiou JM, Walfridsson U, Carlhäll CJ. Echocardiographic and Biochemical factors predicting arrhythmia recurrence after catheter ablation of atrial fibrillation - an observational study. Front Physiol 2019;10:1215.

Kristin Zeiler and Ida Blystad, PIs.

Epistemology and Post-Covid Syndrome – an Interdisciplinary Study

Now that the world recovers from the most serious part of the pandemic, we need to find out more about the disease and the different symptoms connected to the Covid-19 virus. Several research projects are ongoing. In 2021 Professor Kristin Zeiler and colleagues at Linköping University and Linköping University Hospital received a substantial grant from the Swedish Research Council for a new interdisciplinary approach of trying to understand post-covid syndrome.

"This is both challenging and developing – and incredibly stimulating to be forced to think about and adopt to a new way of conducting research, outside the comfort zone."

Ida Blystad

When talking about post covid syndrome, most people know someone who suffered a little more from the virus than the average person. We know so little about the disease and need to try to gain more knowledge about the challenges of the covid-19 now that the worst part of the pandemic is behind us.

Kristin Zeiler, professor and director of the Centre for Medical Humanities and Bioethics is the principal investigator of the SEK 30 million interdisciplinary project with the title Biomedicine, Clinical Knowledge, and the Humanities in Collaboration: A Novel Epistemology for Radically Interdisciplinary Health Research and Policy-Work on Post-Covid-19 Syndrome.

The project is divided into five subprojects, where CMIV is part of subproject two that aims to understand patients' experience of fatigue in post-covid-syndrome and its underlying characteristic disease mechanism. This is done through an innovative approach where the research team not only combines a clinical assessment including neuropsychological tests, magnetic resonance imaging (MRI) and analysis, cytokine profile analysis, and a qualitative phenomenological philosophy analysis, but also cross-reads and triangulates the results from these different analytic steps.

Ida Blystad is leader of the radiology approach.

– What I think is so special is that we are trying to create an understanding and a collaboration on different levels. For example, at the magnetic resonance imaging (MRI) exams we have already looked at the structure and now we are trying to focus on function and quantitative analyses, i.e., the connectivity and the microstructure of the tissue, Ida explains. On earlier conventional MRI exams of post-covid brains there has not been a clear pattern of what is happening, but only some non-specific changes.

Subproject two is co-led by Kristin and by Richard Levi, professor at the Department of Rehabilitation Medicine, at Linköping University Hospital. He and his colleagues at this department perform the clinical assessment to see that the fatigue symptoms are not due to any other underlying cause, as well as neuropsychological tests, while colleagues from different parts of Linköping University perform the cytokine profile analysis, the qualitative phenomenological interviews, and the phenomenological philosophy analyses. The cross-reading and triangulation across the different analyses is a joint task for the research team.

– Possible patterns and differences will be examined across the distinct kinds of analysed data. As an example, the qualitative phenomenological philosophy analysis can identify phenomenologically different qualities of fatigue or different kinds of fatigue in PCS, and such results will then be cross-read with the clinical assessment, the cytokine profile analysis, and the MRI analyses, with the aim of furthering the understanding of fatigue in PCS, says Kristin.

The researchers have diverse scientific backgrounds.

– We have completely different frameworks of how to conduct research, working with various different perspectives and methodologies, such as philosophical, qualitative, and different kinds of quantitative methodologies. It is incredibly interesting and developing to be able to collaborate in a group like this, Ida continues.

– Many of us have been working in interdisciplinary projects for long, and the project builds on a pilot study that combined perspectives from rehabilitation medicine, philosophy, and the qualitative social sciences. Even so, it brings together perspectives from the humanities, the social sciences, the clinical practices, and biomedicine that rarely are combined, and subproject two brings together perspectives and methods from the natural sciences that have

Ida Blystad and Richard Levi, PIs.

Kristin Zeiler, Sofia Morberg Jämterud, Eleanor Byrne, Ulrika Birberg Thornberg, Deneb Boito and Anestis Divanoglou.

more of a third-person perspective, with a focus on the body as measurable in different ways, and perspectives and methods for the analysis of subjective experience of illness, that have more of a first-person perspective, Kristin says. This makes it both unique and challenging. It's exciting and requires curiosity of perspectives other than one's own, and continuous conversations across several fields, Kristin continues.

The project also contains sub-projects that dig deeper into the very conditions for interdisciplinary research of this kind, examining how choices of perspectives and methods impact on what knowledge is being produced and how methods can be combined. Its overall objectives are to contribute a better understanding of post-covid syndrome, its emergence as a diagnosis, its expressions, implications and co-constituting factors through multifaceted analyses, and to contribute to the treatment of the patients.

– The project focuses on post-covid syndrome, but the work that we do in elaborating ways of combining perspectives and methodologies in different interdisciplinary ways is also intended to contribute to discussions about the interdisciplinary health research, its conditions, analytic gains and challenges more broadly. To me, these are exciting conversations that we need to have, Kristin concludes.

MRI Neurology Imaging Biomarkers

Project information

PROJECT NAME

Post-Covid Fatigue and Cognitive Impairment: subproject within the project Biomedicine, Clinical Knowledge, and the Humanities in Collaboration: A Novel Epistemology for Radically Interdisciplinary Health Research and Policy-Work on Post-Covid-19 Syndrome.

PROJECT LEADER

Ida Blystad, Richard Levi and Kristin Zeiler

MAIN PROJECT PARTICIPANTS

Richard Levi, Anestis Divanoglou, Ulrika Birnberg Thornberg, David Engblom, Eleanor Byrne, Sofia Jämterud Morberg, Felipe León, Evren Özarslan, Deneb Boito, Anders Tisell, Ida Blystad, Kristin Zeiler

GRANTS

VR Grant: Interdisciplinary Research Environment Call (2022-2027).

KEY PUBLICATIONS

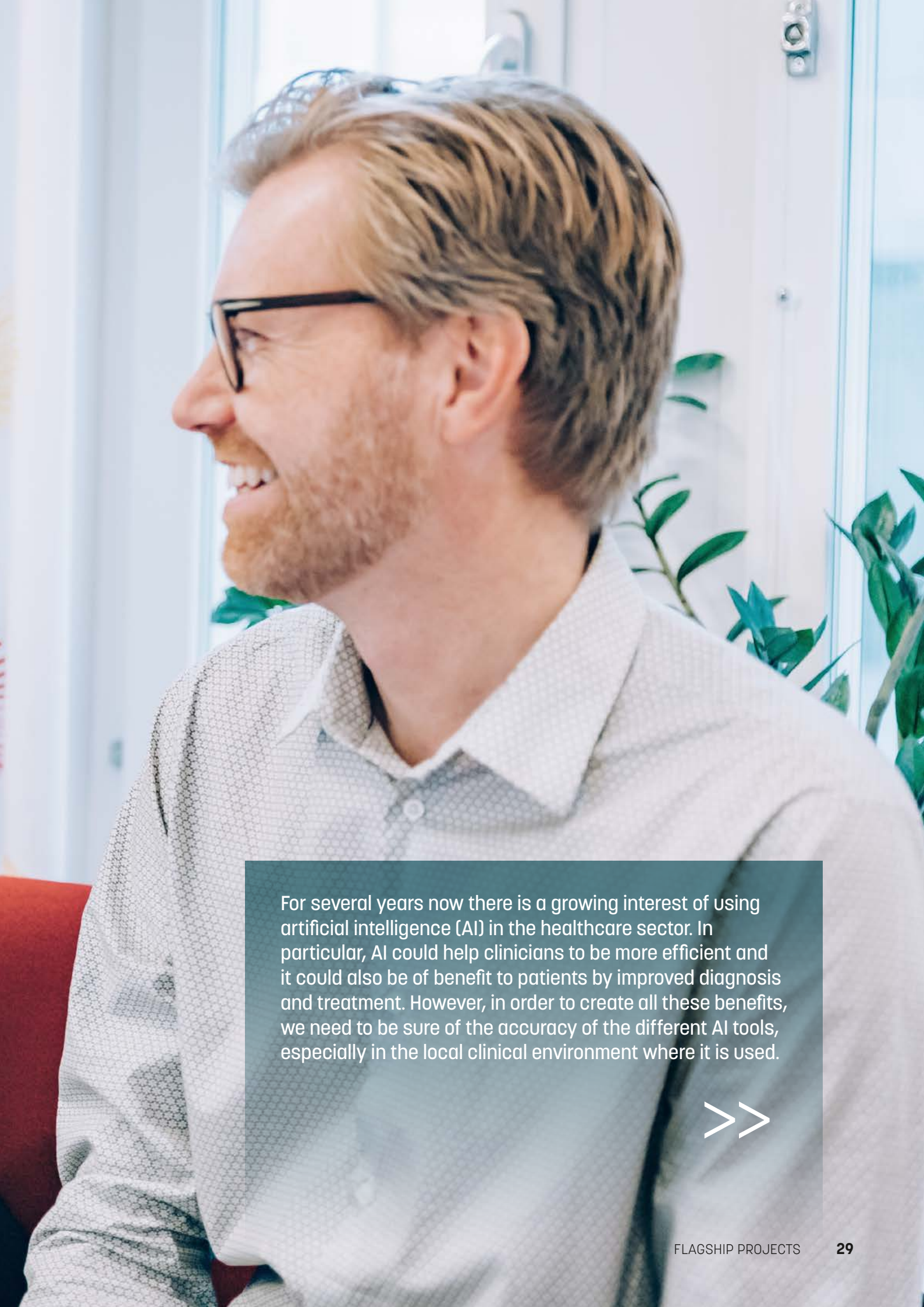
Varela, F.J. 1996. Neurophenomenology. A Methodological Remedy for the Hard Problem. Journal of Consciousness Studies 3(4): 330-349.

Hellgren, L. et al. 2021. Brain MRI and neuropsychological findings at long-term follow-up after COVID-19 hospitalisation: an observational cohort study. BMJ Open 11(10). doi: 10.1136/bmjopen-2021-055164.

Wahlgren C. et al. 2022. Rehabilitation needs following COVID-19: Five-month post-discharge clinical follow-up of individuals with concerning self-reported symptoms. EClinicalMedicine. Jan; 43:101219. doi: 10.1016/j.eclinm.2021.101219.

Catrin Nejdeby and Claes Lundström, PI.

AIDA Incubator for AI Validation Platforms (AIDA-VAI)



For several years now there is a growing interest of using artificial intelligence (AI) in the healthcare sector. In particular, AI could help clinicians to be more efficient and it could also be of benefit to patients by improved diagnosis and treatment. However, in order to create all these benefits, we need to be sure of the accuracy of the different AI tools, especially in the local clinical environment where it is used.

In clinical practice, e.g., within radiology and pathology, AI has proven to be useful, by helping clinical problem solving and speeding up the diagnostic process. However, AI also comes with risks. Some critics claim that the benefits of AI have been overestimated.

There are different types of risks connected with the use of AI tools such as patients being harmed due to incorrect AI predictions on diagnosis of life-threatening diseases or prioritization of interventions. There are also the risks of misusing the AI tool, i.e., if the user is not aware of how to use it correctly and by that harming the patient. In order to trust AI solutions there is also a need for transparency of the machine learning models to see that there is no bias in their recommendations. To understand these potential quality issues, and to keep them in check in clinical use, care providers must have the capacity to validate AI applications before and after implementation.

Claes Lundström is adjunct professor and arena leader of AIDA, Analytic Imaging Diagnostic Arena, which is a national arena for research and innovation in medical image analysis. Within AIDA there is a research project called AIDA Incubator for AI validation platforms (AIDA -VAI). The mission of the incuba-

Catrin Nejdeby, Håkan Gustafsson and Claes Lundström, PI.

tor is to facilitate the development of new national collaborations on AI validation, referred to as platforms.

There are three pilot platforms within the project. The main pilot project is VAI-B, a validation platform for AI in breast radiology with Fredrik Strand at Karolinska Institutet as project manager and Sophia Zackrisson from Lund as vice project manager. The second platform is also in radiology and the third in pathology. Apart from the pilot platforms, the purpose of the incubator is to build a general capability in Swedish healthcare to efficiently create validation platforms for additional areas as needs arise.

– If we look at radiology, we have roughly 200 CE-approved AI solutions that can be legally purchased and implemented by healthcare. Due to the CE approval, we know that they have a basic performance, but what we have learnt is that they still must be validated by the care providers. It is not at all certain that their performance will meet the expectations when they are implemented. So, this means that each care provider must evaluate whether it works for them, Claes explains.

There is not only one way of running health care. The workflows differ between countries, hence also the expectations on the AI solutions differ.

– The supplier may think of one way to use the specific AI solution, but at the hospital in question there might be other things that the users are hoping for from the same solution. As one example, some are looking for support alongside an experienced doctor meanwhile others are in the need of managing things when the senior doctor is not around and a more junior doctor would be supported, Claes continues. Different questions arise also due to variations in acquisition equipment and patient populations. By using a validation platform all those questions can be mapped to what the products can do locally. These questions are part of the validation and need to be answered before starting the procurement process.

The platform would act as a national supporting function for testing new tools and new versions. A reason for national collaboration is that proper validation efforts would be difficult for some care providers to perform. If you look at a small hospital, they typically would not have the capability to consider all these tests, so national platforms makes it easy for everyone to benchmark AI solutions, even on their own local data if desired. It is also possible for the vendors to test their own algorithms to see if they work properly.

– The needs of the care providers must be our guide. The incubator will hopefully facilitate great improvements in health care in the future, Claes concludes.

Computed Tomography | MRI | Digital Microscopy | Other | Neurology | Oncology | No Method Development

Project information

PROJECT NAME

AIDA Incubator for AI Validation Platform

PROJECT LEADER

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

MAIN PROJECT PARTICIPANTS

Håkan Gustafsson, Catrin Nejdeby, Maria Kvist

GRANTS

Vinnova, grant (2021-02617)

KEY PUBLICATIONS

Lundström C, Lindvall M. Mapping the Landscape of Care Providers' Quality Assurance Approaches for AI in Diagnostic Imaging. Journal of digital imaging. 2022 Nov 9:1-9.

Hedlund J, Eklund A, Lundström C. Key insights in the AIDA community policy on sharing of clinical imaging data for research in Sweden. Scientific Data. 2020 Oct 6;7(1):1-6.

A group of researchers and clinical staff in front of the MR scanner.

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.

POPULAR SCIENTIFIC SUMMARY
Mischa Woisetschläger

Photon Counting in Pancreatic Ductal Adenocarcinoma

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 (PhDAC)

PROJECT LEADER

Mischa Woisetschläger, Department of Radiology, University Hospital Linköping

MAIN PROJECT PARTICIPANTS

Lilian Henriksson, Petter Quick, Nils Elander, Hakon Blomstrand, Bergthor Björnsson, Anders Persson

GRANTS

RFoU (2022)

KEY PUBLICATIONS

Blomstrand, H., et al., Real world evidence on gemcitabine and nab-paclitaxel combination chemotherapy in advanced pancreatic cancer. BMC Cancer, 2019. 19(1): p. 40.

Blomstrand, H., et al., Clinical characteristics and blood/serum bound prognostic biomarkers in advanced pancreatic cancer treated with gemcitabine and nab-paclitaxel. BMC Cancer, 2020. 20(1): p. 950.

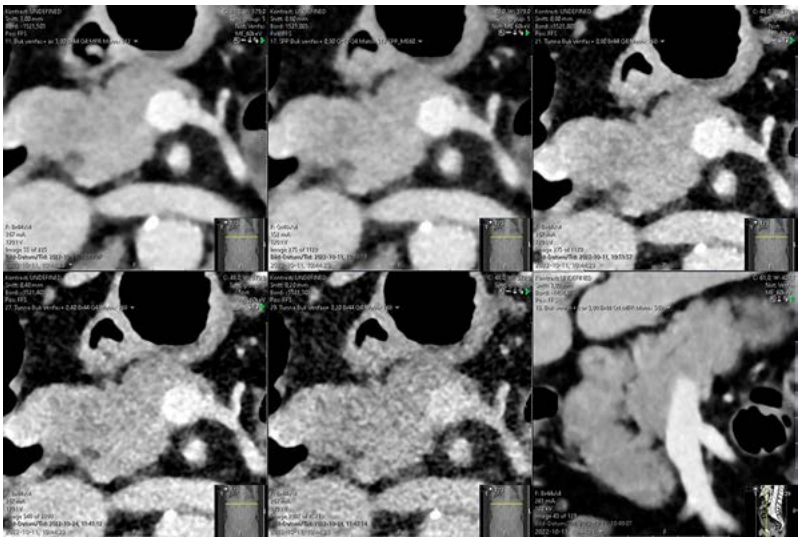


Figure 1. Different reconstructions from the arterial phase of a pancreas, showing high resolution images from the Naeotom ALPHA.

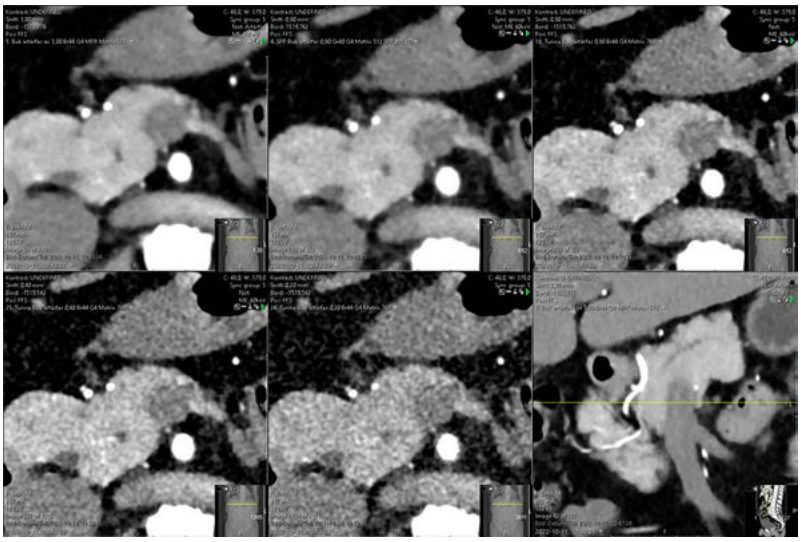


Figure 2. Different reconstructions from the venous phase of a pancreas, showing high resolution images from the Naeotom alpha.

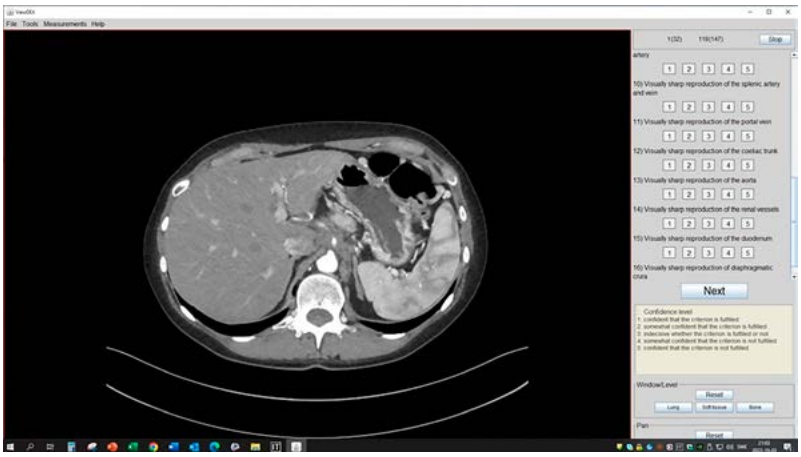


Figure 3. Screenshot of the evaluation done on data from the Force and the Count. The software used is Viewdex 3.0. The image quality evaluation was done with the criteria for the pancreas from the European guidelines on quality criteria for computed tomography.

POPULAR SCIENTIFIC SUMMARY
Mischa Woisetschläger

Abdominal Synthetic MRI

Background: 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 three 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 maybe 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 prostate and MR rectum). The quantitative information from tumor and plain tissue will be correlated with different clinical parameters, as well as probability assessments of tumor disease (i.e. PI-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.

The project is ongoing and data collection is nearly finished for the prostatic part. An interim analysis showed that there might be potential in differentiating lesions that are very similar to their surroundings by quantitative measures, but more data were necessary.

MRI | Oncology | Gastrointestinal | Acquisition | Imaging Biomarkers

Project information

PROJECT NAME

Implementation of Synthetic MRI in the Abdomen

PROJECT LEADER

Mischa Woisetschläger, Department of Radiology, University Hospital Linköping

MAIN PROJECT PARTICIPANTS

Nils Dahlström, Marcel Warntjes, Wolf Bartholomä, Bengt Noren, Mohammed Mahran

GRANTS

Percy Falk Stiftelse
Forsknings- och stipendieförvaltningen

KEY PUBLICATIONS

Warntjes JB, Dahlqvist O, Lundberg P. Novel method for rapid, simultaneous T1, T2*, and proton density quantification. Magn Reson Med. 2007;57(3):528-37.

Blystad I, Warntjes JBM, Smedby Ö, Lundberg P, Larsson E-M, Tisell A (2017), Quantitative MRI for analysis of peritumoral edema in malignant gliomas. PLoS ONE 12(5): e0177135. https://doi.org/10.1371/journal.pone.0177135.

Synthetic MRI of the Knee: Phantom Validation and Comparison with Conventional MRI, Neil M. Kumar, Benjamin Fritz, Steven E. Stern, J. B. Marcel Warntjes, Yen Mei Lisa Chuah, Jan Fritz, Radiology 2018; 289:465-477.

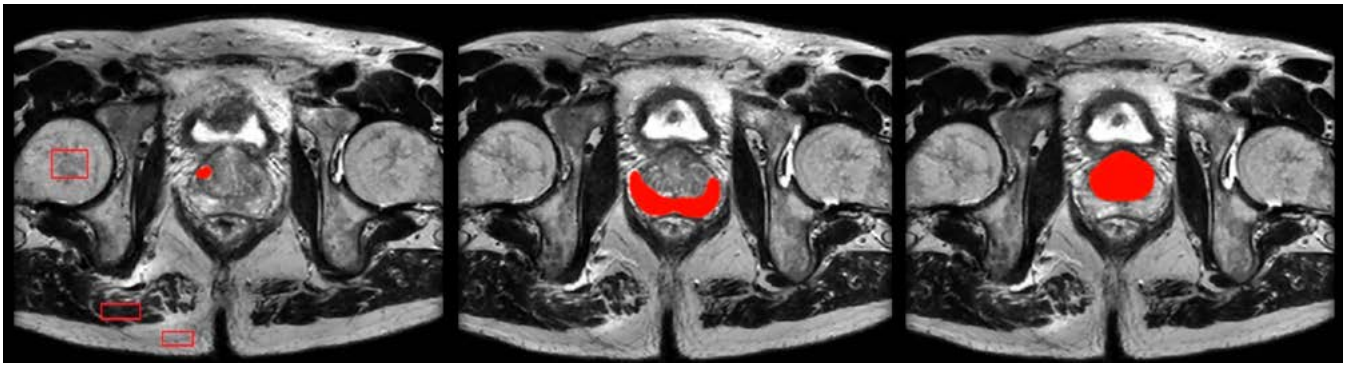


Figure 1. Left: ROIs of Benign Prostatic Hyperplasia (BPH), bone, fat; Center: Peripheral Zone (PZ); Right: Transitional Zone (TZ).

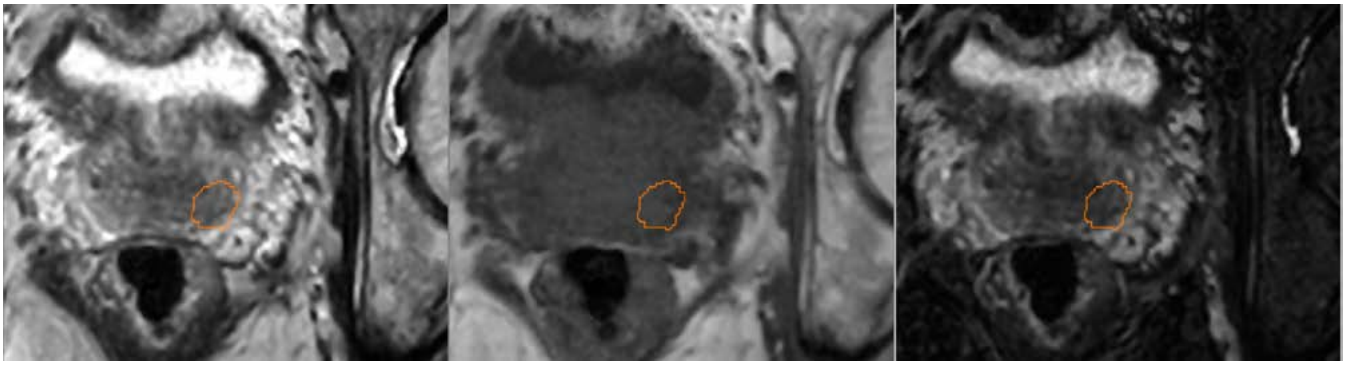


Figure 2. Example of a tumor with very similar characteristics as the surrounding tissue. Indicated on T2W, T1W and T2-STIR.

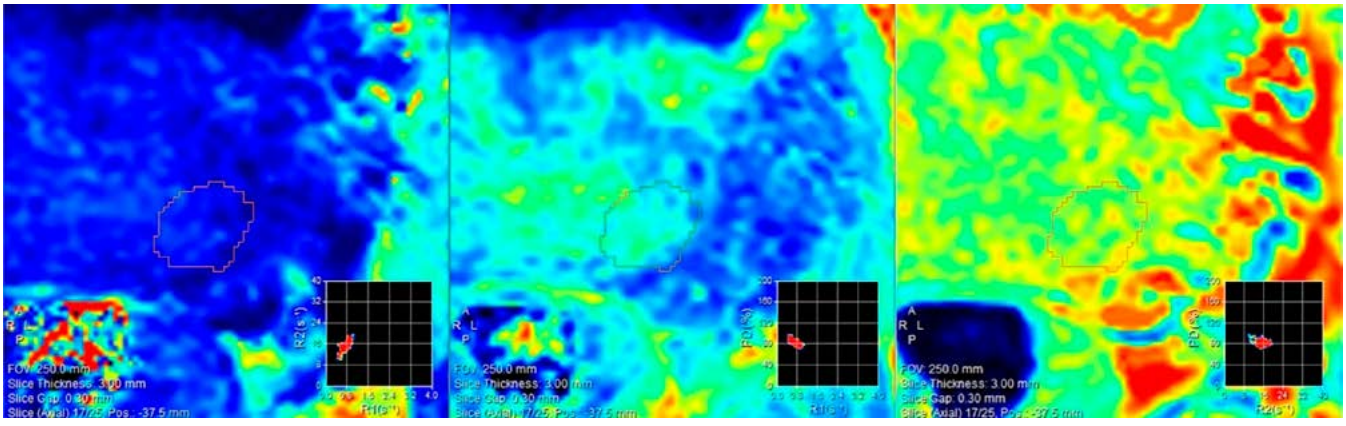


Figure 3. Same tumor on R1, R2 and PD maps: No visual differences between tumor and surrounding tissue.

POPULAR SCIENTIFIC SUMMARY
Bharti Kataria

Evaluation of Reconstruction Methods in CT

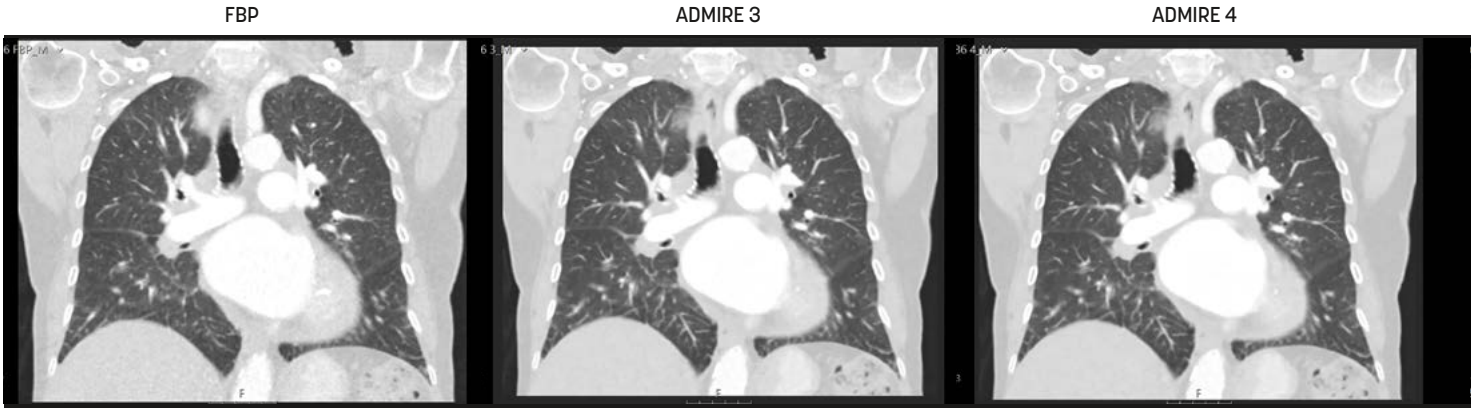
All diagnostic x-ray examinations use ionizing radiation, hence it is imminent to produce images of good diagnostic quality while simultaneously keeping the radiation dose to human organs as low as reasonably achievable (ALARA principle) to minimise detrimental radiation effects. Abdominal and thoracic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

Image quality in CT is related to the radiation exposure. A reduced exposure can lead to 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 (ADMIRE); 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 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. 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 IR 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) has been evaluated by radiologists and preliminary results are expect in the last quarter of 2022. Another 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

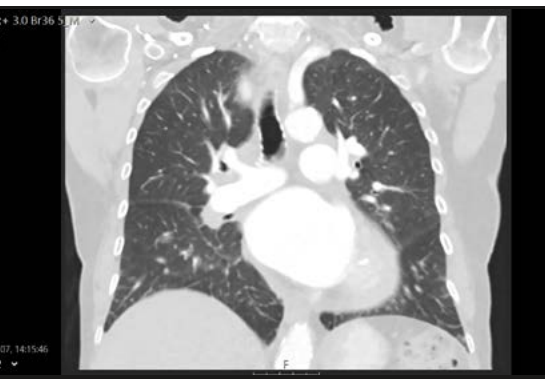


Patient images from a Thoracic CT examination using reconstruction algorithms Filtered Back Projection (FBP) and iterative reconstruction (ADMIRE) strengths 3, 4 and 5.

image quality over time, a re-analysis of the data from two studies (Kataria et al, 2018, 2020) were performed by introducing the time variable in the logistic regression models. In both materials results suggest that radiologists increasingly dislike the image quality produced by ADMIRE 5 over time for at least for two image criteria (liver parenchyma and overall image quality). In the time perspective of weeks or months, no learning effect (reflected in a gradually more positive attitude towards the new algorithm) could be demonstrated.

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 Althén

GRANTS

ALF (2017, 2018, 2021)
FoU (2017-2021)
Patientsäkerhetsforskning (2018-2019)
RFoU (2017-2022)

KEY PUBLICATIONS

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

Kataria B, Sandborg M, Öman J, Smedby Ö. Learning effects in visual grading assessment of new reconstruction algorithms in abdominal Computed Tomography, 16 August 2022, PREPRINT (Version 1) available at Research Square [https://doi.org/10.21203/rs.3.rs-1944960/v1] (Submitted för peer review).

POPULAR SCIENTIFIC SUMMARY
Peter Lundberg

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 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 are 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 Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

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

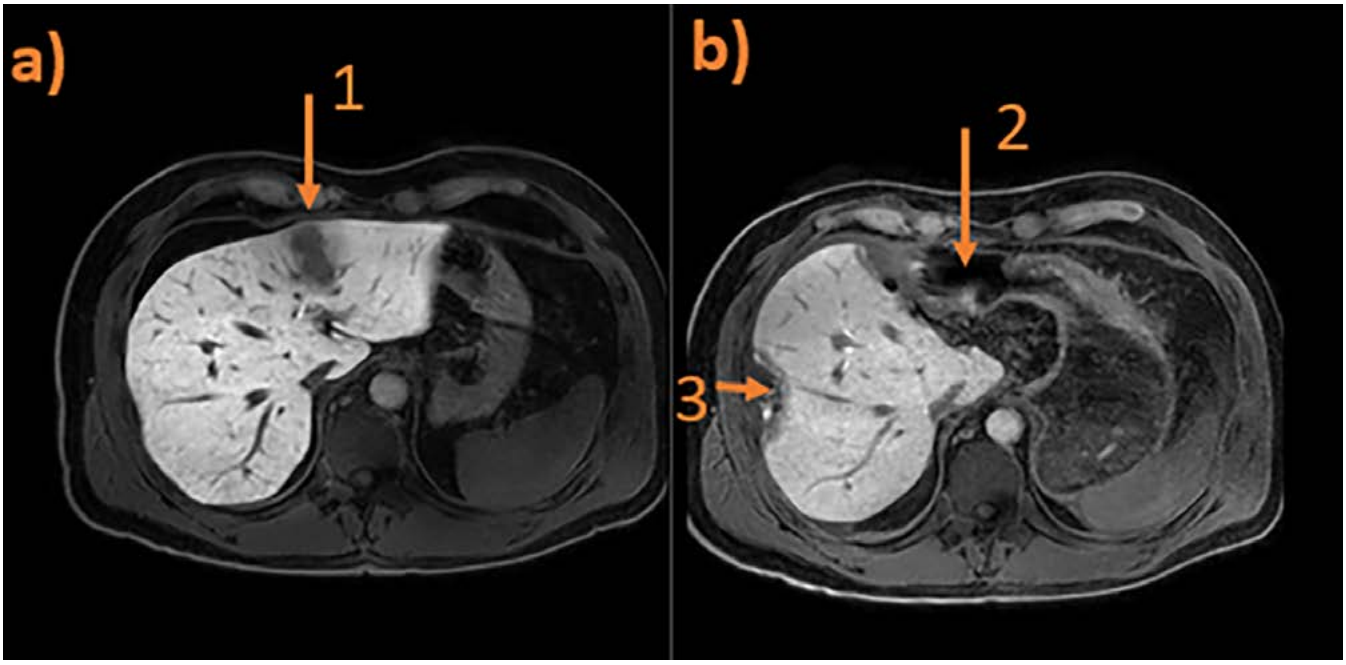
GRANTS
Swedish Research Council (VR/NT) (2021-2024/2025)
VINNOVA (2013-2017)
Swedish Research Council (VR/NT) (2015-2018/2019)
ALF (2019-2022)

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.



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].

POPULAR SCIENTIFIC SUMMARY
Peter Lundberg

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 inflammation, 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 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.

MRI | Gastrointestinal | Acquisition | Modeling | Visualization | Imaging Biomarkers

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 Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

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

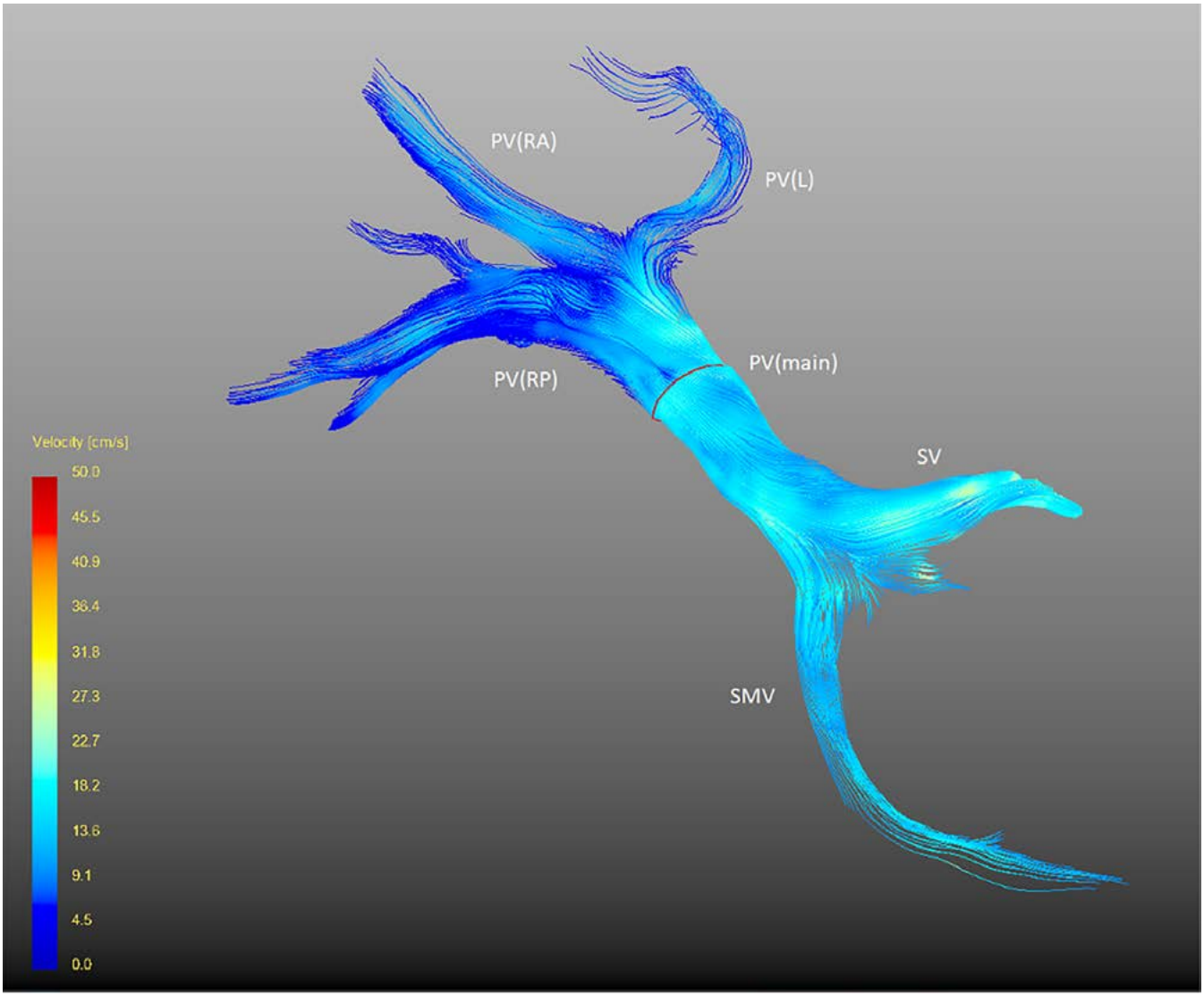
Swedish Research Council (VR/NT) (2021-2024/2025 etc)
ALF (2019-2022)

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).

Nasr P, Ignatova S, Lundberg P, Kechagias S, Ekstedt M (2021) Low Hepatic Manganese Concentrations in Patients with Hepatic Steatosis - A Cohort Study of Copper, Iron and Manganese in Liver Biopsies Journal of Trace Elements in Medicine and Biology Manuscript Number: JTEMB-D-21-00056R1.



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].

POPULAR SCIENTIFIC SUMMARY
Susanna Walter

Neuroplasticity in Irritable Bowel Syndrome

The present project is a longitudinal intervention study to determine the direction of brain-gut interactions in irritable bowel syndrome (IBS). We want to understand if and how brain alterations in IBS are changing together with symptom relief or alternately if brain alterations persist despite change in symptoms. By performing this study, we will also be able to understand whether peripheral alterations in the gut change in relation to symptom relief, and whether this change is, or is not, reflected by central alterations. During the latest years our study group has contributed with several important findings to the IBS brain-gut research by performing cross sectional and case-control studies.

IBS is a chronic pain disorder characterized by abdominal pain and disturbed bowel function often accompanied by extraintestinal symptoms such as anxiety, depression, or chronic fatigue. IBS is a disorder of disturbed bidirectional communication between the brain and the gut, referred to as gut-brain axis alterations. Based on the findings of our latest study evaluating multiple factors along the brain-gut axis in IBS and healthy controls we have designed the present project. Using functional MRI, structural MRI, and MR spectroscopy, we were able to identify altered brain function and structure in IBS patients. Alterations in brain function and structure were also related to both to symptoms and to colonic mucosal barrier integrity and we have been able to find a relationship between microbiota, symptoms, and brain function in the IBS patients and altered neurotransmitter concentration in insula and medial prefrontal cortex, two regions important for symptom generation in IBS. Altogether our recent findings, in agreement with those of other research groups, strongly suggest the occurrence of neuroplastic brain alterations in IBS. Now the next step is to understand whether and how the brain alterations found in IBS are affected by a change in symptoms or whether these alterations are persisting despite changes in symptoms. For this we perform this longitudinal multimodal treatment study with the aim to assess brain structure and function in relation to change in symptoms.

MRI | Gastrointestinal | Imaging Biomarkers

Project information

PROJECT NAME

Neuroplasticity in Irritable Bowel Syndrome. A longitudinal follow-up study of gut-brain axis alterations (MAGONT)

PROJECT LEADER

Susanna Walter, Department of Health, Medicine and Caring Sciences. Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS

Åsa Keita, Paul Hamilton, Maria Engström, Peter Lundberg, Nawroz Barazanji, Julia Gustavsson, Mike Jones

GRANTS

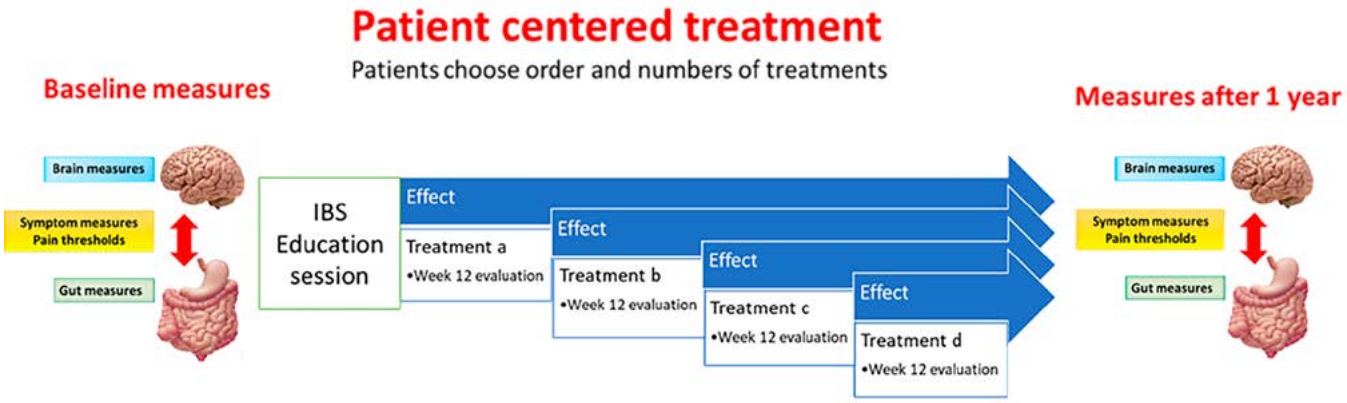
ALF (until 2024)

KEY PUBLICATIONS

Irritable bowel syndrome in women: Association between decreased insular subregion volumes and gastrointestinal symptoms. Barazanji N, Paul Hamilton J, Icenhour A, Simon RA, Bednarska O, Tapper S, Tisell A, Lundberg P, Engström M, Walter S. Neuroimage Clin. 2022;35:103128. doi: 10.1016/j.nicl.2022.103128. Epub 2022 Jul 28. PMID: 36002966.

Vasoactive intestinal polypeptide plasma levels associated with affective symptoms and brain structure and function in healthy females. Simon RA, Barazanji N, Jones MP, Bednarska O, Icenhour A, Engström M, Hamilton JP, Keita ÅV, Walter S. Sci Rep. 2021 Jan 14;11(1):1406. doi: 10.1038/s41598-020-80873-2. PMID: 33446759.

Interactions between gut permeability and brain structure and function in health and irritable bowel syndrome. Witt ST, Bednarska O, Keita ÅV, Icenhour A, Jones MP, Elsenbruch S, Söderholm JD, Engström M, Mayer EA, Walter S. Neuroimage Clin. 2019;21:101602. doi: 10.1016/j.nicl.2018.11.012. Epub 2018 Nov 17. PMID: 30472166.



Gut-brain measures before and after a longitudinal treatment study.

POPULAR SCIENTIFIC SUMMARY
Peter Lundberg

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

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

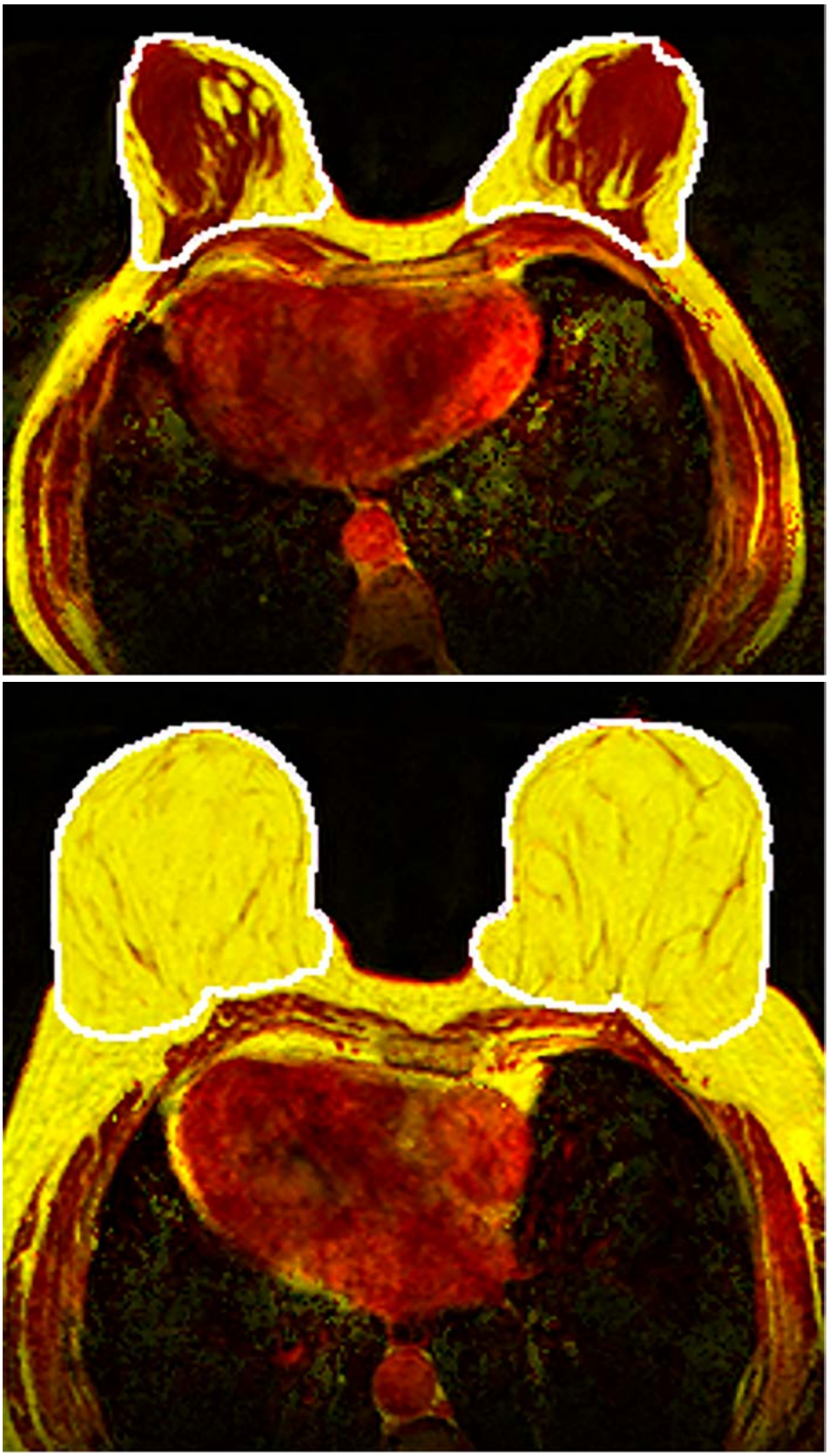
GRANTS

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.

Lundberg P, Forsgren M, Tellman J, Kihlberg J, Rzepecka A, Dabrosin C (2022) Breast density is strongly associated with multiparametric magnetic resonance imaging biomarkers and pro-tumorigenic proteins in situ, Br J Cancer. 2022 Sep 22. doi: 10.1038/s41416-022-01976-3.



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.

POPULAR SCIENTIFIC SUMMARY
Håkan Gustafsson

Artificial Intelligence in Breast Cancer Screening

The purpose of this research project is to assess whether the use of artificial intelligence (AI) can lead to improved diagnostic quality and at the same time safely reduce the workload for the radiologists in the double reading mammography screening program in Östergötland, Sweden. The introduction of AI in the breast cancer screening program in Östergötland will be investigated over several years in several phases where AI gradually takes more space in the decision-making process.

The overall aim is to increase the cancer detection rate without affecting the recall rate and (by, for example, reduce the number of interval cancers) and at the same time substantially reduce the radiologist´s workload by reducing the need for double reading for those cases with low probability of cancers.

In the first phase (data inclusion completed early 2022, analysis ongoing) an AI decision support system (Transpara version 1.7, Screenpoint Medical) was implemented in the breast cancer screening program. Between September 2021 and February 2022, 15 468 women were included in the study from the biannual breast cancer screening program in Östergötland, Sweden. The screening exams were double read independently by two breast radiologists according to normal clinical practice, but also assessed by the AI system acting as an independent third reader. The AI system assigned each examination a score on the scale of 1–10 with increasing likelihood of cancer for higher scores.

In a retrospective simulation, the AI system was implemented as a triaging tool where examinations with a low risk (score < 7) were selected for single reading, while exams with an elevated risk (score r 7) were selected for double-reading according to the standard clinical protocol.

This triaging strategy would lead to a 33.8 % workload reduction and 52 out of 53 screen-detected cancers were picked up by the AI system and received an AI score> 7. This shows the potential that replacing one reader in a breast cancer screening workflow with an AI system for the low risk cases could safely reduce the workload by 33.8 % with no cancers being missed. This study is the first phase of the prospective clinical trial ongoing in Östergötland.

In the coming phases of the research project, AI will take an increased scope in the decision-making process. Next step will be to, parallel to continued analysis of the ongoing analysis of the prospective study in phase 1, replace one of the radiologists with AI in the double reading for those examinations having a low transpara score (see figure).

Phase 2 of the research project is planned to start during 2023.

Other | Oncology | AI/Data analytics

Project information

PROJECT NAME

Artificial Intelligence in Breast Cancer Screening in Region Östergötland (AIM-RÖ)

PROJECT LEADER

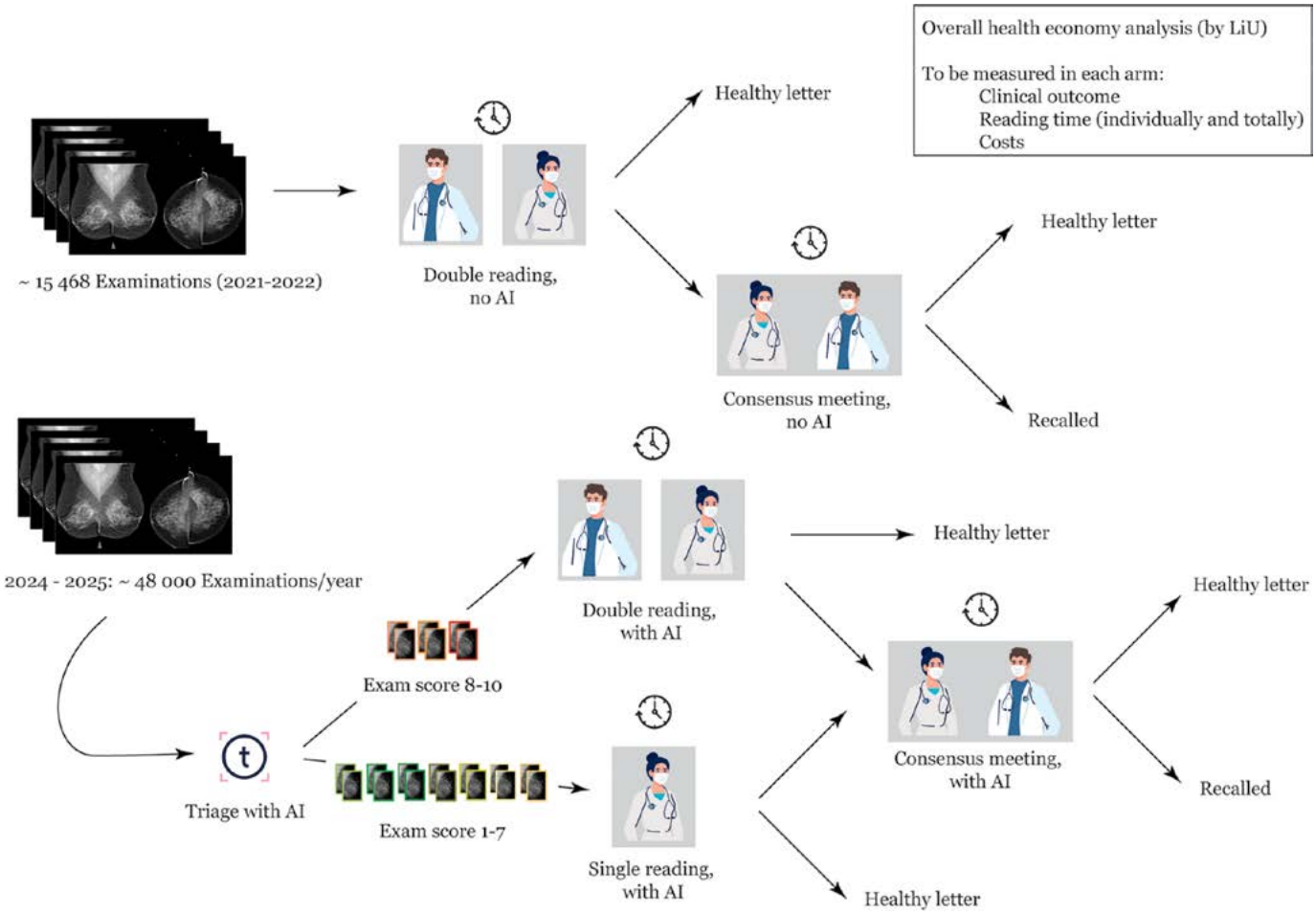
Håkan Gustafsson, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS

Pantelis Gialias, Maria Kristoffersen Wiberg

GRANTS

AIDA clinical evaluation (2021)



Phase 2 of the study: AI in the arbitration process and partial single reading.

POPULAR SCIENTIFIC SUMMARY
Erik Tesselaar

Advanced CT of the Hand and Wrist

The hand and wrist are complex anatomical structures. Their function depends on the integrity of bones, joints and ligaments. Imaging modalities are routinely used for diagnosing fractures, joint malalignment, degenerative and inflammatory changes as well as for the assessment of healing and the position of protheses. Because of the complex anatomy and wide spectrum of diagnostic challenges, computed tomography (CT) plays an important role, providing multiplanar reconstructions and better diagnostic accuracy (Müller et al., 2020; Welling et al., 2008).

Conventional CT, also known as energy-integrating detector CT (EID-CT) has limited spatial resolution, which can make it difficult to correctly diagnose pathologies such as subtle fractures, small joint incongruencies or changes in osteoporotic bone. Despite substantial technical improvements in image reconstruction over the last decade, the use of the EID-CT in diagnosis and follow-up of hand and wrist pathology remains limited because of the limited spatial resolution, the relatively high radiation dose compared to plain radiography and the severity of artifacts in the presence of metallic implants.

The recent introduction of photon-counting detector CT (PCD-CT) has made it possible to visualize structures in the wrist with higher spatial resolution while, at the same time, image noise is reduced due to the inherent properties of photon-counting detectors. Also, with PCD-CT, metal artifacts can be reduced by using virtual monochromatic images (VMI) combined with high kVp imaging, tin filtration, and metal artifact reduction (MAR) (Figure 3).

In our studies, we have so far observed that the availability of spectral information combined with high spatial resolution and low noise is very valuable in visualizing bone structures and reducing metal artifacts. In the near future, we will investigate whether PCD-CT is able to better visualize intra- and peri-articular soft tissue lesions and to evaluate the accuracy of extracted information of bone quality from the PCD-CT data.

Computed Tomography | Musculoskeletal | Acquisition

Project information

PROJECT NAME
IMPACT

PROJECT LEADER
Erik Tesselaar, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS
Nina Kämmerling, Mårten Sandstedt, Ronald Booij, Simon Farnebo, Anders Persson

GRANTS
ALF (Student till Docent)
RFOU

KEY PUBLICATIONS
Kämmerling N, Sandstedt M, Farnebo S, Persson A, Tesselaar E. Assessment of image quality in photon-counting detector computed tomography of the wrist - An ex vivo study. Eur J Radiol. 2022 Sep;154:110442. doi: 10.1016/j.ejrad.2022.110442. Epub 2022 Jul 13. PMID: 35849959.

Booij R, Sandstedt M, Tesselaar E and Farnebo S. Photon counting detector computed tomography (PCD-CT) - an emerging technology in hand and wrist imaging. Journal of Hand Surgery (European Volume) (JHS), in press.

Booij R, Kämmerling N, Oei E, Person A, Tesselaar E. Assessment of visibility of bone structures in the wrist using normal and half of the radiation dose with photon-counting detector CT. Manuscript.

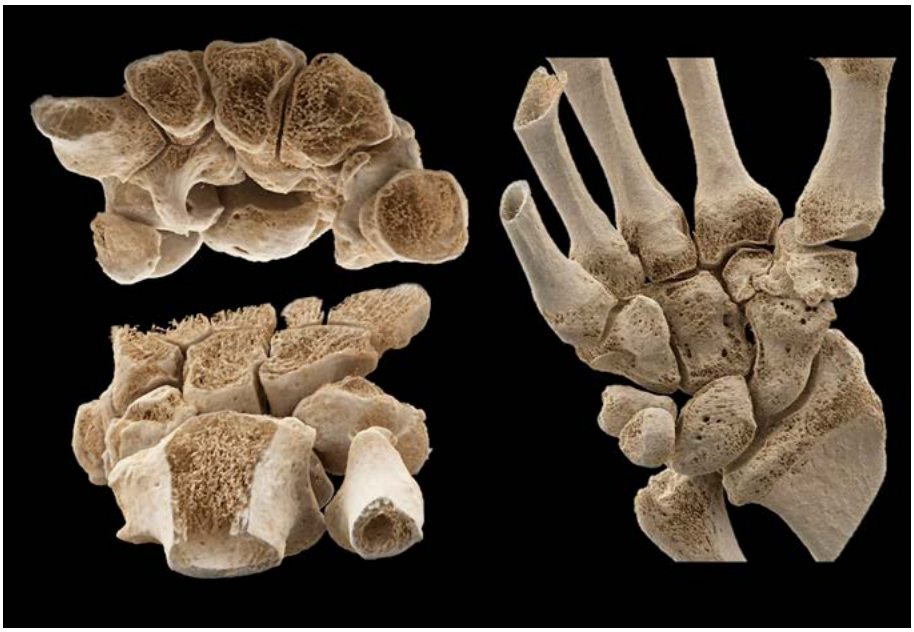


Figure 1. Three-dimensional visualization of the carpal bones using cinematic rendering. Input images were reconstructed with 0.2 mm slice thickness, combined with a sharp reconstruction kernel (Br92) and a large image matrix (1024 x 1024).

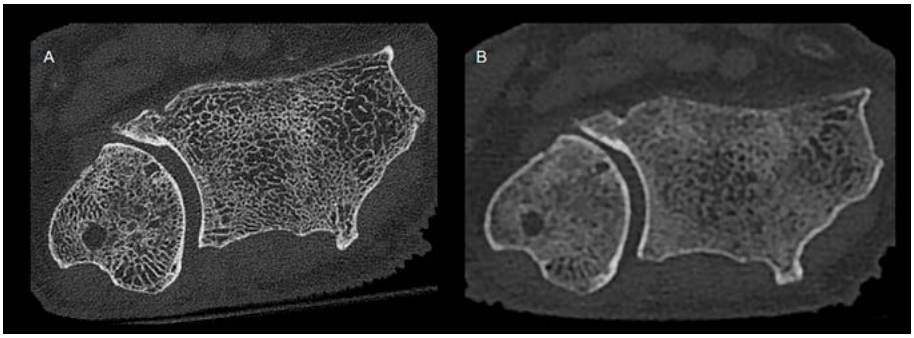


Figure 2. Axial images of the DRUJ obtained from a (a) clinically used photon-counting detector CT protocol with a spatial resolution of 0.2 mm with half of the dose compared with the EID-CT image in a state-of-the art EID-CT protocol (b), with a maximum spatial resolution of 0.3–0.4 mm acquired at a clinically used CTDIvol of 12 mGy.
DRUJ: distal radio-ulnar joint; CT: computer tomography; EID: energy-integrating detector.

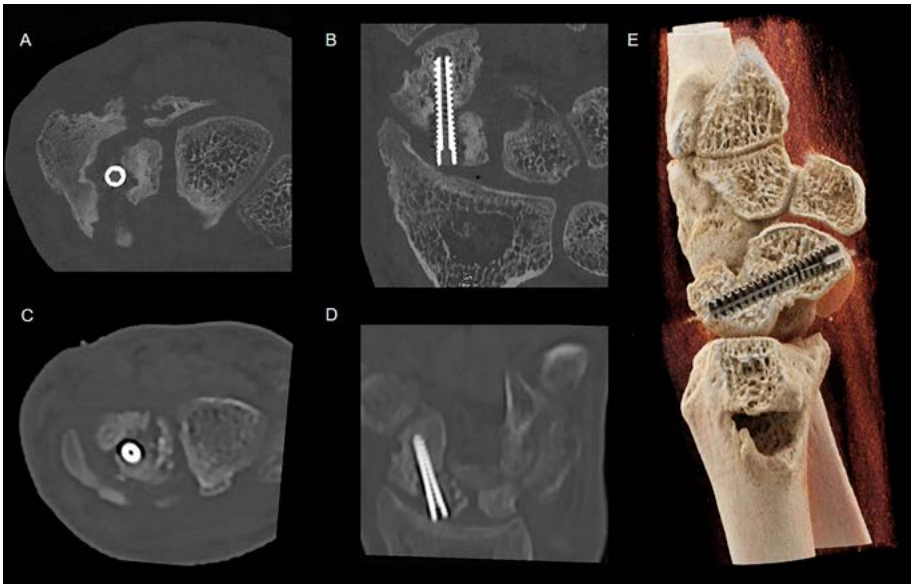


Figure 3. Scaphoid fracture with screw of a 20-year-old male. Scan was acquired with a dedicated spectral shaping (tin filtration) protocol with ultra-high-resolution kernel (Br89). (a,b) Greyscale images in the axial (a) and coronal (b) plane of the PCD-CT; (c,d) greyscale images in the axial (c) and coronal (d) plane of a state-of-the-art EID-CT 2 weeks before the PCD-CT and (e) cinematic rendering of the screw in the scaphoid obtained using PCD-CT.
PCD-CT: photon counting detector computer tomography.

POPULAR SCIENTIFIC SUMMARY
Hanna Björnsson Hallgren

Accurate Trial on Acute Rotator Cuff Tears

Rotator cuff tear is a very common and disabling condition that can be related to acute trauma such as falling on the shoulder. A tear is associated with symptoms such as pain in abduction, abduction weakness and night pain. The incidence of such rotator cuff tears is reported to be between 23–32% and the number of surgeries performed to treat these tears is increasing.

According to a mechanical rationale an operative approach is advocated to treat rotator cuff tears. In such operation the torn tendon is re-attached to it's bony insertion and an additional acromioplasty may be performed to acquire room for the repair and to improve healing. Most of these operations are performed arthroscopically. After the operation patients are referred to physiotherapy after a short period of immobilization. There is conflicting evidence on the benefit of surgery in the treatment of rotator cuff tears. In case of truly degenerative tears, it may be that a primary non-operative approach should be preferred. However, this may not be the case with traumatic tears with acute symptoms. Furthermore, it is arguable whether truly traumatic tears exist, and whether it is in fact a degenerative process, which ultimately causes the tendon tear.

In order to find out the true efficacy of surgical treatment of acute, trauma related rotator cuff tears involving mainly the supraspinatus tendon, we have designed this randomized placebo-controlled efficacy trial set out to investigate the difference in efficacy of rotator cuff repair in the treatment of symptomatic supraspinatus tears after trauma. We are currently recruiting patients for the trial and will randomize 180 patients in one of the two treatment arms (placebo surgery or arthroscopic repair). Up to now we have randomized over 90 patients. The primary outcome measure is function and pain.

MRI | Ultrasound | Musculoskeletal | No Method Development

Project information

PROJECT NAME

Accurate Trial on Acute Rotator Cuff Tears

PROJECT LEADER

Hanna Björnsson Hallgren, Orthopeadic department University Hospital Linköping

MAIN PROJECT PARTICIPANTS

Johan Scheer, Theresa Holmgren, Per Widholm, Ville Äärimaa, Stefan Moosmayer

KEY PUBLICATIONS

Acute Cuff Tear Repair Trial (ACCURATE): protocol for a multicentre, randomised, placebo-controlled trial on the efficacy of arthroscopic rotator cuff repair.
Ryösä A, Kukkonen J, Björnsson Hallgren HC, Moosmayer S, Holmgren T, Ranebo M, Bøe B, Äärimaa V; ACCURATE study group. BMJ Open. 2019 May 19;9(5).

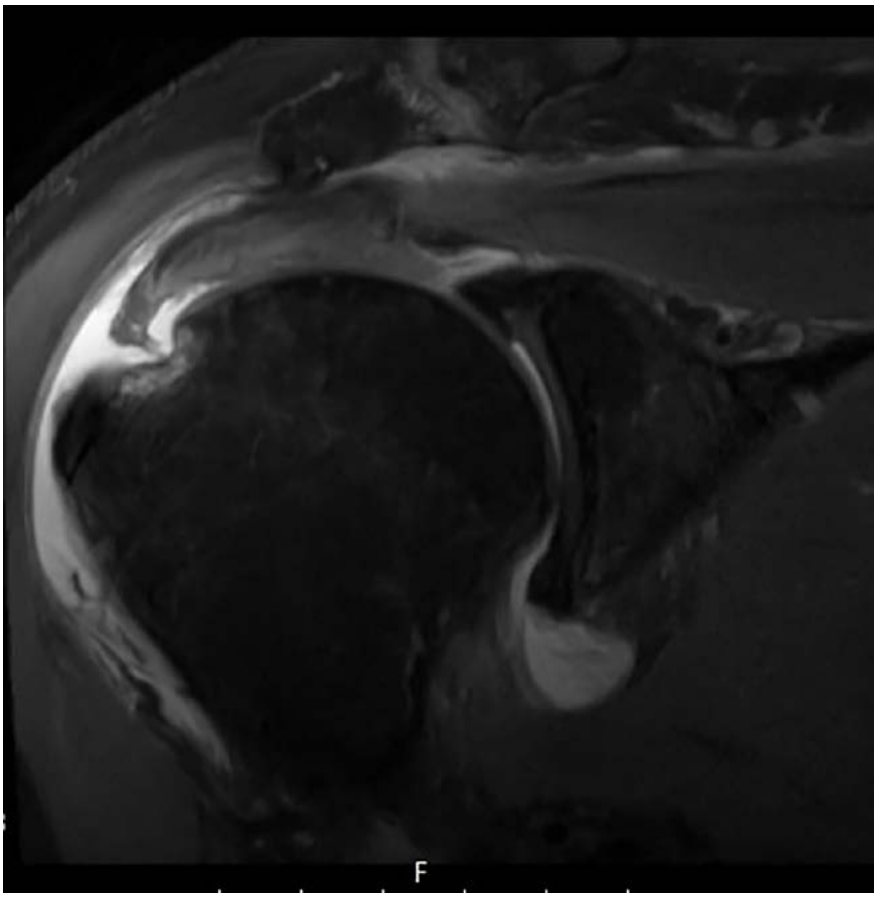


Image 1. This MRI image taken at the CMIV lab with a specific MRI protocol illustrates a frontal view of the shoulder and a typical complete supraspiantus tear and surroundig effusion.

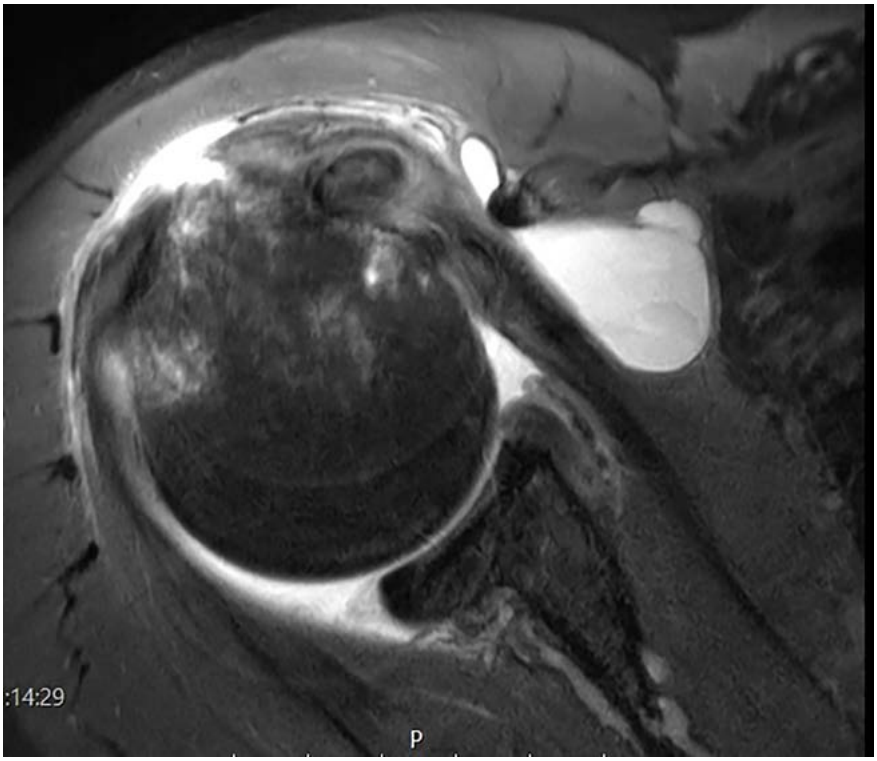


Image 2. This image presents the same shoulder and the same injury in a transverse view.

POPULAR SCIENTIFIC SUMMARY
Jörg Schilcher

PHARAOH

In Sweden roughly 17,000 hip replacements are performed each year. The initial fixation of the prosthesis through a process called osseointegration is very important for the long-term outcome of the joint replacement. If the implant is not properly integrated into the bone, there is a high risk of implant loosening.

Pain and discomfort are indicators of a joint replacement implant coming loose. Until now, neither clinical, radiological or any other tools have been available to reliably assess if the implants still is connected properly to the underlying bone (osseointegration) or if the experienced pain might be related to other sources of pain. Plain radiographs are the gold standard to detect if an implant has become lose and to differentiate implant loosening from other sources of pain. This technique is good as a screening tool for severe loosening, but is poor to differentiate early loosening. Some newer techniques such as computed tomography performed in different positions, MRI or positron emission tomography appear promising tools to assess loosening, but have not been tested in large clinical studies.

New methods, to directly assess osseointegration instead of loosening would help clinicians to detect whether symptoms such as pain are caused by loosening of the implant or by something else at a much earlier stage. Improved diagnostics in these situations can prevent unnecessary surgeries and thereby unnecessary suffering for patients.

Photon-counting detector computed tomography (PCD-CT) provides major improvements in image resolution compared to conventional energy-integrating detector CT (EID-CT), possibly allowing better visualization of osseointegration. This is mainly because PCD-CT offers a higher resolution due to its new detector design. Also, PCD-CT may be better at handling heavy materials such as stainless steel that is often present in implants, causing artifacts on CT images that hamper adequate assessment.

In our project, we have investigated the quality of images acquired using PCD- CT of extracted acetabular cups, i.e. hip implants that have been taken out of the patient during revision surgery and that contain a certain amount of bone remnant from the patient on the implant. The aim was to let radiologists evaluate how well the connection between the metal implant and the bone can be visualized using different scanning parameters. The idea is that an intact connection between bone and implant rules out that symptoms might be related to a loosened implant. Also, we aimed to compare whether the image quality is improved compared with the conventional CT. In addition to the radiologists' opinion, we have measured certain features such as noise and sharpness in the images in order to evaluate the performance of PCD-CT.

In extracted acetabular cups, we found a significant improvement in image quality when using PCD-CT compared to EID-CT in the visualization of bone-implant interface and the bone architecture of newly formed bone.

The current study is limited to extracted material from two patients, making it difficult to estimate the effect of surrounding soft tissues on image quality and to extrapolate these findings to a broader cohort of patients. Therefore, we will continue this project by studying patients with suspected implant loosening. In these patients we will further investigate the clinical value of PCD-CT in the assessment of osseointegration.

Computed Tomography | Musculoskeletal | Acquisition | Visualization

Project information

PROJECT NAME

Photoncounting CT for Radiographic Assessment of Osseointegration in Humans

PROJECT LEADER

Jörg Schilcher, Department of Orthopedics, Department of Clinical and Experimental Medicine, Division of Surgery, Orthopedics and Oncology

MAIN PROJECT PARTICIPANTS

Mischa Woisetschläger, Erik Tesselaar, Ronald Booij, Edwin Oei

KEY PUBLICATIONS

Woisetschläger M, Booij R, Tesselaar E, Oei E, Schilcher J. Improved visualization of osseointegration in acetabular cup implants using photon-counting detector computed tomography. Manuscript.

Figure 1. Retrieved acetabular cup implant (left) with newly formed bone integrated with the porous surface of the implant (middle, with courtesy of Thor Balkhed, Linköping University) and the clinical CT image of the cup acquired using conventional CT before revision surgery (right). Due to the limited spatial resolution, the visibility of the interface between the bone and the implant is not good enough to evaluate whether there is adequate osseointegration.

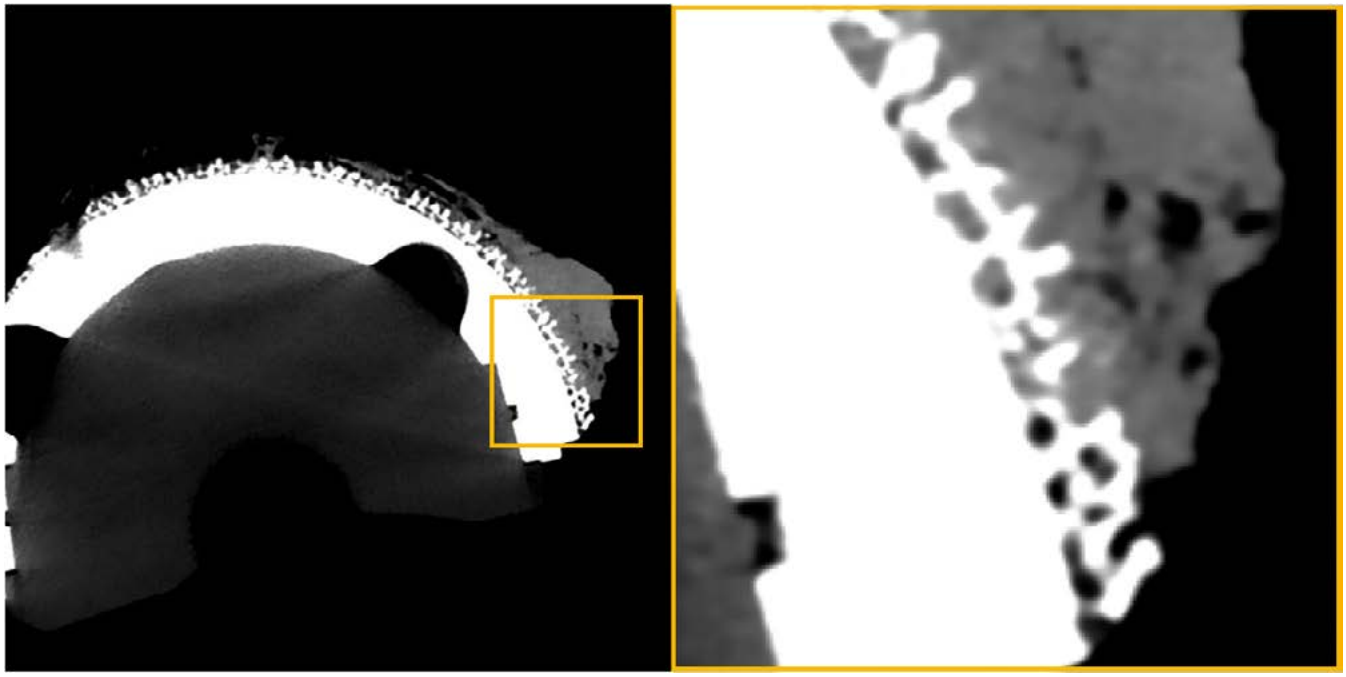


Figure 2. Visualization of the implant-bone interface with PCD-CT. The ingrowth of bone tissue into the porous structure on the implant surface can clearly be seen.

POPULAR SCIENTIFIC SUMMARY
Eva Klintström

Bone Analysis for Reducing Osteoporotic Fractures

People suffering from osteoporosis have increased risk for fractures. When studying osteoporosis, the amount of mineral 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 mineral content. The internal bone microstructure consists of a network of thin bone structures called trabeculae. This can be measured by different parameters like thickness, number and the distances between them. Measurements of the compact bone structure, with porosities, is of high importance. Earlier, the 3D microstructure of humans could be studied only by microscopy and by micro-computed tomography (micro-CT) of specimens removed from the body.

This project aims to study the 3D structure of bone structure in living humans, by using clinical methods available in a radiological department, in particular CT devices. Since the bone trabeculae often are less than 0.1 mm thick, the limited resolution of CT may be a problem. We have therefor focused on examinations from CT devices at high resolution. The main goal is to develop automatic 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, with many papers from our group published in different journals. Another CT device with high resolution is photon-counting detector (PCD) CT. This is a very novel technique available only in a few radiology departments around the world. One of the devices is installed at CMIV. This technique is very promising since it allows high resolution also of central body parts like the hip and vertebrae where osteoporotic fractures are common. All other devices, so far, are able to image bone microstructure only in the peripheral skeleton like wrist and lower leg. A paper from our research group is recently publish in the journal of European Radiology Experimental where PCDCT showed strong correlations to micro-CT regarding trabecular bone microstructure.

A clinical study in cooperation with Department of Endocrinology at Linköping University is ongoing. CBCT data of forearm and mandible is compared to dual energy X-ray absorptiometry (DXA) data on patients examined regarding osteoporosis. On the segmented CT-data sets, we analyse bone cortical and trabecular structure and bone mineral content. Bone strength by finite element modelling (FEM), is also analysed. Our segmented data, presented in previous studies, correlates well with results from FEM analyses. In the future, we hope that our automatic segmentation method will be useful in early detection of osteoporosis. With better tools to measure the structure of the 3D bone structure, 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 | Visualization

Project information

PROJECT NAME

Bone microstructure, strength and composition derived from imaging data of 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

Benjamin Klintström, Mischa Woisetschläger, Örjan Smedby, Rodrigo Moreno, Anna Spångéus, Alexander Malusek, Ronald Booij

GRANTS

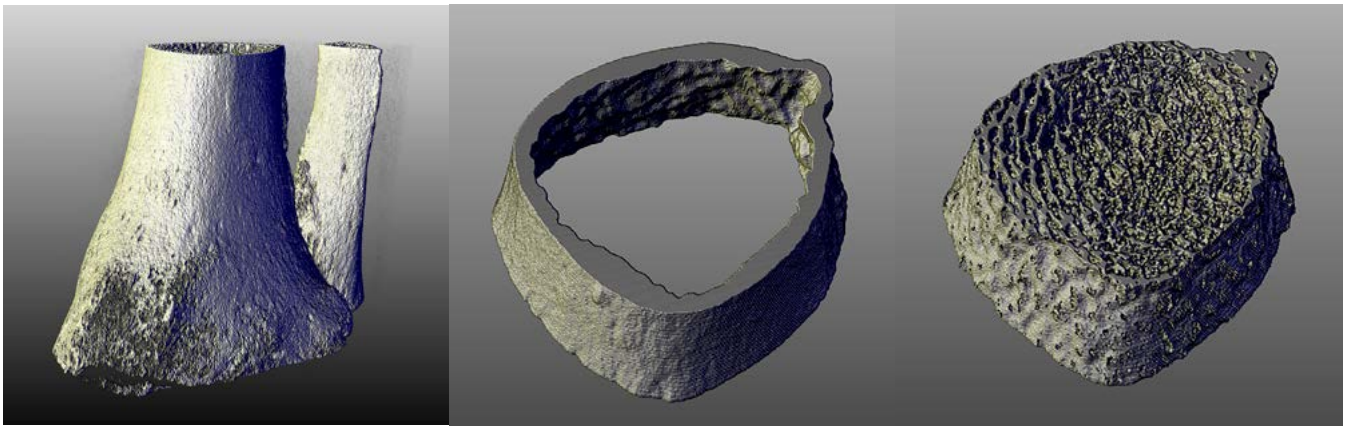
ALF Grants, Region Östergötland

KEY PUBLICATIONS

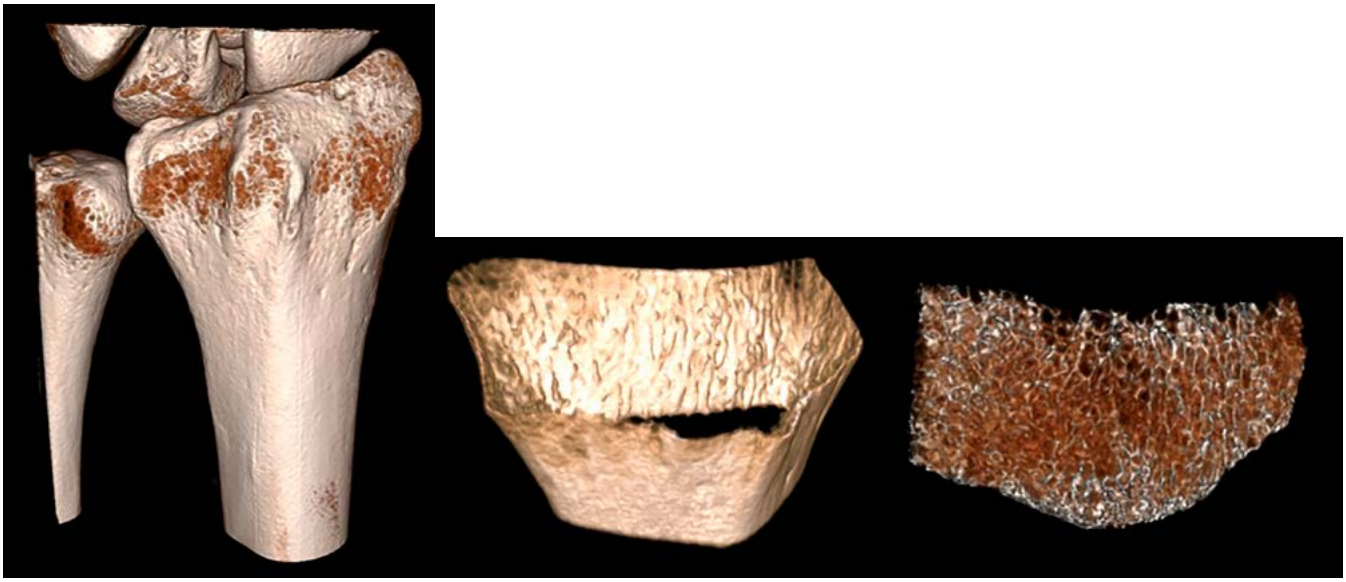
Klintström, B., Henriksson, L., Moreno, R., Malusek A., Smedby Ö., Woisetschläger M., Klintström E. Photon-counting detector CT and energy-integrating detector CT for trabecular bone microstructure analysis of cubic specimens from human radius. Eur Radiol Exp 6, 31 (2022). https://doi.org/10.1186/s41747-022-00286-w.

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. https://doi.org/10.1016/j.oooo.2018.03.014.

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. DOI: 10.1007/s00256-013-1766-5.



Upper row visualizes part of a lower leg (tibia), 3D from a PCDCT image data set From left to right: Whole volume, Segmented cortical volume, Segmented trabecular volume Courtesy of Ronald Booij, Erasmus MC/CMIV, and Benjamin Klintström KTH.



Upper row visualizes part of the wrist (radius), 3D from a CBCT raw image data set From left to right: Whole volume, Cortical volume, Trabecular volume.

POPULAR SCIENTIFIC SUMMARY
Mats Hammar

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

Anna-Clara Spetz Holm, Hanna Lindblom, Lotta Lindh-Åstrand, Magnus Borga, Janne West, Emilia Berin, Sofia Thorell, Sigrid Nilsson, Moa Henriksson

GRANTS

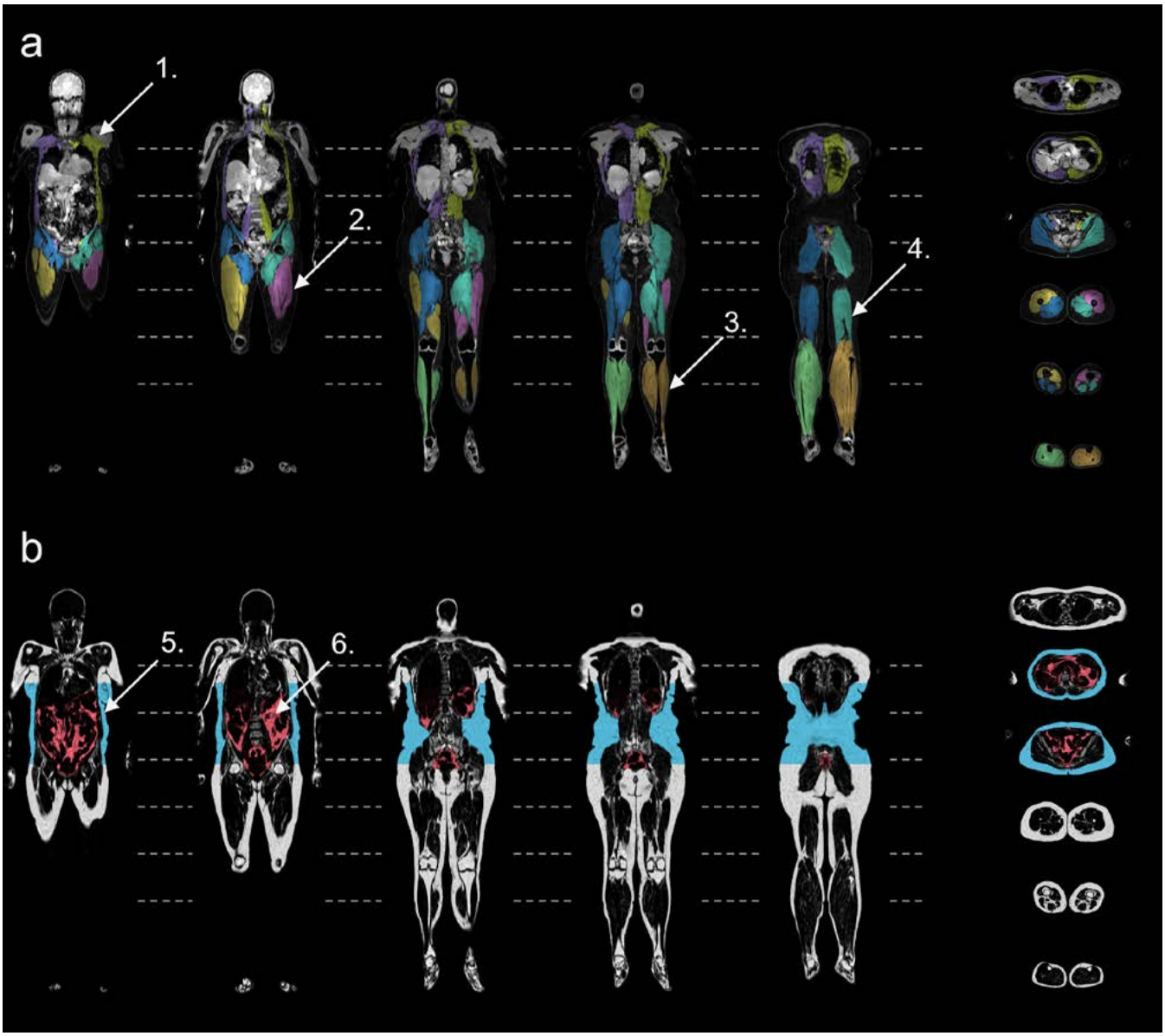
Vetenskapsrådet

KEY PUBLICATIONS

Berin E, Spetz Holm AC, Hammar M, Lindh-Åstrand L, Berterö C. Postmenopausal women's experiences of a resistance training intervention against vasomotor symptoms: a qualitative study. BMC Womens Health. 2022 Jul 30;22(1):320. doi: 10.1186/s12905-022-01900-0. PMID: 35907840; PMCID: PMC9338607.

Nilsson S, Henriksson M, Berin E, Engblom D, Holm AS, Hammar M. Resistance training reduced luteinising hormone levels in postmenopausal women in a substudy of a randomised controlled clinical trial: A clue to how resistance training reduced vasomotor symptoms. PLoS One. 2022 May 26;17(5):e0267613. doi: 10.1371/journal.pone.0267613. PMID: 35617333; PMCID: PMC9135255.

Berin E, Hammar M, Lindblom H, Lindh-Åstrand L, Spetz Holm AC. Effects of resistance training on quality of life in postmenopausal women with vasomotor symptoms. Climacteric. 2022 Jun;25(3):264-270. doi: 10.1080/13697137.2021.1941849. Epub 2021 Jul 9. PMID: 34240669.



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).

POPULAR SCIENTIFIC SUMMARY
Joanna Kvist

The NACOX-study

Anterior cruciate ligament (ACL) injury in the knee joint can result in joint instability, decreased functional performance, reduced physical activity and quality of life. The most important long-term consequence is the increased risk for posttraumatic osteoarthritis (PTOA). The underlying mechanisms behind PTOA are not well understood but altered biological processes due to injury and joint bleeding as well as concomitant structural injuries to the cartilage and the subchondral bone have been suggested to be of relevance. Despite the development of new treatment techniques and extensive research, the complex and multifaceted nature of ACL injury and its consequences are yet to be fully understood.

The overall aim of the NACOX study is to evaluate the natural corollaries and recovery after an ACL injury. There are five main study objectives:

A. To assess biological, psychological and social factors and their relationships to the natural corollaries and recovery after acute ACL injury
B. To evaluate the choice of treatment after acute ACL injury (i.e., ACL reconstruction, ACLR or non-ACL reconstruction, non-ACLR)
C. To evaluate return to sport after acute ACL injury
D. To study knee problems in the short and long term after acute ACL injury
E. To identify proxies (biomarkers and structural risk factors) for early detection of symptomatic and radiographic osteoarthritis

The NACOX study is a multi-centre prospective cohort study of patients with acute ACL injury. At seven sites in Sweden, we have included 275 patients aged 15–40 years, within 6 weeks after primary ACL injury. Patients complete questionnaires at multiple occasions over the 3 years following injury or the 3 years following ACL reconstruction (for participants who have surgical treatment). In addition, a subgroup of 131 patients is followed with extensive imaging modalities, biological samples and clinical examinations.

The study is ongoing, and we are now collecting the 5-years follow-up data. We have 13 publications and several analyses with specific interest on imaging have been done and are planed. Example:

- Diagnostic accuracy of dual energy CT (DECT) for detection of bone marrow lesions in the injured knee using MRI as reference method. Bone marrow lesions can be a telltale sign of a more severe injury in the bone and is usually demonstrated with MRI, but our results show that DECT also can detect these lesions.

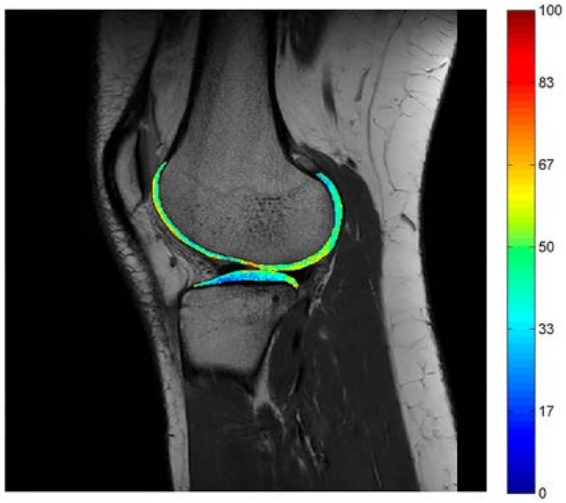


Image 1. Gray scale of a manually segmented cartilage where the cartilage is seen as white color.

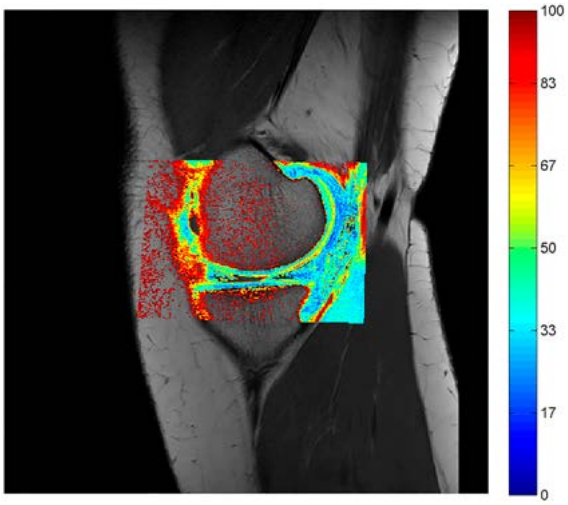


Image 2. Color map of manually segmented knee joint, step before conversion to cartilage image.

- Quantitative MRT analysis of cartilage matrix organization, as measured by T2 relaxation time, of the tibiofemoral joint cartilage after acute anterior cruciate ligament injury, in both the injured and contralateral non-injured knee. Results showed small but statistically significant differences in the subacute phase between ACL-injured and uninjured knee in cartilage T2 relaxation time and cartilage thickness. Future longitudinal observations of the same cohort will allow for better understanding of early development of PTOA.
- Planned review and analyses of the healing potential of the ACL fibers in the non-reconstructed knee, as well as for the concomitant meniscus injuries.

Background: DX T2map

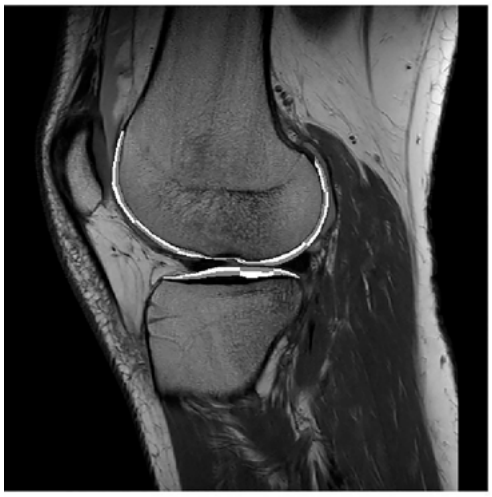


Image 3. Color map of manually segmented cartilage where different colors represent different levels of collagen vs water content in the cartilage.

Computed Tomography | MRI | Musculoskeletal | Acquisition | Visualization | Imaging Biomarkers

Project information

PROJECT NAME

NACOX -Natural corollaries and recovery after acute anterior cruciate ligament injury

PROJECT LEADER

Joanna Kvist, Department of Health, Medicine and Caring Science, Division of Prevention, Rehabilitation and Community Medicine

MAIN PROJECT PARTICIPANTS

Håkan Gauffin, Hanna Tigerstrand Grevnerts, Bashir Tajik Edwardsson, Anders Persson, Ann-Sofi Björkman, Kati Laukkanen, Martin Englund, Richard Frobell, Miika Nieminen, Victor Casula, Seppo Koskinen, Rolf Scheiderbauer

GRANTS

Swedish Medical Research Council (2015-2020)
Swedish Research Council for Sport Science (2017-2021)
Medical Research Council of Southeast Sweden (2020)
ALF Grants Region Östergötland (2018-2020)

KEY PUBLICATIONS

Kvist, J Gauffin H, Tigerstrand Grevnerts H, Ardern C, Hägglund M, Stålman A, Frobell R. NACOX Cohort Study group. Natural corollaries and recovery after acute ACL injury - the NACOX cohort study protocol. BMJ Open 2018 Jun 27;8(6):e020543. doi: 10.1136/bmjopen-2017-020543.

Casula, V., Tajik, B. E., Kvist, J., Frobell, R., Haapea, M., Nieminen, M. T., Gauffin, H., Englund, M. (2022). Quantitative evaluation of the tibiofemoral joint cartilage by T2 mapping in patients with acute anterior cruciate ligament injury vs contralateral knees: results from the subacute phase using data from the NACOX study cohort. Osteoarthritis and Cartilage. doi: https://doi.org/10.1016/j.joca.2022.02.623.

Cristiani R, van de Bunt F, Kvist J, Stålman A. High prevalence of meniscal ramp lesions in anterior cruciate ligament injuries. Knee Surg Sports Traumatol Arthrosc. 2022 Aug 31. doi: 10.1007/s00167-022-07135-8. Epub ahead of print. PMID: 36045182.

All images are T2-weighted, sagittal MR images of the knee joint.
They are processed with a software called Mokkula and are developed in Finland.

NACOX KNÄSTUDIE

POPULAR SCIENTIFIC SUMMARY
Carl Johan Östgren

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 5,058 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 contrast-enhanced computed tomography coronary angiography (CCTA); CT scanning of the abdomen for the quantification of visceral and subcutaneous adipose tissue, liver fat; and ultrasound analysis for carotid artery atherosclerosis.

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. Furthermore, in addition to the core SCAPIS data collection, participants underwent a comprehensive magnetic resonance imaging examination at 1.5 T for assessment of left ventricular (LV) structure and function (end-diastolic volume, mass, concentricity, ejection fraction), as well as regional body composition.

In a recent publication we showed that ectopic fat is predominantly associated with cardiac remodeling, independently of type 2 diabetes. Visceral fat is associated with T2D independently of liver fat and abdominal subcutaneous adipose tissue.

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 fasting blood samples for both immediate analysis and stored in a biobank 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, Mårten Sandstedt, Elin Good, Fredrik Nyström, Tomas Faresjö, Tomas Lindahl, Tomas Strömberg, Anna Moberg

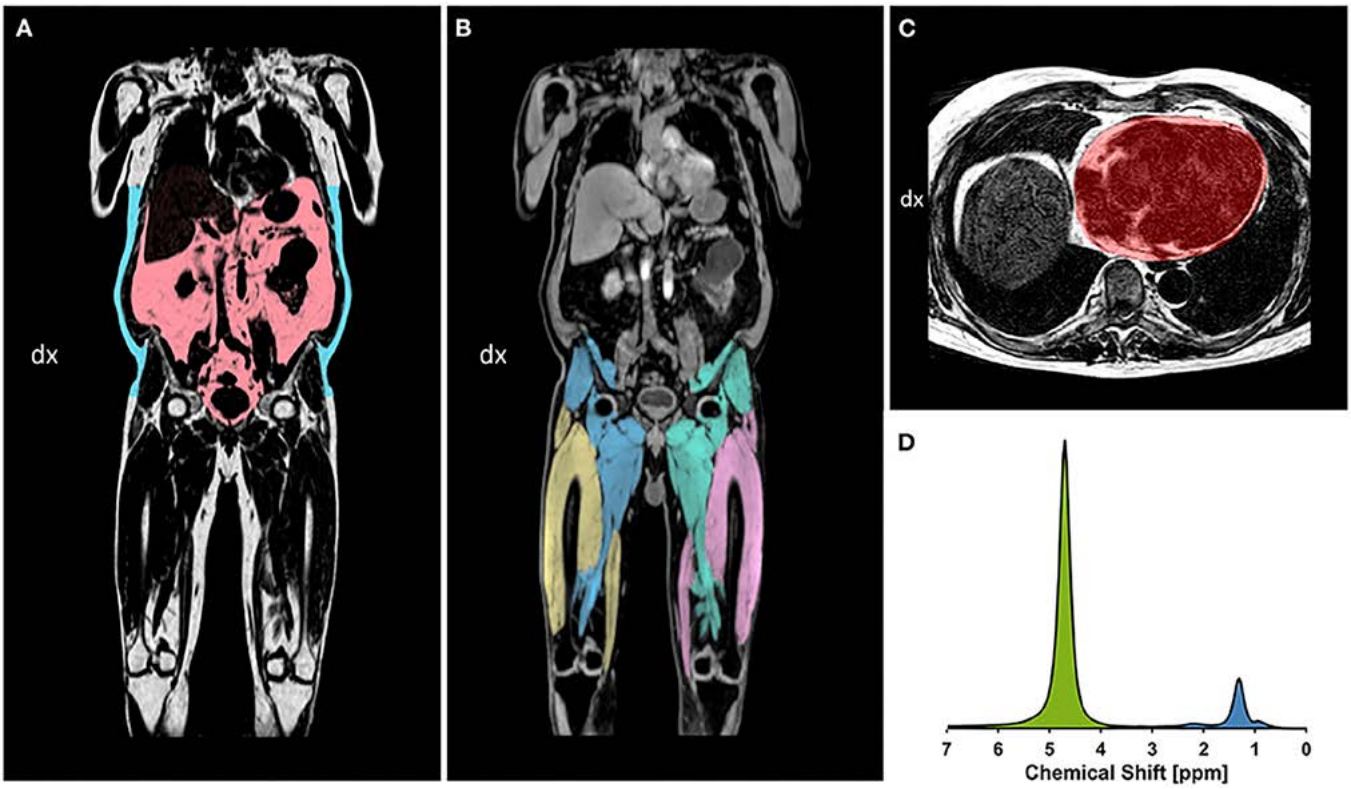
GRANTS
Vetenskapsrådet (2021-2025)
Hjärt-Lungfonden (2022-2024)
ALF-medel Region Östergötland (2022)

KEY PUBLICATIONS

Edin C, Ekstedt M, Scheffel T, Karlsson M, Swahn E, Östgren CJ, Engvall J, Ebbers T, Leinhard OD, Lundberg P, Carlhäll CJ. Ectopic fat is associated with cardiac remodeling-A comprehensive assessment of regional fat depots in type 2 diabetes using multi-parametric MRI. Front Cardiovasc Med. 2022 Jul 28;9:813427. doi: 10.3389/fcvm.2022.813427. PMID: 35966535; PMCID: PMC9366177.

Jonasson H, Bergstrand S, Fredriksson I, Larsson M, Östgren CJ, Strömberg T. Post-ischemic skin peak oxygen saturation is associated with cardiovascular risk factors: a Swedish cohort study. Microvasc Res. 2022 Mar;140:104284. doi: 10.1016/j.mvr.2021.104284. Epub 2021 Nov 23. PMID: 34826433.

Muhammad IF, Engvall JE, Persson M, Borné Y, Nilsson PM, Östgren CJ, Engström G. Association of arterial stiffness with coronary artery calcium score in the general-population: the Swedish CArdioPulmonary bioImage study. J Hypertens. 2022 Feb 9. doi: 10.1097/HJH.0000000000003096.



(A,B) example coronal slices of whole-body Dixon MR images. (A) Fat images with the VAT (red) and ASAT segmented (blue). (B) Water images with the segmented thigh muscle groups: right posterior thigh (blue), right anterior thigh (yellow), left posterior thigh (green), and left anterior thigh (pink). (C) Cardiac fat image in transversal view from the 3D Dixon sequence, showing the segmented region of interest (red) following the epicardial border. (D) Liver H-1 MR spectrum obtained at 1.5 T, showing the water resonance at 4.76 ppm (green), and the major fatty-acyl chain resonances at 1.21 ppm (methylene), as well as 0.9 ppm (methyl) and 2.2 ppm (alpha-olefinic etc.) (blue). All lipid resonances were included in the integration procedure.

POPULAR SCIENTIFIC SUMMARY
Petter Dyverfeldt, Ebo de Muinck

Carotid MRI

Atherosclerotic plaque in the carotid artery bifurcation is a common cause of ischaemic stroke, a major cause of cardiovascular mortality and morbidity. However, clinical stroke assessment has for many years been based on the degree of lumen narrowing caused by the plaque in the carotid artery. Even if there is a correlation between plaque size and cardiovascular events, this approach risks a consistent misclassification of strokes caused by small plaques. In fact, a large number of strokes tend to be classified as "unknown cause". More research on small plaques is necessary to determine whether small size plaques are a larger problem than previously thought. The necessity to advance our clinical and scientific knowledge in this area is further underscored by the finding that up to 10% of the Swedish population between 50–64 years have asymptomatic carotid plaques >2.7 mm. An improved understanding of such plaques, including the ability of MR imaging to identify plaque features that predict future plaque development and events, can open up for improved selection of patients for thrombendarterectomy and high intensity medical treatment.

The overall purpose of this project is to evaluate carotid magnetic resonance imaging (MRI) in a population-based cohort and explore the natural course of MRI-identified plaque features as well as the capability of MRI-identified plaque features to predict future events such as stroke. In addition to MRI, we have via the Swedish CArdioPulmonary bioImage Study (SCAPIS) access to data on blood pressure, biomarkers, medical history, lifestyle, coronary computed tomography, etc. in a unique population-based cohort of middle-aged individuals.

In this project, we will investigate baseline characteristics of carotid plaques in our SCAPIS subcohort of 600 middle-aged individuals with asymptomatic carotid plaques. We will also perform a repeat MRI 8 years after the initial MRI to study the natural course of carotid plaques in asymptomatic individuals. Finally, the predictive capability of MRI-based characterization of morphological and compositional plaque features will be explored in relation to events such as stroke and myocardial infarction.

MRI | Other | Cardiovascular | AI/Data analytics | Imaging Biomarkers

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

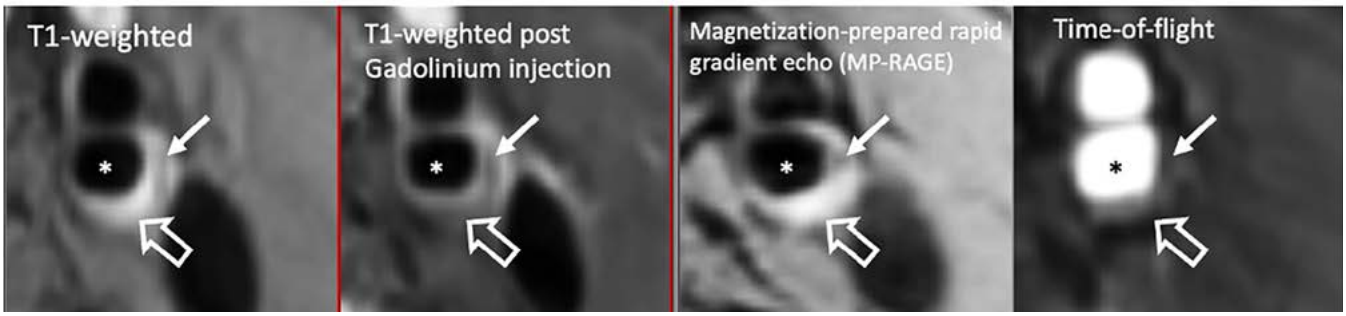
ALF Grant, Region Östergötland
Henry and Ella Margareta Ståhl foundation
Hälsofonden, Linköping University and Region Östergötland
Swedish Research Council, project grant

KEY PUBLICATIONS

Good E, Ziegler M, Warntjes M, Dyverfeldt P, de Muinck E. Quantitative magnetic resonance imaging assessment of the relationships between fat fraction and R2* inside carotid plaques, and circulating lipoproteins. Journal of Magnetic Resonance Imaging 2022; 55: 1260-1270.

Ziegler M, Alfraeus J, Bustamante M, Good E, Engvall J, de Muinck E, Dyverfeldt P. Automated Segmentation of the Individual Branches of the Carotid Arteries in Contrast-Enhanced MR Angiography using DeepMedic. BMC Medical Imaging 2021; 21(1):1-10.

Ziegler M, Good E, Engvall J, Warntjes M, de Muinck E, Dyverfeldt P. Towards Automated Quantification of Vessel Wall Composition using MRI. Journal of Magnetic Resonance Imaging 2020; 52: 710-719.



MR images in patient with carotid plaque. The images were acquired with T1-weighted, post-Gadolinium contrast T1-weighted, MP-RAGE and time-of-flight MR imaging. Image location is just distal to the carotid artery bifurcation. Asterix: internal carotid artery lumen. Solid arrow: calcification as characterized by low signal intensity in all images. Open arrow: Intraplaque hemorrhage as characterized by hyperintense signal on the T1-weighted and MP-RAGE images in combination with hypointense signal on the post-Gadolinium contrast T1-weighted and time-of-flight images.

POPULAR SCIENTIFIC SUMMARY
Petter Dyverfeldt

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

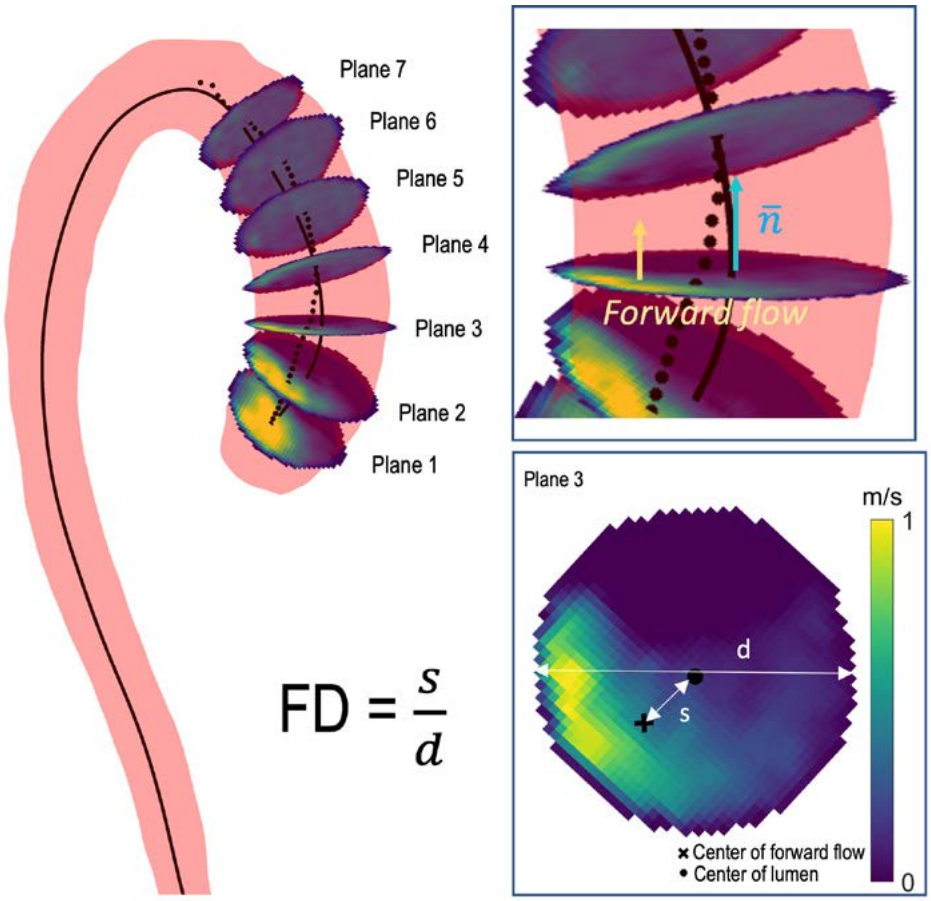
Petter Dyverfeldt, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS

Chiara Trenti, Filip Hammaréus, Elisabeth Logander, Marcus Lindenberger, David Kylhammar, Aleksandra Trzebiatowska-Krzynska, Jan Engvall, Lena Jonasson, Eva Swahn

GRANTS

ALF Grant, Region Östergötland
Linköping University Strategic Research Area in Circulation and Cardiovascular Metabolic Risk Factors
Medical Faculty at Linköping University, co-financing of PhD Student



Flow displacement (FD) is a promising hemodynamics marker of ascending aortic dilation. Flow displacement is defined as the displacement of the "center of mass" of forward flow normalized by the vessel diameter. In this example, flow displacement is measured at seven locations in the ascending aorta by automatic positioning of equidistant planes along the aorta centerline.

POPULAR SCIENTIFIC SUMMARY
Tino Ebbers

4D Flow MRI

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

Sometimes small abnormalities occur at birth or by disease, cardiovascular diseases are often found in obesity, diabetes and an aging population. The heart can compensate for these to some extent, but they can also lead to inefficient pump function and sometimes to a cascade of more severe abnormalities.

Despite the primacy of flow, cardiac diagnostics still rely almost exclusively on tools focused on morphological assessment. Flow characteristics are often assumed rather than measured directly. Suitable non-invasive tools for characterizing and measuring flow dynamics are needed to push our medical effectiveness to the next level.

The objective of this project is to develop the next generation of methods for the non-invasive quantitative assessment of cardiovascular diseases and therapies by focusing on blood flow dynamics, with the goals of earlier and more accurate detection and improved management of cardiovascular diseases.

The project makes use of a method for flow quantification using MRI which allows for simultaneous measurement of time-resolved, three-dimensional (time + 3D = 4D) blood flow velocity and turbulence intensity. This method, which was pioneered at CMIV, reveals blood flow patterns in the heart and the large vessels. By combining this approach with modelling approaches, more knowledge can be obtained from the measured data about the cardiovascular system under different conditions.

Cardiovascular blood flow is still to a large extent unknown. In order to define relevant parameters, development of analysis and visualization approaches and studies of normal and abnormal blood flow have to be performed in chorus.

Studying cardiovascular blood flow dynamics in patients and healthy subjects will improve our understanding of the roles of flow dynamics in health and disease, leading to improved cardiac diagnostics, novel assessments of pharmaceutical, interventional, and surgical therapies, and promoting exploration of new avenues for management of cardiac disorders can facilitate treatment of cardiovascular patients with higher quality and lower costs.

MRI | Cardiovascular | Acquisition | Modeling | AI/Data analytics | Simulation

Project information

PROJECT NAME

Assessment of Cardiovascular Blood Flow Using 4D flow MRI and Physiological Modelling

PROJECT LEADER

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

MAIN PROJECT PARTICIPANTS

Carl-Johan Carlhäll, Jan Engvall, Petter Dyverfeldt, Gunnar Cedersund, Federica Viola, Kajsa Tunedal

GRANTS

Swedish Research Council (2019-2022)
Swedish Research Council (2023-2026)

KEY PUBLICATIONS

Bustamante M, Viola F, Engvall J, Carlhäll CJ, Ebbers T. Automatic Time-Resolved Cardiovascular Segmentation of 4D Flow MRI Using Deep Learning. Journal of Magnetic Resonance Imaging, 2022.

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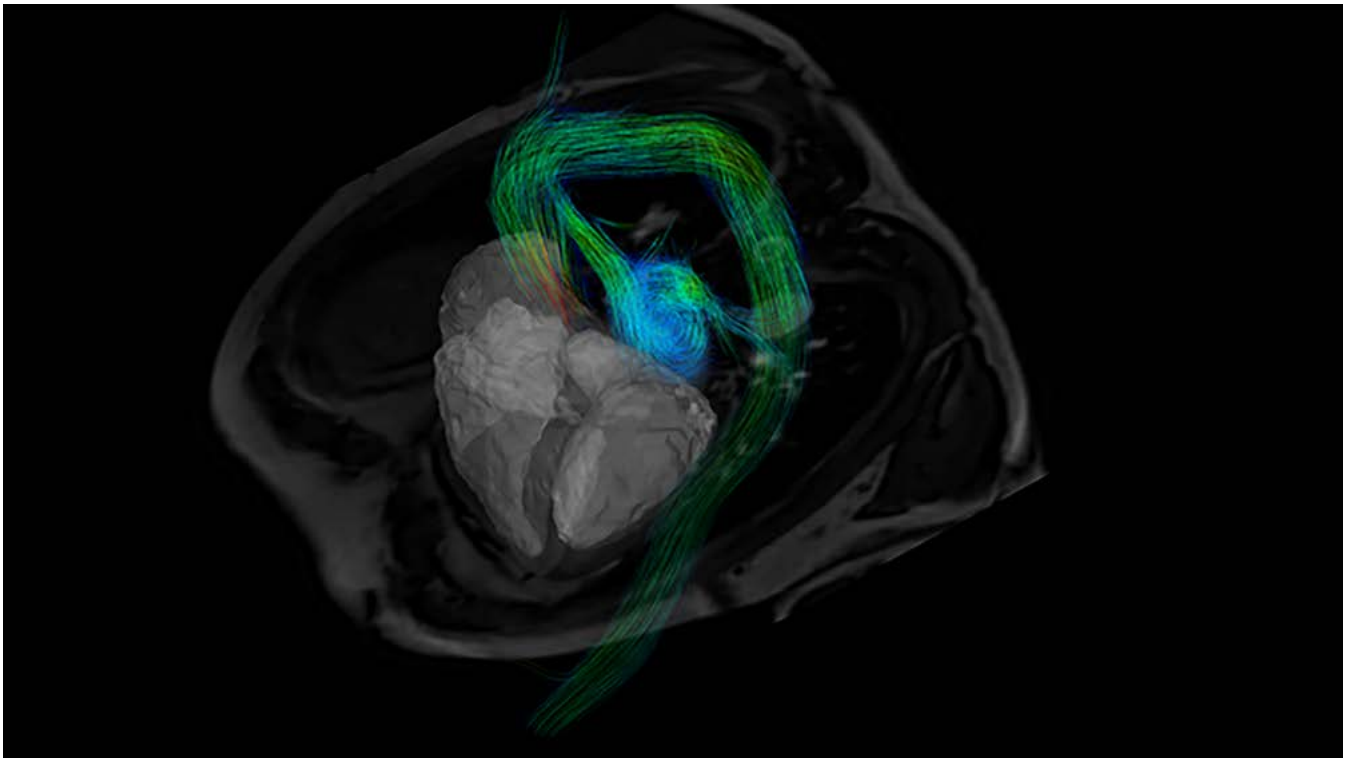
Garg P, Swift AJ, Zhong L, Carlhäll CJ, Ebbers T, Westenberg J, Hope MD, Bucciarelli-Ducci C, Bax JJ, Myerson SG. Assessment of mitral valve regurgitation by cardiovascular magnetic resonance imaging, Nature Reviews Cardiology, 1-15 2019.



Streamlines visualization of blood flow in the aorta and the left-atrium at systole. Segmentations of the cardiac cavities (gray) were created automatically using atlas-based segmentations.

POPULAR SCIENTIFIC SUMMARY
Tino Ebbers

4D Flow CT

Advanced computed tomography (CT) allows for amazing visualization of the human body including the beating heart. However, the complex interactions of blood flow, which is crucial in the diagnosis and treatment planning of many diseases, are not fully reflected by these images. Magnetic resonance imaging (MRI) and ultrasound are able to measure functional data like blood flow, but at a low resolution. Furthermore, these techniques are not able to predict the changes in blood flow after surgical treatment.

This project aims to extract blood flow data from CT images of the heart using image-based simulations. The goal is earlier and more accurate detection as well as improved management of cardiac diseases.

Even though many forms of functional imaging data and modelling approaches are currently available, a gap persists between modelling and experimental research. This project has bridged the gap by developing and evaluating an approach in which intracardiac flow fields are computed based on patient-specific high-resolution cardiac CT data. The heart is segmented, and advanced registration techniques are used to track the heart wall. Using computational techniques usually employed by the automotive or aerospace industry, detailed intracardiac and vascular blood fields are obtained.

The results show that the 4D Flow CT method can produce blood-flow patterns that are qualitatively and quantitatively similar to the current reference standard 4D Flow MRI, but at higher resolution. The high resolution also allows the simulated data to reveal processes that could not be studied before, like the coagulation of blood or the occurrence of turbulence in the blood flow.

One clinical application that is explored is in atrial fibrillation. These patients have an increased risk of blood cloths forming in the atrium and by migrating to the brain or coronary arteries they may induce a stroke or heart attack. We are building a model that can identify where the blood cloths are forming. The goal is that the information from this model may be used to identify patients at risk.

The simulation-based approach potentially allows for studies of what-if scenarios where different treatment options can be explored. This is challenging, as the heart is complex and adapts to changes in demand and constrains. A model is a simplified version of reality and there has to be a balance in the amount of details included and clinically usability.

Computed Tomography | Cardiovascular | Acquisition | Modeling | Simulation

Project information

PROJECT NAME

Simulation of Time-Resolved, Three-Dimensional Cardiac Blood Flow from Computed Tomography (4D flow CT)

PROJECT LEADER

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

MAIN PROJECT PARTICIPANTS

Jonas Lantz, Anders Persson, Carl-Johan Carlhäll, Matts Karlsson, Bente Konst, Lilian Henriksson, Sophia Bäck, André Da Luz Moreira, Linus Ohlsson

GRANTS

Swedish Heart Lung Foundation (2022-2023)
Visual Sweden / MeDigiT (2022-2023)
WASP/DDLS (2022-2024)
Swedish Research Council (2023-2026)

KEY PUBLICATIONS

Lantz J, S 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 2021, 116.

Lantz J, Gupta V, Henriksson L, Karlsson M, Persson A, Carlhäll CJ, Ebbers T. Impact of Pulmonary Venous Inflow on Cardiac Flow Simulations: Comparison with In Vivo 4D Flow MRI, Annals of biomedical engineering 2019; 47 (2), 413-424.

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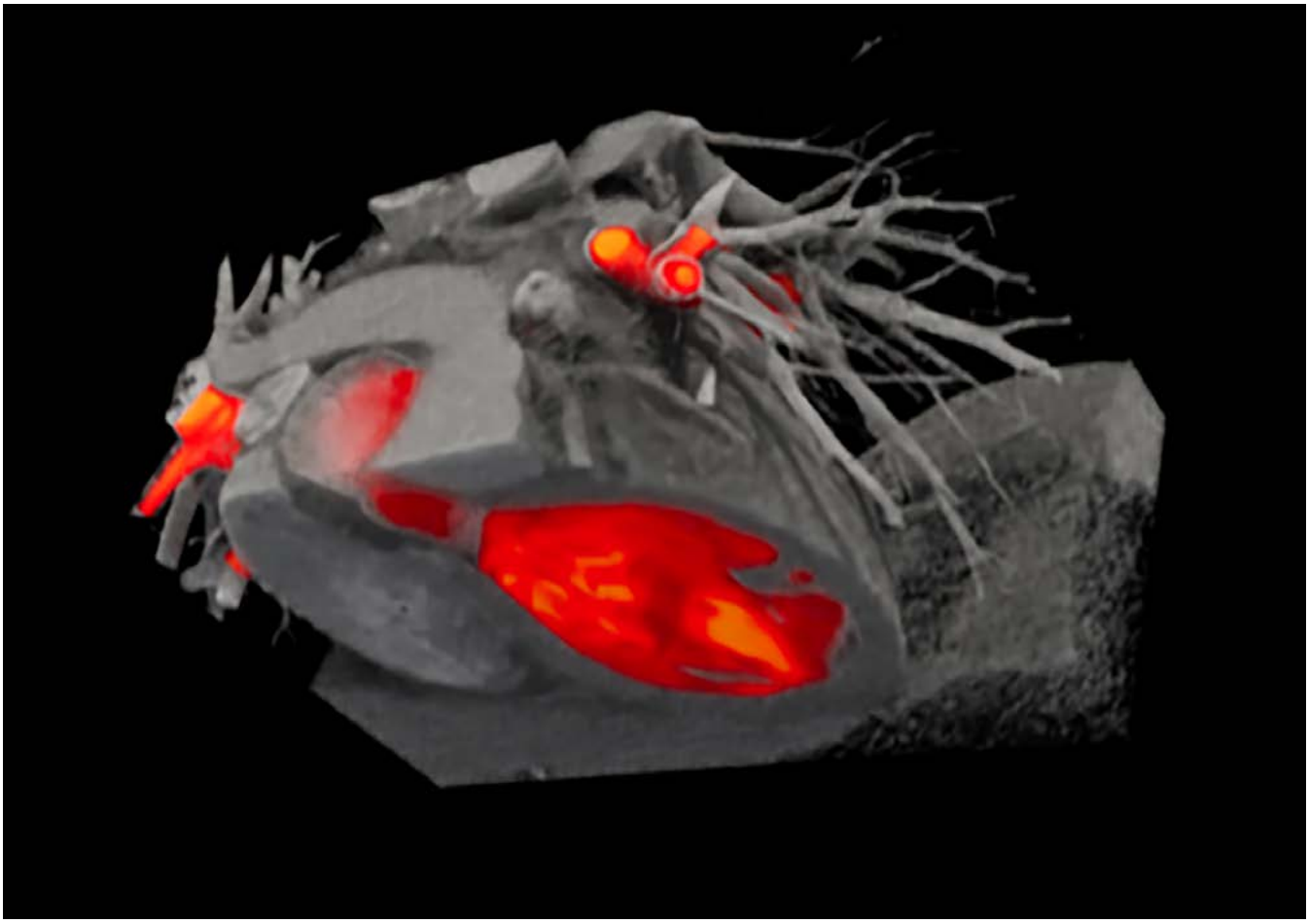

Volume rendering of the blood flow in a patient with a dilated left ventricle.

POPULAR SCIENTIFIC SUMMARY

Miguel Ochoa-Figueroa

Digital nuclear cardiology and AI in the diagnosis of myocardial ischemia

Myocardial perfusion imaging (MPI) is one of the most common cardiological examinations performed all over the world and is used for diagnosis and risk assessment in patients with suspected coronary artery disease (CAD). The technique provides important information on ischemia, myocardial injuries and left ventricular ejection fraction, among others.

One of the deepest developments MPI has experienced in the last decades is the introduction of cadmium-zinc-telluride (CZT) detectors. In Scandinavia, the jump from conventional sodium iodide (Nal) based cameras into dedicated CZT cardiac cameras took place in Linköping University Hospital in 2014, being the first Hospital in Scandinavia to install a camera of this kind. Taking advantage of this we have performed a study (1) to evaluate the performance of this camera in our CAD population. Additionally, we evaluated if there were any differences in the diagnostic performance of the MPI when the stress test was performed as a cycling test, a pharmacological test, or a combination of both. All patients where further evaluated with invasive coronary angiography (ICA), which is the standard of truth.

Our research has shown that the D-SPECT camera achieves satisfactory results in patients with CAD with an overall diagnostic accuracy of 86%, Sensitivity 93%, Specificity 54%, PPV 90% and NPV 63%, not finding significant differences when the stress test was performed as a cycling test, a pharmacological test or as a combination of both, something which could help us in the future in the clinic when taking the decision of which kind of stress test we should use in our patients.

A limitation of this technology has been the numbers of artefacts in the MPI images, which are mainly due to obesity, patient movement during the study and technical issues. These artefacts are the Achilles heel of the test as they are the main cause of false positive results. To address this problem, we have conducted a study (2), using an artificial intelligence attenuation correction software (AI-ACS) to avoid artefacts. The study has shown that the use of the AI-ACS achieves significant better results specially, increasing the specificity from 54% without AI-ACS to 85% when using AI-ACS. In conclusion, this AI technology is very promising, and it might have tackled the Achilles heel of CZT MPI once and for all.

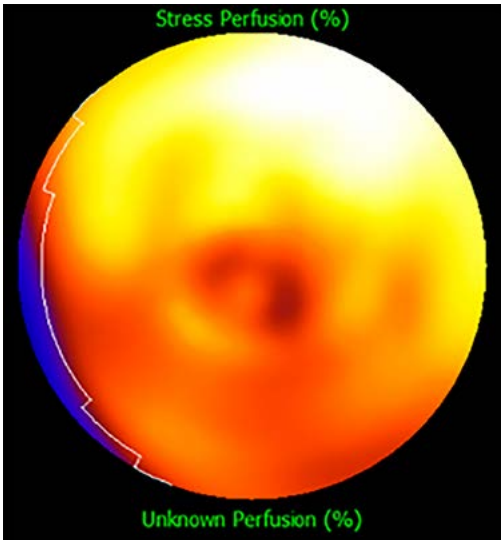

Figure 1. Bulls-eye stress MPI without DLACS showing infero-septal and apical perfusion defects which were fixed in the upright and supine positions and only partially reversible on the rest test.

70 y.o. female, 165 cm height, 71 kg weight and BMI 26. DM type II and smoker, no previous cardiac background known. Recently diagnosed with gastric cancer which plans to be operated. A heart echocardiography has been performed as part of the pre-op work up, which was suspicious for apical hypokinesia. Referred to MPI to rule out ischemia.

One of the aims of our project has been to develop an AI tool for automatic evaluation of myocardial ischemia as well as the estimation of the degree of coronary artery stenosis using MPI images. Our published data show very promising results (3). The implications of our findings for the health care system are sustainable since the information provided from the AI tool, using a non-invasive approach, could result in avoiding the ICA intervention, reducing radiation exposure to the patients and the number of hospitalizations.

In the future we will continue including more patients to create a more robust AI as well as looking for new variables which can help us achieve better results with our AI tools.

Other | Cardiovascular | AI/Data analytics

Project information

PROJECT NAME

Novel developments in nuclear cardiology using a cardio-dedicated digital gammacamera and artificial intelligence for the diagnosis of myocardial ischemia.

PROJECT LEADER

Miguel Ochoa-Figueroa, Department of Radiology, Region Östergötland

MAIN PROJECT PARTICIPANTS

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GRANTS

Vinnova-Medtech4Life program – AIDA
Mats Paulssons stiftelse (2022)

KEY PUBLICATIONS

Ochoa-Figueroa M, Frias-Rose J, Good E, Sanchez-Rodriguez V, Davidsson A, Pagonis C. Diagnostic performance of different cardiac stress protocols for myocardial perfusion imaging for the diagnosis of coronary artery disease using a cadmium-zinc-telluride camera with invasive coronary angiography correlation. Rev Esp Med Nucl Imagen Mol (Eng Ed). 2022 Sep 11:S2253-8089(22)00084-2. doi: 10.1016/j.remnie.2022.09.001. Epub ahead of print.

Ochoa-Figueroa M, Davidsson A, Sanchez-Rodriguez V, Ressner M, Norberg P, Good E, Frias-Rose J, Pagonis C. The role of a deep learning attenuation correction software in the performance of MPI using a cardio dedicated CZT camera with ICA correlation. Eur J Nucl Med Mol Imaging. 2022; 49 (Suppl 1): S136-7.

Arvidsson I, Davidsson A, Oveergard NC, Pagonis C, Åström K, Good E, Frias-Rose J, Heyden A, Ochoa-Figueroa M. Deep learning prediction of quantitative coronary angiography values using myocardial perfusion images with a CZT camera. J Nucl Cardiol. 2022. https://doi.org/10.1007/s12350-022-02995-6 Epub ahead of print.

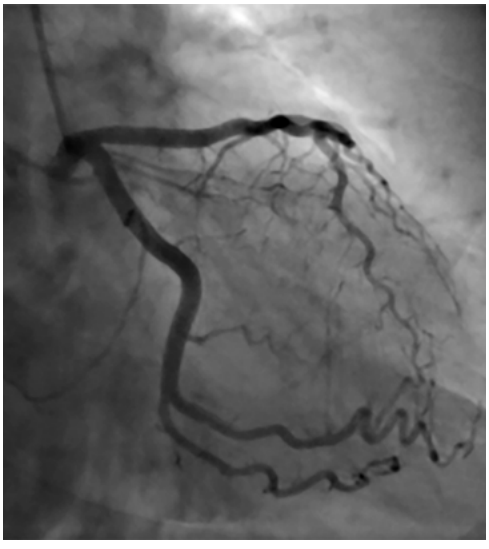

Figure 2. The patient underwent ICA, due to the MPI result, showing no obstructions in the coronary arteries.

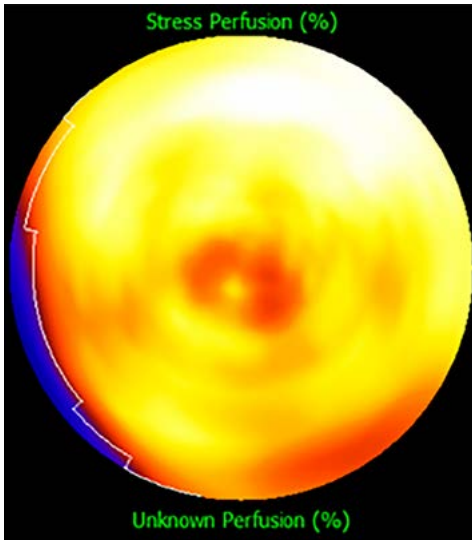

Figure 3. Stress MPI using DLACS showing an almost "normal" image, something that could have prevented the ICA in this patient.

POPULAR SCIENTIFIC SUMMARY
Tomas Bjerner

Computational integrated diagnostics panorama for liver cancer

Diagnostic practice in hepatocellular carcinoma (HCC) is challenging since there is a continuum of lesions developing from benign to malignant. Our primary medical research direction is towards future refinement of LI-RADS leading to improved treatment of HCC patients and surveillance of patients at risk to develop HCC. One example of such refinement is to reduce the number of falsely suspected HCC cases in radiology, for which unnecessary and potentially harmful punctures are performed.

In the long term, the clinical aim of the proposed line of investigation is to contribute to improved diagnostics of all liver malignancies by full integration of multi-scale, multi-modal data. During this initial project, contributions will be made constituting important milestones on this path. We plan to compile 20 data sets constituting an integrated diagnostic panorama for HCC patients. Based on this unique data collection, we will conduct proof-of-concept studies towards both medical and technical research questions.

The data to be collected in the integrated diagnostics panorama includes in-vivo radiology, ex-vivo radiology, pathology, and genomics, with the high-resolution photon counting CT being a particularly important resource. In this proof-of-concept phase, the computational research track in focus is upstream enrichment AI, i.e., improving radiology precision through what can be learned from data sources downstream. A central objective in the project is also to establish an effective process for collecting integrated diagnostic data and to establish a structured platform for the data and associated metadata.

Computed Tomography | MRI | Digital Microscopy | Other | Oncology | Acquisition | AI/Data analytics | Simulation

Project information

PROJECT NAME

Computational integrated diagnostics panorama for liver cancer

PROJECT LEADER

Tomas Bjerner, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS

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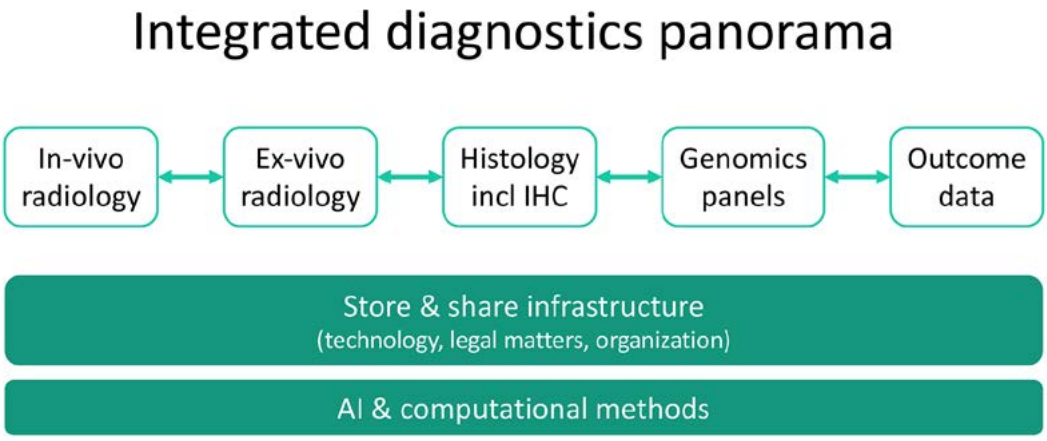
GRANTS

LiU Cancer

KEY PUBLICATIONS

Lundström CF, Gilmore HL, Ros PR. Integrated diagnostics: the computational revolution catalyzing cross-disciplinary practices in radiology, pathology, and genomics. Radiology. 2017 Oct;285(1):12–5.



An overview of the Integrated Diagnostics Panorama concept.

POPULAR SCIENTIFIC SUMMARY
Claes Lundström

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.

The activities in the AIDA program 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. The third component is the meeting place AIDA organizes, with frequent cross-disciplinary workshops and meet-ups, providing valuable knowledge and exchanges.

The AIDA operations build on the infrastructure and services provided by AIDA Data Hub. The hub includes a tailor-made technology platform for efficient AI development, with the flagship resource being the heavy-load computational system DGX-2 shared between the groups across the country. A key achievement is the capacity to securely handle sensitive personal data on the system. AIDA Data Hub also provides sharing services for clinically relevant data available for AI research. Currently 6 TB of such data is available, so far having been shared with researchers in 28 countries around the world.

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 2021 a SciLifeLab Facility within the Bioinformatics Platform (NBIS).

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, Darren Treanor, Miguel Ochoa-Figueroa, Petter Dyverfeldt, Evren Özarslan, Anders Eklund, Tino Ebbers, Martin Lindvall, Karin Stacke

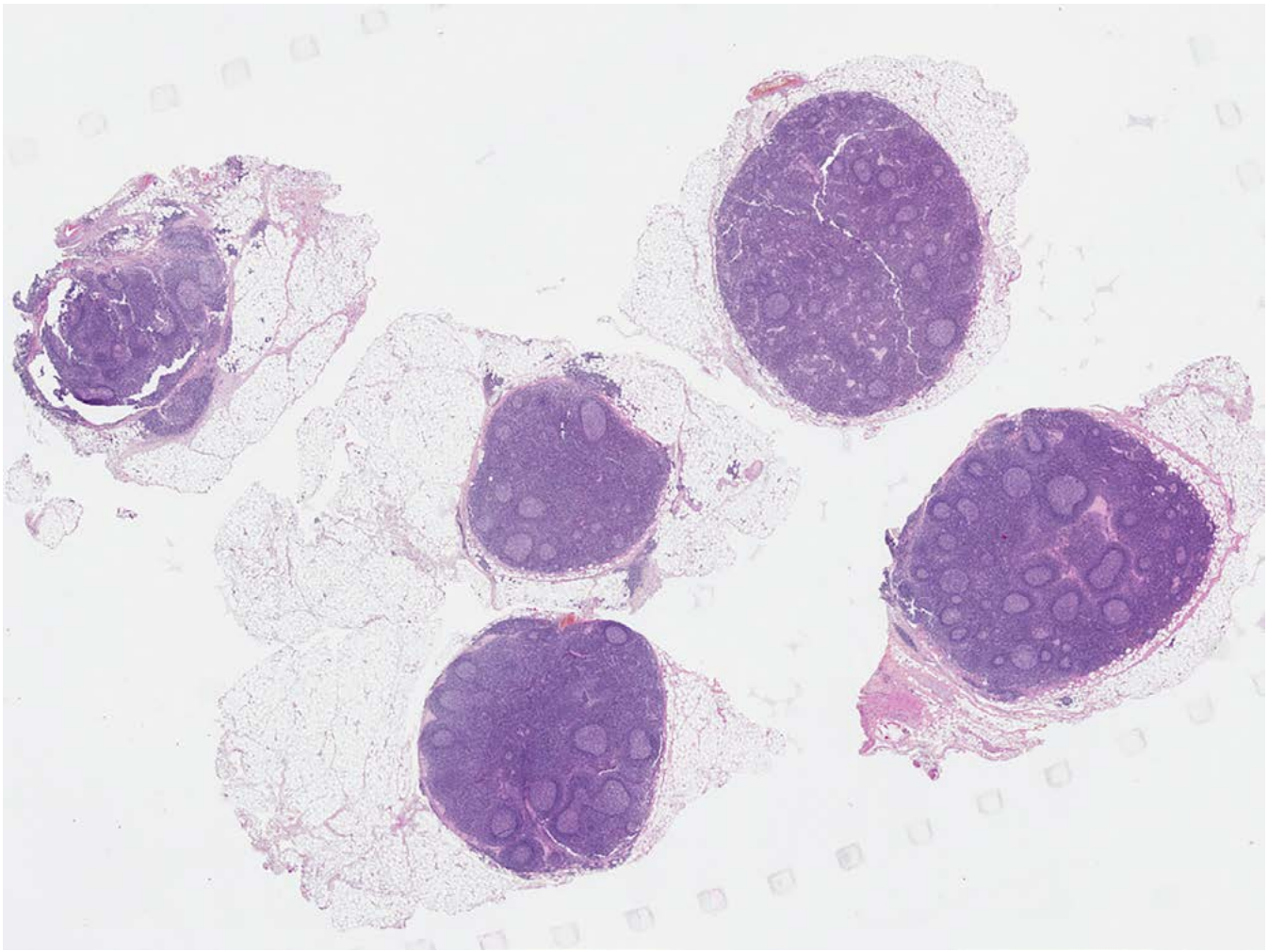
GRANTS
VINNOVA

KEY PUBLICATIONS

Etminani, K., Soliman, A., Davidsson, A., Chang, J. R., Martínez-Sanchis, B., Byttner, S., ... & Ochoa-Figueroa, M. (2022). A 3D deep learning model to predict the diagnosis of dementia with Lewy bodies, Alzheimer's disease, and mild cognitive impairment using brain 18F-FDG PET. European journal of nuclear medicine and molecular imaging, 49(2), 563-584.

Jakub Olczak, John Pavlopoulos, Jasper Prijs, Frank FA Ijpma, 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).



An example from the LNCO2 data set, showing a whole slide pathology image with colon lymph nodes.
The LNCO and LNCO2 data sets are one of the biggest shared histology data sets in the world.

POPULAR SCIENTIFIC SUMMARY
Joel Hedlund

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, are developing the world's biggest repository for sharing of pathology data. The Bigpicture repository is now in pilot production mode, aiming to commence large scale archive operations phase in March 2023. The 6-year, €70 million project called Bigpicture, will herald a new era in pathology.

In June 2022, the Bigpicture repository received its first three datasets, consisting of whole-slide pathology images and associated clinical metadata, from Region Östergötland in Sweden, Medical University of Vienna in Austria, and University Medical Center Utrecht in the Netherlands. The data that is amassed will enable development of groundbreaking AI tools for clinical diagnostics and drug development.

Center for Medica Image Science and Visualization (CMIV) at Linköping University engages heavily in Bigpicture. CMIV is responsible for the technical infrastructure in collaboration with the Swedish ELIXIR node at the SciLifeLab Bioinformatics platform NBIS and the Finnish ELIXIR node at 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-controlled platform, in which both large-scale data and AI algorithms 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 respected, 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 | Cardiovascular | Neurology | Oncology | Musculoskeletal | Gastrointestinal | Gynecological | Pulmonary | Metabolism | Acquisition | Modeling | AI/Data analytics | Visualization | Imaging Biomarkers

Project information

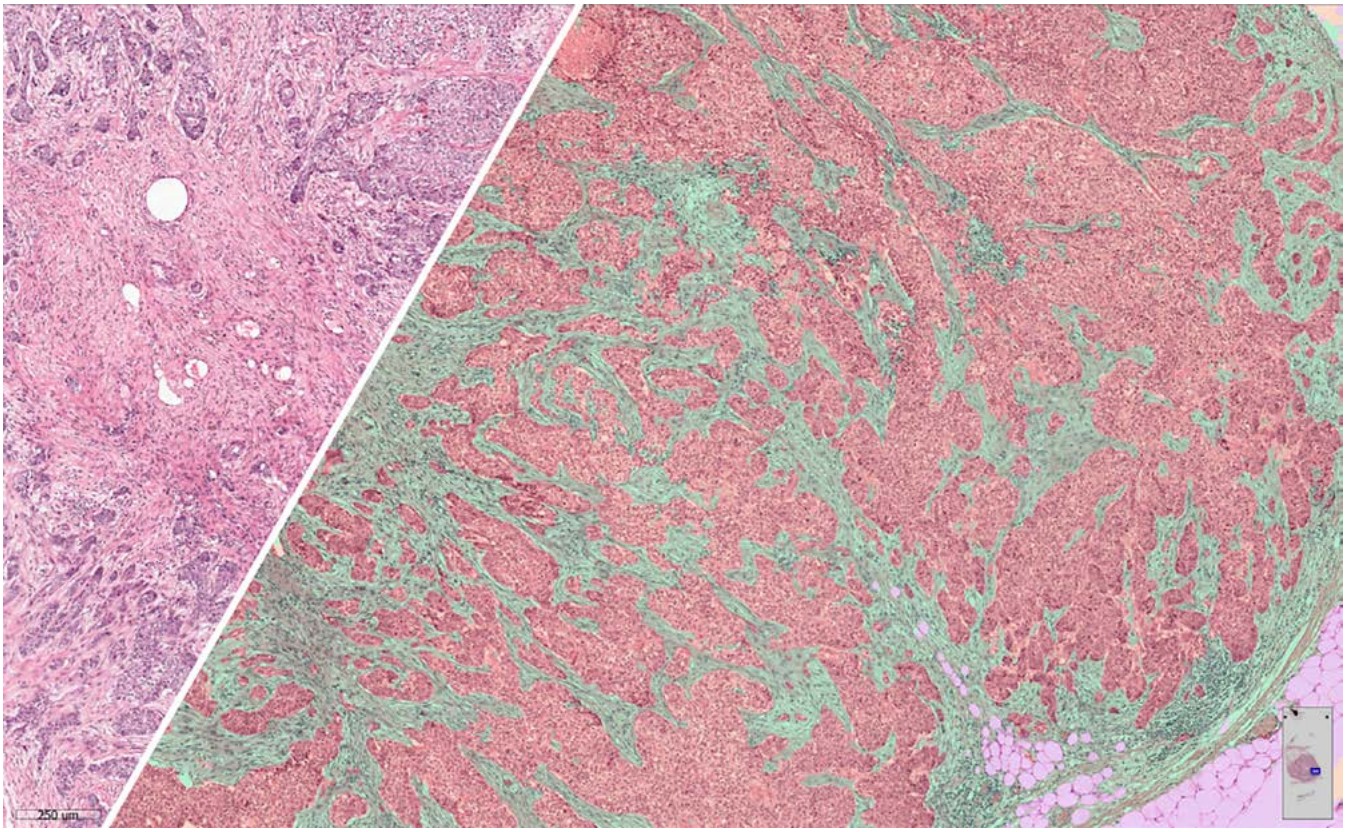
PROJECT NAME
Bigpicture

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

MAIN PROJECT PARTICIPANTS
Claes Lundström, Caroline Bivik Stadler, Darren Treanor, Anna Bodén, Håkan Gustafsson, Betül Eren Keskin, Shreyas Shivakumara, Jesper Molin, Catrin Nejdeby

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.



Close-up view of a breast cancer histopathology slide using standard hematoxylin and eosin staining, shown here before vs. after (top-left vs. bottom-right) an AI algorithm that can recognize breast cancer was used to color the cancerous cells red and the healthy cells green. The image shows only a small portion of the full microscopy slide, as indicated by the blue rectangle in the thumbnail image at the bottom-right. The scale indicator on the bottom left indicates the length of 250µm at this level of magnification.

POPULAR SCIENTIFIC SUMMARY
Michael Sandborg

Comparison of CT Technical Image Quality of Using PCCT and EID

Detection of low-contrast lesions are important in computed tomography. Its detection is limited by image noise since patient exposure need to be reasonably low while maintaining sufficient image quality for diagnosis. Figures of merit such as the signal-to-noise ratio, SNR, show limited positive correlation to the detection rate by human observers since humans are influenced by correlated noise. However, the channelized Hotelling model observer (CHO) have shown positive correlation with human observers as found by Racine et al (Radiat. Prot. Dosim., 169, 1–4, 73–77, 2016).

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).

The use of the model observer concept, (where a computer algorithm mimics the radiologists) minimizes the bias found with human observers. This enables us to compare and analyze a range of imaging parameters e.g., patient exposure, reconstruction kernel, mono-energetic reconstruction etc., which are typically selectable in clinical imaging protocol implementation. This will facilitate the careful balance between low-contrast resolution and patient exposure known as optimization. With the clinically released photon counting CT system (NAEOTOM Alpha, Siemens Healthineers), we aim to further explore the noise advantages of a photon counting detector and to correlate our results with patient clinical 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

Henrik Elgström, Jonas Nilsson Althén, Alexandr Malusek, Erik Tesselaar, Yuting Wang

GRANTS

RFoU (2022)

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 Läkarprogrammet, 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, May 2022. Supervised by Alexandr Malusek.

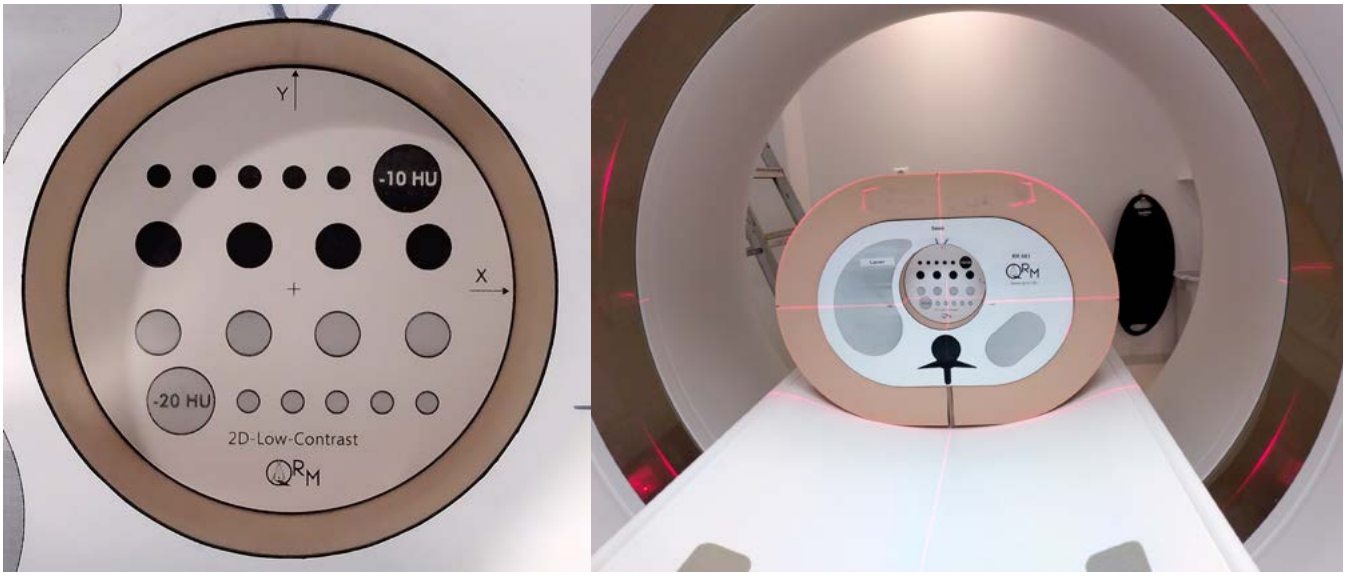


Figure 1. (a) A low-contrast phantom from QRM positioned in the gantry of the CT scanner (from Wang 2022).

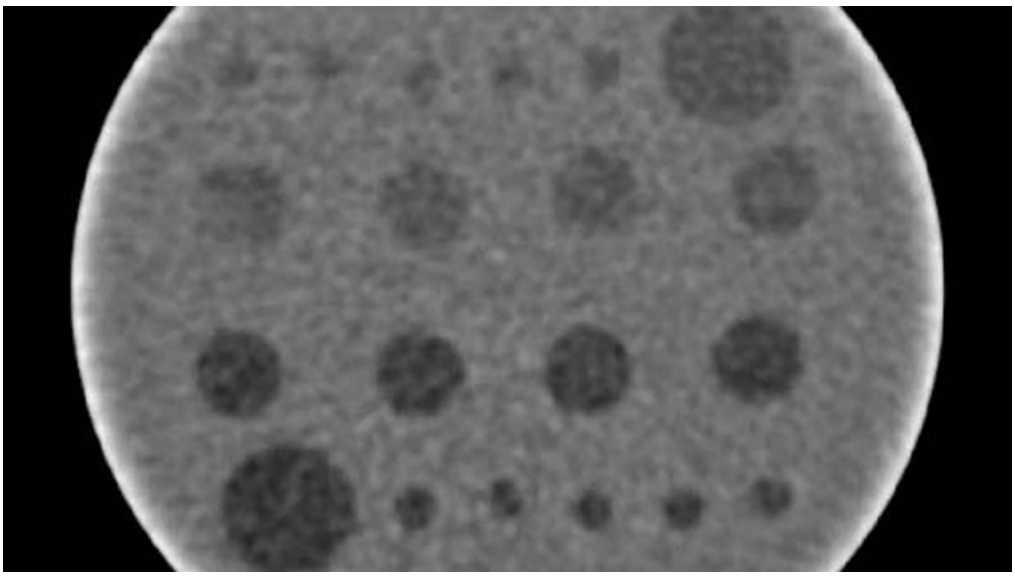


Figure 2. A CT image of the QRM phantom insert. The -10 HU and -20 HU contrast rods had diameters of 5, 8, and 15 mm (from Wang 2022).

POPULAR SCIENTIFIC SUMMARY
Åsa Carlsson Tedgren

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 continue to 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.

Computed Tomography | Oncology | Musculoskeletal | Modeling | AI/Data analytics | Simulation

Project information

PROJECT NAME

TCDECT – Tissue Classification using Dual Energy CT and Iterative Reconstruction

PROJECT LEADER

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

MAIN PROJECT PARTICIPANTS

Alexandr Malusek, Maria Magnusson, Michael Sandborg, Gudrun Alm Carlsson

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, Björnfot 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.

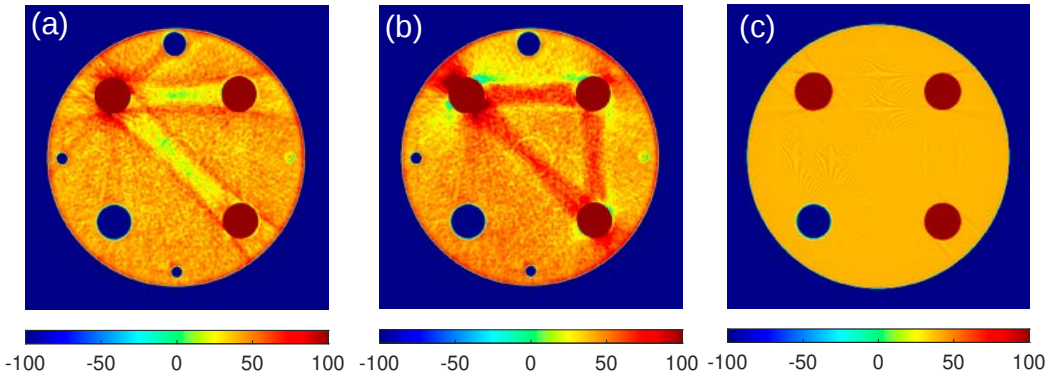


Figure 1. Images of a cylindrical PMMA phantom containing aluminium, low density polyethylene, and Teflon inserts reconstructed at 40 keV using Monoenergetic Plus (a) without and (b) with iBHC, and (c) DIRA. The range of CT numbers has been adjusted to emphasize the beam hardening artifact. Taken from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

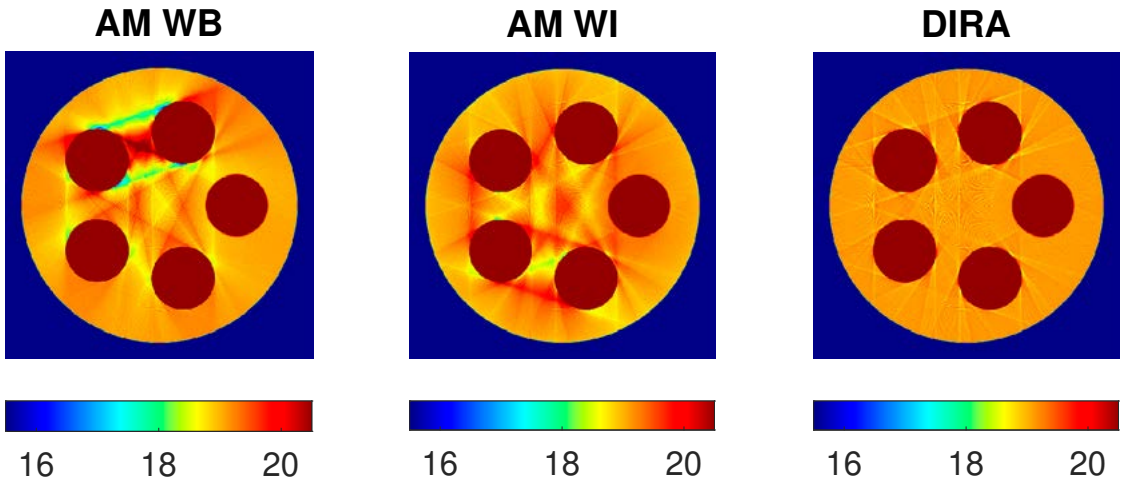


Figure 2. Images of a cylindrical protein phantom containing water, bone and iodine solution inserts reconstructed at 50 keV by the Alvarez-Macovski method using (a) the (water, bone) and (b) (water, iodine) doublets. (c) A reconstruction by DIRA using the (lipid, protein, water) triplet in the protein 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/ncab097under 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.

POPULAR SCIENTIFIC SUMMARY
Åsa Carlsson Tedgren

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 192Ir, 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 192Ir 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. The aim of this project is to evaluate and further develop these in the 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. We have recently evaluated an in-house developed adjustment tool, developed to improve clinical treatment plans upon spatial properties (Morén et al 2019). Quantitative evaluation of clinical plans to be operated on by the adjustment tool was complemented by a paired observer study. Visual grading methods with origin in radiology were used to our knowledge for the first time in grading radiotherapy treatment plans. Eight oncologists experienced with prostate brachytherapy participated and chose the adjusted plans in the majority of cases. A manuscript is currently under revision. In the next step we will focus on cervix cancer.

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

Frida Dohlmar, Michael Sandborg, Björn Morén, Torbjörn Larsson

GRANTS

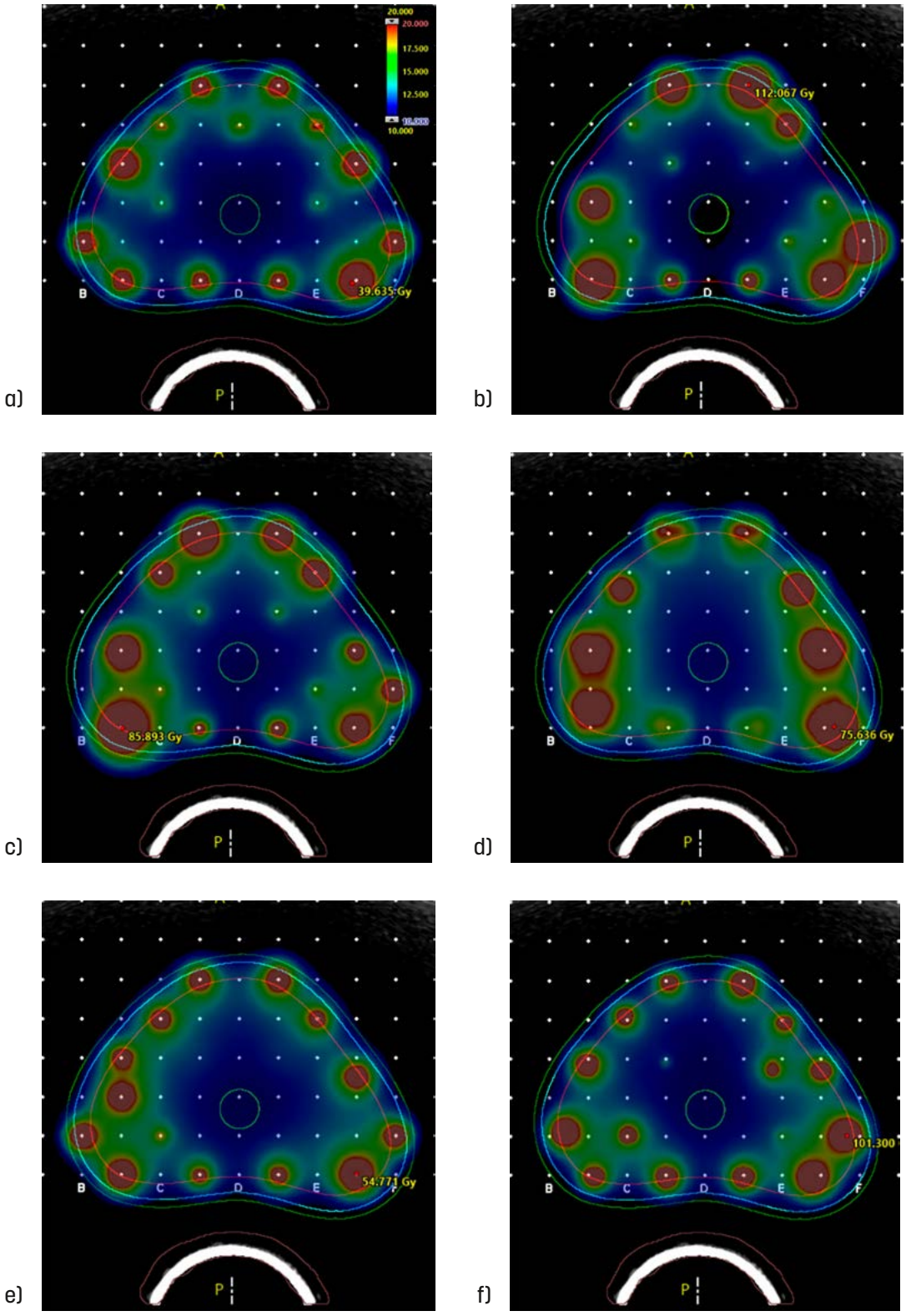
VR-NT (2020-2023)
Cancerfonden (2019-2021)
LiU Cancer (2020-2021, 2021-2022)
Region Östergötland "student till docent" (2021-2022)

KEY PUBLICATIONS

Dohlmar 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.

Moren 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 (Dohlmar 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 Dohlmar et al (2021) under CC BY.

POPULAR SCIENTIFIC SUMMARY
Peter Lundberg

AIMPLANT

The project "AI-based medical record screening for patient-safe MRI examination" involves development of an innovative AI-based method to significantly increase patient safety prior to a magnetic resonance imaging (MRI) scan. The method is based on automatic identification of "implant terms" through context processing of patient records.

When a patient today has or is suspected of having an implant, the procedure to obtain such is in fact entirely manual, it is also laborious and involves a range of experts with specialized knowledge. Hence, it is very important to speed up the current procedure and at the same time make the process both more accurate and reliable. It is very difficult to know whether a patient has an implant or not, because a patient usually does not know the model of implant or even the presence of one. In addition, even if implants have been removed, left-behind leads may be overlooked. About 30.000 MRI examinations are performed annually in Region Östergötland, and an increasing number of the patients have implants.

From a technical perspective, the project's main challenge is to automatically and correctly identify one small number of highly specialized implant terms scattered in a text mass of millions of words, unstructured and often 'noisy' text documents. It is thus difficult to create a model that can automatically detect the presence of implants or other dangerous objects prior to an MRI examination.

Implant terms can be words indicating devices such as "pacemaker", "shunt", "stent", "prosthesis", "nail", "metal clips", "electrode" and the like. But medical records are linguistically very difficult texts, written by medical practitioners, who usually use a wide range of medical 'shorthand'. This is not only based on common medical jargon, but contains also a host of unpredictable word abbreviations and spelling variants of the same word (including typos), numbers, model numbers and the like. To meet this challenge, we use state-of-the-art AI-based methods based on deep learning.

MRI | Cardiovascular | Neurology | Oncology | Musculoskeletal | Gastrointestinal | AI/Data analytics

Project information

PROJECT NAME
AIMPLANT

PROJECT LEADER
Peter Lundberg, Department of Health, Medicine and Caring Sciences. Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS
Anders Tisell, Yosef Al-Abasse, Johan Kihlberg, Maria Santini, Arne Jönsson, Håkan Gustavsson

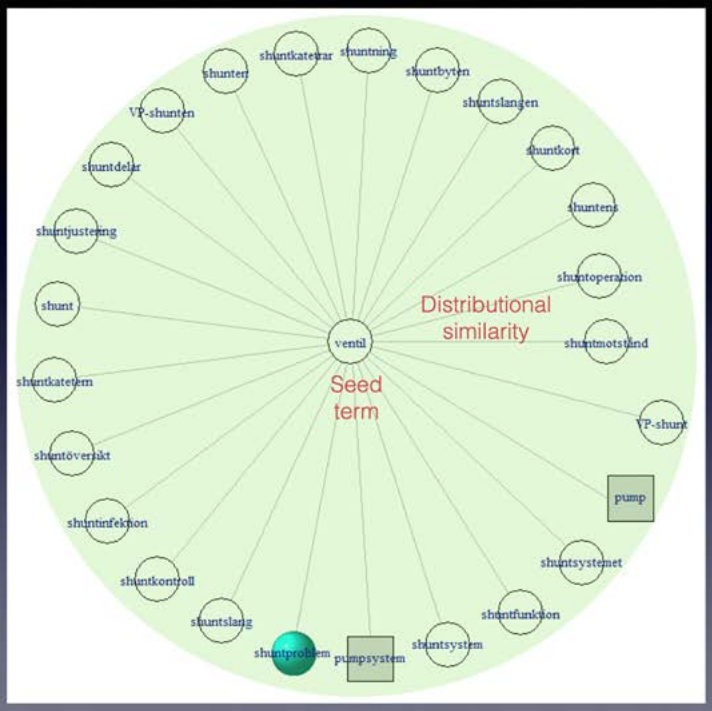
GRANTS
MedTech4Health, Vinnova

KEY PUBLICATIONS

Jerdhaf O, Santini M, Lundberg P, Bjerner T, Al-Abasse Y, Jönsson A (2022) Evaluating Pre-Trained Language Models for Focused Terminology Extraction from Swedish Medical Records, LREC 2022 Workshop Language Resources and Evaluation Conference, 20-25 June, Marseille, 2022.

Danielsson B, Santini M, Lundberg P, Al-Abasse Y, Jönsson A, Eneling E, Stridsman M (2022) Classifying Implant-Bearing Patients via their Medical Histories: A Pre-Study on Swedish EMRs with Semi-Supervised GAN-BERT, LREC 2022 Workshop Language Resources and Evaluation Conference, 20-25 June, Marseille, 2022.

Jerdhaf, O., Santini, M., Lundberg, P., Karlsson, A., & Jönsson, A. (2021, June). Focused Terminology Extraction for CPSs The Case of" Implant Terms" in Electronic Medical Records. In 2021 IEEE International Conference on Communications Workshops (ICC Workshops) (pp. 1-6). IEEE.



Term similarity

BERT: uses a search term (e.g., "ventil") to identify semantically similar terms that indicate implants. The term "*ventil*" (en: valve) is indicative of the presence of implants as much as the terms "*shunt*" and all its variants (**circles**), while some terms are not indicative of implants (**squares**);

Some other terms like those in **grey** squares are controversial and the domain experts disagree on whether they indicate the presence of implants or not.

The length of the lines represents the relatedness of the terms to "ventil", according to BERT.

POPULAR SCIENTIFIC SUMMARY

Peter Lundberg, Neda Hai-Hosseini

Improved diagnosis of pediatric brain tumours using AI-based digital pathology

Clinical pathology is one of the cornerstones of healthcare when it comes to medical diagnostics. Diagnostics is carried out mostly at the cellular level of tissue that is classified and assessed according to various criteria. A survey of a biopsy contains many separate sub-analyses that help develop different treatments. The fast medical development, for example in cancer healthcare, is moving towards the possibility of individually adapted care (what is called 'precision medicine') which places ever higher demands on efficiency and quality in clinical pathology.

For example, cancer investigations are already very resource-intensive today, and such investigations will likely continue to increase sharply in both number and scope in the future. This is due to both the increasing proportion of elderly and more healthy aged population as advanced technology developments. This places great demands on the diagnostic tools in clinical pathology, which are developing at the same rapid pace as the rest of cancer healthcare. The trend is not unique to cancer healthcare, but similar developments are seen in a large number of disease areas.

Development of new advanced decision support in pathology will therefore be necessary to streamline and further strengthen diagnostic safety. Digitalization of clinical pathology has opened the possibility of using rapid developments in artificial intelligence (AI) and 'machine learning' to develop AI-based support systems, for example image analysis for clinical decision support. A particular challenge for developing AI-based tools is that the amount of training data needed is normally severely limited and often not even available to the research groups and companies that are knowledgeable in the field.

In this project, we have the goal to digitalize a national pediatric brain tumour biobank (Barntumörbanken, BTB) and archive the dataset for licensed access. Moreover, we aim to explicitly develop and implement AI algorithms and similar methods as a diagnostic supplement in tumours of the central nervous system in children. The vision is that the AI-based tools, after validation, can be used as a clinical decision support and thus increase safety and precision in clinical pathology and thus benefit future patients greatly.

Digital Microscopy | Neurology | Oncology | AI/Data analytics | Imaging Biomarkers

Project information

PROJECT NAME

Improved diagnosis of central nervous system tumours in both children and adolescents using AI-based digital pathology

PROJECT LEADERS

Peter Lundberg, Department of Medical and Health Sciences, Division of Diagnostics and Specialist Medicine
Neda Hai-Hosseini, Department of Biomedical Engineering, Division of Biomedical Engineering

MAIN PROJECT PARTICIPANTS

Per Nyman, Ida Blystad, Iulian Emil Tampu, Johanna Nordmyr, Anders Eklund

GRANTS

Barncancerfonden
LiU Cancer
Joanna Cocozzas stiftelse för barnmedicinsk forskning
Forsknings-ALF Region Östergötland

The image shows the histology slides from Barntumörbanken that are digitalized in the SmallPicture.

POPULAR SCIENTIFIC SUMMARY
Mattias Ekstedt

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 257 individuals, whereof 223 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 Bergram, Carl-Johan Carlhäll, Gunnar Cedersund, Tino Ebbers, Nils Dahlström, Martin Henriksson, Fredrik Iredahl, Stergios Kechagias, Peter Lundberg, Patrik Nasr, Karin Rådholm, Christian Simonsson

GRANTS

Region Östergötland ALF-Grant
Mag-tarmfonden
Rut och Rikard Juhlin
Svenska Läkaresällskapet
Bengt Ihre-fonden

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.

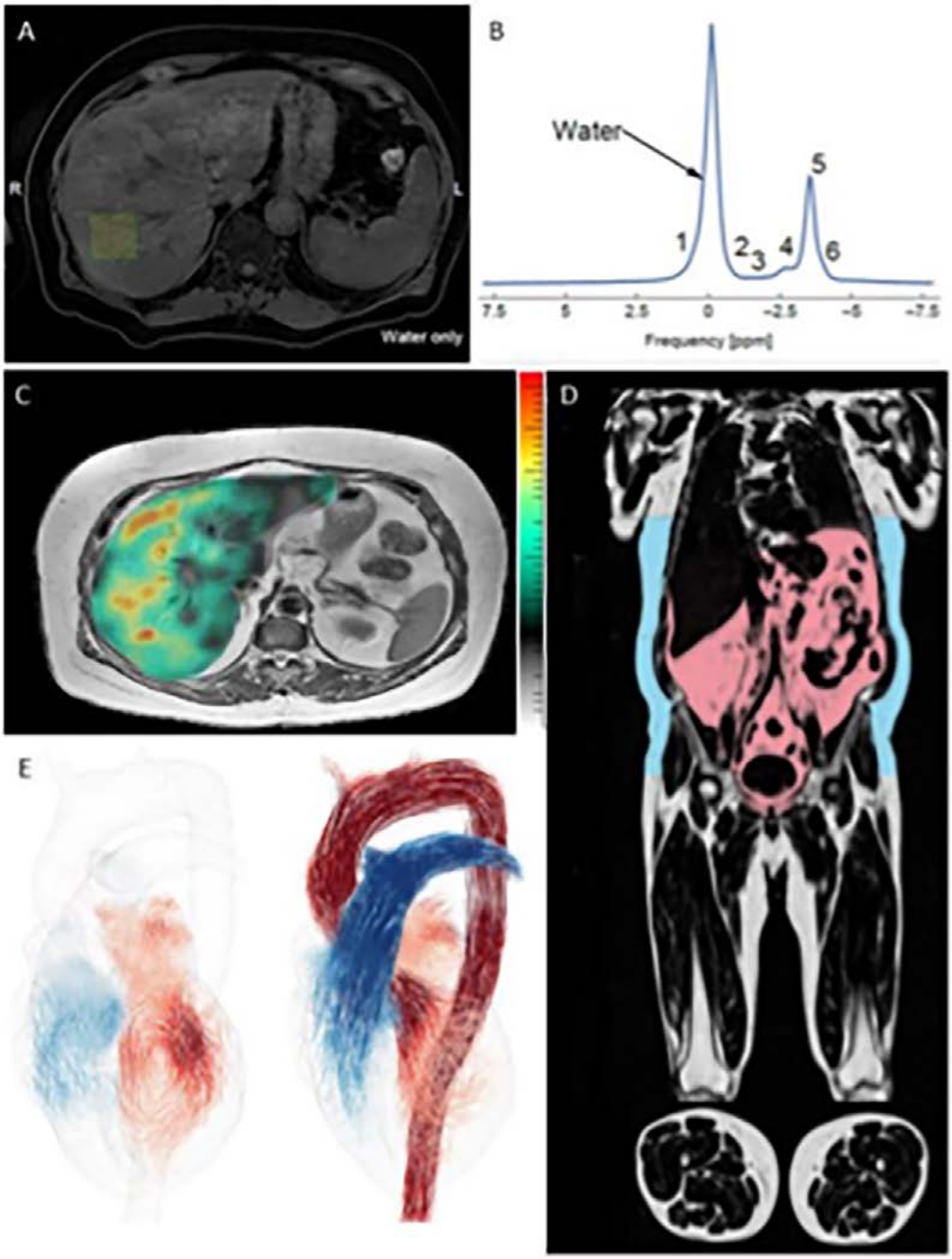


Image A shows the representative water MR image with 547 the placement of a proton magnetic resonance spectroscopy (^{1}H-MRS) voxel in the right hepatic lobe. Image B shows in vivo ^{1}H-MRS spectrum for water and fat. Image C shows MRE for a cirrhotic NAFLD patient. Image D shows a whole-body water-fat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

POPULAR SCIENTIFIC SUMMARY
Tino Ebbers

MeDigiT

A medical digital twin is a computer model that contains so much information about a patient that it can work as a digital copy. The digital twin can be used to simulate disease progression and treatment response before the patient has begun a medication or a surgical procedure.

Medical Digital Twin, MeDigiT, is a platform project financed by Visual Sweden aiming to facilitate the use of individualized digital models in healthcare for better diagnostics, more individualized treatment of illness, and simplified and improved education for healthcare professionals. The platform also aims to create and promote a network for research and exchange of knowledge and experience between Linköping University, Region Östergötland and companies in medical visualization.

The platform was formed in early 2019 and has since then connected several partners and created demonstrator projects in several areas.

One of the demonstrator projects, a collaboration between CMIV, Clinicum, Sectra and Region Östergötland, investigates the use of time-resolved digital twins in teaching. The project has developed an interactive software for visualization of the heart and moving joints, where the images are collected using advanced computed tomography (CT). The solution has been evaluated in the education of physiotherapists and physicians.

Another MeDigiT demonstrator projects is focusing on CMIVs cutting edge research on imaging of the cardiovascular system. Using simulations of heart flow based on CT images, individualized digital twins are tested for diagnosis and treatment evaluation in heart disease. The research aims, amongst others things, at improving valve surgery and risk assessment of blood clot formation in atrial fibrillation. Others participating in the project are Siemens and Region Östergötland.

In collaboration with Scandinavian Real Heart and Region Östergötland, a unique digital twin of an artificial heart has been created. The artificial heart has a design not previously used and the possibility to use time-resolved CT and MRI data provides valuable knowledge of the heart's function in the development of the product.

We also explore the use of digital twins covering the metabolism and cardiovascular physiology of the whole body, which is of interest for AstraZeneca, amongst others. In collaboration with AMRA, a usability study is conducted to investigate how information from digital twins can be presented to physicians and patients.

Access to digital, functional models of the organs in the body offers invaluable opportunities for research and for the development of products related to visualization of medical data.

Computed Tomography | MRI | Cardiovascular | Musculoskeletal | Metabolism | Modeling | AI/Data analytics | Visualization | Simulation | 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
Tilda Herrgårdh, Anders Persson, Nils Dahlström, Gunnar Cedersund, Jonas Lantz, Kajsa Tunnedal, Sophia Bäck, André Da Luz Moreira, Linus Ohlsson, Federica Viola, Twan Bakker

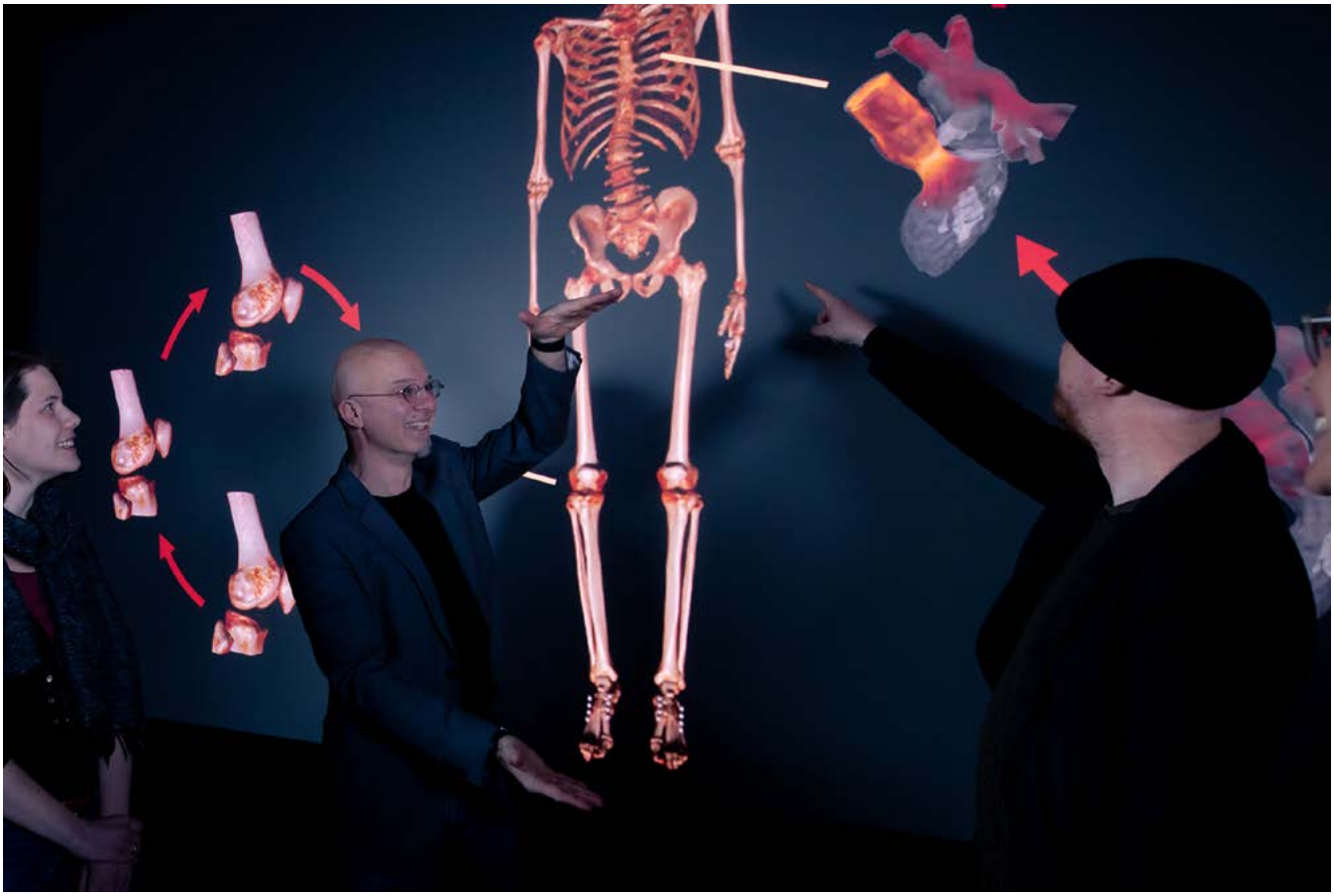
GRANTS
Visual Sweden 2022-2023

KEY PUBLICATIONS

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

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

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



Sophia Bäck, Tino Ebbers and Gunnar Cedersund.

POPULAR SCIENTIFIC SUMMARY
Rebecca Böhme

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

Rebecca Böhme, Department of Biomedical and Clinical Sciences, Center for Social and Affective Neuroscience

MAIN PROJECT PARTICIPANTS

Reinoud Kaldewaij, Paula Salamone, Adam Enmalm, Andrea Johansson Capusan, Lisbet Severin, Markus Heilig, Håkan Olausson

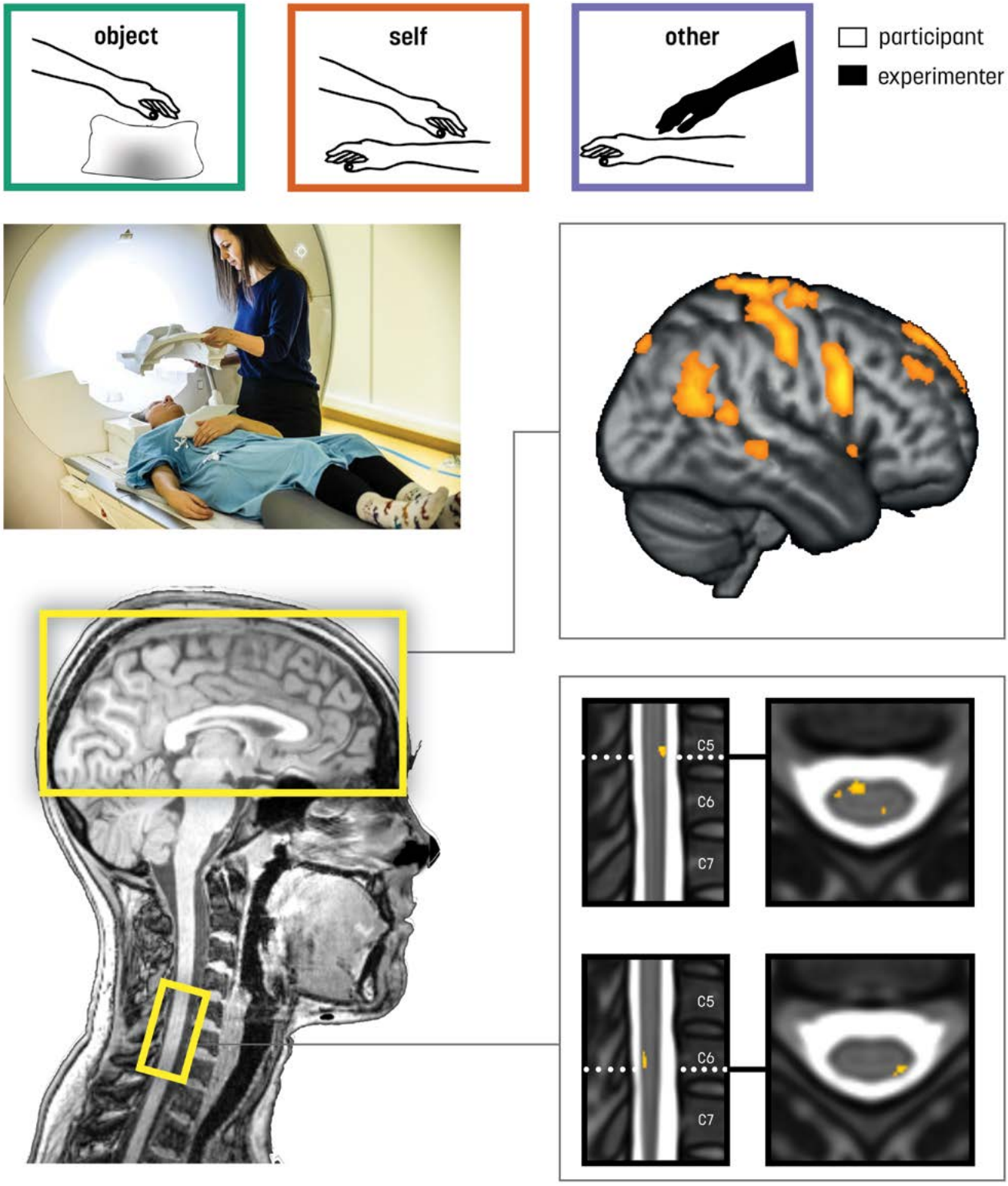
GRANTS

Vetenskapsrådet startbidrag (2019)
Åke Wiberg stiftelse
FORSS
ALF RÖ

KEY PUBLICATIONS

Boehme, R., Karlsson, M. F., Heilig, M., Olausson, H., & Capusan, A. J. (2020). Sharpened self-other distinction in attention deficit hyperactivity disorder. NeuroImage: Clinical, 102317.

Boehme R, Hauser S, Gerling G, Heilig M, Olausson H. Distinction of self-produced touch and social touch at cortical and spinal cord levels. Proceedings of the National Academy of Sciences (PNAS), Jan 22, 2019.



During the self-other-touch task, participants touch their own forearm, an object or are touched by someone else, while lying in the MRI scanner. Simultaneous MRI of the brain and spinal cord reveals regions that show differences in activation depending on the type of touch that participants produce and receive.

POPULAR SCIENTIFIC SUMMARY

Anneli Peolsson

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

Anneli Peolsson, Department of Health, Medicine and Caring Sciences, Division of Prevention, Rehabilitation and Community Medicine

MAIN PROJECT PARTICIPANTS

Anette Karlsson, Bijar Ghafouri, Tino Ebbers, Maria Engström, Margaretha Jönsson, Karin Wåhlén, Thobias Romu, Magnus Borga, Eythor Kristjansson, Hilla Sarig Bahat, Dmitry German, Peter Zsigmond, Gunnel Peterson, Nils Lund

GRANTS

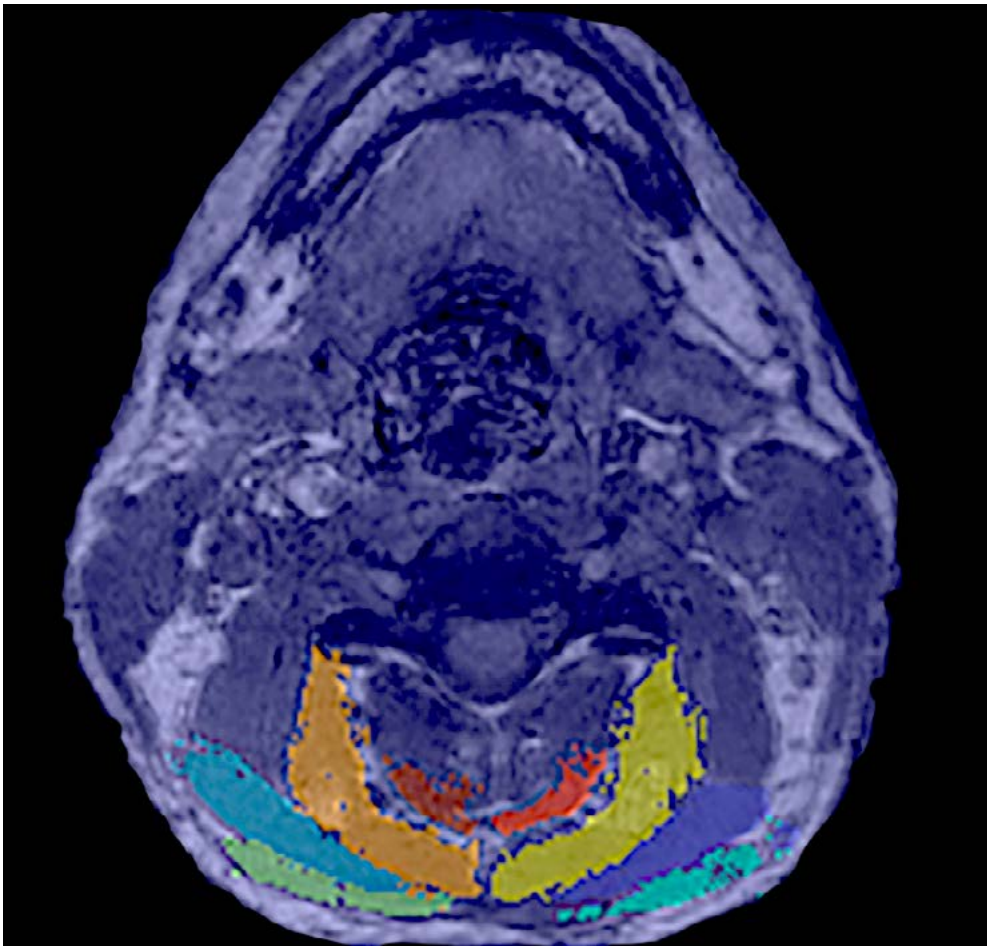
Swedish Research Council
Vinnova
Region Östergötland

KEY PUBLICATIONS

Björkkvist J, Peterson G, Peolsson A. Ultrasound investigation of dorsal neck muscles during neck rotation exercise. Which muscles are in use? J Manipulative Physiol Ther, 2020 Sep 3;S0161-4754(20)30070.

Kashfi P, Karimi N, Peolsson A, Rahnama L. The effects of deep neck muscle-specific training versus general exercises on deep neck muscles thickness, pain and disability in patients with chronic non-specific neck pain: protocol for a randomized clinical trial (RCT). BMC Musculoskeletal Disorders 2019;20:540.

Moodie K, O´Leary S, Tucker K, Phil S, Peolsson A. Are ultrasound measurements of muscle deformation well correlated with force and electromyography? J Manipulative Physiol Ther 2020;43:284-293.



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.

POPULAR SCIENTIFIC SUMMARY
Maria Engström

Image-Based Biomarkers of Brain Disorders (IBBB)

The research project focuses on the interpretation and modelling of blood oxygen level dependent (BOLD) responses in functional MRI (fMRI) and cerebrovascular reactivity (CVR) imaging. The research aims to 1) deepen the knowledge about the neurovascular coupling and changes in cerebral blood flow that underlies BOLD responses measured by MRI, 2) develop novel methods for CVR measurements, and 3) obtain model-based imaging biomarkers for clinical decision support.

Previously, we have developed mathematical models 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.

Our first model rejected the hypothesis of brain metabolism being the driving force behind the BOLD response in fMRI and we have shown that neural inhibition can explain so-called negative BOLD responses. By our modelling approach we can describe interactions in 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). We have extended the mathematical BOLD model to include 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 (Sten et al., 2021). Future research aims at mechanistic modelling of cognitive networks. In parallel with mechanistic mathematical modelling, we also work with cognitive network modelling using standard methods. We have recently shown that the relation between perceived fatigue (extreme tiredness) and brain connectivity differs between patients with irritable bowel syndrome (IBS) and healthy subjects (Fig. 1).

We are presently developing a medical technology device for CVR measurements by hypercapnia challenge i.e., induction of changes in cerebral blood flow by CO2 administration. The aim is to enable CVR measurements in patients with subarachnoidal haemorrhage at risk of cerebral vasospasm. A pilot study on a healthy subject show promising result (Fig. 2) and regulatory work is progressing. Future research aims to develop a mechanistic model that describes changes in BOLD responses to hypercapnia challenge.

MRI | Neurology | Acquisition | Modeling | AI/Data analytics | Visualization | 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

MAIN PROJECT PARTICIPANTS

Gustav Magnusson, Gunnar Cedersund, Henrik Podéus, Nicolas Sundqvist, Charalampos Georgiopoulos, Lovisa Tobiesson

GRANTS

Swedish research council (2019 - 2022)
Swedish Brain Foundation (2022 - 2023)

KEY PUBLICATIONS

Sebastian Sten, Gunnar Cedersund, Fredrik Elinder, Maria Engström. A quantitative analysis of cell-specific contributions and the role of anesthetics to the neurovascular coupling. NeuroImage, 2020; 215:116827.

Sebastian Sten, Henrik Podéus, Nicolas Sundqvist, Fredrik Elinder, Maria Engström, Gunnar Cedersund. A multi-data based quantitative model for the neurovascular coupling in the brain. BioRxiv, 2021. doi: https://doi.org/10.1101/2021.03.25.437053.

Anna-Karin Norlin, Susanna Walter, Adriane Icenhour, Åsa V Keita, Sigrid Elsenbruch, Olga Bednarska, Michael P. Jones, Rozalyn Simon, Maria Engström. Fatigue in Irritable bowel syndrome is associated with plasma levels of TNF-α and mesocorticolimbic connectivity. Brain Behavior and Immunity. 2021; 92: 211-220.

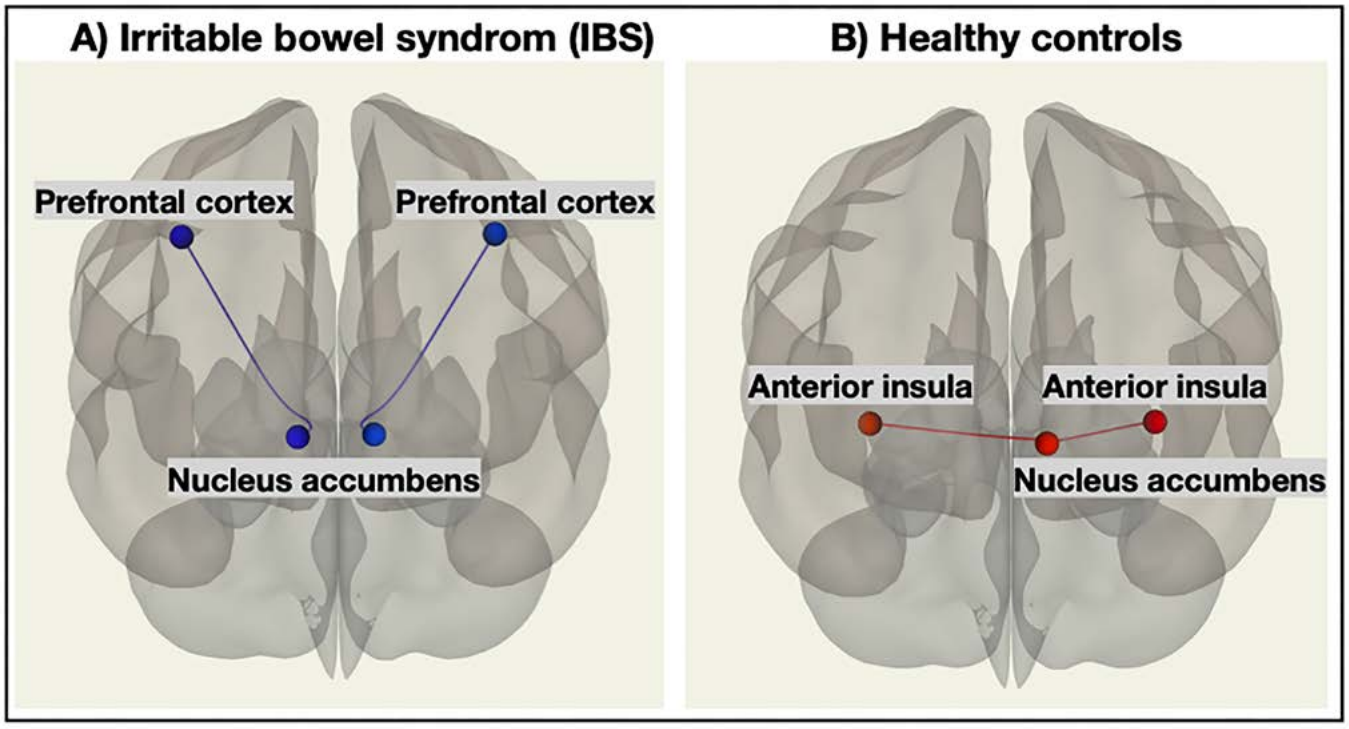


Figure 1. Different functional connectivity related to perceived fatigue in A) irritable bowel syndrome (IBS) and B) healthy controls.

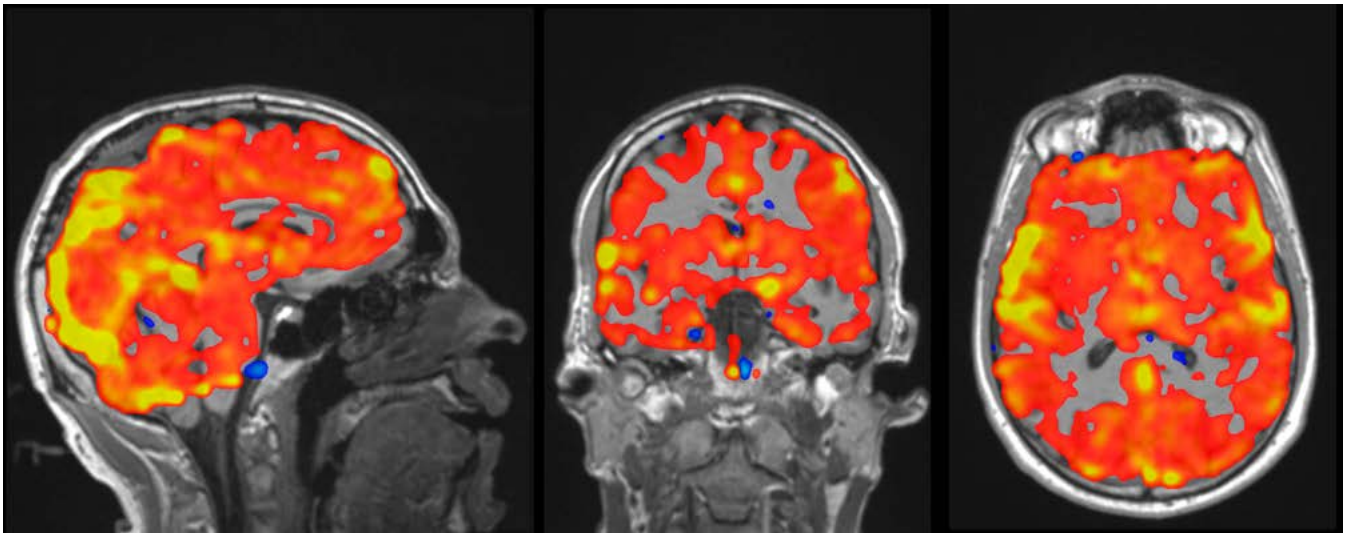


Figure 2. Cerebrovascular reactivity (CVR) at hypercapnia challenge in healthy subject.

POPULAR SCIENTIFIC SUMMARY
Marcel Warntjes

High Resolution MR Quantification in 3D

Magnetic Resonance Images are very sensitive to tissue differences and a high contrast is achieved between various tissue types and pathology. MRI is, however, a qualitative method, where images must be subjectively interpreted by a radiologist. Typically, no values are given, for example for absolute tissue properties or for tissue volumes. At CMIV a method was developed to measure physical properties for MRI, to provide numbers and statistics of a patient rather than user-dependent interpretation. The acquisition, called QALAS, is a 3D method providing similar high resolution in all directions. The scan time for the 3D sequence is about 6 minutes, measuring the most important characteristics for MRI: the R1 relaxation rate (1/T1), the R2 relaxation rate (1/T2) 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.

There are commercially available software products that can automatically segment the brain into smaller brain structures. The volumes, and the change of these volumes over time, can be used to monitor a patient with a neurodegenerative disease. A question was whether the synthetic images based on MR quantification were appropriate as input data to these programs and would render similar results as conventional images as input. If this were the case, there would no longer be a need for scanning the conventional acquisitions which are dedicated for brain segmentation, saving valuable examination time. A study was conducted where the repeatability and reproducibility of conventional and synthetic images was evaluated on NeuroQuant, a program providing a segmentation of 12 brain structures. The study showed both input data provided similar precision although some bias was detected between the methods.

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.

MRI | Other | Neurology | Oncology | Acquisition | Modeling | Visualization | Simulation | Imaging Biomarkers

Project information

PROJECT NAME

High Resolution MR Quantification in 3D

PROJECT LEADER

Marcel Warntjes, Department of Medical and Health Sciences, Division of Cardiovascular Medicine

MAIN PROJECT PARTICIPANTS

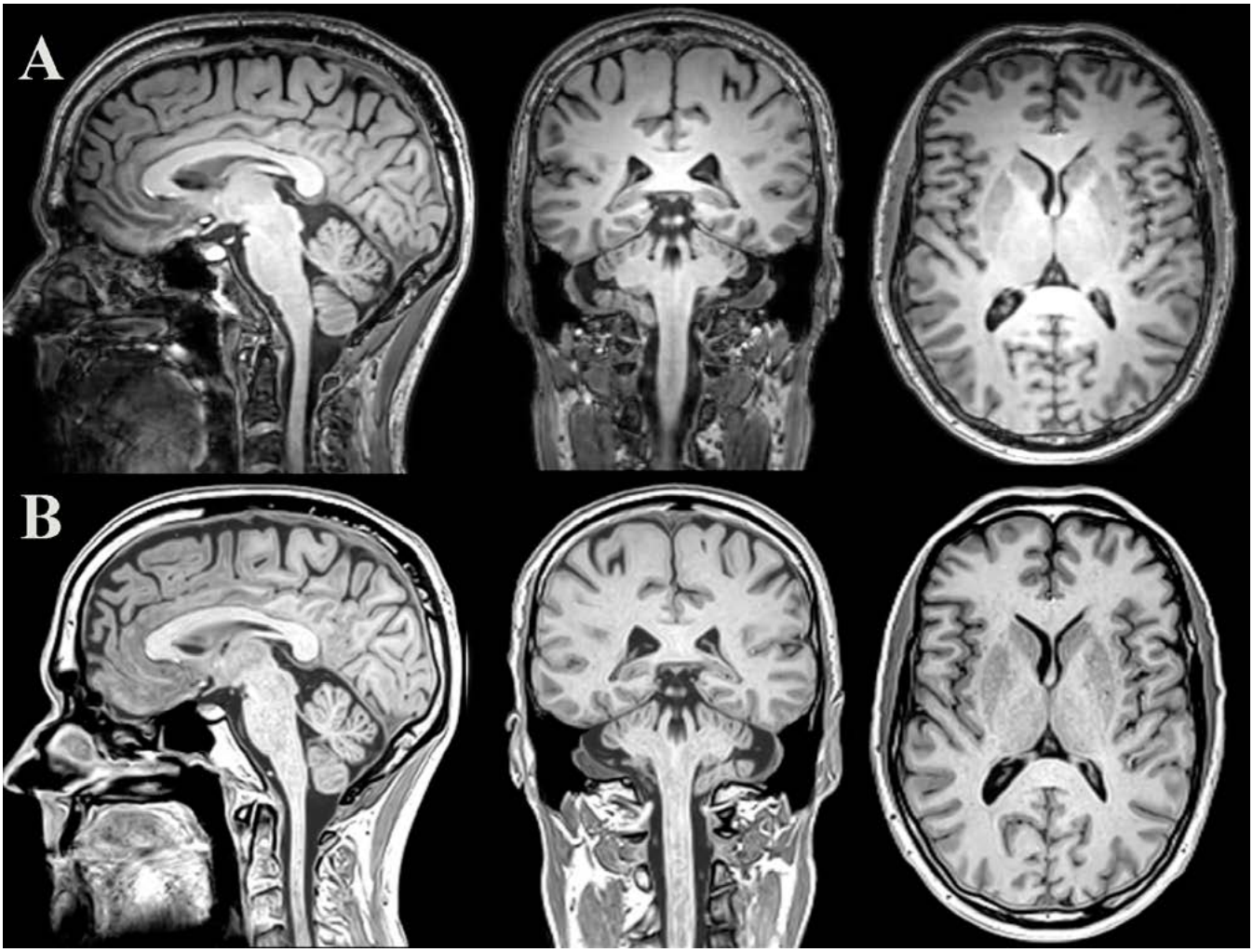
Ida Blystad, Peter Lundberg, Anders Tisell, Peter Johansson, Catharina Petersen, Johanna Alfredsson, Anette Karlsson, Ken Hwang, Borjan Gagoski, Shohei Fujita

KEY PUBLICATIONS

Kvernby S, Warntjes M, Haraldsson H et al. Simultaneous three-dimensional myocardial T1 and T2 mapping in one breath hold with 3D-QALAS. Cardiovasc Magn Reason 2014;16:102. DOI: 10.1186/s12968-014-0102-0.

Fujita S, Hagiwara A, Hori M et al. Three-dimensional high-resolution simultaneous quantitative mapping of the whole brain with 3D-QALAS: An accuracy and repeatability study. Magn Reson Imaging 2019;63:235-243. DOI: 10.1016/j.mri.2019.08.031.

Fujita S, Yokoyama K, Hagiwara A et al. 3D Quantitative Synthetic MRI in the Evaluation of Multiple Sclerosis Lesions. AJNR Am J Neuroradiol 2021;42:471-478. DOI: 10.3174/ajnr.A6930.



An example of conventional (A) and synthetic (B) 3D-T1W images in a sagittal, coronal and axial reformat. Both acquisitions have a scan time of 6:10 minutes. The study showed that for brain structure volume detection it does not matter whether the input image data is conventional or synthetic.

POPULAR SCIENTIFIC SUMMARY
Markus Heilig

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 light and heavy social drinkers (N=60 in total). In order to assess the behavioral mechanisms, a behavioral study preceeded the currently presented sutdy in the magnetic resonance imaging (MRI) scanner. The results from the behavioral study are presented in Figure 1 and Figure 2. We used the "Concurrent Choice Alcohol Food (CCAF)" task, a novel task modified from Hogarth et al. 2018, to investigate the decision-making process behind choosing between two mutually exclusive alternative rewards presented concurrently (Figure 1, left). In the behavioral study, we found that drinking habits and the value of the alternative reward shape choice preference for alcohol-related stimuli. While heavy drinkers chose alcohol more, in both groups choice preference for alcohol was reduced when the alternative reward had greater value (Figure 1, right). 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 female 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. In the behavioral study, we did not observe a negative social bias in heavy social drinkers. However, and only in heavy drinkers, we found that alcohol use severity, measured with the Alcohol Use Disorders Identification Test (AUDIT), predicted negative feedback towards others. This finding suggests that social behaviour can be affected negatively at early stages of harmful alcohol use. The study in the MRI scanner is ongoing and data collection is planned to be completed by the end of 2022.

MRI Neurology No Method Development

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, María del Carmen Cortes Molina

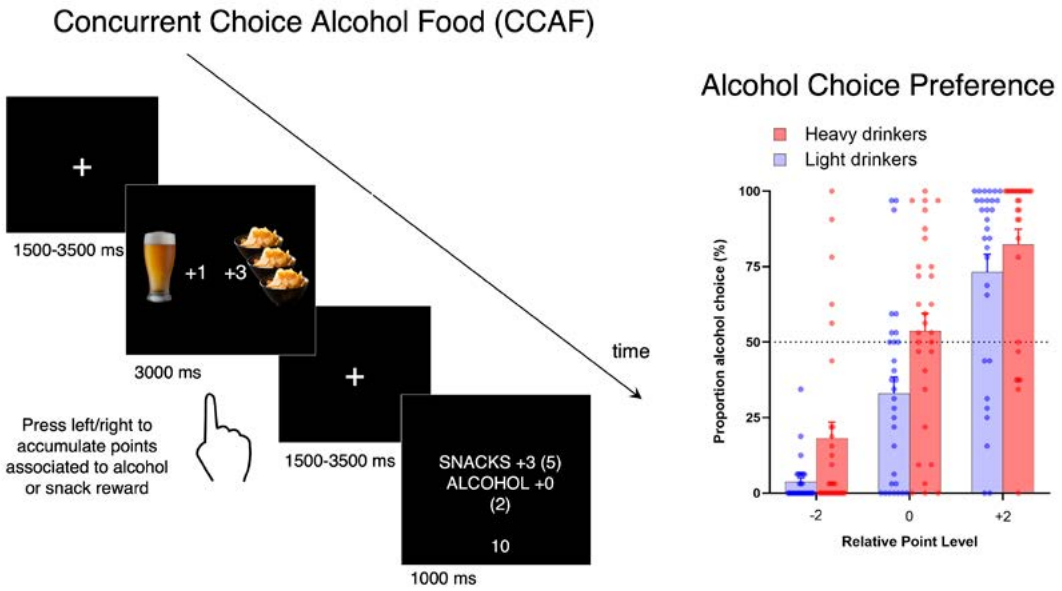


Figure 1. **Left.** Concurrent Choice Alcohol Food (CCAF) task design. In this task, participants were instructed to accumulate points associated with alcohol or snacks, which could then be redeemed at the end of the ression with the respective reward. Each alcohol and snack picture were associated to either 1 or 3 points, shown on the side of the picture, creating three relative point levels. When both pictures were associated with either 1 or 3 points, then the relative point levels were equal (0). When the relative point level changed it could be in favor of alcohol (+2) or snacks (-2).
Right. The percentage of trials on which alcohol was chosen (y-axis) is shown according to the relative point level (x-axis: -2, 0 or +2), for both heavy (red) and light (blue) drinkers. Bar charts showing increased percentage of alcohol choice in heavy drinkers ($F_{2,56}$ = 8.07, p = 0.06, ηp^2 = 0.7). In both groups, increased choice preference for alcohol was observed when relative point level was in favor or alcohol ($F_{2,112}$ = 124.4, p < 0.001, ηp^2 = 0.7).

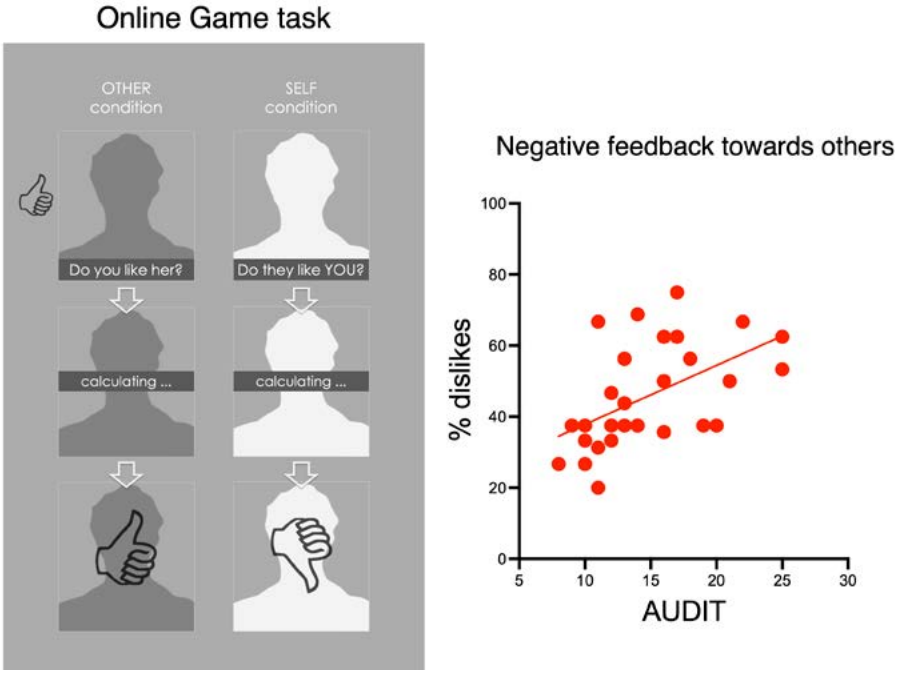


Figure 2. **Left.** Online game task design. Participants engaged in a simulated online game in which they decided and indicated whether they liked or disliked pictures of other adolescents. Similarly, other putative players also judged the participants' pictures. The pictures consisted of neutral frontal face photos. Each trial of this rapid event-related design consisted of three epochs: the question phase, the anticipation phase and the outcome phase (Perini et al. 2018 Sci Rep, 2019 BP:CNNI).
Right. Alcohol use disorder severity predicted negative feedback towards other players (β = 1.66, t = 3.19, p < 0.004).

POPULAR SCIENTIFIC SUMMARY
Anders Eklund, Evren Özarslan

ASSIST

Swedish healthcare is facing major challenges in the coming years. One in three people in Sweden will get cancer at some point in their lives, and many of them will receive radiation therapy. Due to the recent pandemic, a large health care debt has accumulated. In the coming years, Swedish healthcare must handle this debt, while performing regular care. This challenge can be addressed only through more efficient planning and treatment strategies.

In the ASSIST project, the main goal is to boost efficiency of healthcare, by taking advantage of the advances made in deep learning, wherein a computer is trained to perform various tasks. Radiation therapy is an effective treatment method for tumours, complementing surgery and chemotherapy. However, radiation therapy demands time-consuming preparations that involve acquisition of medical images, segmenting the tumour and risk organs, and developing a treatment plan for treating as much of the tumour as possible without harming healthy tissue. Deep learning can be used in all these steps, to shorten the time for planning, which leads to increased patient throughput and shorter queues.

To determine the most effective treatment plan for tumour patients, there is pressing need for observations sensitive to small-scale changes within the brain. In the ASSIST project, we develop models and data analysis techniques for advanced magnetic resonance imaging (MRI) for delineating the tumour border accurately, thereby aiding the deep learning algorithms to be employed for treatment planning.

A general problem with deep learning for medical images is access to training data, which is complicated by GDPR and ethical rules. In ASSIST, we develop methods for so-called 'federated learning,' wherein computers can be trained without sending medical images between hospitals. We also develop methods to create realistic synthetic medical images, see the figure below, which can be shared freely because they do not belong to a specific patient.

MRI | Neurology | Oncology | Acquisition | Modeling | AI/Data analytics | Imaging Biomarkers

Project information

PROJECT NAME

Automation, Surgery Support and Intuitive 3D Visualization to Optimize Workflow in Image Guided Therapy Systems

PROJECT LEADERS

Anders Eklund, Evren Özarslan, Department of Biomedical Engineering, Division of Biomedical Engineering

MAIN PROJECT PARTICIPANTS

Ida Blystad, Deneb Boito, David Abramian, Iulian Emil Tampu, Muhammad Usman Akbar, Neda Haj-Hosseini, Magnus Herberthson

GRANTS

VINNOVA (2021 - 2024)

KEY PUBLICATIONS

Tampu, I. E., Blystad, I., Haj-Hosseini, N., Eklund, A., Deep learning-based brain tumor segmentation using quantitative MRI, ISMRM, 2022.

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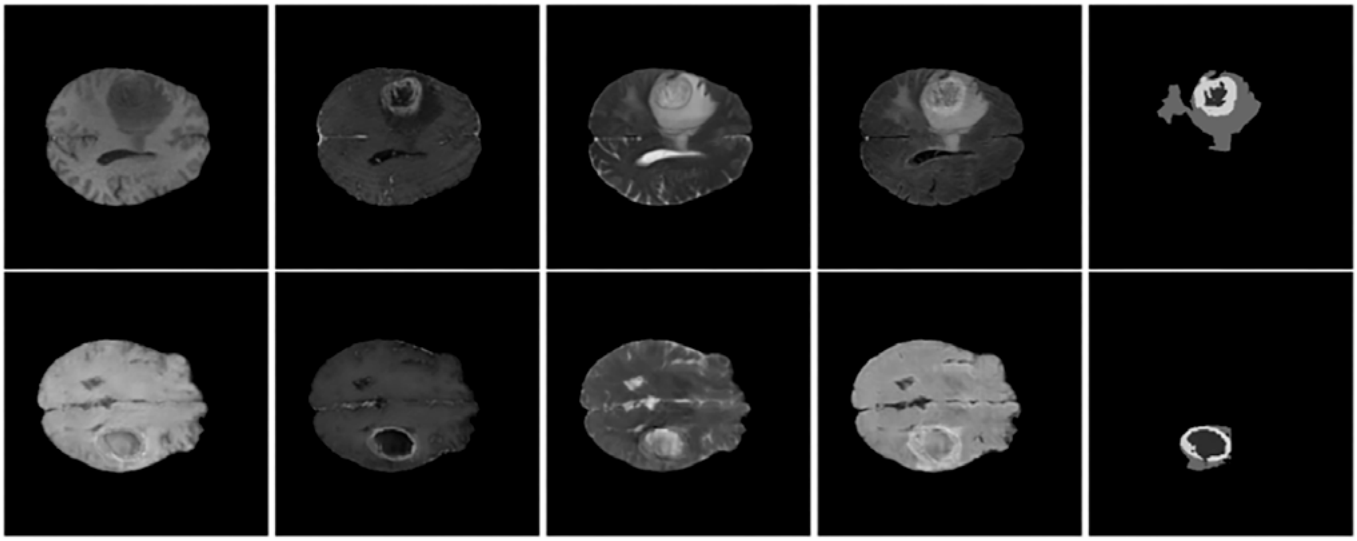
Afzali M, Pieciak T, Jones DK, Schneider JE, Özarslan E. Cumulant expansion with localization: A new representation of the diffusion MRI signal. Front Neuroimaging, 2022; 1:958660.

Boito D, Yolcu C, Özarslan E. Multidimensional diffusion MRI methods with confined subdomains. Front Phys, 2022; 10:830274.



Top row: a real 5-channel image. Bottom row: a synthetic 5-channel image generated by a generative adversarial network (GAN). From left to right: T1-weighted MR image, T1-weighted MR image after gadolinium contrast, T2-weighted MR image, FLAIR MR image, segmentation mask representing different parts of the brain tumor.

POPULAR SCIENTIFIC SUMMARY
Peter Lundberg

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 functions, 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

Peter Lundberg, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS

Anders Tisell, Ida Blystad, Per Thunberg, Karin Åberg, Göran Lidén, Karine Elihn, Gunilla Wastensson, Bernt Bergström, Louise Fornander, Göte Mölleby

GRANTS

FORTE

Welding in progress.

POPULAR SCIENTIFIC SUMMARY
Hans Lindehammar

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

Hans Lindehammar, Department of Clinical Neurophysiology, University Hospital Linköping

MAIN PROJECT PARTICIPANTS

Helena Gauffin, Mats Svantesson, Paul Hamilton, Katarina Henell Eklund

GRANTS

Sinnescentrum, Region Östergötland
Föreningen Margarethahemmet

KEY PUBLICATIONS

Contribution of EEG/fMRI to the definition of the epileptic focus. Pittau F, Dubeau F, Gotman J. Neurology 2012;78:1479-1487.

The hemodynamic response to interictal epileptic discharges localizes the seizure-onset zone. Khoo HM, Hao Y, von Ellenrieder N et al. Epilepsia 2017;58(5):811-823.

Clinical benefit of presurgical EEG-fMRI in difficult-to -localize focal epilepsy: A single-institution retrospective review. Kowalczyk MA, Omidvarnia A, Abbott DF et al. Epilepsia 2020;61:49-60.

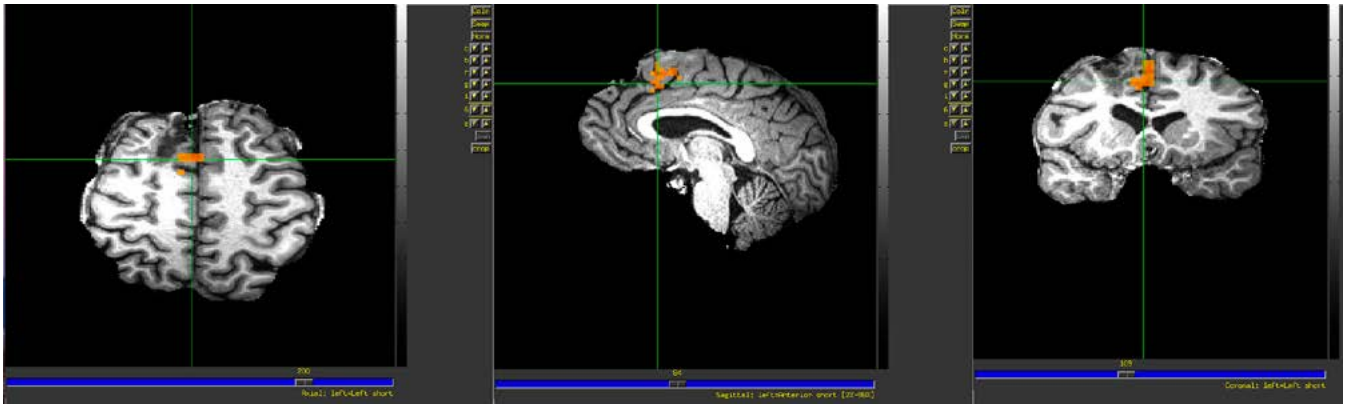


Figure 1. The most significant BOLD-changes correlated to epileptiform activity in a patient with epilepsy that was earlier operated for focal cortical dysplasia in the left frontal lobe.

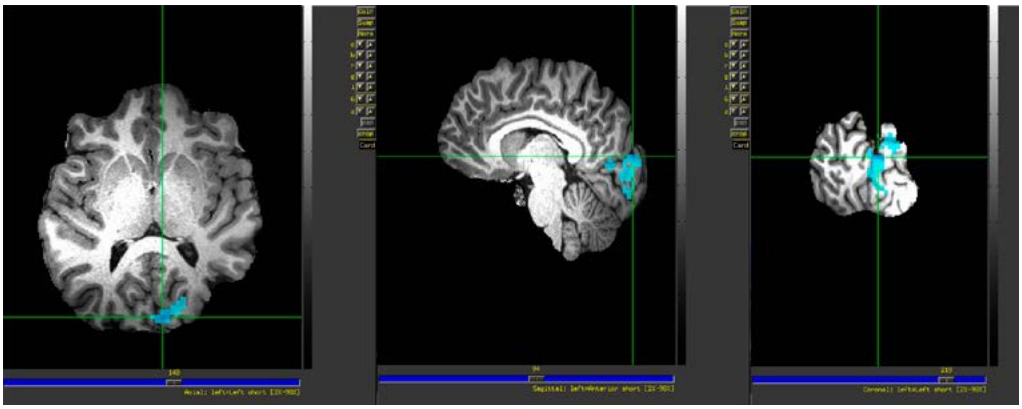


Figure 2. The most significant BOLD-changes correlated to epileptiform activity in a patient with epilepsy that was earlier operated for focal cortical dysplasia in the right occipital lobe.

Image 1. Patient and nurses by the MR scanner.

POPULAR SCIENTIFIC SUMMARY
Anders Tisell

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

Anders Tisell, Department of Health, Medicine and Caring Sciences. Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS

Peter Lundberg, Ida Blystad, Maria Kristoffersen Wiberg, Annika Malmström, Anna Ljusberg, Faris Durmo, Pia Sundgren and Linda Knutsson

GRANTS

Liu Cancer
ALF
RFoU
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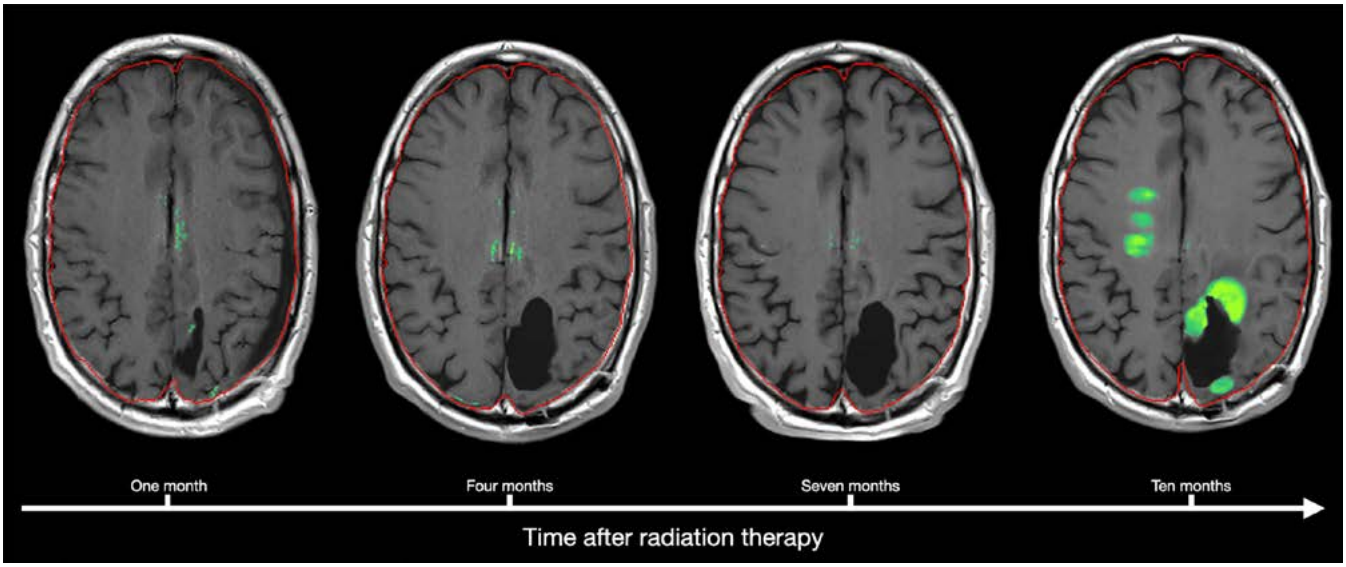
KEY PUBLICATIONS

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.

Blystad I, Warntjes JBM, Smedby Ö, Lundberg P, Larsson E-M, Tisell A (2017) Quantitative MRI for Analysis of Peritumoral Edema in Malignant Gliomas, PLoS ONE, 2017 May 23;12(5):e0177135. doi: 10.1371/journal.pone.0177135. eCollection 2017. PMID: 28542553.

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.



Example patient with tumor reoccurrence. Synthetic T1w images post contrast injection at four different time points after radiation therapy with concomitant temozolomide. A mask of automatic detection of contrast enhancement from the qMIR data is shown in green overlay.

POPULAR SCIENTIFIC SUMMARY
Anders Tisell

SESNIC

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 advocates 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

PROJECT LEADER

Anders Tisell, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS

Johan Mellergård, Peter Lundberg, Jan Ernerudh, Ida Blystad, Magnus Vrethem, Jonas Lind, Maria Kristoffersen Wiberg, Marcel Warntjes, Kristina Söderberg, Azad Mohammad and Anna Eklund

GRANTS

Swedish Research Council
FORSS
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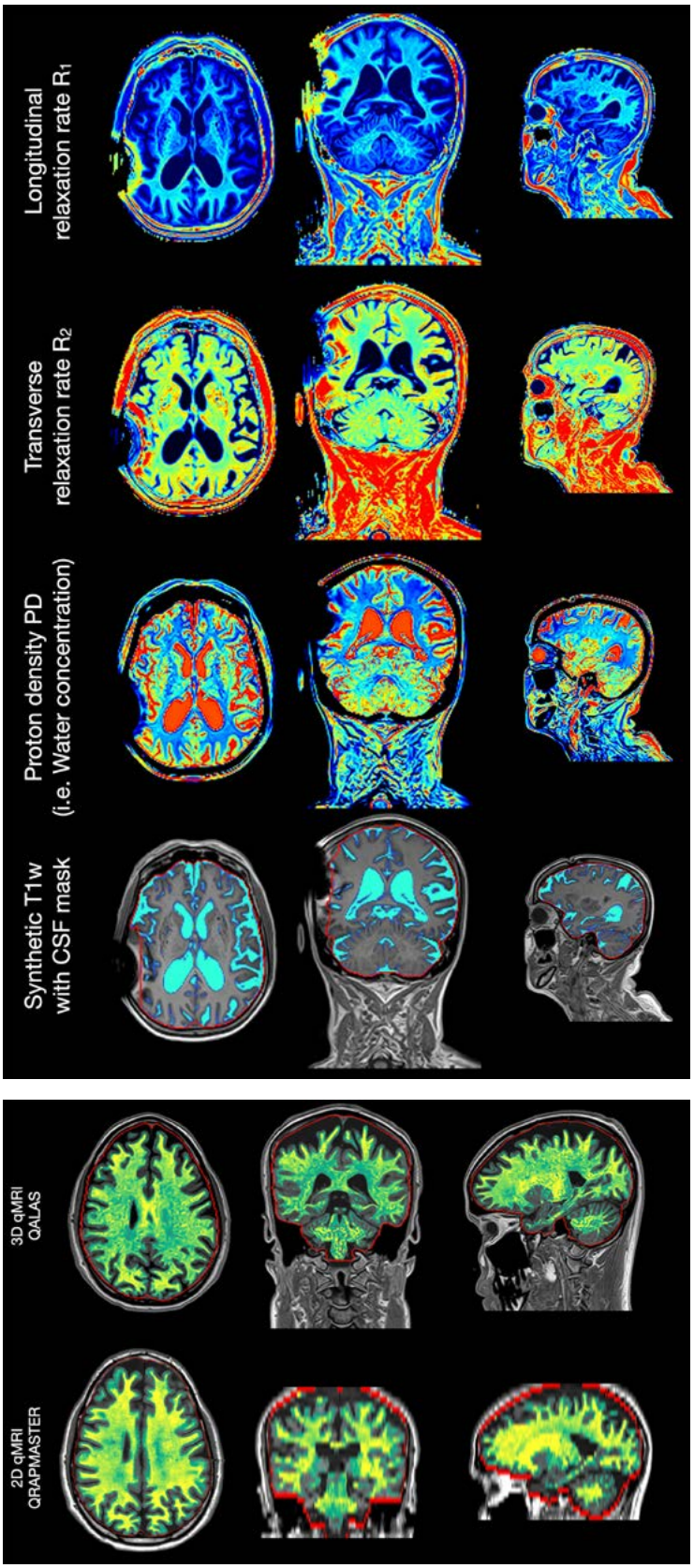
KEY PUBLICATIONS

Max Borgström, Anders Tisell, Hans Link, Elisabeth Wilhelm, Peter Lundberg, Yumin Huang-Link "Retinal Thinning and Brain Atrophy in Early MS and CIS" Acta Neurol Scand. 2020;10.1111/ane.13282.

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.

Mellergård J, Tisell A, Blystad I, Gronqvist A, Blennow K, Olsson B, Dahle C, Vrethem M, Lundberg P, Ernerudh J (2017) Cerebrospinal fluid levels of neurofilament and tau correlate with brain atrophy in natalizumab-treated multiple sclerosis. Eur J Neurol 24: 112-121.



Comparison of 2D and 3D qMRI. The example is synthetic T1w with estimated myelin concentration showed as a green/yellow overlay of a 32 years old MS patient.

POPULAR SCIENTIFIC SUMMARY
Anders Tisell

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 AI/Data analytics

Project information

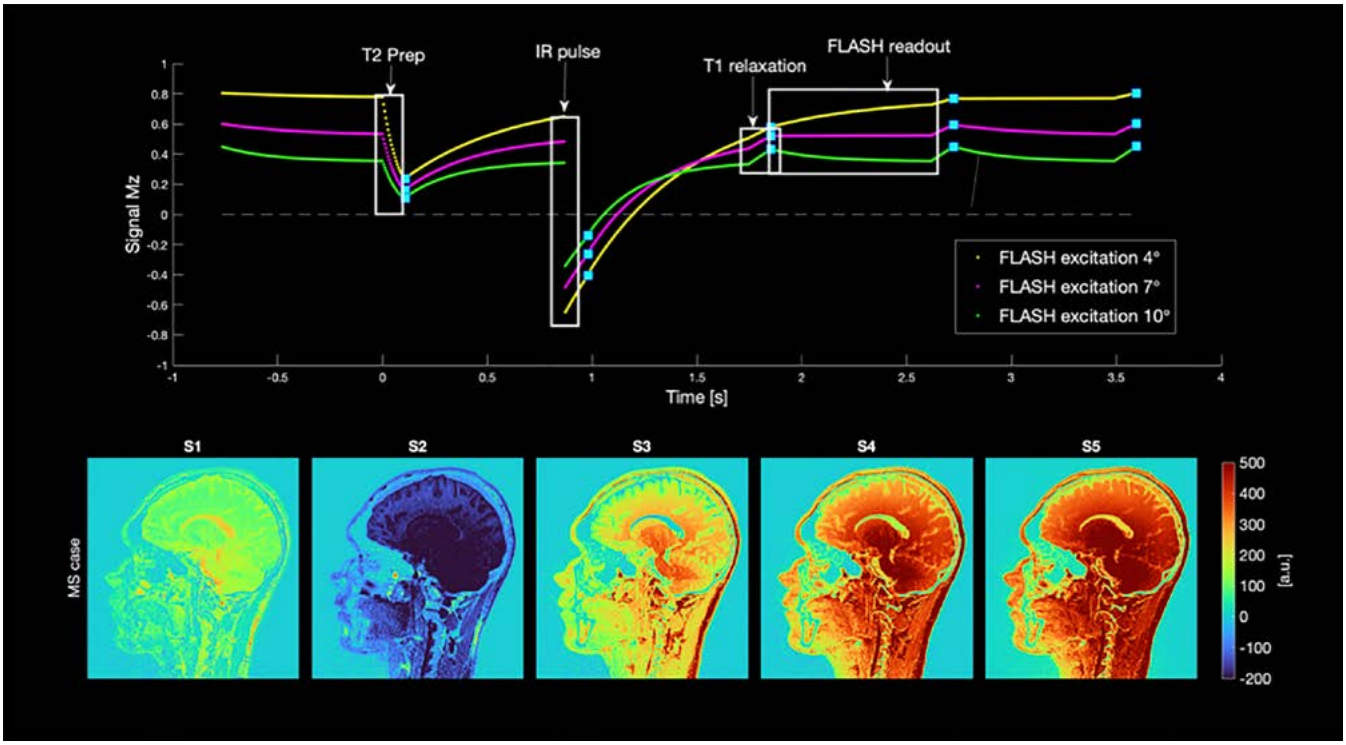
PROJECT NAME
Implementing QALAS on Siemens

PROJECT LEADER
Anders Tisell, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine

MAIN PROJECT PARTICIPANTS
Peter Lundberg, Frederik Testud, Marcel Wrantjes, Aditya Tejaswi

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.



3D qMRI images from a 6 min scan of an idiopathic hydrocephalus patients that had undergone shunt surgery. Quantitative maps of R1, R2 and PD in the top three rows and synthetic T1w images with CSF mask in blue overlay in the bottom row. The artefact for the magnetic valve in the shunt system is local and limited to ca 2 cm.

Anders Persson, Anders Eklund, Mona Cederholm, Catrin Nejdeby, Peter Lundberg, Mattias Ekstedt, Eva Klintström, Tino Ebbers and Håkan Gustafsson.

Kick-off – Research School and Scientific Council

As previous years except from the pandemic year we had a kick-off for the research school, the scientific council together with the management group. Two days well spent.

Every autumn the scientific council has a kick-off retreat together with the research school and the management group. This is an occasion to meet and have some free time together, which often is the most important time and often results in new collaborations in various research areas.

This year we spent two days in Vadstena. Among others, the PhD students gave presentation pitches to the council of their different research projects and the scientific council had time to discuss future strategies of CMIV.

The research school had some time spent on their own with team building activities focusing on the senses and they also had a seminar on graphical abstracts and how to improve these.

All in all, two days well spent.

Team building activity with the research school.

PhD student presentations to the research school and research council.

Lunch together.

Team building activity.

Peter Lundberg, Milda Pocevičiūtė, Iulian Emil Tampu, Håkan Gustafsson, Anna Ljusberg, Deneb Boito, Sophia Bäck, Gustav Magnusson.

Milda Pocevičiūtė, Sohaib Ayaz Qazi, Shan Cai, Marjan Firouznia, Chiara Trenti, Iulian Emil Tampu, Federica Viola in Wranne theater.

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 35 PhD students of 10 different nationalities admitted to the research school. Here a selection of them presents their research.

David Abramian

fMRI Methods for Brain Tumour Treatment

Primary brain tumors account for 2% of new cancer diagnoses, with some 300,000 new cases globally each year. Although not the most prevalent cancer type, they require challenging treatment procedures, and, if malignant, have a poor prognosis.

Stereotactic radiosurgery (SRS) is increasingly being considered as a suitable treatment option for achieving tumor control of small brain tumors. Unlike surgical resection, where the skull is opened and the tumor tissue cut out, SRS allows tumors to be removed non-invasively. This is achieved by precisely focusing multiple beams of radiation inside the skull, delivering a high radiation dose to a well-delimited region, where the target tissue is destroyed.

Although SRS can be performed with great spatial precision, it is unavoidable to deliver some radiation to the healthy parts of the brain. It is therefore essential to minimize the radiation dose delivered to any regions of the brain that could cause a functional deficit to the patient. While it is common to consider risk organs that can be visually identified, such as the optic nerve and cochlea, it is rare to also consider the eloquent regions of the brain, responsible for sensory, motor, and linguistic abilities, as they cannot be readily identified from the anatomical images typically acquired for SRS.

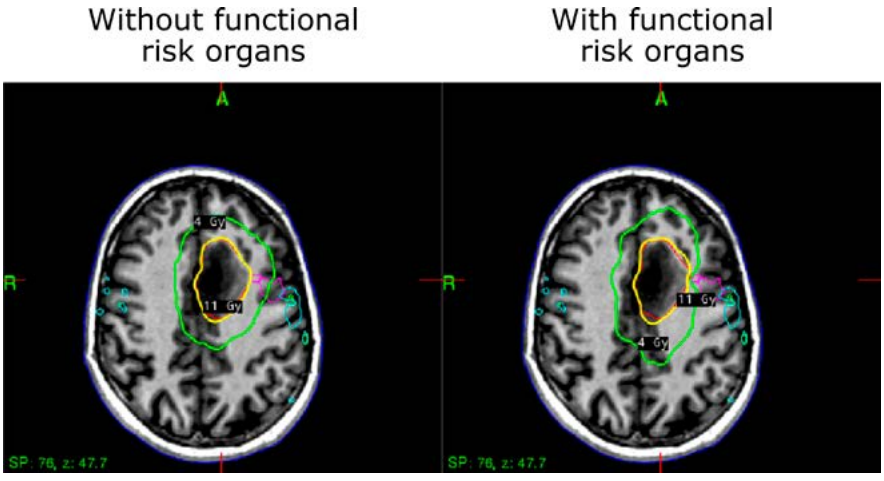
In this project, in collaboration with pioneering SRS company Elekta, we have developed a procedure for considering such functional risk organs in SRS treatment planning. We used functional MRI data, an MRI modality used to map the functional regions of the brain, to identify the motor and speech areas of patients, and loaded these onto Elekta's treatment planning software. Using Elekta's automatic treatment optimization software, we showed that the inclusion of functional risk organs can substantially reduce the radiation dose to the eloquent brain regions, and thus minimize the risk of future functional deficits for the patients.

PROJECT INFORMATION

Project
Methods for Analyzing fMRI 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.



Example treatment plans not considering (left) and considering (right) functional risk organs. In both cases the region receiving the prescribed radiation dose (thick yellow line) closely conforms to the tumor (thin red line). However, in the former case, there is also a high radiation dose (thick green line) delivered to an eloquent brain region (thin magenta line). In the latter case, the radiation dose is shaped to avoid the eloquent brain region. Other eloquent brain regions (thin green and cyan contours) are far from the tumor, and thus do not receive a high radiation dose.

Wolf Claus Bartholomä

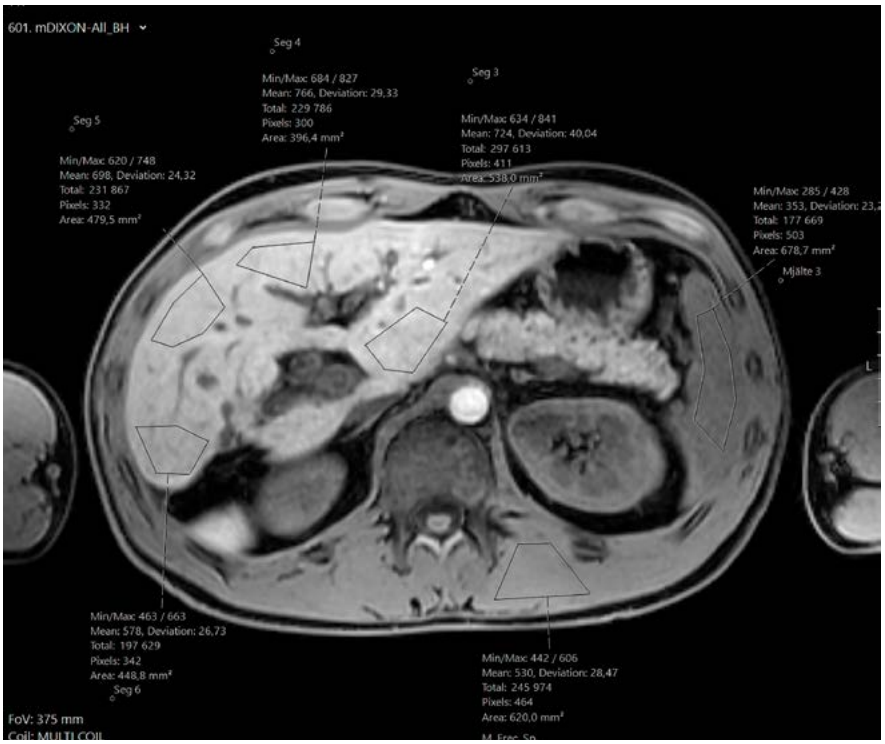
Nordic Post Hepatectomy Liver Failure (PHLF) Study

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 who usually have an otherwise healthy liver), as well as patients with hepatocellular cancer and biliary cancer, who usually have diffuse liver disease (HCC) or very heterogenous liver parenchyma due to biliary disease (biliary cancer). However, these studies have been quite limited in the number of included patients, averaging around 70 individuals.

Our PHLF study, internally called LIFE2, is a retrospective Nordic multicenter study where CMIV and Linköping University Hospital are cooperating with hospitals in Stockholm, Göteborg, Uppsala, Copenhagen, Umeå 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 392 patients who underwent hepatectomy – some with verified posthepatectomy liver failure, some without. It is our 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 than a small population from a single national liver center. This can help optimizing liver surgery and preoperative planning to help further reduce live threatening complications caused by posthepatectomy liver failure.



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

PROJECT INFORMATION

Project

Nordic Post Hepatectomy Liver Failure (PHLF) Study

Supervisors

Peter Lundberg, Nils Dahlström, Mischa 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.

Ann-Sofi Björkman

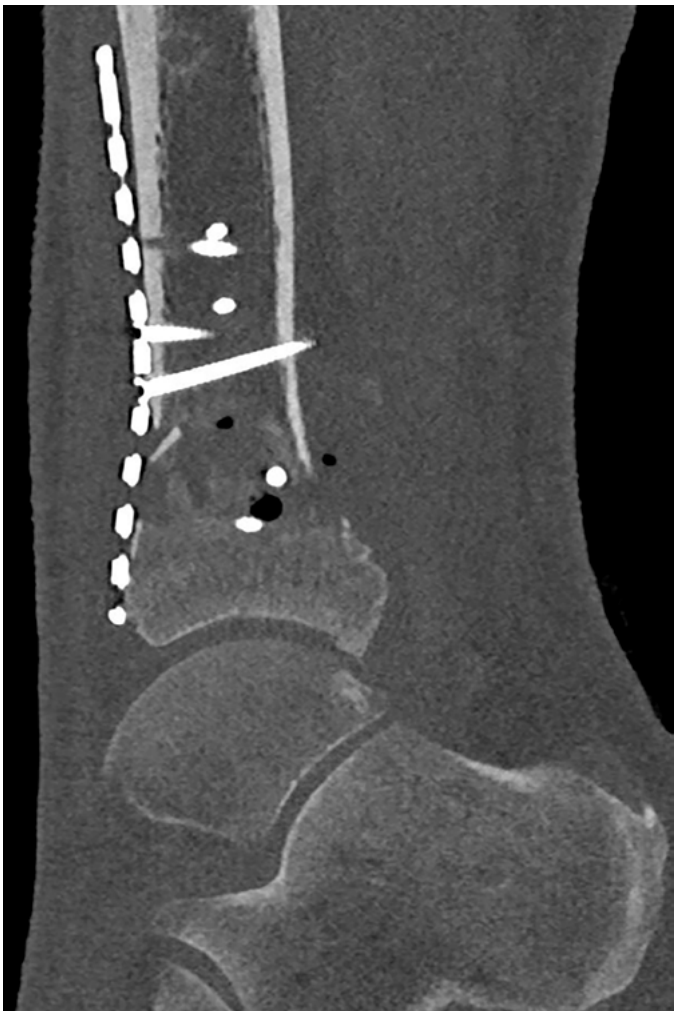
Spectral CT for the Musculoskeletal System

Imaging of musculoskeletal tissues such as bones, joints and soft tissue can be done with different techniques. Magnetic resonance imaging (MRI) is good at visualizing soft tissues such as muscles and ligaments but is time consuming and unsuitable for some patients. Computer tomography (CT) is good at fracture detection, fast, widely available, and suitable for almost all patients but the visualization of soft tissues is limited. Recent technical developments within the field of computer tomography, the photon counting detector CT (PCD-CT), might improve image quality and for some patients replace the need of an MRI examination.

In the PCD-CT, x-ray photons are directly converted to an electrical signal and counted, in contrast to the conventional detector where photons are first converted to visible light before generating the electrical signal. This increases the spatial resolution, reduces image noise, and makes it possible to reduce the radiation dose. Also, the PCD-CT has the potential to discriminate different types of tissues as well as to remove certain elements from the image, such as calcium in bone, to visualize previously hidden information. Further, some evidence suggest that it might improve imaging of body parts with metal implants such as orthopedic plates and screws.

Metal cause artifacts that are seen as bright and dark streaks in the image. These artifacts can obscure important structures and degrade image quality significantly.

In the FORT study patients with fractures to the knee or ankle that require surgery with metal plates and screws are imaged in the PCD-CT in addition to the conventional CT examination performed after surgery. The aim is to find the best settings for the PCD-CT to reduce metal artifacts and provide better image quality when visualizing bone, the joint surface, soft tissues and the placement of the metal plate and screws as well as to compare it to the conventional CT.



An example of a fractured ankle, that has been repaired with a metal plate and screws, imaged in the photon counting detector CT (PCD-CT).

PROJECT INFORMATION

Project
Spectral CT for the Musculoskeletal System

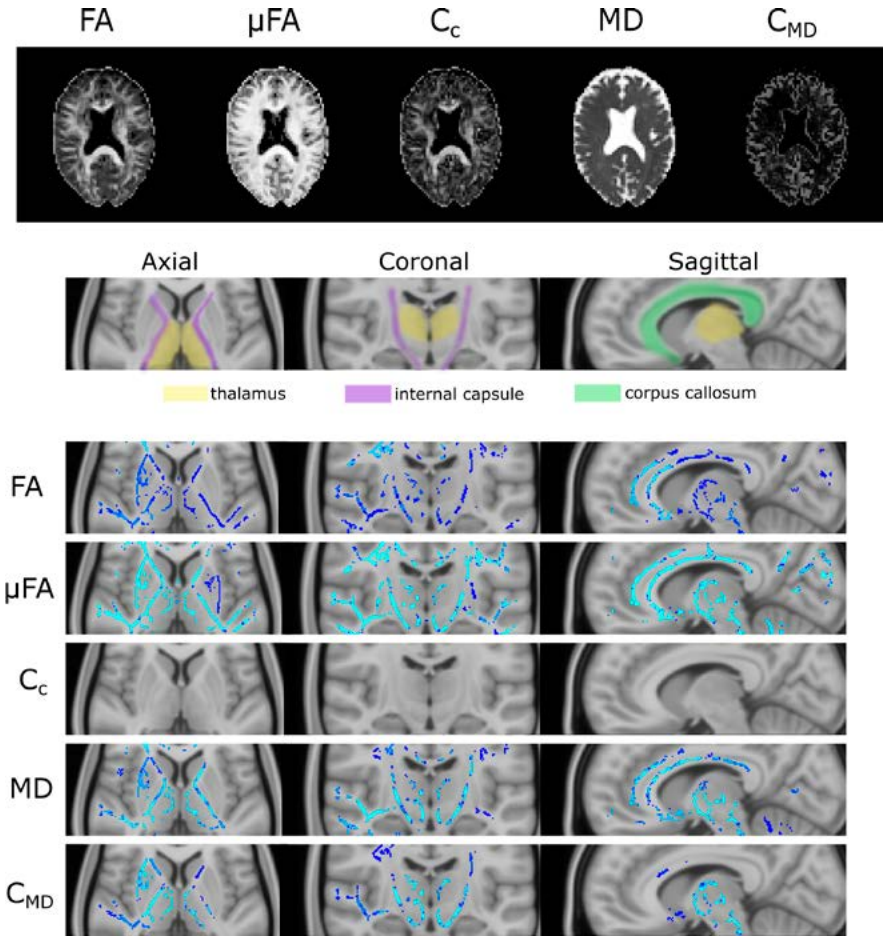
Supervisors
Anders Persson, Seppo K Koskinen, Håkan Gauffin, Alexandr Malusek

Short CV
Doctor of Medicine (MD), Linköping University, 2010.
Resident in Radiology, Radiology Department at Linköping University Hospital 2012–2020.
Radiologist, Radiology Department at Linköping University Hospital 2020–.
PhD student 2020–.

Deneb Boito

Neural Tissue Composition via Diffusion MRI

Diffusion MRI is an imaging technique that allows the study of heterogenous 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 have led to the development of new methods. These are 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. Recently, we developed an estimation framework in which positivity constraints are enforced. This increases the reliability and robustness of the metrics obtained with such method thus facilitating its translation into clinical practice. The top row of the figure contains examples of the different metrics relating to different features of the tissue microstructure obtainable with said method. The bottom part of the figure shows an example application of how, by employing these metrics, it is possible to detect microstructural changes in the brain white matter of patients previously hospitalized for Covid-19 infection.



The figure shows on top several maps relating to different features (voxel (FA) and cellular (μFA) level anisotropy, cells' orientation coherence (Cc), voxel average diffusivity rate (MD), and variation in cells' sizes (CMD)) of the tissue microstructure. On the bottom, the figure shows the locations in the blue-light blue voxels where changes in the brain white matter microstructure could be detected through the metrics obtained employing this diffusion MRI method.

PROJECT INFORMATION

Project

Unraveling the intravoxel neural tissue composition using advanced diffusion MRI

Supervisors

Evren Özarslan, Ida Blystad, Anders Eklund, Magnus Herberthson

Short CV

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

Sophia Bäck

Blood Flow and Stasis in Atrial Fibrillation

Arial 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.

In the current study of the project, we calculated how long blood stays inside the left atrium in patients diagnosed with atrial fibrillations and patients without atrial fibrillation. We did this by extracting the motion of the blood from time resolved cardiac CT and using this motion as a boundary condition in computational fluid dynamics simulations.

We found that the average time blood stays inside the left atrium was less than one cardiac cycle for the participants without atrial fibrillation. For most AF patients, blood stayed more than one cardiac cycle in the atrium. We could also confirm that the LAA is the region in the atrium where blood stays the longest. One reason why blood stays longer in the atrium could be that the atria of the AF patients were larger.

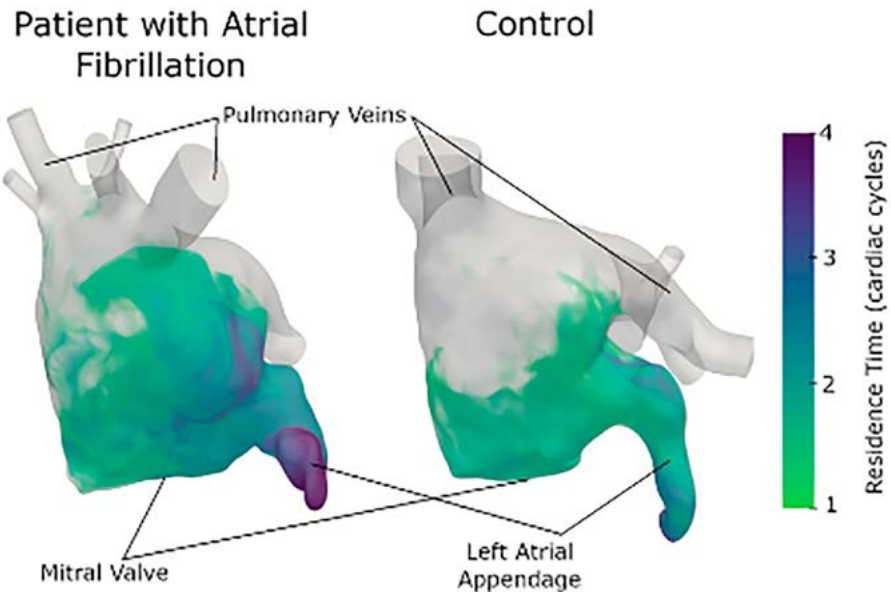
In the future, this technique could support treatment decisions in AF patients by giving more insights on the patient specific risk of stroke based on the individual blood flow in the left atrium.

PROJECT INFORMATION

Project
Assessment of Blood Flow and Stasis in Atrial Fibrillation

Supervisors
Tino Ebbers, Jonas Lantz, Carl-Johan Carlhäll, Anders Persson

Short CV
Chair of CMIV research school, January 2021–June 2022.
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.



3D visualization of left atrium of a Patient with atrial fibrillation (right) and a control (left). Green and blue colored areas indicate that blood has stayed for more than one cardiac cycle.

André Da Luz Moreira

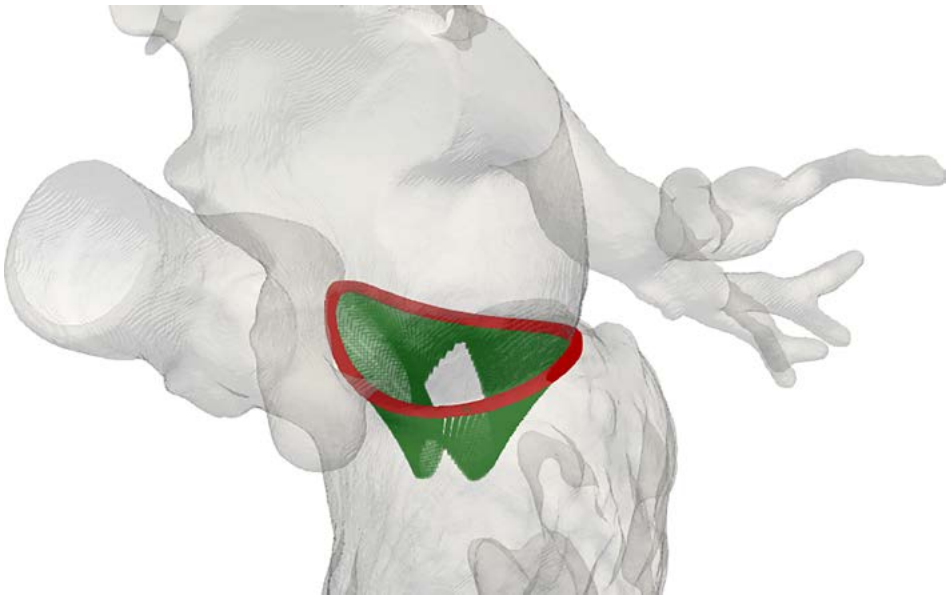
Modelling and Simulation of Mitral Valve Function and Cardiac Hemodynamics

The mitral valve (MV) is located between the left atrium and the left ventricle and is crucial in the efficient pump function of the heart. If closed, it blocks blood from flowing back into the atrium while it exits through the aorta. When open, it allows blood to flow unimpeded to fill the ventricle (while the aortic valve is closed). We are able to see the valve using cardiac imaging, but its effect on cardiac function, for healthy and diseased cases, is not fully understood.

It is possible to simulate subject-specific cardiac hemodynamics utilising time resolved computed tomography (CT) images and computational fluid dynamics (CFD). Utilising geometry and motion information from CT, we feed a CFD model, from which the blood flow is simulated. Previous studies have compared this technique to 4D Flow MRI measurements, with very good agreement, indicating how valuable it can be in understanding blood flow. We can use 4D flow CT to study the effect of normal and abnormal mitral function on the blood flow, but this requires a more accurate representation of the valve than what is currently available.

For this purpose, models of the valves may be used to approximate their geometry, such that more realistic flow is obtained. This project focuses on the improvement of the representation of the mitral valve in 4D Flow CT, for evaluation of its function and impacts in blood flow in the left ventricle.

At this stage the work is focused on the development of a parametric mitral valve model, based on not only CT, but also on specific types of MRI images that allow its visualisation during a cardiac cycle. The model uses mathematical descriptions for some components of the valve, as well as newly developed approaches that are being tested for describing the shape of the MV's leaflets, for example. Later this model will be included in fluid simulations, allowing not only for an analysis of the flow in a patient's heart and how it is influenced by the mitral valve, but also for studying how changes to the valve's geometry may affect this flow and hopefully assist in clinical cases in the future.



Parametric MV model example shown on patient segmentation of the left heart from CT.

PROJECT INFORMATION

Project

Modelling and simulation of patient specific mitral valve function and cardiac hemodynamics

Supervisors

Tino Ebbers, Anders Persson, Matts Karlsson, Farkas Vanky, Jonas Lantz

Short CV

Von Karman Institute for Fluid Dynamics, MSc. project in simulation and analysis of experimental results of liquid sloshing in microgravity, 2019.

Linköping University, MSc. in Aeronautical Engineering with specialization in aircraft aerodynamics, 2017–2019.

Universidade Federal de Minas Gerais, dual degree in Mechanical and Aeronautical Engineering, 2005–2010.

Linköping University, Research Engineer at the Unit of Cardiovascular Sciences, 2019–2021.

Dallas Airmotive, Maintenance and quality control engineer in aircraft engines for civilian and military customers in Brazil and Latin America, 2011–2016.

Frida Dohlmar

Dosimetric Evaluation and Development of New Methods for Automated Brachytherapy Treatment Planning

Brachytherapy is a type of radiation therapy where a small iridium-192 radioactive source is used to irradiate tumors from within. This is done by inserting catheters/needles or applicators (instruments designed to fit the anatomy of different disease sites) into or close to the tumor. The source stops at predefined positions in the catheters/applicators for a certain time to give the prescribed absorbed dose. It is commonly used for prostate and cervical cancer in combination with external beam radiation therapy.

Treatment planning of brachytherapy is the decision making of how the source is to move inside the catheters/applicators. This can be done manually, by deciding each source position and the time the source should stay in these. Nowadays automated treatment planning is often used where an optimization tool decides how long the source should stop in each position. The treatment planner sets up criteria on the dose to the tumor and the sensitive tissues around. Treatment planning is performed after insertion of the catheters/applicators, while the patient awaits treatment under anesthesia. It is hence important that the process is fast.

Treatment planning for prostate cancer was for long done manually. At least 80–90 source positions are used for each treatment plan, so it is time demanding to adjust these in a trial-and-error process. Optimization tools yield more heterogenous dose distributions than manual planning, therefore, manual adjustments are often needed. A new type of optimization tool has been developed to perform the adjustments automatically. This tool was tested on 25 previously treated prostate patients. The treatment plans with and without the automated adjustments were compared, using quantitative measures and an observer study with 8 oncologists. The adjusted plans were preferred in the majority of the cases. The observer study was important because the quantitative measures do not tell us the whole truth about the plan quality.

In cervical cancer brachytherapy the international recommendations are to use manual treatment planning as the commercial optimization tools in today's treatment planning systems are not providing dose distributions that fulfill treatment aims. The currently available optimization tools and a methodological usage of additional optimization volumes aimed to steer them will be used to explore how the weaknesses of the tools can be overcome. Such knowledge could be used to develop an improved optimization model for treatment planning for cervical cancer.

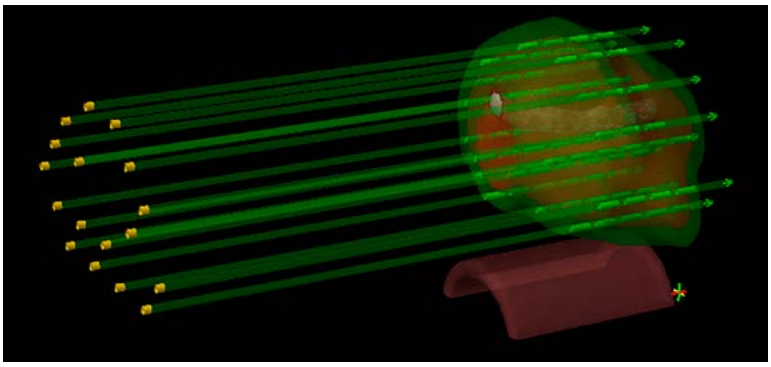


Figure 1. 3D-presentation of a brachytherapy treatment for prostate cancer. The red volume is the prostate, the green is the treatment volume, the brown is the rectum. Urethra can be seen as the light green in the center of the prostate. The green arrows are the catheters, and the green boxes are the source positions.

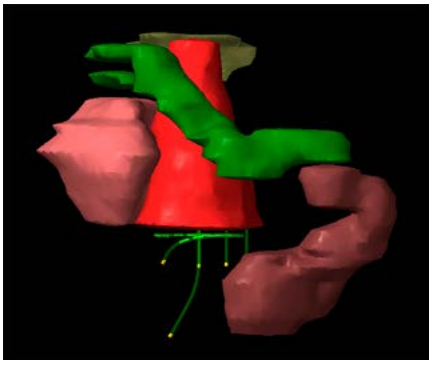


Figure 2. 3D-presentation of a brachytherapy treatment for cervical cancer. The red volume is the treatment volume, the pink is the bladder, the brown is the rectum, the green is the sigmoideum and the yellow is the bowel. The green lines below the treatment volume are the applicator and catheters, and the green boxes are the source positions.

PROJECT INFORMATION

Project

Dosimetric Evaluation and Development of New Methods for Automated Brachytherapy Treatment Planning

Supervisors

Åsa Carlsson Tedgren, Torbjörn Larsson, Michael Sandborg och Björn Morén

Short CV

Master of Science in Medical Physics, 2009.
Medical Physicist, Blekingesjukhuset, Karlskrona, 2009–2010.
Medical Physicist, Region Östergötland, 2010–present.

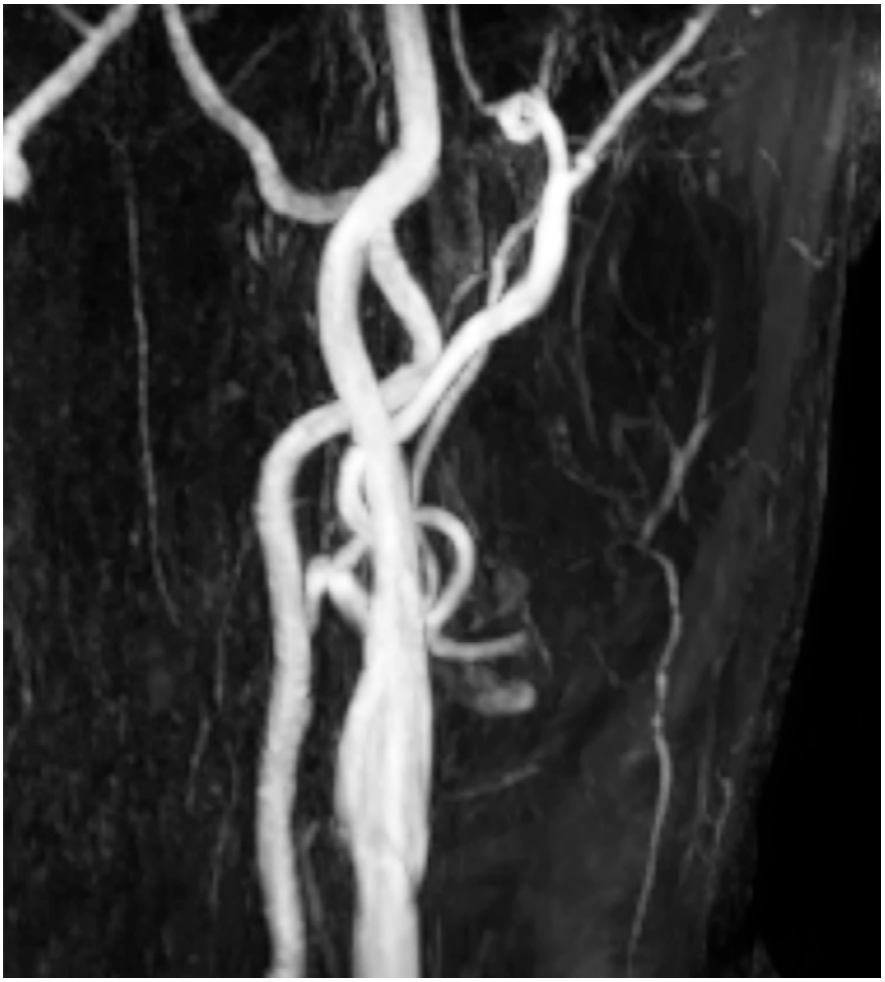
Elin Good

SCAPIS Carotid MRI

Swedish CArdioPulmonary bioImage Study, (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 aged 50–64 years. In Linköping we included 5,058 study participants between 2015 and 2018, and the individuals underwent extensive examinations including cardiovascular imaging. All individuals had a carotid ultrasound scan, and all presenting with a thickening of the carotid arterial wall were offered a complementary MRI of the carotid arteries, for the assessment of atherosclerotic plaques.

Linköping has now become a centre point for the national analysis of carotid MRI data. On a national level, 607 carotid MRI examinations were performed within SCAPIS, but half of these were performed in Linköping (315 carotid MRI). Therefore, the extensive data analysis of SCAPIS carotid MRI is coordinated from here. Based on this exclusive material our research group will investigate associations between plaques in the carotid arteries and plaques in the coronary arteries, we will try to identify plaque features that are associated with an increased cardiovascular risk and eventually evaluate the use of carotid MRI as a prognostic marker in an asymptomatic cohort.

In a complementary local sub study to SCAIS, we have invited healthy subjects for carotid MRI, to enable the comparison between healthy arteries and arteries with carotid plaques. Are there differences in the composition of the vessel wall? Do individuals with carotid plaques have different blood flow and hemodynamic patterns compared to healthy individuals? This is an ongoing project where we recently closed the inclusion of healthy individuals. We are now looking forward to extract MRI data from the approximately 150 healthy individuals, to analyse in relation to the 300 individuals with atherosclerosis. Our intention is for this work to contribute to further knowledge on the pathology of plaque vulnerability, and the development of improved diagnostic imaging techniques.



3D reconstruction of carotid MRI.

PROJECT INFORMATION

Project
SCAPIS Carotid MRI

Supervisors
Petter Dyverfeldt, Ebo de Muinck

Short CV
Degree of Master of Science in Medicine. Medical School, Linköping University. 330 ECTS, 16 January 2012.
Fellowship in Cardiology and Internal Medicine. Linköping University Hospital, Mar 2015 onward.
Certified MD. Swedish National Board of Health and Welfare, Feb 28 2015.
Various internships, Jan 2012-Feb 2015.

Lilian Henriksson

Coronary Computed Tomography: Stenosis Evaluation and Calcium Score

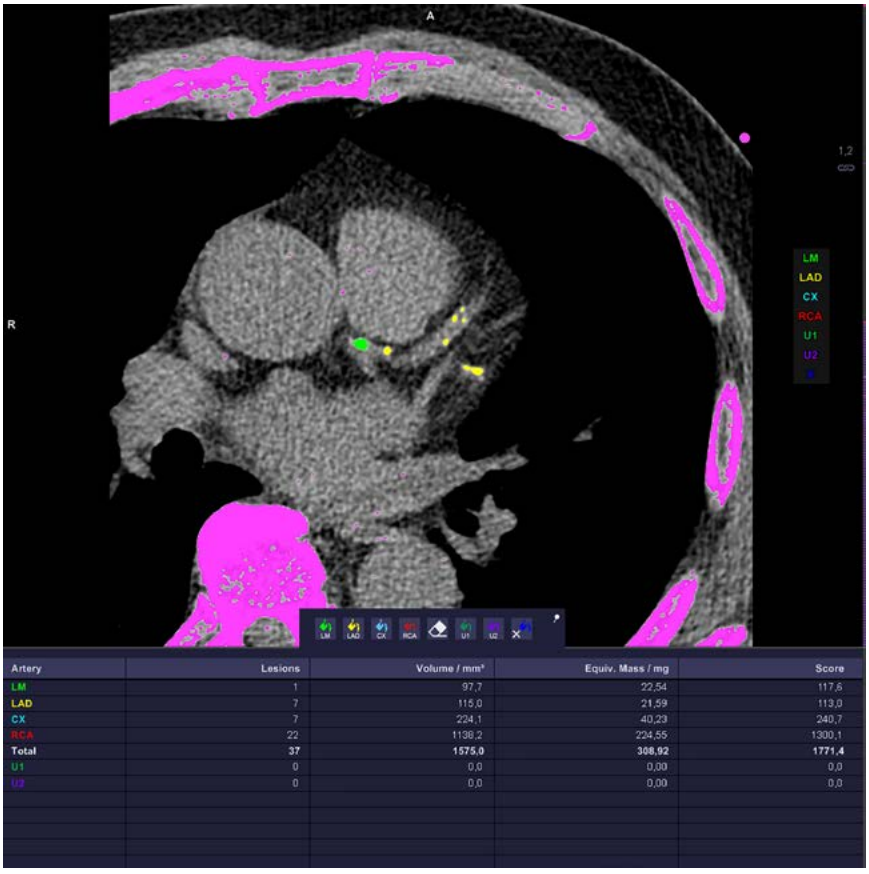
A healthy coronary artery wall does not contain calcifications. If calcifications are present this is a specific sign of coronary artery disease (CAD). The extent of coronary artery calcifications (CAC) has also shown to be proportional to the degree of CAD. The amount of CAC can be measured with calcium 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 30,000 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 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 5,000 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.



Artery	Lesions	Volume / mm³	Equiv. Mass / mg	Score
LM	1	97,7	22,54	117,6
LAD	7	115,0	21,59	113,0
CX	7	224,1	40,23	240,7
RCA	22	1138,2	224,55	1300,1
Total	37	1575,0	308,92	1771,4
U1	0	0,0	0,00	0,0
U2	0	0,0	0,00	0,0

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.

PROJECT INFORMATION

Project
Coronary Computed Tomography: Stenosis Evaluation and Calcium Score

Supervisors
Anders Persson, Jan Engvall, Tino Ebbers, Mischa Woisetschläger

Short CV
Radiology nurse, 2005
M.Sc. medical science, 2013
CT Research nurse, 2015
PhD student, 2017

Sofia Jarkman

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?

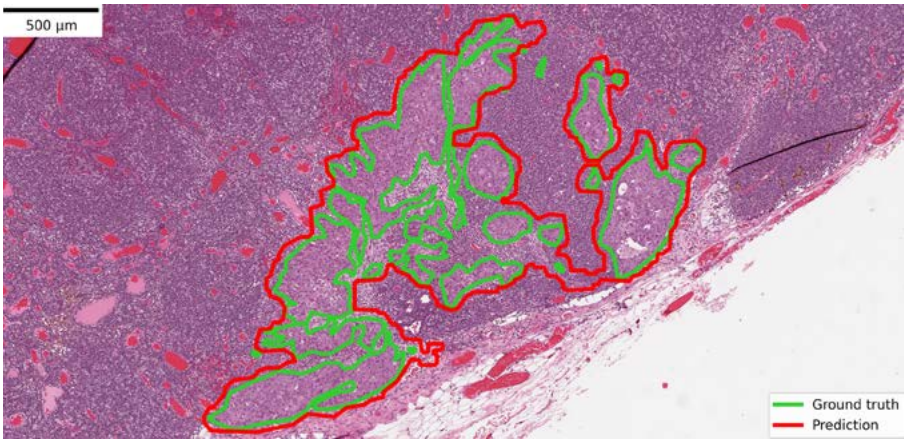
We initially focus on evaluating an algorithm for detecting lymph node metastases in breast cancer cases. The algorithm is developed by the Computational Pathology group at Radboud University medical center in Nijmegen in the Netherlands. An important step is to be able to transfer or generalize an algorithm 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. The generalizability of the algorithm was then tested both on data of the same type it was trained on (sentinel lymph nodes), but also on data with a slight change in indication (lymph nodes from axillary dissections). Both datasets generated from same type of patient group, topography, and diagnosis group. A drop in performance was seen for both scenarios, but especially for the axillary nodes. To mitigate the performance drop retraining was needed. (Jarkman, S.; Karlberg, M.; Poceviγiγtγ, M.; Bodén, A.; Bándi, P.; Litjens, G.; Lundström, C.; Treanor, D.; van der Laak, J. Generalization of Deep Learning in Digital Pathology: Experience in Breast Cancer Metastasis Detection. Cancers 2022, 14, 5424. https://doi.org/10.3390/cancers14215424).
The next step will be to assess potential clinical value with the model and user interface design in a clinical setting.

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
Specialist in Clinical Pathology, Linköping University Hospital, 2021-present.
Residency in Clinical Pathology, Linköping University Hospital, 2016-2021.
Medical degree, Lund University, 2013.



Example of ground-truth annotation and model prediction detection area overlapping. (Jarkman, S.; Karlberg, M.; Pocevičiūtė, M.; Bodén, A.; Bándi, P.; Litjens, G.; Lundström, C.; Treanor, D.; van der Laak, J. Generalization of Deep Learning in Digital Pathology: Experience in Breast Cancer Metastasis Detection. Cancers 2022, 14, 5424. https://doi.org/10.3390/cancers14215424).

Robin Kämpe

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

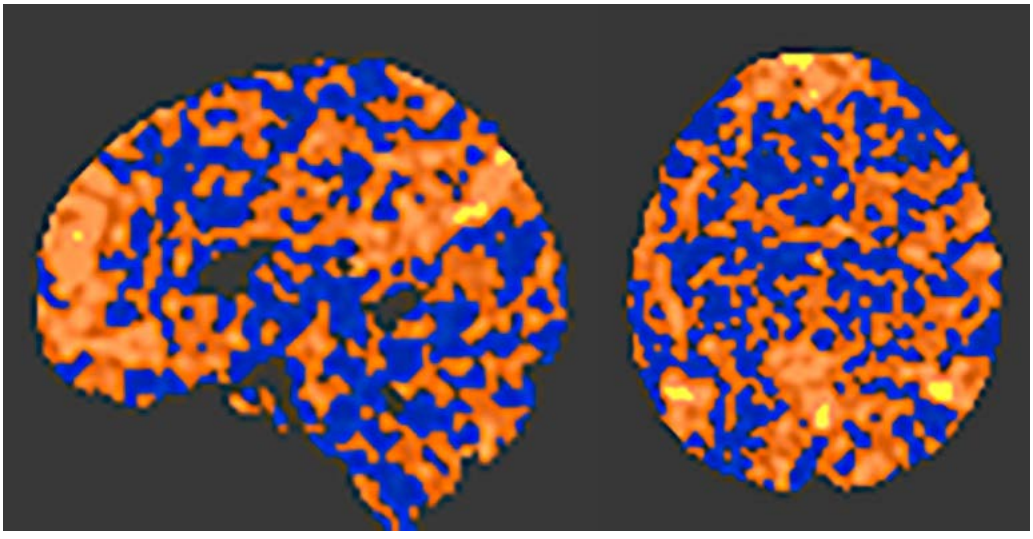
Diagnostic Center, MR-physics, Part time employee, Region Östergötland, Medical/MRI physicist, 10/2022-present.

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.



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.

Anna Ljusberg

Myelin Changes in Brain after Radiation Therapy

About 1,400 patients every year are diagnosed with brain tumor and about 50% of them are gliomas. Gliomas arise in the glial cells which main function is to support and protect the nerve cells. Gliomas can be both mild and severe where over-all survival time is short for the severe types, most patients decease within a couple of years. Treatment consist of surgery followed by a combination of chemotherapy and radiation therapy. After completed therapy the patient is regularly followed every 3rd month. Diagnosis, treatment planning and evaluation is performed using MRI. In this project quantitative MRI has been used for detection of changes in normal appearing white matter in the brain. The white matter consist of nerve fibers and a protective layer of myelin. Both chemotherapy and radiation therapy aim at killing the cancer cells but unfortunately also effect the surrounding tissue. When planning radiation treatment, it is hard to aim only at the tumor site, doses are spread over the surrounding tissue illustrated in the image. The aim of this study is to see how the dose levels from radiation therapy effect the white matter. Preliminary results show that there is a decrease in myelin concentration and increase of water concentration which indicates that the protective layer of myelin is damaged by radiation. For low doses of radiation there seems to be a repair mechanism but unfortunately for higher doses (over 30 Gy) the damage seems to be permanent at least during the follow-up time. We believe this method will improve radiation therapy in the future by estimating the risk and effects on white matter and the levels of dose the tissue tolerates.

PROJECT INFORMATION

Project

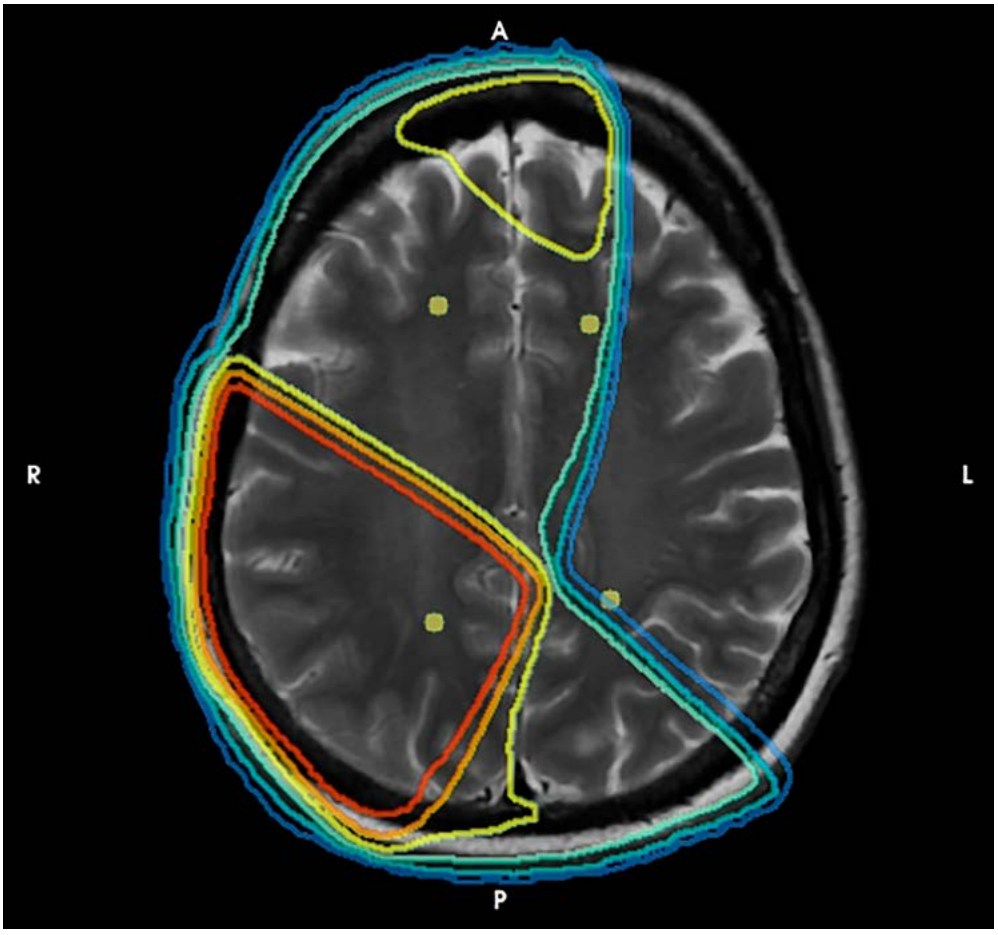
Quantitative MR for diagnosis and treatment of brain tumors

Supervisors

Anders Tisell, Ida Blystad, Emelie Adolfsson, Peter Lundberg

Short CV

Master of science in medical physics, 2013 Lund University.
Medical physicist, radiation therapy, Linköping University hospital, 2015-present.



MR-image of the brain with different dose levels indicated by the different colored lines. Blue and green lines corresponds to low doses while yellow, orange and red are high dose areas. The yellow circles are examples of the regions in which measurement has been done.

Gustav Magnusson

Cerebrovascular Reactivity studies

Many neurological diseases, such as stroke, brain tumor and small vessel disease are connected, directly or indirectly, to the brain's vascular function. Vascular autoregulation is an important aspect of the overall vascular function which assures a reliable supply of oxygen and nutrients to the brain as well as removal of biproducts such as carbon dioxide (more on this further down) in the face of changes in other physiological parameters, such as blood pressure. Autoregulation is what stops you from fainting when you stand up quickly, even though you might experience some transient dizziness before the regulation kicks in.

One way to probe the autoregulation of the brain is to use a technique called Cerebrovascular Reactivity, or CVR. It works by applying a blood flow stimulus and at the same time measure the resulting change in blood flow to produce a measurement of the blood vessels reactivity. This reactivity shows how well, or not well, the vessels are responding to the stimulus and can thus be seen as measurement of underlying regulatory function.

The standard way to perform CVR measurement is to provoke a blood flow change by changing the systemic carbon dioxide level of the body while at the same time monitoring the cerebral blood flow with magnetic resonance imaging or transcranial doppler. Carbon dioxide is a natural occurring waste product in the body which is being produced by the cells and transported away to the lungs by the blood and then exhaled out. Because of this central function, the body has several mechanisms to sense the carbon dioxide level, both in the blood and tissue, and alter its blood flow accordingly.

There exist multiple ways to alter the carbon dioxide level in body, however, the preferred way for a reliable and reproducible stimulus is to alter the carbon dioxide concentration in the inhaled gas, inhaled-CO2-CVR. There exist multiple systems to perform CVR measurement this way. None exists today though, that works together with a ventilator. Therefore, a large group of patients that are being ventilated and might benefit from CVR measurement has to be excluded.

To solve this, we have constructed a system, iCO2 CVR System, that works together with a ventilator to administer a fix amount carbon dioxide in the inhaled gas and thus enable inhaled-CO2-CVR measurements for ventilated patients, see figure 1. Soon, we hope to be able to use the system to study CVR in subarachnoid hemorrhage patients, which is a severe type of stroke with high mortality and a large portion of patients being ventilated.

PROJECT INFORMATION

Project

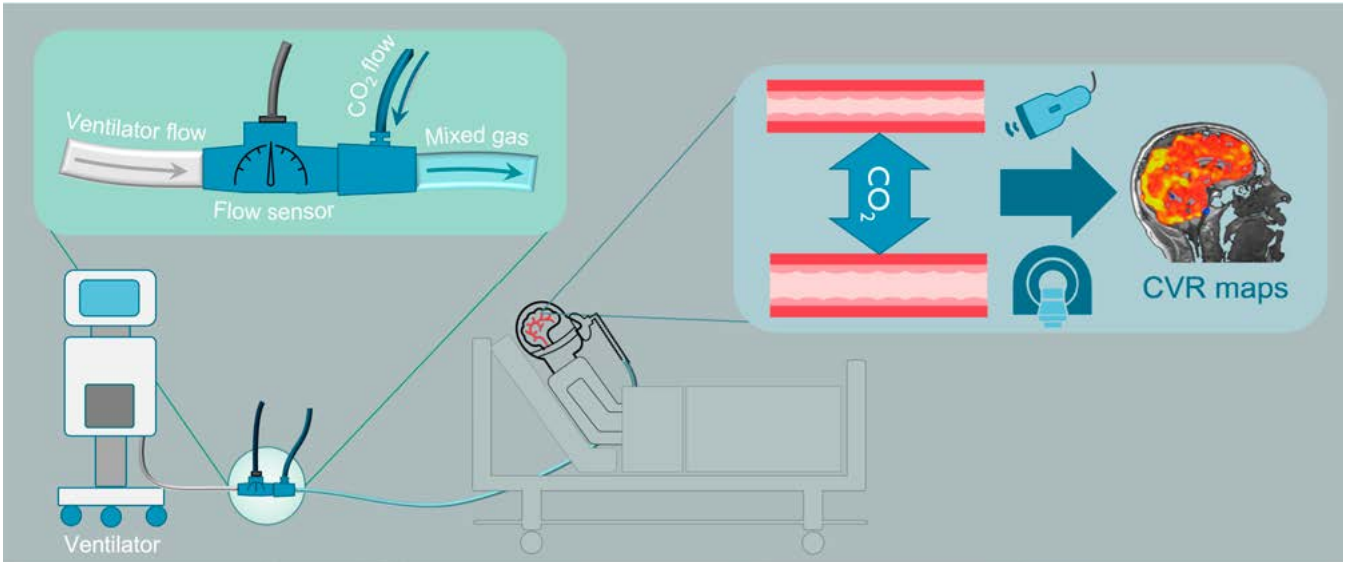
Magnetic Resonance Imaging Studies on Cerebrovascular Reactivity

Supervisors

Maria Engström, Anders Tisell, Lovisa Tobieson, Gunnar Cedersund, Charalampos Georgiopoulos

Short CV

Bachelor and master's degree in engineering physics from Chalmers University.
Research assistant at Gothenburg University.
Research engineer at Linköping University
Vice-chair CMIV Reseach school.



The constructed system, iCO2 CVR System, that has been built to enable inhaled-CO2-CVR measurements for ventilated patients. It works by measuring the flow from the ventilator, using a flow sensor, and then adds an additional flow of high concentration CO2 using a mass flow controller, MFC, to achieve a target CO2 concentration in the mixed gas. By controlling the proportion of the additional gas, various CO2 concentration can be targeted.

Marcus Malmqvist

Patomechanism of Idiopathic Scoliosis

Scoliosis is a disorder of the spine characterized by a deformity in three dimensions. It affects the coronal, sagittal and axial plane of the spine. 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. The deformation naturally affects the thorax in the form of thoracic hypokyphosis and vertebral rotation, especially in patients with severe thoracic scoliosis. Reduced pulmonary function is seen in this patient group. Recent studies have shown that a consequence of the deformity may be right-sided bronchial narrowing and chest intrusion by the endothoracic hump, suggesting an obstructive component of the pulmonary dysfunction seen.

When surgically correcting severe scoliosis there are different methods. One is posterior spinal fusion (PSF) which includes a posterior approach, pedicle screw insertion and deformity correction via the posterior column. Another method is the anterior selective fusion via thoracotomy which includes rib head resection and deformity correction via the anterior column. When correcting thoracolumbar curves, the diaphragm is sectioned.

While pros and cons of these methods have been extensively debated and many comparative studies have been published, knowledge on the effects of these surgical methods on both pulmonary function and the morphology of the thorax and the airways is lacking.

In this project we aim to address this by measuring the segmental lung volumes and bronchial cross-sectional area on 3D reconstructed computed tomography scans, pulmonary function measured with spirometry in patients with thoracic scoliosis before and after undergoing anterior fusion with thoracotomy. We also aim to investigate the true 3D aspect of morphological thoracic and respiratory obstruction and the difference between these two surgical methods.

PROJECT INFORMATION

Project
Idiopathic Scolioisis - Patomechanism and Morphology

Supervisors
Hans Tropp, Ludvig Vavruch

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

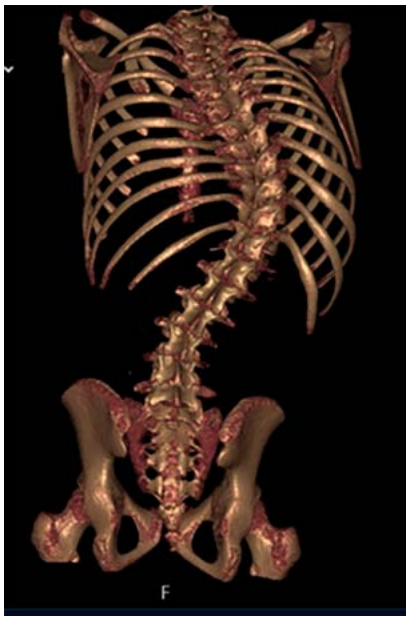


Figure 1. A 3D reconstruction of the scoliotic spine.

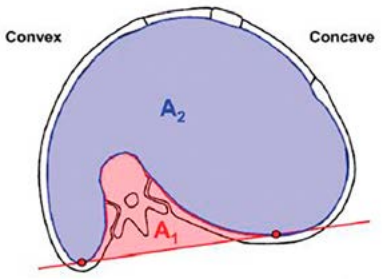


Figure 2. An axial illustration of the scoliotic thorax.

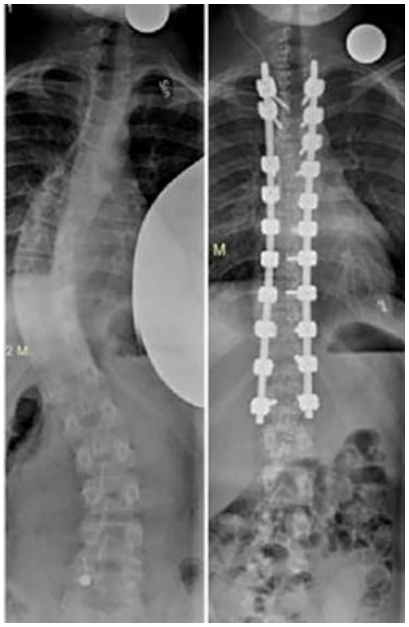


Figure 3. Before and after posterior spinal fusion.

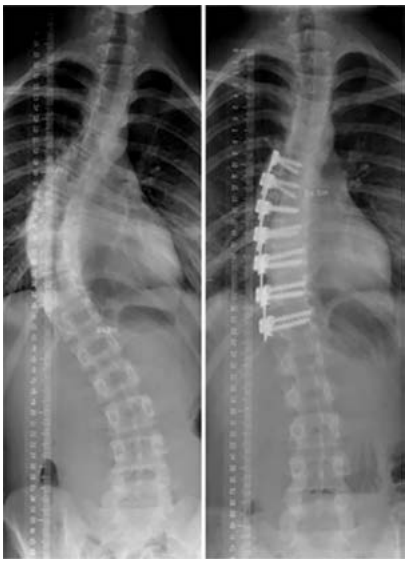


Figure 4. Before and after anterior spinal fusion.

Per Nyman

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

This research seeks to validate new techniques including quantitative MRI (qMRI) and APT-Chemical Exchange Saturation Transfer (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, 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 implementations 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 qMRI measurements (QALAS) and functional MRI 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 (Barntumörbanken, 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

Supervisors

Peter Lundberg, Jan Hillman, Ida Blystad Ulf Samuelsson

Short CV

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.

Linus Ohlsson

Cardiac Motion and Blood Flow in LVAD Patients

Mechanical circulatory support is, alongside heart transplantation, the last treatment step in advanced heart failure and the use has increased rapidly during the last decade. The development of Left Ventricular Assist Devices (LVADs) is one of the major contributing factors to this increase. This therapy has previously only been indicated while waiting for a heart transplant but can now also be established as a destination therapy for patients who, for various reasons, cannot undergo a heart transplant.

Even though these pumps have made great technical progress in the last decade, serious complications, and adverse events, such as blood clot formation, infections, valve leakage or impaired right ventricular function remain. This patient group is thus continuously followed up by the healthcare system to optimize the treatment and reduce the risk of complications. In this follow-up routine, above all, cardiac transthoracic ultrasound has been used as an imaging method. However, ultrasound of these patients is challenging, and it is difficult to get an overall understanding of the treatment's impact on the heart. Furtherly, there is limited previous research regarding whether more advanced medical imaging methods could contribute to an increased understanding of LVADs and its impact on the heart.

Computed Tomography (CT) can acquire time-resolved images over the cardiac cycle and enables analyzes of both cardiac geometry, movements, and computerized blood flow calculations. Until very recently, however, radiation levels, contrast requirements, and metal artifacts would have made CT a challenging modality to thoroughly examine patients with LVADs. Now, however, the recent launch of photon-counting CT enables image acquisition with lower iodine contrast demands, radiation requirements as well as reduced metal artefacts. This new medical imaging modality can therefore potentially generate increased understanding and benefit for patients with LVADs, something that this project intends to investigate.

The overall aim of the project is to investigate and describe the heart during treatment with LVAD. This is done by exploring the heart's internal geometry, movements, and blood flow during the treatment and how these aspects relate to the flow rate of the pump. It will also explore the cardiac adaptation during the post-operative period.

PROJECT INFORMATION

Project

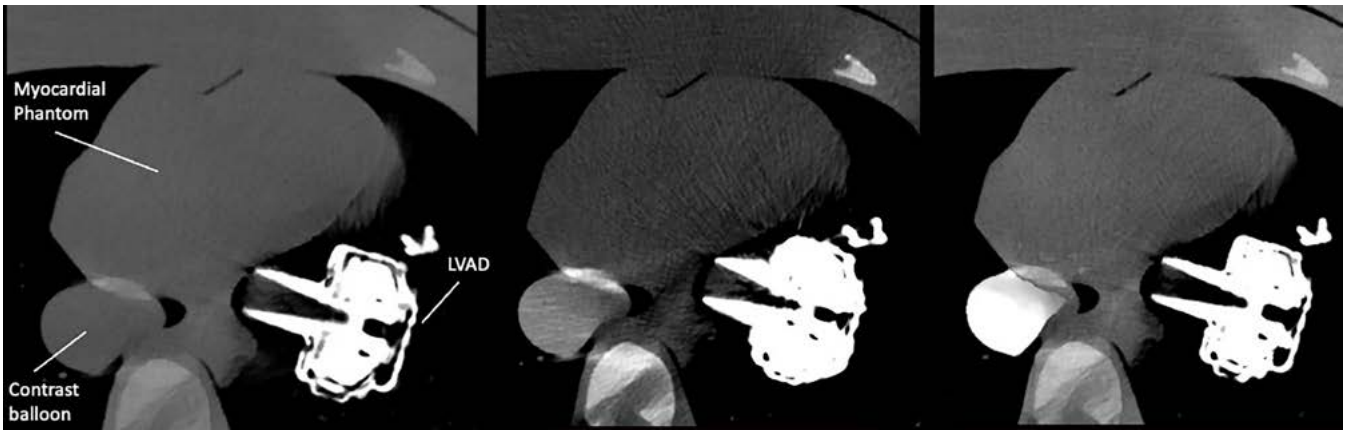
Cardiac adaption, wall motion and hemodynamics in patients with left ventricular assist devices explored with computed thomography and computational fluid dynamics

Supervisors

Tino Ebbers, Hans Granfeldt, Éva Tamás

Short CV

PhD-student, Medical Science, Department of Health, Medicine, and Caring Sciences (HMV), Linköping University, 2022-.
Research assistant, Department of Health, Medicine, and Caring Sciences (HMV), Linköping University, 2022.
Amanuensis of anatomy, Department of Biomedical and Clinical Sciences (BKV), Linköping University, 2020-.
Union President, Consensus - the student union of the Medical Faculty, Linköping University, 2021-2022.
Chairman, Medical Association, Linköping University, 2020-2021.
Initiated the Medical Program, Linköping University, 2018-.



Results of work together witch post-doc Bente Konst and visiting PhD student Jack Xu on reducing metal artefacts from LVADs in a thorax-phantom. The dataset to the left is reconstructed with a high keV level, reducing most of the artefacts but extinguishes iodine contrast. The image in the middle is instead reconstructed with a low keV level, preserving the iodine contrast but increases the artefacts. The image to the right is a result of material decomposition images using dual-energy ratios where pixels demonstrating iodine-like characteristics are transferred to the high keV image, reducing both artifacts while preserving iodine attenuation.

Milda Pocevičiūtė

XAI Applied to Histopathology Image Analysis

Introduction of digital pathology enabled research on Artificial Intelligence (AI) systems that are designed to assist pathologists in their daily tasks. These systems can not only improve efficiency of a pathology laboratory, but also reduce the well-known inter-doctor variability in some diagnostic tasks such as determining if a cancer has metastasized. 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 in the target task 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 system 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". This can be achieved by developing ad-hoc methods that generate visualisations or some measurements separately from the AI prediction. Alternatively, some AI frameworks have in-built explainability features, for example, so-called attention maps, that enables them to provide the prediction and XAI visualisation at the same time. An example of such an in-built attention map is provided in the figure. Here, the areas in a H&E stained lymph node section that is most likely to contain cancer cells are highlighted in red.

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

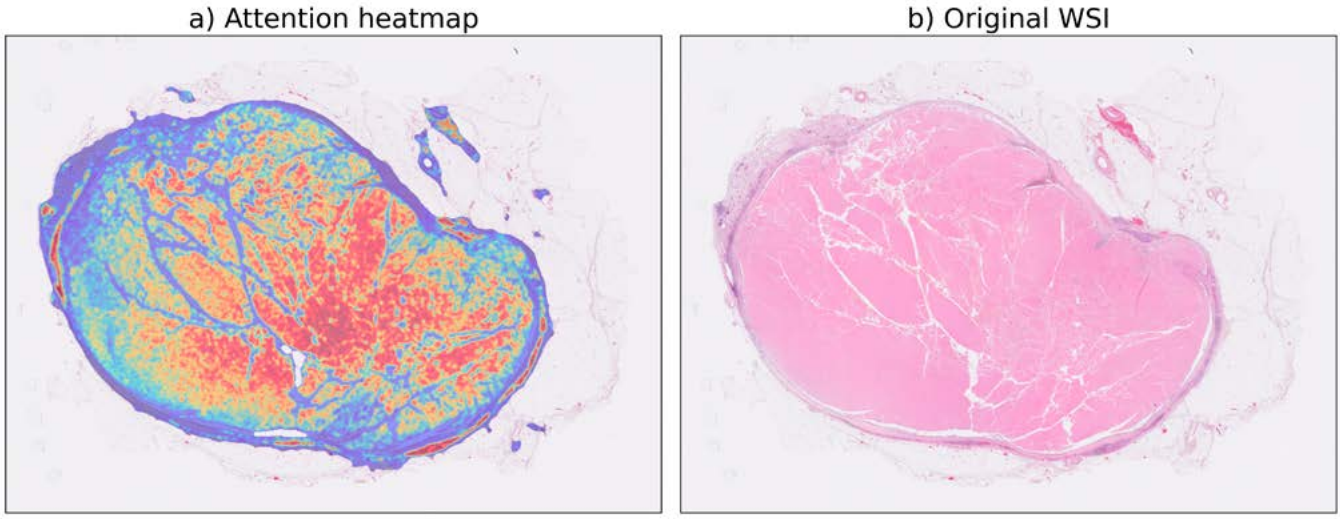
Explainable AI applied to histopathology image analysis

Supervisors

Claes Lundström, Gabriel Eilertsen, Stina Garvin

Short CV

Lancaster University, BSc Hons. Financial Mathematics, 2011 September-2014 June.
SEB bank Lithuania, Client Service Coordinator, 2014 August-2015 April.
Affecto Lithuania, Junior Specialist, 2015 April-2017 June.
Linköping University, MSc Statistics and Machine Learning, 2017 August-2019 June.
Linköping University, PhD candidate, 2019-August-now.



a) Attention heatmap that indicates which areas of the whole slide image (WSI) of a lymph node section contributed most to the tumour prediction by an AI. b) Original whole slide image (WSI) of the H&E stained lymph node section that was processed by the AI.

Christian Simonsson

Combining Systems Biology and MRI to Investigate NAFLD

The worldwide obesity epidemic is increasing the prevalence of *alcoholic fatty liver disease* (NAFLD), which will be a future health problem. This is because NAFLD can progress into more dangerous conditions. The progression of NAFLD involves many different steps (Figure 1, Left), starting with the accumulation of fat in the liver. Fatty liver can in some cases promote the development of chronic hepatic inflammation, *non-alcoholic steatohepatitis* (NASH). Prolonged inflammation leads to damage and the formation of scar tissue (fibrosis), if the scarring becomes very severe it is denoted liver cirrhosis. Liver cirrhosis is non-reversible and can lead to liver failure which can be fatal. Cirrhosis can also promote the development of liver cancer, *hepatocellular carcinoma* (HCC). Liver diseases are also heterogenous expressed in the liver, making it hard to detect, with e.g., biopsies (Figure 1, Middle). To this cause, we want to investigate the possibility of using non-invasive MRI biomarkers (Figure 1, Right) to be able to detect e.g., NASH progression as early as possible.

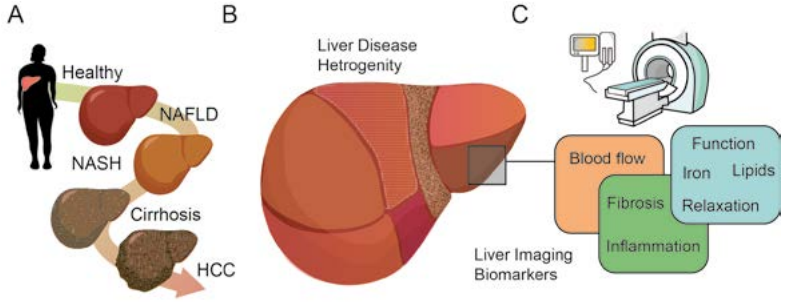


Figure 1. A) Progression of NAFLD. B) Heterogeneity of liver disease C) imaging bio markers used in our multi-modal MRI examinations.

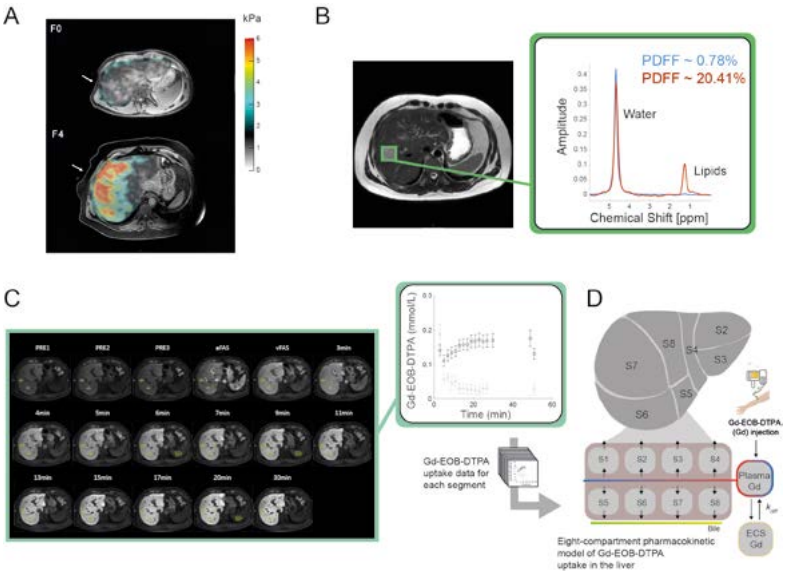


Figure 2. Example of images and methods from the multi modal MRI examinations. A) Elastogram from MRE, showing the liver stiffness for two different patients, one healthy (F0) and one with severe fibrosis (F4). B) Example of 1H-MRS spectra to measure PDFF for two different cases, one healthy and one with high fat accumulation. C) Images from dynamic contrast enhanced MRI. Times-series images create a contrast agent uptake curve which can be used for system biology modelling. D) Our eight-compartment model used to quantify the uptake of contrast agent in each liver segment.

In my PhD project I am involved in several studies which focuses on collecting imaging data from patients from the whole spectra of NAFLD progression. From relatively healthy patients to end-stage patients with cirrhosis and/or HCC (Figure 1, Left). We investigate patients using multi-modal MRI examinations, where we measure a lot of different biomarkers (Figure 1, Right). Here are some examples. In all studies we look at 3D magnetic resonance elastography (MRE) to measure liver tissue biomechanical properties correlated to fibrosis and inflammation (Figure 2A), and quantification of hepatic fat accumulation, via 1H-MRS proton density fat fraction (PDFF) (Figure 2B). In some of our studies we also make use of dynamic contrast enhanced (MRI) in combination with systems biology modelling to quantity global and regional liver function (Figure 2C and D). These are just phew examples of all the data we collect in the studies.

The long-term aim of our research is to better characterize each patient in the early to intermediate stages of disease progression, with a higher degree of precision. Also, to gain insights into new possible biomarkers, for better assessment at end-stage points. Lastly, to also gain insights into key underlaying mechanisms behind the progression of NAFLD.

PROJECT INFORMATION

Project

Investigating the progression of NAFLD using multi-modal MRI and systems biology modelling

Supervisors

Peter Lundberg, Gunnar Cedersund, Mattias Ekstedt, Elin Nyman

Short CV

M.Sc. in Engineering Biology, Linköping University (2018).

Susann Skoog

Comparison of EID-CT and PCD-CT in Assessment of Coronary Arteries

Cardiovascular disease is one of the major causes of death and disability in the world. Risk assessment of cardiovascular diseases is thus important, as there may be potential major advantage in early detection and treatment of coronary artery disease.

During the last decades coronary computed tomography angiography (CCTA) has been increasingly used as an imaging modality for diagnosing coronary artery disease. CCTA stands out among other diagnostic modalities with an excellent negative predictive value and an ability to image various stages of atherosclerosis. The emerging role of CCTA has been acknowledged by the 2019 Guidelines of the European Society of Cardiology recommending the use of computed tomography (CT) as a first-line tool for the evaluation of patients with stable disease.

Despite technological developments CCTA performed by energy-integrating detector CT (EID-CT) still has some remaining disadvantages. EID-CT CCTA still has limited spatial resolution and soft-tissue contrast which impairs diagnostic for small arteries and the evaluation of lumen adjacent to calcifications and stents, as well as evaluation of non-calcified plaques.

The latest step in CT technology is the photon counting detector CT (PCD-CT). Compared with the EID-CT the PCD-CT has better spatial resolution and soft-tissue contrast, reduced level of noise, and less blooming and beam-hardening artifacts.

My research area is to compare examination with our conventional/EID CT and the PCD-CT.

Our first study was to evaluation the possibility of converting the well-established calcium score Agatston score (AS) into the new technology. We investigated cadaveric hearts in the two machines. Our results show an excellent correlation and good agreement between AS derived from an EID-CT and ac PCD-CT.

We have just started a study to compare the quality of coronary arteries assessment between an EID-CT and a PCD-CT. We will also compare the assessment of coronary plaque composition between the two machines. In an up-coming study we will compare lumen-stenos evalution between EID-CT- PCD-CT and invasive coronary angiography.

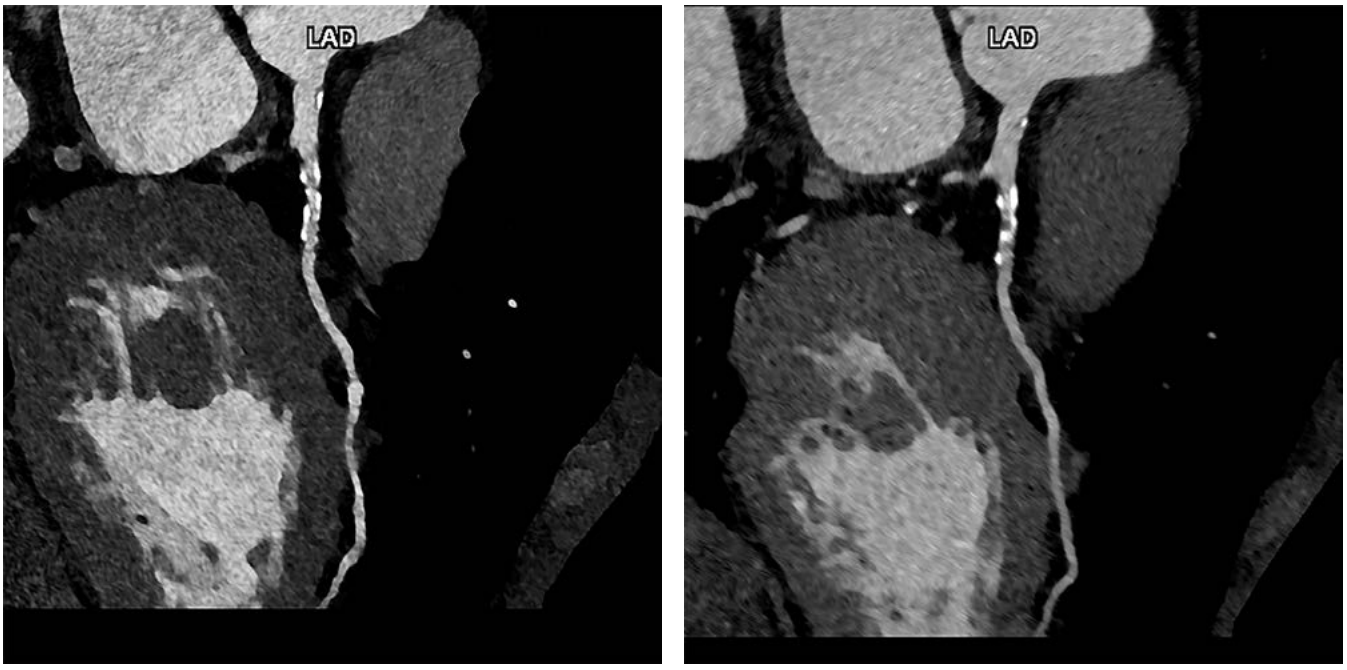
PROJECT INFORMATION

Project
Comparison of EID-CT and PCD-CT in assessment of coronary arteries

Supervisors
Håkan Gustafsson, Anders Persson, Mårten Sandstedt

Short CV
Consulting thoracic radiologist

A B



Coronary calcification appearance in PCD-CT (A) and EID-CT (B).

Iulian Emil Tampu

Quantitative MRI for Brain Tumor Detection

Gliomas are tumors that affect one of the most sensitive and functional parts of our body: the brain. In the clinical routine, magnetic resonance (MR) images are used for diagnosis and treatment planning of gliomas, where clinicians try to balance the extent of treatment area with possible collateral effects. One of the aspects that improves overall patient survival is the ability to target, through therapy, all the active tumor region. Unfortunately, not all active tumor, which can be the source of tumor re-growth, is visible in the conventionally acquired MR images (cMRI).

Quantitative MRI (qMRI) is an advanced imaging modality that measures relaxation properties of the brain tissue and has shown potential in highlighting tumor-like regions extending the visible tumor area. In this project, we train deep learning models for tumor detection using either cMRI or qMRI as input data. Deep learning explainability methods are then applied on the trained models to visualize what regions are used by the algorithm for the detection task.

By studying the differences between the tumor regions used by models trained on cMRI and qMRI, a new way of looking at the tumor area is investigated. This could increase our understanding of the tumor information available in the MRI data, for future improvements in treatment planning.

PROJECT INFORMATION

Project

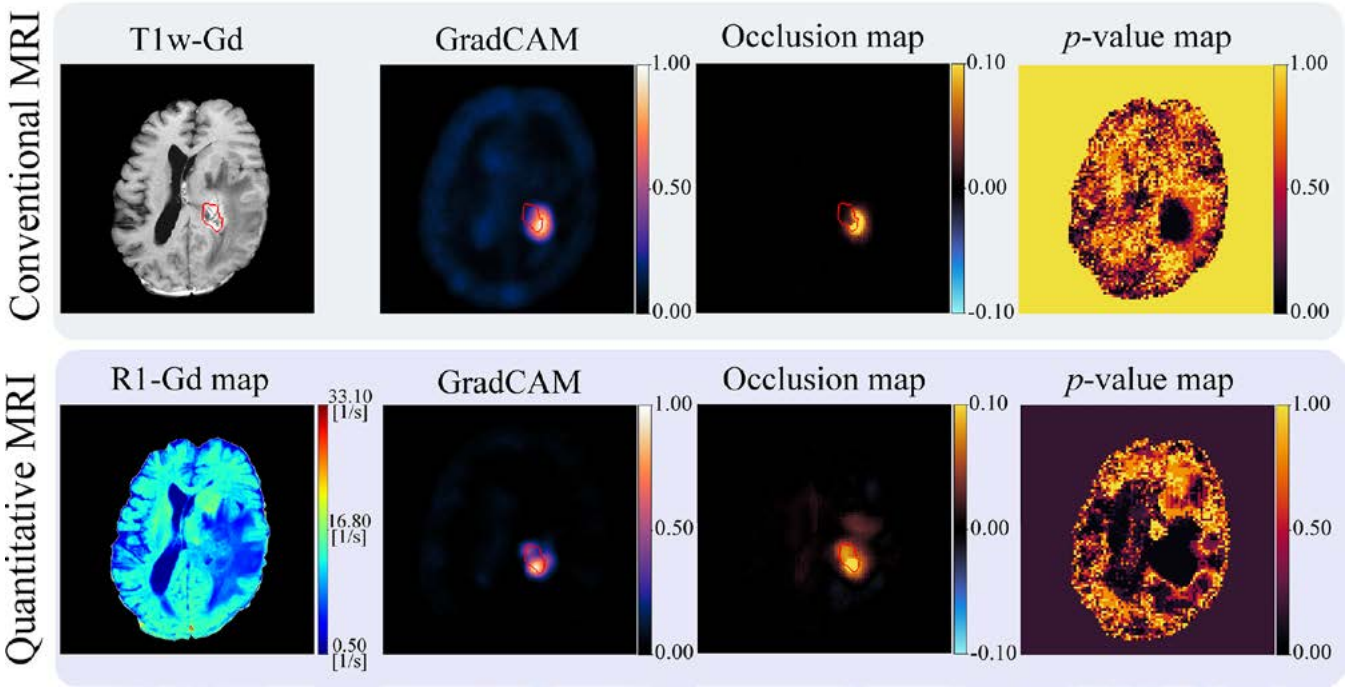
Leveraging qMRI through deep learning for brain tumor detection

Supervisors

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

Short CV

University of Padova, BSc in Biomedical Engineering, 2013-2016.
Linkoping University, MSc in Biomedical Engineering, 2017-2019.
Linköping University, Department of Biomedical Engineering, Research Engineer, June 2019-January 2020.
Linköping University, PhD candidate, February 2020-now.



Contrast of the tumor region generated by model explainability analysis (GradCAM and Occlusion mapping) for models trained on conventional MRI (top row) and quantitative MRI (bottom row) data. Bright regions in both GradCAM and occlusion maps (second and third columns) highlight regions in the brain that the models used for the tumor detection. In the p-value maps (forth column), lower values indicate brain regions whose occlusion lowers the models' predicted probability of detecting the tumor. The manual annotation of the tumor is shown as a red line over-imposed to the anatomical T1w-Gd image, GradCAM and occlusion map images.

Chiara Trenti

Nonsize Factors in Aortic Dilation

Aneurysmal dilation 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 small aneurysms and thus do not fall within the current guidelines for elective aneurysm surgery. We lack scientific understanding and clinical tools to properly manage individuals with aortic dilation.

The main objective of this project is to investigate if aorta dilation 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 dilation 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 dilation.

Recently, we investigated how hemodynamics is altered in dilated patients with bicuspid aortic valve and aortic valve insufficiency. In this case, the aortic valve does not close properly in the diastolic phase, during the filling of the ventricles. The project was carried out in a collaboration with the University of Calgary, Canada. The selected patients had undergone a defined cardiovascular magnetic resonance (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 to compute wall shear stress, which represent the shear action of blood on the aortic wall.

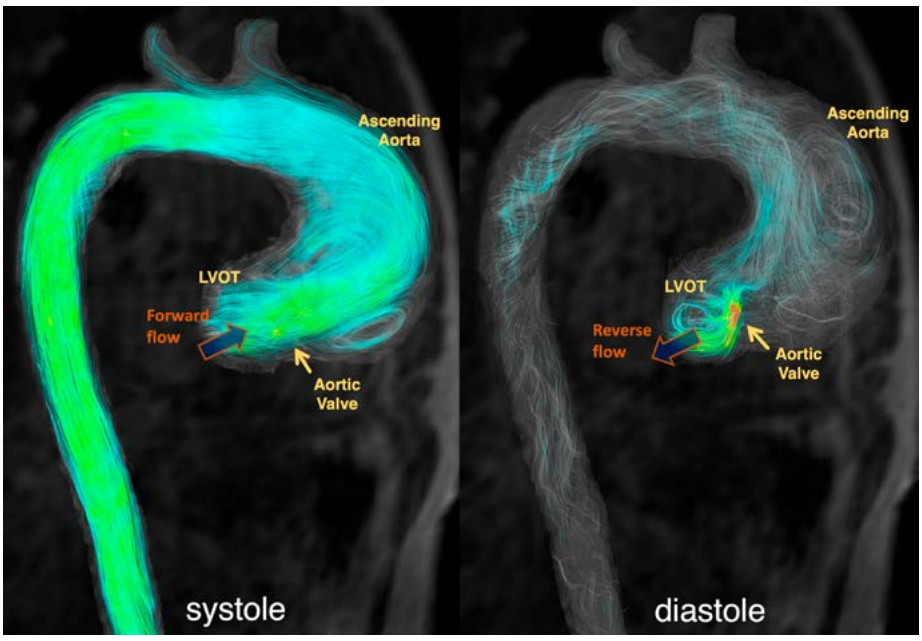
Patients with bicuspid aortic valve and insufficiency experienced elevated oscillatory shear flow in the ascending aorta, probably related to the pendulum volume: since the valve does not close during the filling of the ventricles, extra volume of blood enters from the aorta through the aortic valve, which is ejected volume in the next systolic phase. The oscillating extra volume of blood in the cardiac phases results in elevated oscillatory shear on endothelial cell that form the inner layer of the aortic wall. This mechanism could potentially enhance the degradation of the aortic wall, contributing to the development of aortic dilation.

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.



Visualization of the blood flow in the ascending aorta from 4D flow CMR in systole and diastole in a patient with bicuspid aortic valve and regurgitation. During filling of the ventricles, the aortic valve does not close, allowing the blood to flow back from the aorta to the left ventricle. LVOT = Left Ventricular Outflow Track.

Kajsa Tunedal

A Cardiovascular Model for Blood Pressure Regulation

High blood pressure, or hypertension, is one of the most common health issues today with one third of all adults worldwide affected and it is twice as common in patients with type 2 diabetes (T2D). Additionally, hypertension is a risk factor for cardiovascular diseases such as coronary artery disease, atrial fibrillation, stroke, and renal failure. To better understand the cause of hypertension and what happens in the cardiovascular system during hypertension, one can study the blood pressure and blood flow regulation, together called hemodynamics, where a high blood pressure requires the heart to work harder to pump blood through the body.

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 hemodynamic parameters such as blood pressure or aortic stiffness.

In this project, we combine 4D flow MRI data with a cardiovascular model 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 compare model-derived hemodynamic parameters such as the contraction and relaxation of the left atrium between hypertensive, T2D patients, and controls. Additionally, the personalized model can make patient-specific predictions of future scenarios such as disease progression or treatments. 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

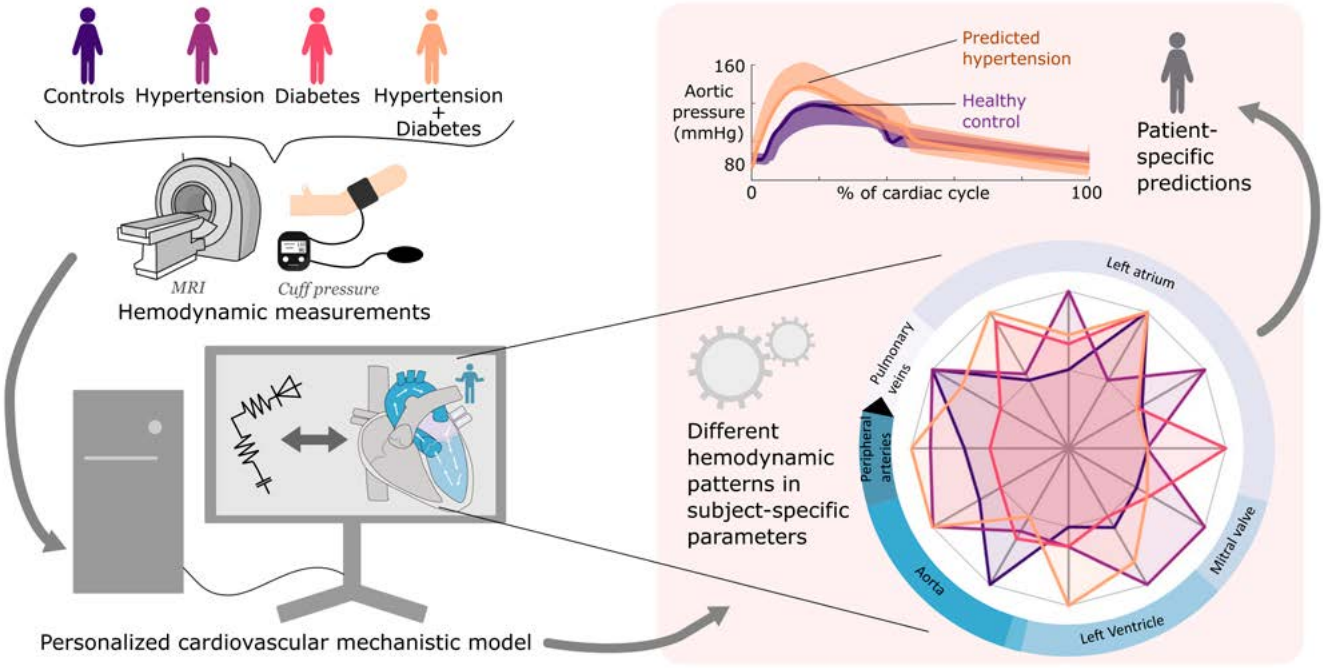
A cardiovascular mechanistic avatar for blood pressure regulation

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.



Overview of the use of 4D flow MRI combined with a personalized cardiovascular model to assess differences in hemodynamic parameters and make patient-specific predictions of disease progression.

Federica Viola

Improving Post-Processing of Cardiovascular 4D Flow MRI

Time-resolved three-dimensional phase-contrast magnetic resonance imaging (4D flow MRI) is a type of acquisition that permits measurement of velocities in any direction in the whole volume acquired, lending itself well for flow visualization and quantification. One of the most interesting features of 4D flow MRI is the retrospective placement of analysis planes, which allows for the assessment of flow volumes through vessels and shunts(1). At present, widespread use of 4D flow in the clinical setting is hindered by technical limitations, like sub-optimal data quality hampered by phase errors, limited temporal-spatial resolution, and long scan time.

To adapt 4D flow MRI to the clinical workflow, the impact of its limitations must be assessed, and efficient post-processing techniques must be developed to improve data quality and facilitate data handling. The potential advantages of 4D flow MRI compared to the golden standard techniques are many, but faster and more accurate methods are necessary.

The first part of this project is indeed devoted to solving some of the technical issues and limitations of 4D flow MRI. We have first compared faster 4D flow MRI sequences, finding an optimal balance in terms of reduced scan time and resulting data quality(2). After that, we have developed a deep-learning-based cardiovascular segmentations approach (a CNN network), for improved data handling and automated segmentation of the regions of interest, such as the heart chambers and the vessels (3). In the third study we will focus on developing a new technique for removing a specific phase error from the data, the background offset. The plan is to exploit deep learning networks, due to their proved outstanding performance in a variety of imaging tasks. In the following studies we will focus on developing cardiac applications for 4D flow MRI, such as methods for the assessment of diastolic function and for evaluating the effect of mitral valve repair surgery.

PROJECT INFORMATION

Project
Improving Post-Processing of Cardiovascular 4D Flow MRI

Supervisors
Tino Ebbers, Petter Dyverfeldt, Carl-Johan Carlhäll, Farkas Vanky

Short CV
Research Engineer at the Unit of Cardiovascular Science at the Linköping University Hospital, November 2014–Current.
MSc in Biomedical Engineering at Linköping University, Sweden, Sept 2012 –Sept 2014.
BSc in Electronic Engineering at Università Degli Studi Di Palermo, Palermo, Italy with highest honors; 110/110 cum laude, October 2002–July2007.

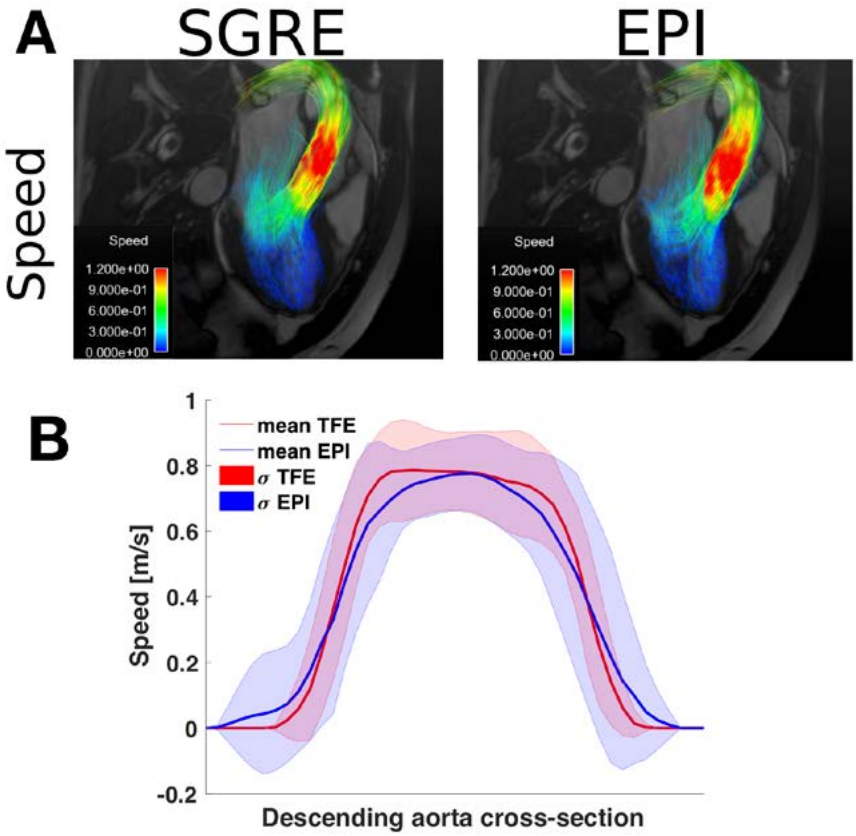


Figure 1. Comparison between two fast 4D flow- based sequences, SGRE and EPI. A: Streamlines plotted on a reference left sided 3ch-image. Streamlines do not show any visible abnormal velocity profile. B: Speed at peak systole through a cross-section of the thoracic descending aorta in SGRE (red) and EPI (blue) data. Mean values of all subjects are represented as solid lines, and standard deviation as shaded areas(2).

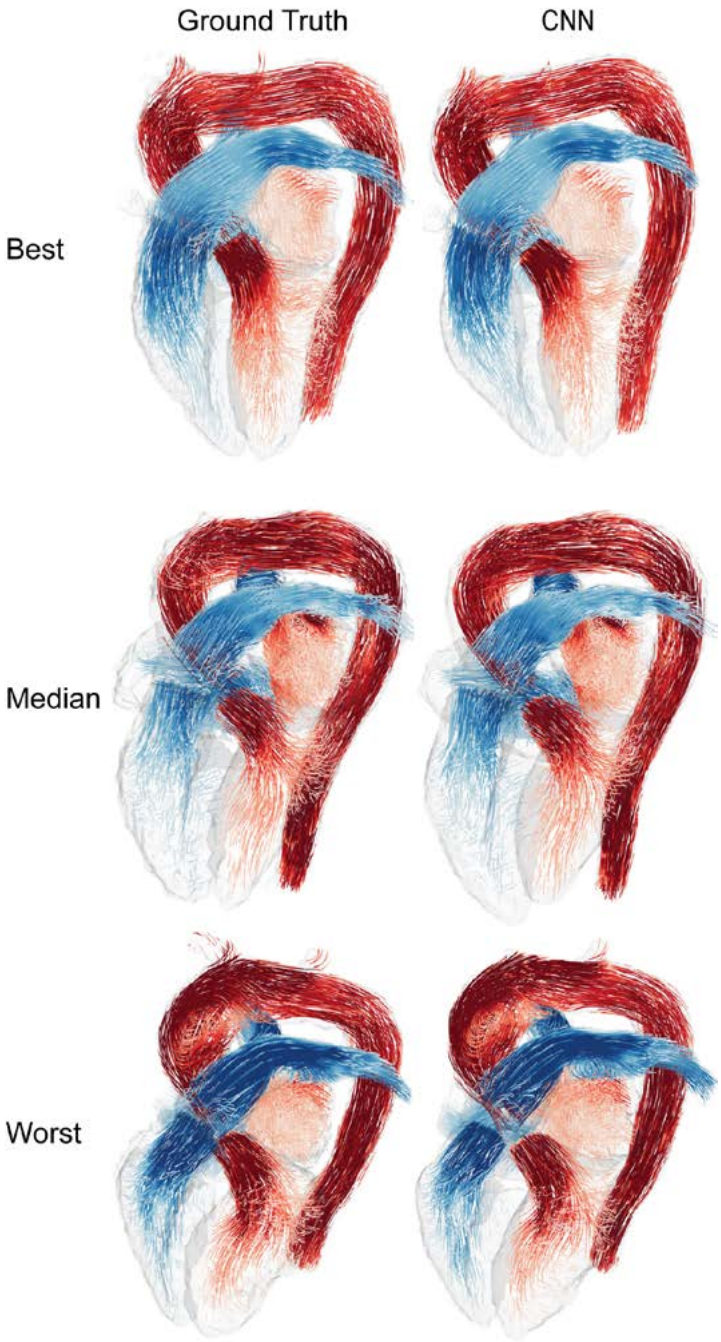


Figure 2. Flow streamlines generated at a mid-systolic timeframe using the ground truth and CNN results for the best, median, and worst Dice scores. Dice scores of 0.96, 0.91, and 0.86, respectively. Pulmonary flows are depicted using shades of blue, and systemic flows using shades of red. Streamlines were generated independently for each region included in the segmentation(3).

The Philips Ingenia 3.0T MR scanner.

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 **NAEOTOM 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 eyesight 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 Nanozoomer 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.

The 4K projector room.

Sophia Bäck, Kajsa Tunedal and Twan Bakker in a meeting room at CMIV.

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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Marcel Warntjes	Senior Staff Scientist

Milda Pocevičiūtė and Federica Viola.

Publications

The CMIV research efforts lead to a steady stream of scientific publications. An overview of the 2022 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.

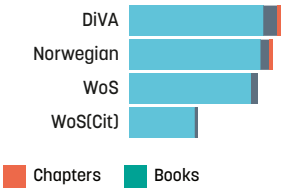
Bibliometric Analysis

1. Basis for analysis, 2018-2022

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

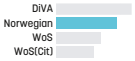
[1] Publications in DiVA
[2] Publications based on the Norwegian model
[3] Publications in Web of Science
[4] Publications in citation analysis



[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.

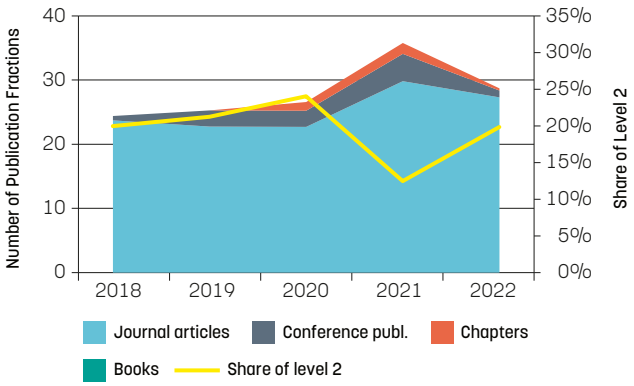
At each new section of the analysis, the symbol in the top right corner will mark the selection being used.

2.a Norwegian model, 2018-2022

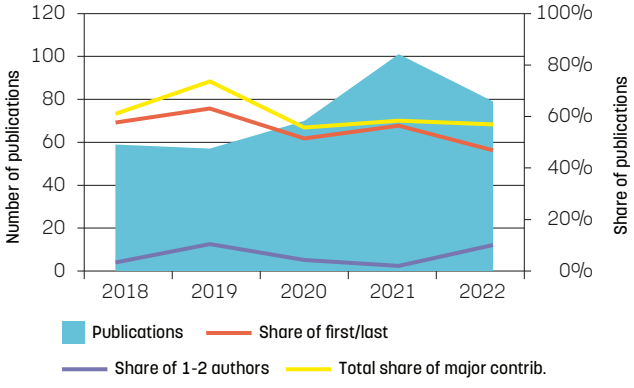


Publications published in journals and by publishers in the Norwegian list	Number of publications	Number of publication fractions	Share of level 2
Journal articles	331	126.3	21%
Conference publications	23	11.0	0 %
Chapters	8	3.4	5 %
Books	0	0.0	0 %

Share of level 2, total: 25 %



2.b Author position, 2018-2022

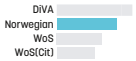


Publication fraction refers to the share of a publication originating from the department. For example, if two out of four authors are affiliated with the department, the fraction is 0.5.

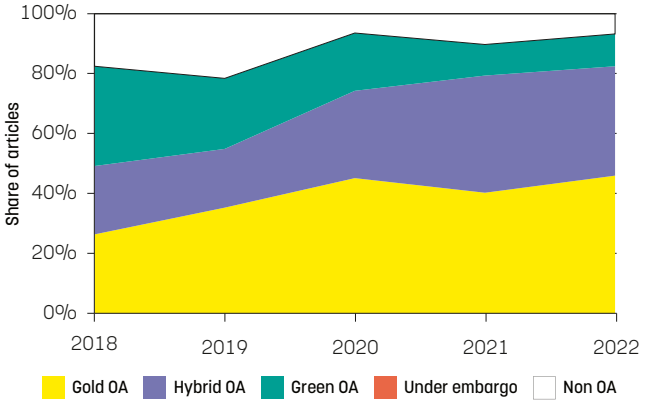
In the Norwegian model, the included publication channels are divided into two levels – 1 (scientific) and 2 (scientific and leading in its field of research). Level 2 publication channels comprise a maximum of 20 percent of channels in their research field.

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.

3. Open access, 2018-2022

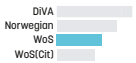


Share of open access publications (incl. OA after an embargo period):	
Journal articles	88%
Conference publications	30%
Chapters	25%



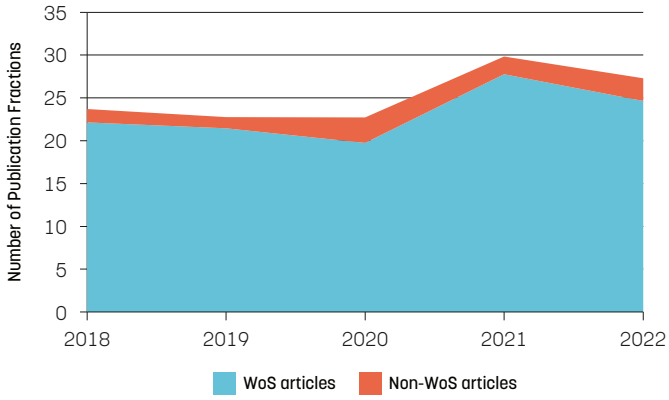
Open Access (OA) publications have been identified with the help of data from Unpaywall (unpaywall.org). The diagram shows articles according to Open Access type. OA data for articles has been supplemented with data from our own customized algorithm. Gold Open Access is defined as articles published 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.

4. Coverage in Web of Science, 2018-2022



	Number of publications	Number of publication fractions
Journal articles and conference publications *	328	125
Coverage		
Journal articles: 95 %		
Conference publications: 55 %		

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

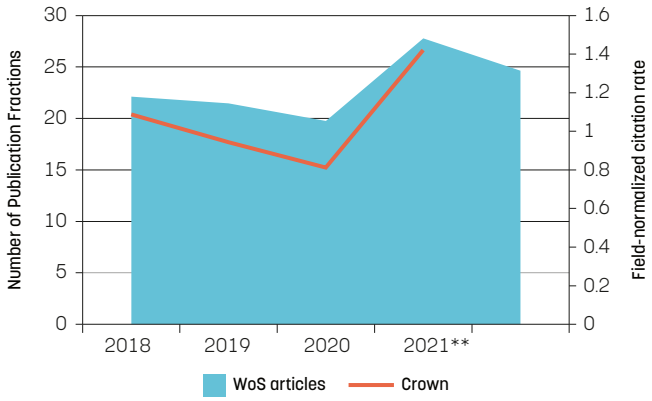


The analysis is based upon Clarivate Analytics Web of Science. For a citation analysis to be relevant and reliable, a sufficient basis is required. To give an indication of the coverage of journal articles in the database, the number of publications/fractions in the database is displayed. All citation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

5. Citation analysis, 2018-2021

DiVA
Norwegian
WoS
WoS(Cit)

	Number of publications	Number of publication fractions
Journal articles *	167	66.8
Results, field-normalized		
Field-normalized citation rate (crown): 0.98		
Share of highly cited articles (top 10 %): 13 %		
Share of uncited articles: 12 %		
Ranking of Journal Impact Factor (JIF), average: 0,69		



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.

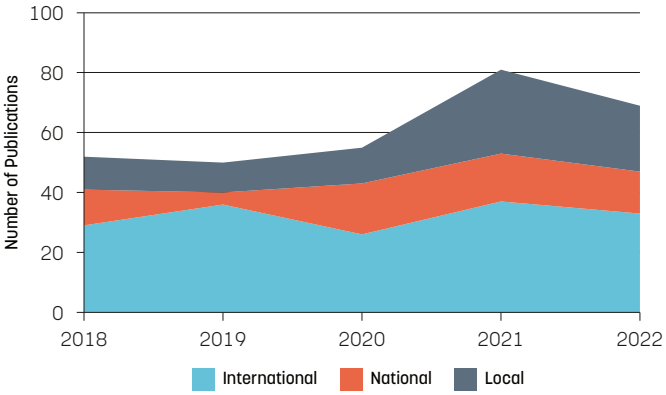
- Field-normalized citation rate (Crown): a measure of impact of articles included in the analysis that provides acomparison with the international average for the same subject area, year and type of article, where 1 is the globalaverage. Field normalized rate of citation is fractionalized, i.e. the number of authors affiliated with the department istaken into account. Self-citations are excluded. The average field normalized citation rate for universities in Swedenduring 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 citedpublications 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. Itprovides a comparison for the average number of citations for the journals chosen for publication with the globalaverage number of citations for journals in the same field. I.e, a value of 0.9 means that the chosen journals forpublication are on average cited 10% less than journals in the same field(s).
- SNIP: normalized journal indicator based on data from Scopus.

*Articles, reviews and letters in WoS.
**The results for last year's articles should be interpreted with great caution. Thecitation rate for newer articles is generally low, leading to individual items causing high impact on the average rate.

6. Co-authorship - geographical, 2018-2022

DiVA
Norwegian
WoS
WoS(Cit)

Share of articles with international co-authorship	52 %
Share of articles with national co-authorship	21 %
Share of articles with local co-authorship	27 %



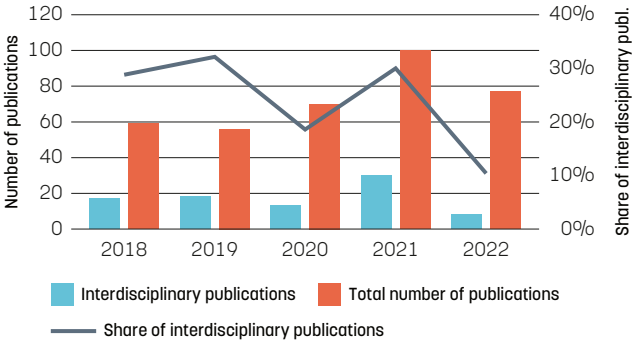
Share of publications in WoS where department authors have co-authored with international, national or local collaborators (academic as well as non-academic). Local co-authors refers to other LiU authors. This category also includes single authors. International collaborations are also displayed, since 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.

7. Interdisciplinary authorship (LiU faculties), 2018-2022

DiVA
Norwegian
WoS
WoS(Cit)

Publications with interdisciplinary authorship*	
Number	86
Share	24 %

*Publications with more than one faculty.



The share of co-authorship per type of partner and number of co-publications with specific companies/agencies are calculated per publication. The classifications are based on authors' external affiliations in DiVA, where at least one author has an external affiliation identifies as collaboration outside of academia. The types of collaborations included are companies and Swedish government agencies.

Publications 2022

CMIV affiliated researchers are written in bold.

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Part of the research school are heading to lunch. Chiara Trenti, Twan Bakker, Sophia Bäck and Gustav Magnusson.

Annual accounts

During 2022 CMIV had a turnover of more than 58 million.
The financial result for CMIV in 2022 was SEK 1.119 thousand.

During the fiscal year 2022 CMIV had several ongoing grant research projects. AIDA – Analytic Imaging Diagnostics Arena continued its work, being funded by VINNOVA. 18 projects funded by AIDA together with three clinical fellowship and five clinical evaluation projects started during 2022.

SciLifeLab extended its funding of AIDA data hub during 2022. Research projects SCAPIS (Swedish Heart-Lung Foundation) and MeDigiT (Visual Sweden) continued during 2022. 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.

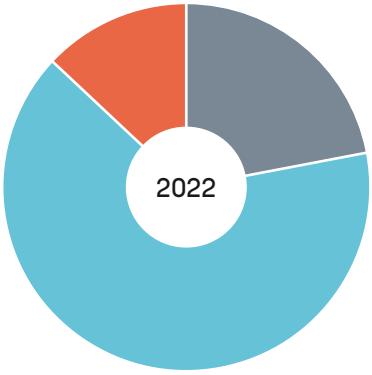
ECONOMIC SUMMARY	2018	2019	2020	2021	2022
Total revenue	**52,059**	**56,266**	**55,007**	**57,384**	**58,794**
EXPENSES					
Staff expenses	-16,711	-20,390	-22,480	-23,660	-23,907
Cost of premises	-6,657	-5,752	-6,647	-6,474	-6,372
Misc. Operating expenses	-18,704	-18,848	-17,928	-19,551	-20,489
Depreciation expenses	-8,129	-8,440	-7,848	-6,878	-6,897
Financial expenses	-151	-126	-11	-4	-10
Total expenses	**-50,051**	**-53,556**	**-54,913**	**-56,568**	**-57,675**
Result of operations	**2,008**	**2,710**	**95**	**815**	**1,119**

Research funding at CMIV 2010–2022

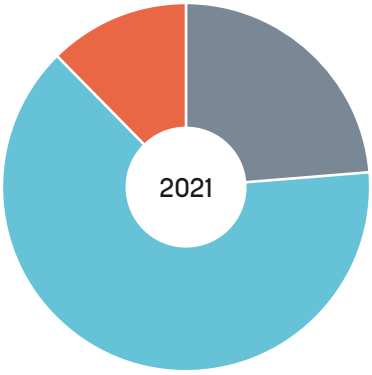
CMIV receives funding from research funds and the industry both directly to the R&D platform and to specific research projects. In addition, the affiliated researchers have their own funding; these grants will, however, not be presented here.

External funds: kSEK 158,377
Industrial funds: kSEK 92,564

CT Research and Clinic (%)

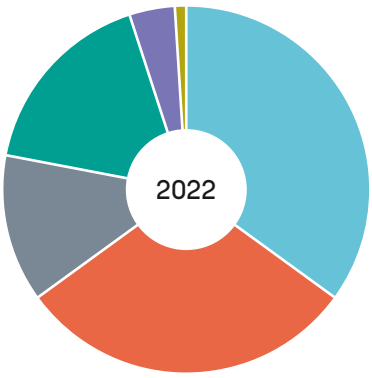


Research, 22
Clinic, 65
Special exams only at CMIV CT, 13

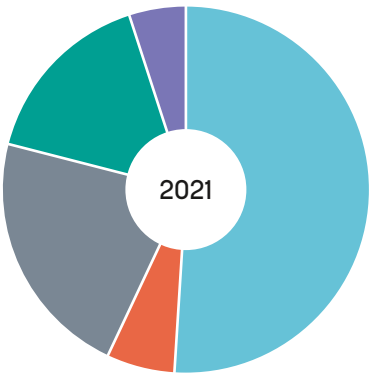


Research, 23
Clinic, 65
Special exams only at CMIV CT, 12

Distribution on Research on the MR Scanners (%)



Neuro, 35
Musculoskeletal, 30
Cardiovascular, 13
Gastro, full body, 17
Development, 4
Pediatric, 1



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

CMIV will continue to make new moves in 2023.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