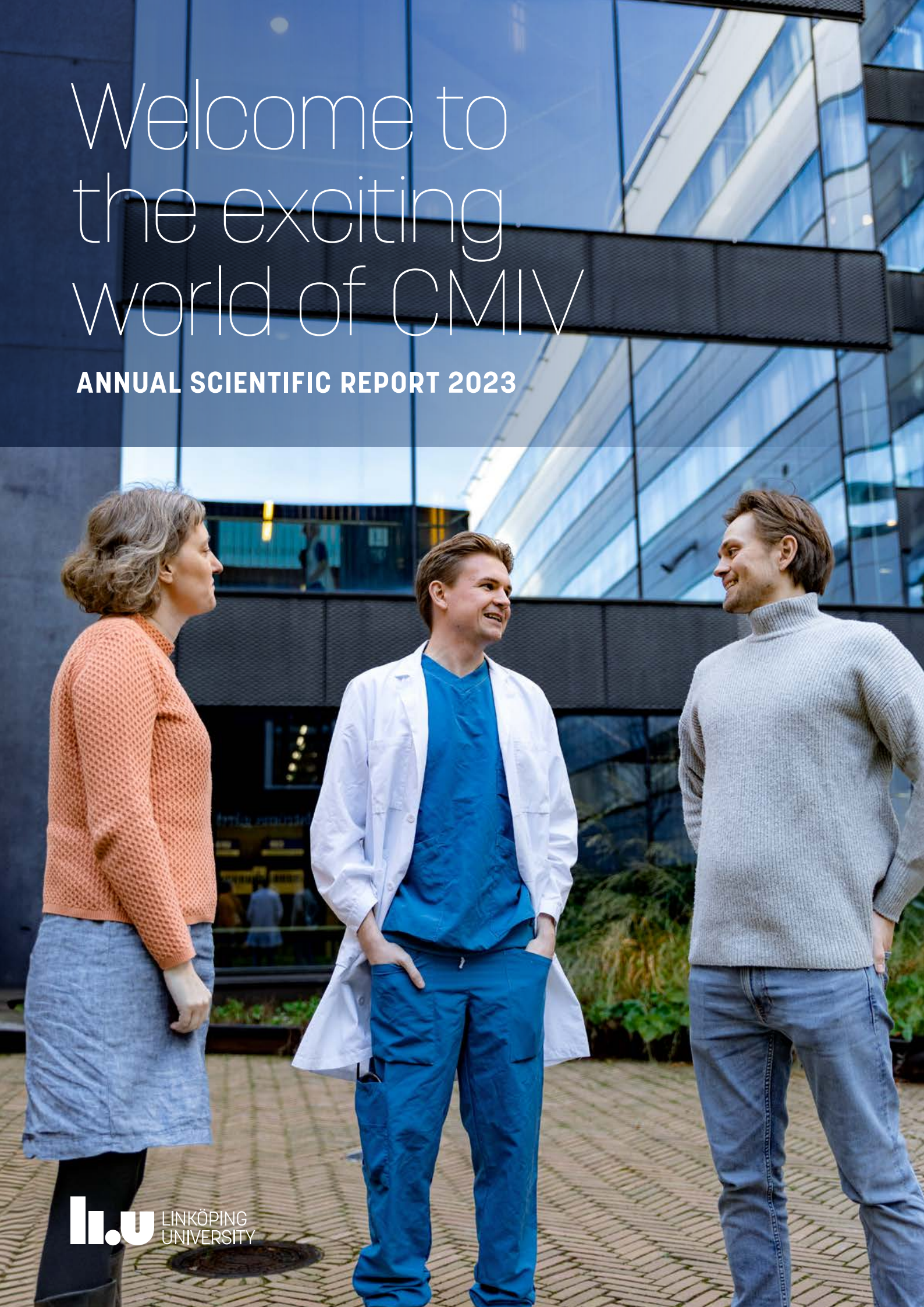
Welcome to the exciting world of CMIV

ANNUAL SCIENTIFIC REPORT 2023



LINKÖPING UNIVERSITY

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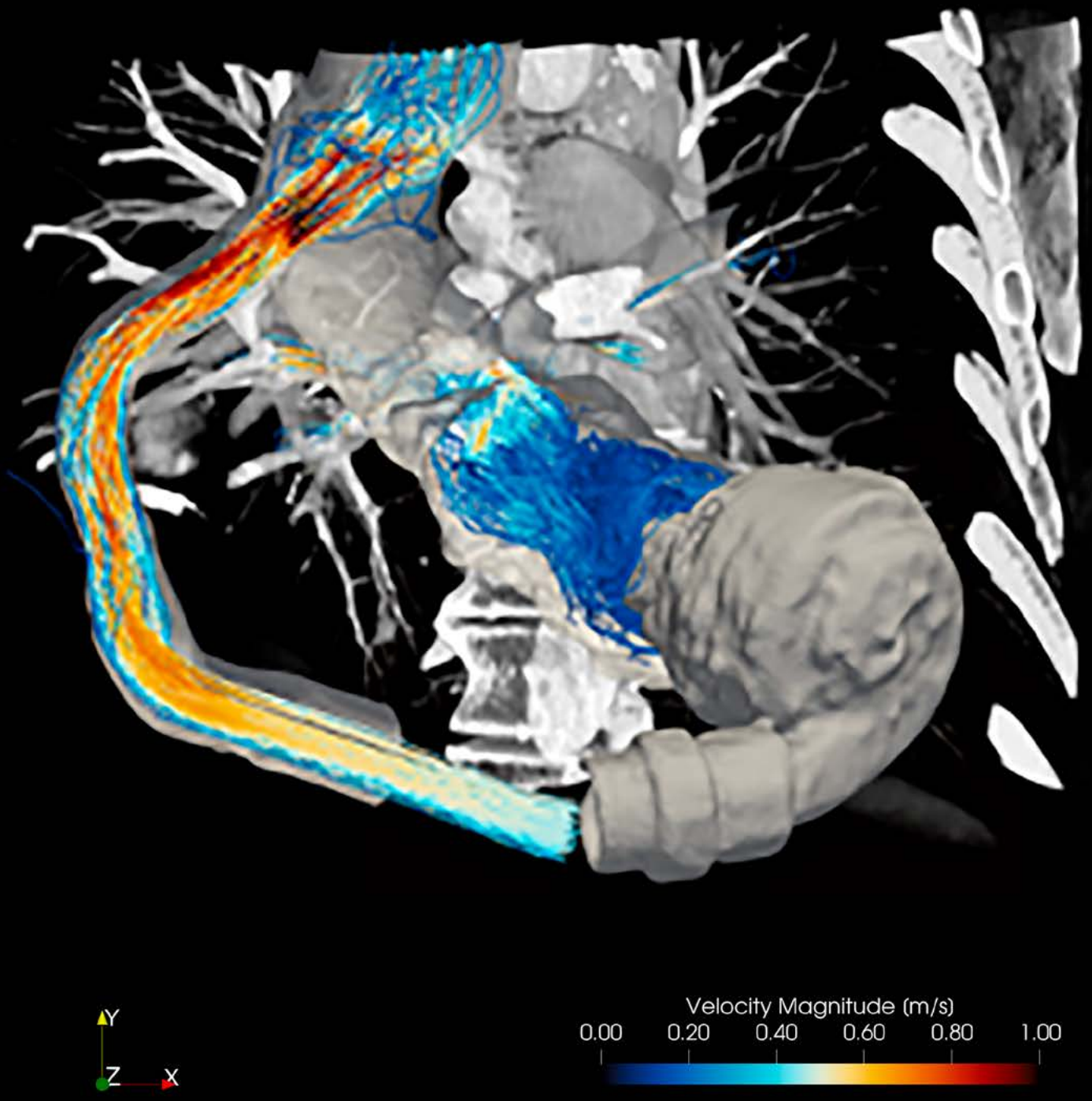

Visualization of intracardiac blood flow patterns in a patient with an implanted left ventricular assist device (LVAD, shown in gray). The analysis is based on photon-counting CT data, allowing computation of blood flow patterns in the left side of the heart and the outflow graft connecting the LVAD with the ascending aorta. Through this technique, researchers and clinicians can acquire hemodynamic information that would otherwise be unattainable. Image by Jonas Lantz & Linus Ohlsson, CMIV.

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Preface

As we reflect on CMIV's journey in 2023, we're feeling proud and excited about the strides we've made. Our spaces have been buzzed with visiting scholars, bringing in fresh ideas and collaborations. It has been truly inspiring to witness clinicians embracing the pioneering photon-counting technology to improve patient outcomes.

Our research community, especially through our graduate school, has shown remarkable unity and productivity. The retreat in Vadstena stands out as two days of rich dialogue and knowledge exchange among our researchers in the scientific council and PhD students, fostering a vibrant academic atmosphere.

Post-pandemic, there has been a surge in interest in CMIV. We've welcomed a wave of national and international visitors, and our participation in scientific conferences has reached new heights.

This year's flagship projects – Bigpicture: Skin Node Data Collection, Exploring the Endocannabinoid System in Trauma-Exposed Individuals, and finally, Global Data Pooling and AI for Optimized Fragility Fracture Prevention – demonstrate our commitment to turning intricate research into practical health solutions.

An important milestone was securing an 8 million SEK grant from Vinnova to establish a comprehensive research database. This forms a strong foundation for pioneering AI and precision medicine research planned for the next two decades, from 2024 to 2044.

As CMIV continues to grow, our strategies pivot towards data-driven imaging, aiming to connect intricate cellular data to the complexities of the human body. Our ultimate aim remains unchanged: to improve patient care and individual health outcomes through our dedication to medical image science and visualization.

2023 reflects our collective efforts. We are grateful for enduring partnerships with the university, healthcare sector, industry, research groups, and our support staff. Together, we've elevated our research, solidifying CMIV as a center of scientific excellence and a guiding light for future medical breakthroughs.

Anders Persson
DIRECTOR OF CMIV

A drill from Parken Zoo, Eskilstuna, examined in both our photon counting CT and our MR scanner.

Highlights

As always, it has been an intensive year and a lot of things have happened.
Join us as we spotlight a selection of CMIV's achievements here.

Continued fruitful cooperation with wildlife parks in Sweden

For zoo veterinarians, it is invaluable to have access to images of wild animals, as these are generally not readily available. For CMIV, this is a way to use the images without having to consider patient confidentiality. Over the years, we have had many wild animals, primarily from Kolmården Wildlife Park, visiting us. Last spring, Parken Zoo in Eskilstuna brought in a drill that was not doing well. He had hit his head, leading to a change in behavior and the onset of self-harming behavior. Therefore, he was examined in both our photon counting CT and our MR scanner.

The drill in the MR scanner.

Siemens Healthineers' Head of CT at CMIV

Dr. Philipp Fischer was an honored guest during a visit at the end of March. Throughout his stay, Dr. Fischer engaged in productive discussions with Prof. Anders Persson and various research groups, focusing on collaborative research initiatives concerning photon counting detector computed tomography. His insightful visit included a comprehensive tour of CMIV, providing an opportunity to interact with our modality managers. He also had the chance to review newly taken images of the drill.

This visit not only bolstered collaboration prospects but also showcased CMIV's innovative strides in imaging technology, reflecting the commitment to advancing healthcare through cutting-edge research and partnerships.

Dr Philipp Fischer, Head of Computed Tomography, Siemens Healthineers together with Prof. Anders Persson at CMIV.

CMIV's Noteworthy Presence at ISMRM

In a modest display of ongoing research efforts, CMIV participated at the ISMRM – The International Society for Magnetic Resonance Imaging in Medicine, 2023 conference in Toronto.

Eight committed researchers and PhD students from CMIV presented a total of 11 abstracts, emphasizing our dedication to advancing the frontiers of medical imaging.

Toronto Skyline and the convention center of ISMRM.

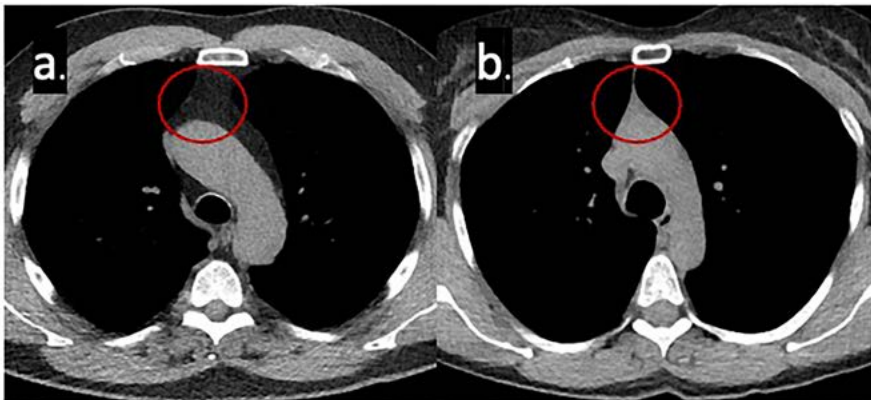
Significant Research Grant from Vinnova

Region Östergötland has received 30 million Swedish kronor from Vinnova to run a four-year project aimed at improving the management of the region's health data. The project is part of the field of information-driven development, which is a component of the Region's investment in precision health. CMIV has received 8 millions of these funds to develop a research database that will later be integrated with Region Östergötland's Health Data Space.

VINNOVA
Sweden's Innovation Agency

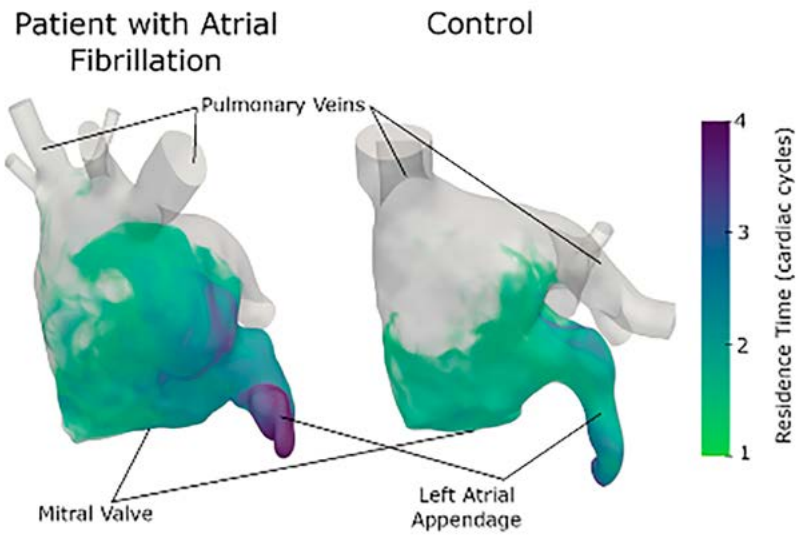
Unveiling Thymus's Influence: Insights into Immune Aging

Mårten Sandström and Lena Jonasson et al have found out that the thymus, often overlooked, might have a significant impact on adult immune systems contrary to prior beliefs. As people age, the glandular tissue in the thymus is replaced by fat. However, a recent study on CT morphology of the thymus reveals this process links to sex, age, and lifestyle. The findings also suggest that the thymus's changes mirror immune system aging, highlighting its potential relevance in understanding immunity as we grow older.



a) Fatty thymic degeneration. b) Preserved thymic tissue.

Revelations in Atrial Fibrillation: Stagnant Blood and Tailored Treatments for Stroke Prevention



In a study on atrial fibrillation by Sophia Bäck et al, they found that even when the heart beats normally, blood tends to pool in the left atrium for extended periods. This stagnant blood increases clotting risks, potentially leading to strokes. Understanding this helps tailor medications for individual patients, reducing stroke and bleeding risks.

'Your Brain' Series on SVT Featuring CMIV

Featured on the Swedish national TV series 'Your Brain' on SVT, CMIV had the honor of hosting two compelling episodes this year. The first episode, exploring the human brain's moral compass, showcased CMIV researcher Irene Perini and PhD student Robin Kämpe as they investigated whether brain size influences moral inclinations.

In the subsequent episode, series host Anders Hansen engaged in a forward-looking discussion with Anders Persson about the future of the brain. Hansen, a prominent psychiatrist and the anchor of the series, highlighted the burgeoning role of AI in medicine, particularly in fields like pathology and radiology.

Anders Hansen and Anders Persson in the Wranne theatre, CMIV.

Iulian Emil Tampu, PhD student, at a teambuilding activity together with CMIV Research School.

The CMIV Landscape

When CMIV was initiated, the vision was to consolidate all components of medical imaging and visualization in one place. Simultaneously, the goal was to establish a novel research environment where scientists, engineers, technicians, and medical doctors could collaborate closely with immediate access to patients – a space fostering seamless integration of research and clinical requirements. Since the start in 2002, CMIV has evolved into this vision, becoming a part of 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 such as 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. Basic research outcomes at the university can be applied in clinical research, leading to scientific publications and advancements in 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. Currently, artificial intelligence and precision medicine are integrated parts of the imaging chain.

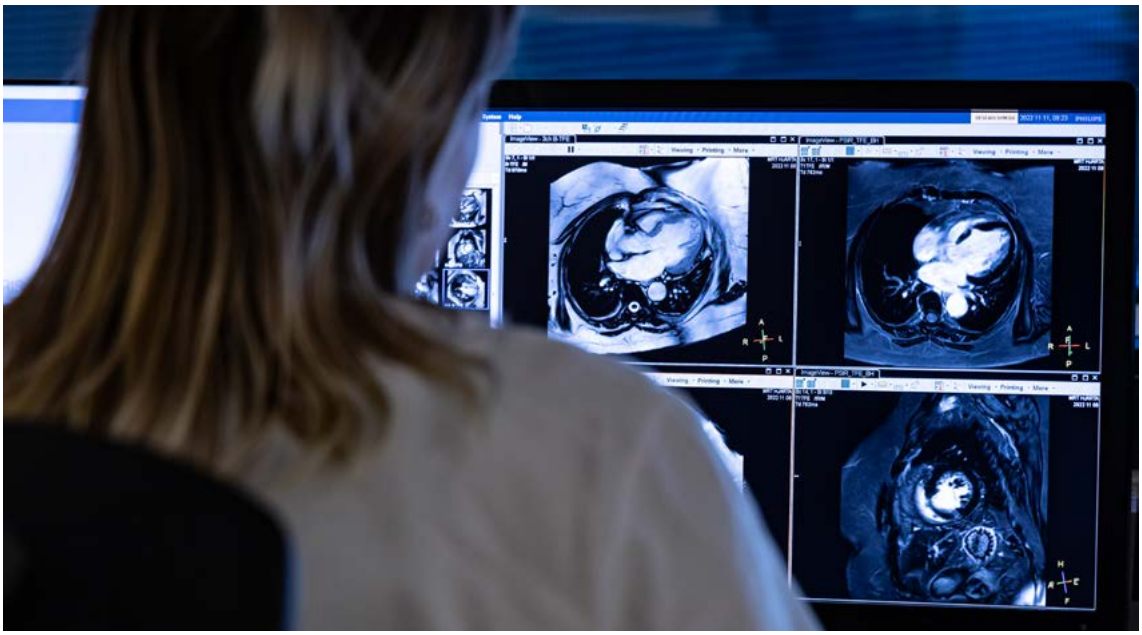
We find ourselves amidst a paradigm shift in healthcare. While focused research and development in every step of the chain remain crucial for continuous improvements in the quality of care, it is equally important to embrace new possibilities and allow research to extend into new dimensions. This adaptability is essential for maintaining a leading position in medical imaging, a principle CMIV is currently incorporating into its research strategies.

The advancements in precision medicine result from rapid developments in several groundbreaking areas. However, the impact of these advancements can be significantly amplified when wisely combined. These areas encompass molecular biology, large-scale genetic sequencing, and artificial intelligence. CMIV is actively positioning itself at the forefront of this development, recognizing the synergies that can arise from integrating these diverse yet interrelated fields.

Precision medicine can be defined as a set of clinical, therapeutic, and diagnostic methods tailored for optimal disease management, taking into account individual variations among patients, often incorporating a genetic profile. Its primary goal is to offer more effective treatments, reduce adverse effects, and improve overall survival rates.

Furthermore, precision medicine extends its advantages to increased possibilities for identifying and, subsequently, preventing or mitigating diseases at an early stage. It facilitates improved disease management for patients and contributes to the reduction of hospital stays.

The CMIV projects defy easy categorization as they dynamically traverse various research areas, consistently seeking inspiration from diverse fields. To provide a visual representation of the CMIV research landscape, we've crafted an overview table using projects from the annual report. The table identifies key areas of involvement, classifying them into three main research domains: imaging data source, biomedical research area, and technical research area. Each of these main areas comprises several sub-areas, capturing the multidisciplinary nature of CMIV's research endeavors.



Nurse in front of the screens at the MR scanner.

IMAGING DATA SOURCE

Traditionally, the predominant data source at CMIV has been magnetic resonance imaging (MRI). This method's versatility allows for extensive opportunities in project-specific development. An additional advantage lies in the use of volunteers without restrictions imposed by radiation dose.

In the realm of computed tomography (CT), the advent of low-dose CT has facilitated larger prospective studies, and clinical examinations can be utilized for potent simulations. Since 2020, CMIV has stood as one of the few clinical research centers worldwide with access to the cutting-edge photon-counting CT technology. The latest photon-counting CT, now clinically approved, features two X-ray tubes and two detectors, offering unprecedented possibilities.

While MRI remains a major data source, there has been a rapid increase in data from digital pathology and photon-counting CT. The researchers' growing need to amalgamate data from diverse sources places substantial demands on infrastructure, particularly for data storage and access to computing power.

CMIV is currently engaged in several exciting studies across these fields. Another emerging area with a growing contribution is microscopy, where the ongoing digitization of clinical routines has paved the way for new applications in image analysis and deep learning.

BIOMEDICAL RESEARCH AREA

CMIV has a rich tradition in cardiovascular and neurology research, with other robust areas including musculoskeletal and gastrointestinal research. However, with new collaborative constellations emerging, projects are shifting away from a singular focus on individual organs, adopting a more holistic approach.

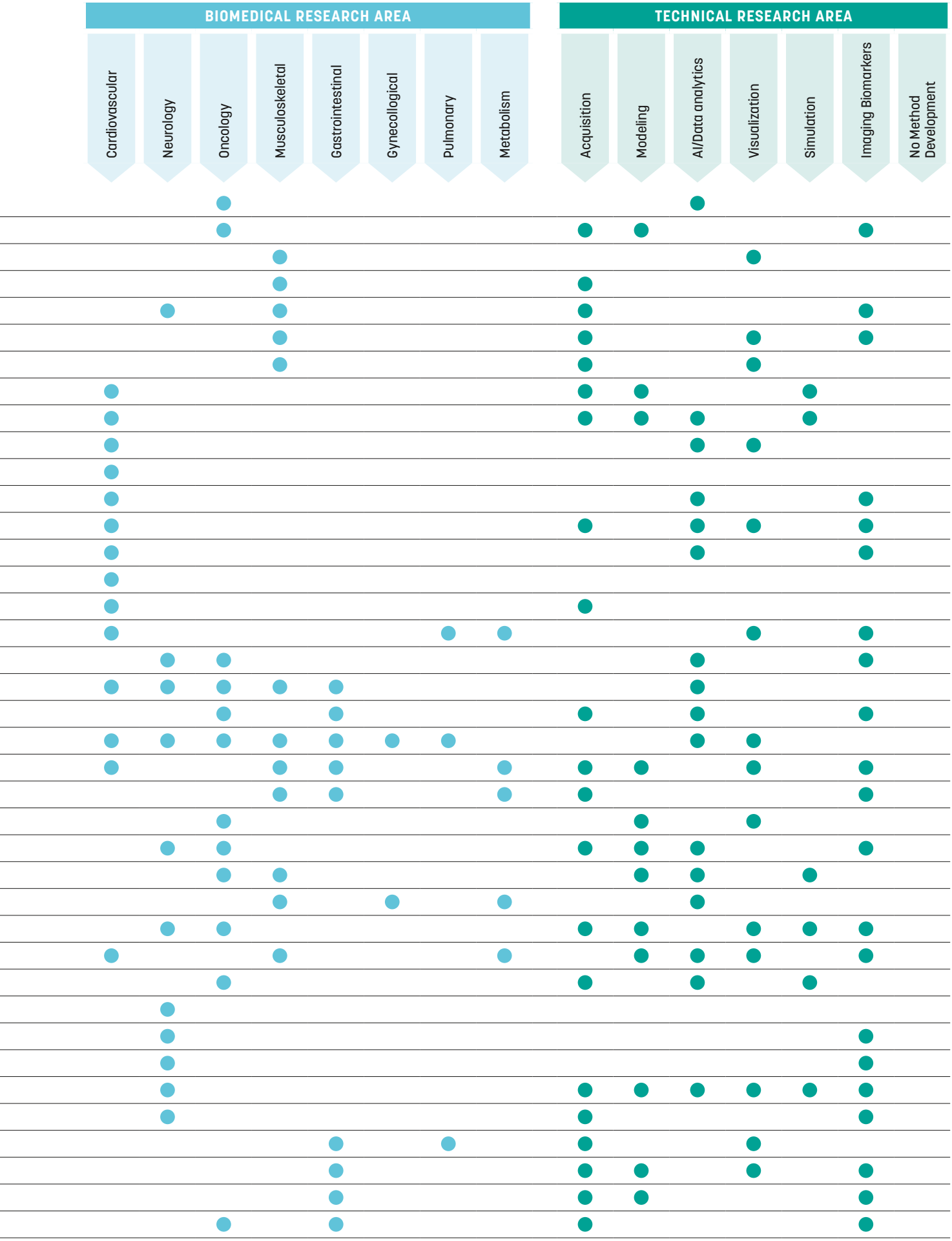
TECHNICAL RESEARCH AREA

A fundamental aspect of CMIV lies in its comprehensive approach, encompassing all technical areas involved in the imaging chain. This cross-disciplinary strategy ensures that scientific endeavors in one technology domain at CMIV benefit from in-depth knowledge of the characteristics of preceding steps and the subsequent utilization of results later in the chain.

The overview reveals a well-balanced distribution of CMIV projects in terms of technical contribution. This spans from data generation through acquisition and simulation to a diverse array of analytics and visualization methods.

A SELECTION OF CMIV PROJECTS DIVIDED BY RESEARCH AREA

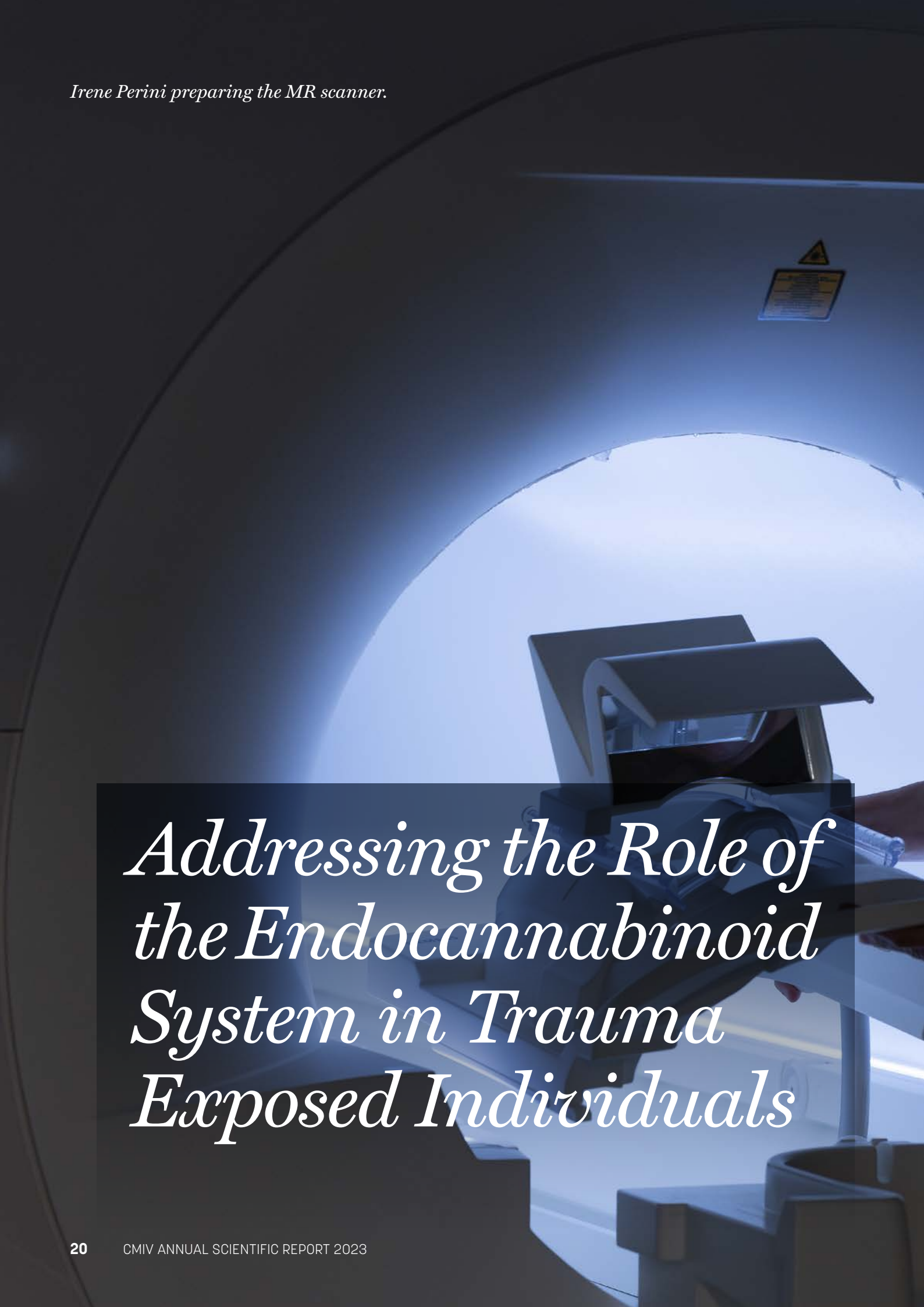
	IMAGING DATA SOURCE				
	Computed Tomography	Magnetic Resonance Imaging	Digital Microscopy	Ultrasound	Other
Artificial Intelligence in Breast Cancer Screening					●
MR-Mammography 3.0		●			
Bone Analysis for Reducing Osteoporotic Fractures	●				
Photon-Counting CT of the Wrist	●				
Pain Mechanisms in Chronic Widespread Pain Including Fibromyalgia		●			
The NACOX-Study	●	●			
PCCT for Radiographic Assessment of Osseointegration	●				
4D Flow CT	●				
4D Flow MRI		●			
Evaluating Antithrombotic Treatment Post-Coronary Artery Bypass Grafting with CT	●				
Chronic Coronary Syndrome in Swedish Primary Care	●			●	●
Predictive Value of Carotid MRI		●			●
MR Turbulence Angiography		●			
Ascending Aortic Dilation		●		●	
Aortic Stenosis - Calcium Burden and its Impact on Left Ventricular Function	●				
Optimizing PCCT in Patients with Metal Devices	●	●			
Swedish CArdioPulmonary bioImage Study (SCAPIS) in Linköping	●	●		●	
Improved Diagnosis of Pediatric Brain Tumours Using AI-Based Digital Pathology			●		
AI-Based Medical Record Screening for Patient-Safe MRI Examination		●			
Photon Counting in Pancreatic Ductal AdenoCarcinoma	●				
AIDA	●	●	●	●	●
EPSONiP		●	●		
The ACCESS-ESLD Study		●			
Evaluation of New Brachytherapy Planning Methods		●	●	●	
ASSIST		●			
Spectral Photon-Counting CT for Radiotherapy	●				
Health Effects of Resistance Training in Postmenopausal Women		●			
Automatic Ventricle Segmentation Using 3D Quantitative MR		●			
Medical Digital Twin	●	●			
Computational Integrated Diagnostics Panorama for Liver Cancer	●	●	●		●
The Behavioral and Neural Mechanisms of Alcohol Choice Preference		●			
Pathophysiology Behind Prolonged Whiplash Associated Disorders		●			
PoCo-19: a Multidisciplinary Study on Fatigue in Patients with Post-Covid Condition		●			
Image-Based Biomarkers of Brain Disorders		●			
Detection and Neurological Effects of Manganese		●			
Evaluation of Reconstruction Methods in CT	●				
Assessment of Hepatic Function in Health and Disease		●			
Liver Function Evaluation		●			
Implementation of Synthetic MRI in the Abdomen		●			


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

Mischa Woisetschläger, Eva Klintström, Jörg Schilcher, Anders Eklund and Erik Tesselaar by the photon counting CT.

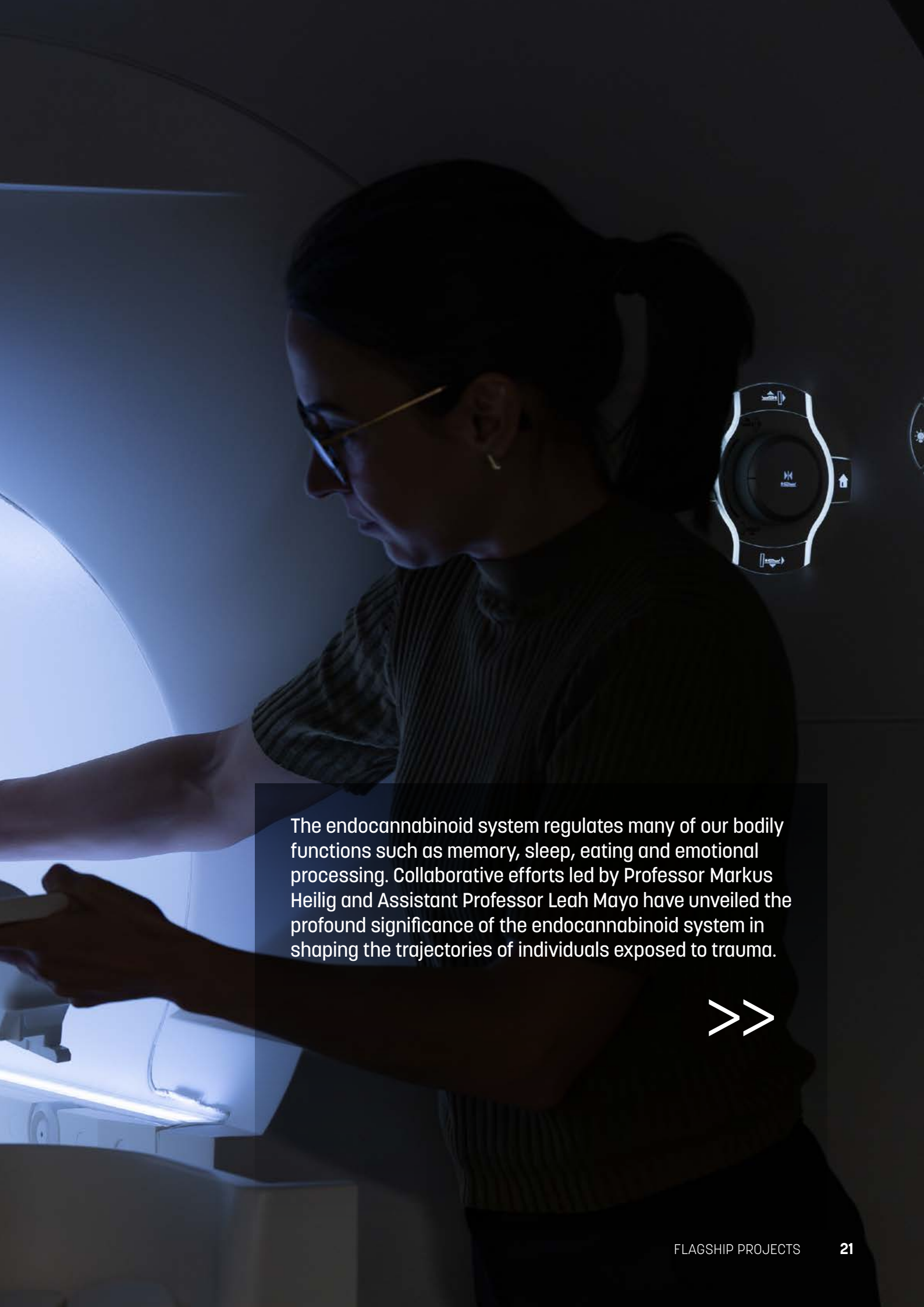
Flagship Projects

The 2023 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.



Irene Perini preparing the MR scanner.

Addressing the Role of the Endocannabinoid System in Trauma Exposed Individuals



The endocannabinoid system regulates many of our bodily functions such as memory, sleep, eating and emotional processing. Collaborative efforts led by Professor Markus Heilig and Assistant Professor Leah Mayo have unveiled the profound significance of the endocannabinoid system in shaping the trajectories of individuals exposed to trauma.

"The prevailing assumption linking early-life trauma to addiction lacked concrete evidence, primarily relying on retrospective self-reporting. Distinguishing between trauma and genetic predispositions posed a challenge", Markus Heilig explains.

By collaborating with researchers at Karolinska they delved deeper and found that a patient cohort that had been prospectively assessed, revealed a threefold increase in addiction risk associated with early-life trauma, even after factoring in genetic influences.

With Leah Mayo's involvement, first as a post doc, the research entered a new phase. It transitioned from statistical associations to in-lab inquiries, aiming to comprehend the mechanisms at play.

The comprehensive data collection involved intricate procedures.

"These individuals were all former patients at the trauma unit, the Elefanten Child and Adolescent Psychiatry unit in Östergötland. We were contacting them trying to track them down and trying to get them into the lab. It was a very difficult process. Some were willing to participate, some were not. All in all, a great team effort", Leah Mayo says.

"Worth highlighting here is the critical importance of highly skilled and passionate research nurses, who have played a pivotal role", adds Markus.

Their perseverance paid off as a hundred individuals, some with addiction and some without, joined the study. The data collection involved a functional magnetic resonance imaging (fMRI) session in the MR scanner with Irene Perini, psychiatric questionnaires, a lot of blood samples and stress test to see how the patients responded to stress. Leah also measured emotion processing together with fear conditioning. A small fraction of these tests has been analyzed and published with the result that the endocannabinoid system played an important role, particularly in those individuals who had been exposed to trauma and did not develop a substance use disorder. "They had a very unique endocannabinoid signature that we think could have conferred a kind of protection and resilience against more maladaptive coping strategies, like using drugs or alcohol", Leah explains.

Leah Mayo, now an Assistant Professor in psychiatry at the University of Calgary and affiliated with Linköping University, continued her research endeavors beyond her postdoc at LiU. Her expertise and dedication have significantly contributed to advancing our understanding of the endocannabinoid system's role in trauma-exposed individuals.

The endocannabinoid system, a pivotal neuro-modulatory network, operates within the body and brain, influencing stress regulation, sleep, memory, and more. Anandamide and 2-AG (2-arachidonoylglycerol), two crucial molecules within this system, emerged as focal points. Elevated levels of anandamide were associated with improved unlearning of fear memories – an essential factor for individuals recovering from trauma.

Professor Markus Heilig.

When Leah was a postdoc, she found that the ability to unlearn fear memories was improved when levels of anandamide were elevated. Either by virtual people's genetics or by a drug that boost those levels.

The implications of these discoveries hold promise for novel treatments. Elevating anandamide levels emerged as a potential therapeutic avenue. Clinical trials investigating this approach alongside psychological interventions for PTSD have sparked industry interest, possibly revolutionizing treatment approaches.

"In the child an adolescence perspective, there are other ways of increasing anandamide, one example is through exercise, which is really useful when one think of children. Through exercise we have seen similar effects", Leah says. Yet, the best way is of course to prevent people from developing a substance use disorder. "You could relatively easily establish through a blood test that this person is traumatized but also low on anandamide, and that is probably a person we should devote some attention to preventive efforts. It is much easier to prevent the development of substances problems than to treat them once they've emerged.", Markus concludes.

Assistant professor Leah Mayo.

MRI Neurology

Project information

PROJECT NAME

Addressing the Role of the Endocannabinoid System in Trauma Exposed Individuals.

PROJECT LEADERS

Markus Heilig & Leah Mayo.

MAIN PROJECT PARTICIPANTS

Irene Perini, Andrea Capusan, Per Gustafsson, Åsa Axén.

KEY PUBLICATIONS

Perini, I., Mayo, L., Johansson Capusan, A., Paul, E., Yngve, A., Kämpe, R., Gauffin, E., Mazurka, R. M. R., Ghafouri, B., Stensson, N., Asratian, A., Hamilton, J. P., Kastbom, Å., Gustafsson, P., Heilig, M. Resilience to substance use disorder following childhood maltreatment: association with peripheral biomarkers of endocannabinoid function and neural indices of emotion Regulation. Molecular Psychiatry, 2023.

Mayo, L., Asratian, A., Lindé, J., Morena, M., Haataja, R., Hammar, V., Augier, G., Hill, M. N., Heilig, M. Elevated Anandamide, Enhanced Recall of Fear Extinction, and Attenuated Stress Responses Following Inhibition of Fatty Acid Amide Hydrolase: A Randomized, Controlled Experimental Medicine Trial. Biological Psychiatry, vol. 87:6, 2020.

Johansson Capusan, A., Gustafsson, P. A., Kuja-Halkola, R., Igelström, K., Mayo, L., Heilig, M. Re-examining the link between childhood maltreatment and substance use disorder: a prospective, genetically informative study. Molecular Psychiatry, 26:7, 2021.

PI Anna Bodén, pathologist, is showing a skin dataset on the screen in Wranne theater.

Bigpicture – Skin Dataset for AI Training and Validation

Pathologists face a significant workload examining numerous microscopic slides and images routinely. Each glass slide contains vital information requiring careful scrutiny and expertise. The demanding workload leads to delay in turnaround time and fatigue, increasing the chances of errors. This highlights the importance of finding solutions to assist pathologists in managing their workload effectively, ensuring accurate diagnoses and maintaining patient care standards.

Bigpicture is a project that will develop and establish a large-scale database of pathology images, enabling development and implementation of artificial intelligence methods. Anna Bodén, an accomplished pathologist at Region Östergötland, serves as the co-lead of Work Package 3 (WP3) and the node coordinator for the skin node, overseeing data collection and management. One general aim of Bigpicture is to collect 3 million whole-slide images, (WSI), from clinical studies (human pathology data from pathology laboratories and biobanks) and non-clinical studies (animal pathology data from pharma companies in EFPIA). Hence, clinical collections are focused on six nodes: skin, lung, renal, liver, cancer, and the clinical trial node. A node coordinator promotes the diversity and strategy for collecting and constructing datasets. Data associated with the skin node will comprise about 10% of the final goal of one million clinical WSI. At present, there is a lack of pathology data mirroring clinical reality for AI training and validation. Therefore, the establishment of good quality and FAIR (Findable, Accessible, Interoperable, and Reusable) use of data collections aimed for collaborations across data owners and users are new grounds to explore.

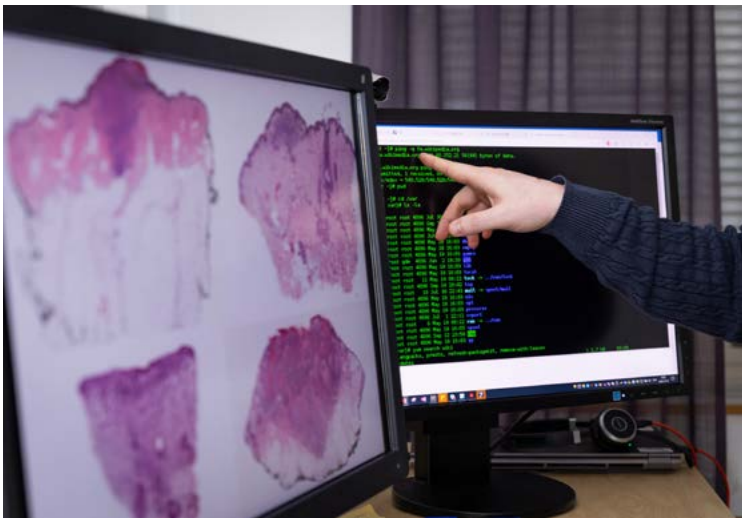
"All AI development should address clinical needs. In exploring potential use cases for a future AI tool, we consider perspectives from pathologists as well as from patients" Anna explains. One identified need is the early detection of melanomas, aiming to expedite the process from surgery to diagnosis. Jeronimo Frias Rose, a pathology resident, conducted background interviews, reviewed different published datasets, and defined key parameters for a versatile dataset ensuring anonymization.

"Traditionally, datasets feature a single representative image per entity", Anna continues. "If we were to implement a melanoma detection algorithm in a clinic setting, it would need to analyze all WSIs generated from a lesion. This introduces unknown variables, such as slides without malignant tissue from the resection margins. It is important to consider these clinical settings and highlight the need for the dataset environment to closely resemble real-world conditions, for a seamless transition to clinical application", Anna emphasizes. However, these assumptions require testing to determine their impact.

The melanoma detection system aims to serve as a prescreening tool, potentially functioning as a form of triage. However, assessing the computational requirements and monitoring the algorithm's behavior over time are crucial considerations. Milda Pocevičiūtė, at CMIV, is focusing on implementing quality control and surveillance metrics to account for evolving data.

The Bigpicture skin dataset, from Region Östergötland, aims to collect around 40,000 anonymized WSIs and descriptive metadata from various skin lesions, including melanoma, basal cell carcinoma, squamous cell carcinoma, and benign outcomes like scar tissue. The overarching goal is to leverage research on AI in clinical settings, enhancing the identification of melanoma. Today, the clinical predictive value is low, leading to many non-melanoma cases with a priority as melanomas. Integrating AI could aid in prioritizing urgent cases, expediting identification, and potentially revolutionizing melanoma diagnosis.

"Our aim is to use AI as a valuable diagnostic aid in the future," concludes Anna.



The image illustrates one collaborative part of dataset creation, selection of good quality pathology images and conversion into a dataset. On the left hand screen four different skin tumours, on the right hand screen the conversion into code and descriptive metadata. As AI models need bigdata, automation tools for extraction, convertion, anonymization and validation are important tools to enhance data access and use and hence development of these are one important foundation.

Anna Bodén, Joel Pettersson, Milda Pocevičiūtė, Erik Gabrielsson, Joel Hedlund, Jeronimo Frias Rose, Jeroen van der Laak, Caroline Bivik Stadler and Darren Treanor.

Digital Microscopy | Oncology | AI/Data analytics

Project information

PROJECT NAME

Bigpicture, WP3, Skin Node Data Collection.

PROJECT LEADER

Anna Bodén

MAIN PROJECT PARTICIPANTS

Caroline Bivik Stadler (Project lead AIDA funded project part), Jeronimo Frias Rose, Joel Pettersson, Maria Madentzoglou, Milda Pocevičiūtė, Erik Yllipää.

GRANTS

RÖ and LiU/CMIV as Bigpicture partners € 600 000 by the EU Innovative Medicines Initiative (IMI). (2021-2027) AIDA funding (2023-2025)

KEY PUBLICATIONS

Bodén et al. (2022). D3.03-Report on defined and first collected datasets. 945358-BIGPICTURE Central Repository for Digital Pathology. https://bigpicture.eu/sites/default/files/2023-04/945358-BIGPICTURE_D3.03_Report%20on%20defined%20and%20first%20collected%20datasets.pdf.

Bigpicture - Background

Center for Image Science and Visualization (CMIV) at Linköping University is engaged in the EU Innovative Medicines Initiative project Bigpicture to construct a large-scale database of pathology images enabling development of artificial intelligence methods. CMIV, with Joel Hedlund in lead in WP2, is responsible for the technical infrastructure, in a joint effort with the SciLifeLab Bioinformatics platform NBIS and ELIXIR-SE and the Finnish ELIXIR node CSC. The project partly builds on experiences from the CMIV-hosted AIDA Data Hub. CMIV Guest Professor Jeroen van der Laak is main coordinator of Bigpicture, and the CMIV efforts include close collaboration with Bigpicture partners Region Östergötland and Sectra.
Bigpicture is a 6-year, €70 million project that will herald a new era in pathology led as a consortium consisting of 45 partners from 15 countries and funded by the EU Innovative Medicines Initiative (IMI). Bigpicture will develop and establish the biggest European repository for sharing of pathology data to accelerate the development of artificial intelligence in medicine.

Global Data Pooling and AI for Optimized Fragility Fracture Prevention

Jörg Schilcher, PI.

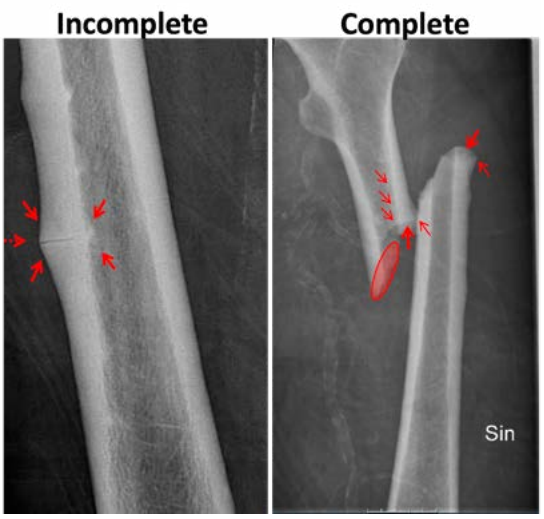
Osteoporosis is a bone disease marked by reduced bone density, increasing the risk of fractures. These fragility fractures are a major healthcare problem worldwide, primarily affecting women over the age of 50. Professor Jörg Schilcher is an orthopedic surgeon at Linköping University focusing his research efforts on fracture healing and how to best prevent fragility fractures using pharmacological interventions with limited side effects.

The journey began in 2006 when Professor Per Aspenberg and PhD candidate Jörg Schilcher together attempted to unravel peculiar femur fractures that occurred in patients on long-term treatment with drugs to treat osteoporosis. Initial attempts to reveal epidemiological aspects of these new fractures by examining X-rays from Östergötland and Lund lead to striking findings – drug treatment against osteoporosis (bisphosphonates) appeared to be causally related to insufficiency fractures in the thigh bone – Atypical Femur Fractures (AFF).

While aiming to bolster bone density, bisphosphonates interfere with bone repair mechanisms, resulting in fractures despite improved bone density. With bisphosphonate treatment extending over longer periods of time, in some patients bone strength diminishes as a result of accumulating microdamage which deteriorates the material properties of the bone ultimately leading to an insufficiency type of fracture. These fractures are unique in their radiographic appearance because the skeleton senses the accumulation of microdamage and starts a healing process (Figure 1). Because of the bisphosphonate treatment, the cascade of bone healing is disrupted and while new bone is added around the fracture (bone apposition), the micro-cracks persist and weaken the structural integrity of the bone. At some point the thigh bone can break with as little trauma as a one leg stance.

"While medications are important in the treatment of osteoporosis and prevention of fragility fractures, they're not the only solution. A combination of complementary measures like exercises, dietary counseling, home modifications, and lifestyle adjustments are likely to be evenly important. These vital components complement medication, forming a robust defense against bone fragility", Jörg explains. The research group around Jörg has been accused of undermining osteoporosis patients' confidence in osteoporosis treatment, as they no longer dare to take the medication due to being much more AFRAID of Atypical Femur Fractures than seeing the benefit of drug treatment. "In our extensive research, pinpointing specific risk factors underlying the development of AFF remains elusive. In Sweden there are roughly 50 patients each year sustaining an AFF, which makes the identification of risk factors a big challenge due to small numbers. To address this, we've started a collaboration with research groups in the USA and Denmark with the aim of pooling data to unravel risk factors leading to AFF", Jörg continues.

One crucial step in treating patients with AFF is a correct diagnosis at the time of fracture. According to the Global Burden of Diseases, Injuries, and Risk Factors Study 2019 there were 178 million new fractures worldwide during 2019. To address this diagnostic challenge, we're using Artificial Intelligence in collaboration with Anders Eklund and Mischa



Incomplete AFF (+ART group) characterized by a radiolucent line surrounded by a focal callus reaction (Left). Complete AFF from +ART group (Right). Both fractures show multiple stress lesions (focal periosteal thickening) along the lateral cortex.

Anna Spångeus,
PI for the AIDA osteoporosis project.

Eva Klintström, Mischa Woisetschläger, Erik Tesselaar, Jörg Schilcher and Anders Eklund by the photon counting CT.

Woisetschläger to assist in the automated identification of these fractures to allow initiation of adequate treatment protocols at the time of presentation.

Patients and physicians seem to overreact to the side effects of bisphosphonates without fully recognizing potential benefits when used correctly. Therefore, the project aims to provide a decision-making algorithm for clinicians helping to decide who to treat, with which medication and for how long. “An algorithm to take patient background factors such as age, gender, drug treatments, and comorbidities into consideration to determine the risk of fragility fractures already exists, but there's nothing to counterbalance the benefit of drug treatment to prevent fragility fractures against the risk of AFF. Specifically in the USA, many patients believe that the risk of AFFs is greater and fractures more serious than normal fragility fractures, so they refuse to take the medication. They are AFRAID”, Jörg concludes.

Medications play a crucial role in averting vertebral compression and hip fractures. Swedish women face a staggering 50% risk of fragility fractures in these areas thus making it very important for patients to regain confidence in multimodality fragility fracture prophylaxis including also the use of drugs. Reinforcing the confidence in osteoporosis treatment is one crucial step towards a reduction in fragility fractures in Sweden and worldwide.

At CMIV's AIDA initiative, spearheaded by Anna Spångeus, extensive osteoporosis studies transcend atypical fracture research. Spångeus's project focuses on AI-driven identification of vertebral fractures within non-skeletal CT scans, crucial for addressing underdiagnosed and undertreated osteoporosis cases. Despite the high prevalence and severe consequences of osteoporotic fractures, healthcare systems struggle to bridge the diagnosis-treatment gap, a pressing concern outlined in national guidelines. The project seeks to rectify this by leveraging AI for automatic vertebral fracture detection and bone quality assessment, aiming to revolutionize care for this patient group.

Musculoskeletal | AI/Data analytics

Project information

PROJECT NAME

AFRAID – Atypical Femur Fracture diagnosis and Risk Assessment using Artificial Intelligence and global Data pooling for optimized fragility fracture prevention.

PROJECT LEADER

Jörg Schilcher, Department of Biomedical and Clinical Sciences, Division of Surgery, Orthopedics and Oncology.

MAIN PROJECT PARTICIPANTS

Hans Peter Bögl, Anders Eklund, Johan Lyth, Karl Michaëlsson, Daphne Wezenberg.

GRANTS

Swedish Research Council. National Institute of Health.

KEY PUBLICATIONS

Schilcher J, Michaelsson K, Aspenberg P. Bisphosphonate use and atypical fractures of the femoral shaft. N Engl J Med 2011;364(18):1728–37. (In English). DOI: 10.1056/NEJMoa1010650.

Zdolsek G, Chen Y, Bogl HP, Wang C, Woisetschlager M, Schilcher J. Deep neural networks with promising diagnostic accuracy for the classification of atypical femoral fractures. Acta Orthop 2021;92(4):394–400. DOI: 10.1080/17453674.2021.1891512.

Schilcher J, Nilsson A, Andlid O, Eklund A. Fusion of electronic health records and radiographic images for a multimodal deep learning prediction model of atypical femur fractures. Computers in Biology and Medicine 2024;168. DOI: 10.1016/j.compbiomed.2023.107704.

Erik Tesselaar at the CMIV retreat in Vadstena.

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
Håkan Gustafsson

Artificial Intelligence in Breast Cancer Screening

The purpose of this research project is to investigate whether the use of AI leads to increased diagnostic safety in mammography screening in Östergötland (measured as a reduced incidence of interval cancer) and at the same time reduces the workload for breast radiologists. Furthermore, the intention is to examine how the use of AI affects the work of radiologists in terms of reading time per examination and whether the specificity and sensitivity are affected when the radiologists have access to AI-based decision support during the reading compared to when they do not have this support.
The hypotheses are as follows:

(1) The use of AI in breast cancer screening in Östergötland increases diagnostic safety. As a result, more cases of breast cancer are detected early, and the incidence of interval cancer decreases.

(2) The reduced workload for radiologists in Östergötland, as evidenced by the data collected in phase 1 of the project (Clinical trial AI-ROL, ID NCT05048095, 2021–2022) can also be demonstrated in a large-scale prospective study.

(3) Through the use of AI-based decision support, not only can double reading be eliminated for cases where AI assesses cancer risk as low, but each examination can also be read more effectively with maintained or improved diagnostic safety.

(4) It is the least experienced radiologists who benefit the most from decision support, both in terms of increased diagnostic safety and increased efficiency.

During 2023–2024, AI will be prospectively implemented in the clinical reading. The AI tool will be used to categorize all mammography examinations into two groups: high cancer risk and low cancer risk. These two groups are defined based on the overall risk score (1–10) provided by the AI algorithm for each examination. AI will replace one of the two radiologists for low-risk examinations, potentially achieving a 33.8% reduction in workload, as was demonstrated in in the phase 1 of the project (2021–2022).

The cancer detection rate (CDR) for each radiologist will be examined to assess whether the use of AI improves diagnostic safety and whether the least experienced radiologists benefit the most from the tool.

Finally, the project will investigate whether AI leads to increased diagnostic safety, measured as an increased cancer detection rate (CDR) and reduced incidence of interval cancer (interval cancer rate – ICR). This has been demonstrated in other studies, but still needs to be proven locally in Östergötland. The implementation of AI in the clinical reading process is expected to demonstrate a reduced incidence of interval cancer during the final year of this proposed project in 2026 when women return for their next screening appointment.

In parallel this project is closely related to the national project VAI-B (Nationell valideringsplattform för AI inom mammografiscreening) headed by Fredrik Strand (Karolinska Institutet).

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, Tomas Bjerner.

GRANTS

Pantelis Gialias: Region Östergötland
Från Student till docent steg 3 - Doktorand (2024-2025)

KEY PUBLICATIONS

VAI-B: A multi-center platform for the external validation of artificial intelligence algorithms in breast imaging. Fernando Cossío, Haiko Schurz, Mathias Engström, Carl Barck-Holst, Apostolia Tsirikoglou, Claes Lundström, Håkan Gustafsson, Kevin Smith, Sophia Zackrisson, Fredrik Strand. Journal of Medical Imaging 10 (2023) 061404 https://doi.org/10.1117/1.JMI.10.6.061404.

Så kan AI valideras för klinisk implementering. Fredrik Strand, Sophia Zackrisson, Håkan Gustafsson. Läkartidningen 120 (2023) 23065.

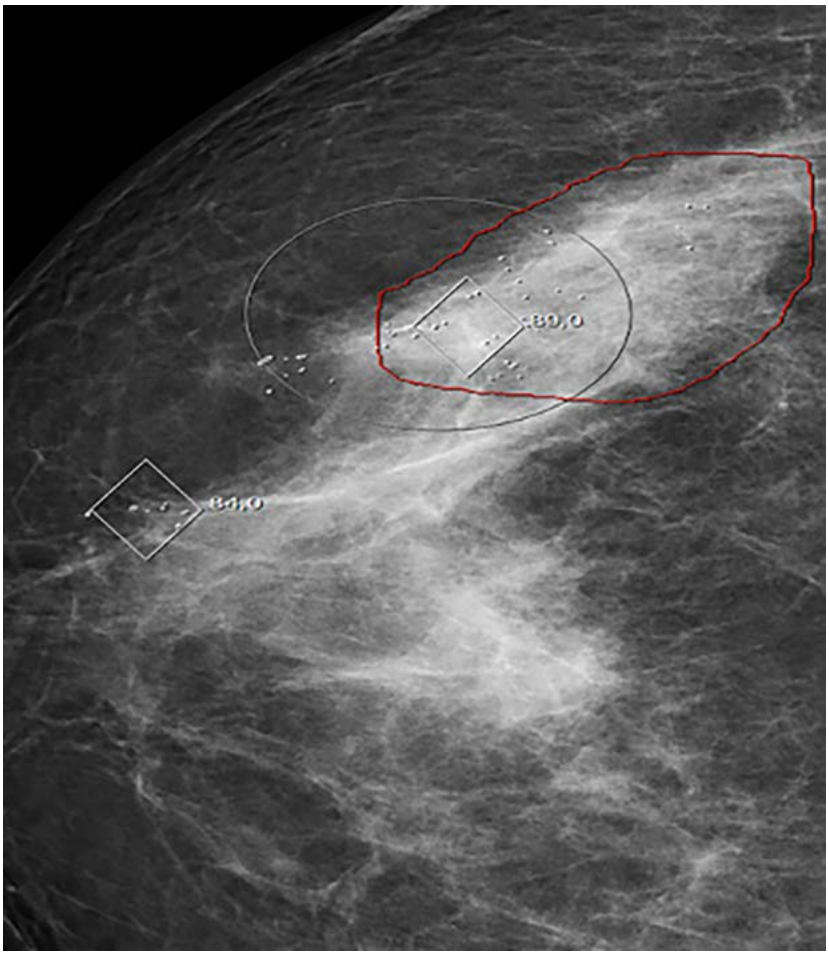


Figure 1. The image shows an example of the use of AI in the mammography screening program. The red marking shows lesion, the white rhombus shows area with calcifications and the white ellipse is a marking made by the radiologist reading the examination.

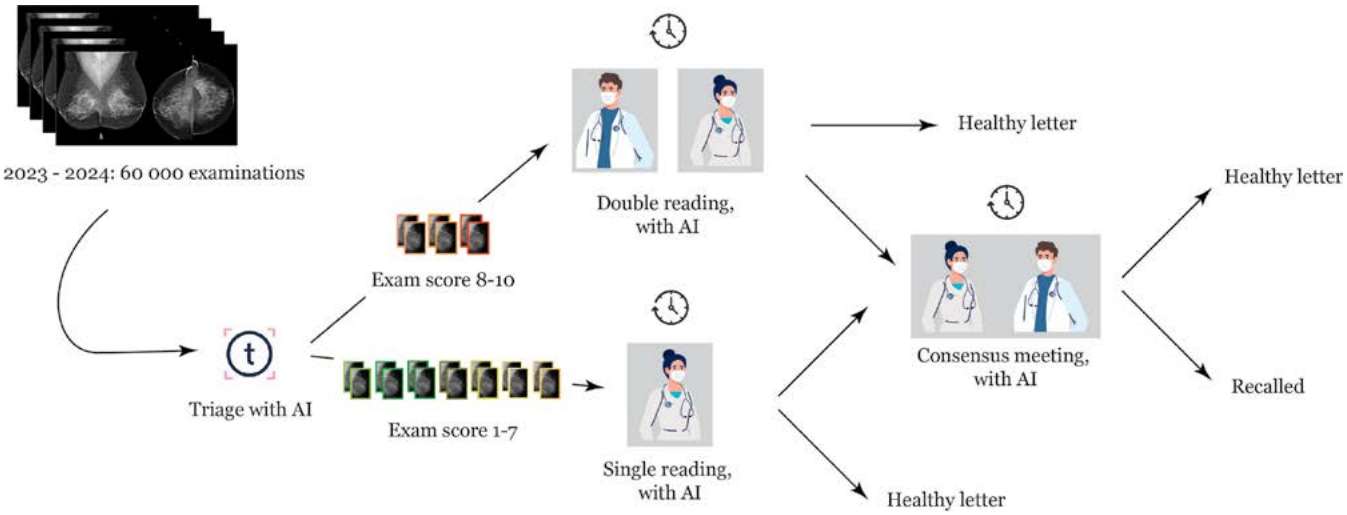


Figure 2. The image shows the current phase of AIM-RÖ: 60 000 examinations will be included in the prospective study. Examinations which AI has assessed as low risk for cancer will be read by one radiologist, whereas examinations assessed as high risk for cancer will be read by two radiologists as normally.

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, Radiation Physics, Department of Medicine and Health.

MAIN PROJECT PARTICIPANTS

Charlotta Dabrosin, Anette Karlsson, Ieva Tomkeviciene, Mikael Forsgren, Jens Tellman, Johan Kihlberg, Maria Kristoffersen Wiberg, Magnus Borga, Marcel Warntjes, Anna Rzepecka.

GRANTS

LiU-Cancer, Cancerfonden

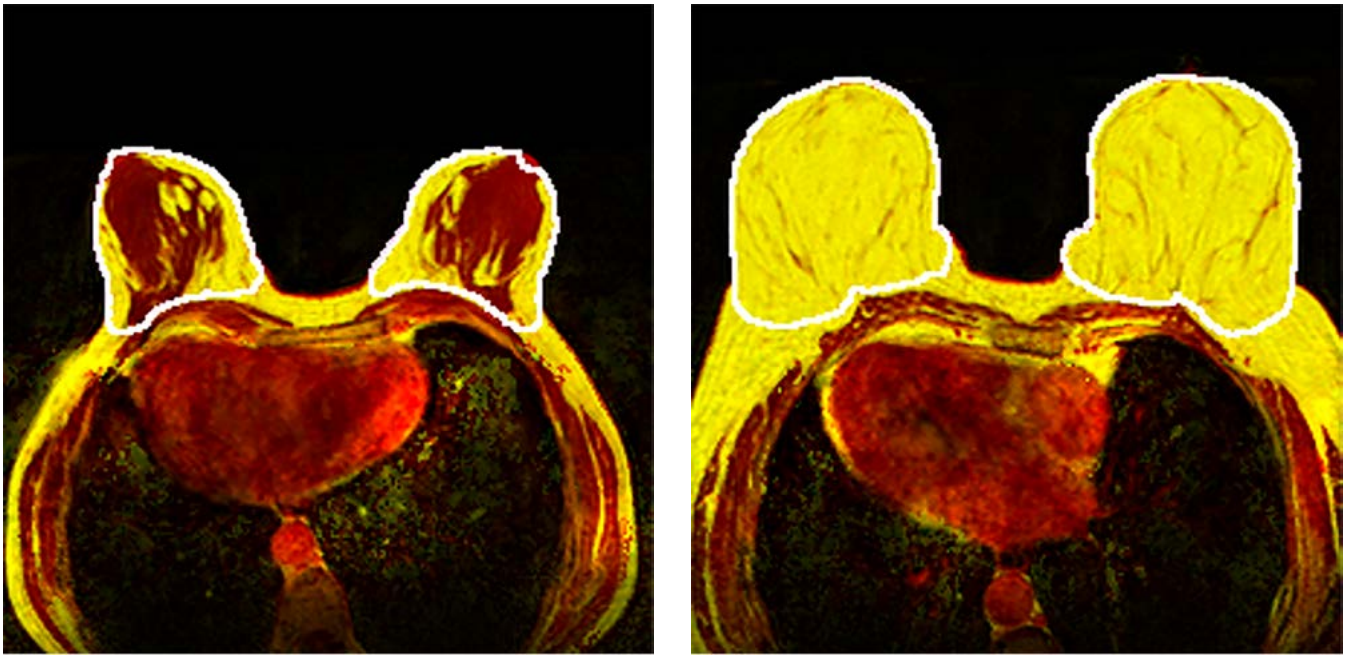
KEY PUBLICATIONS

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.

Lundberg P, Forsgren MF, 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 Nov;127(11):2025-2033. doi: 10.1038/s41416-022-01976-3. Epub 2022 Sep 22.

Ekstrand J, Zemmler M, Abrahamsson A, Lundberg P, Forsgren M, Dabrosin C. (2022) Breast Density and Estradiol Are Major Determinants for Soluble TNF-TNF-R Proteins in vivo in Human Breast Tissue, Front Immunol. 2022 Mar 30;13:850240. doi: 10.3389/fimmu.2022.850240. eCollection 2022, PMID: 35432372.



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

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.

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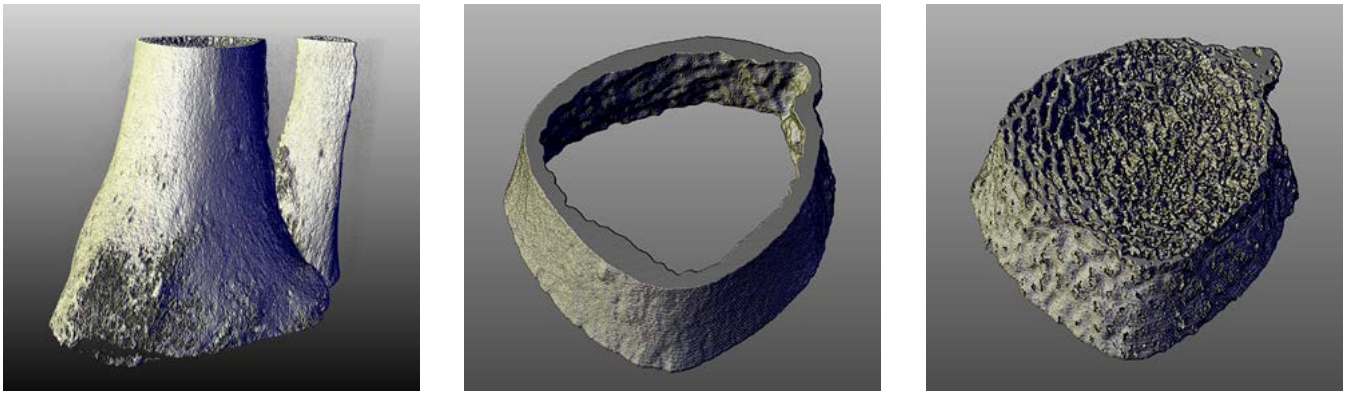
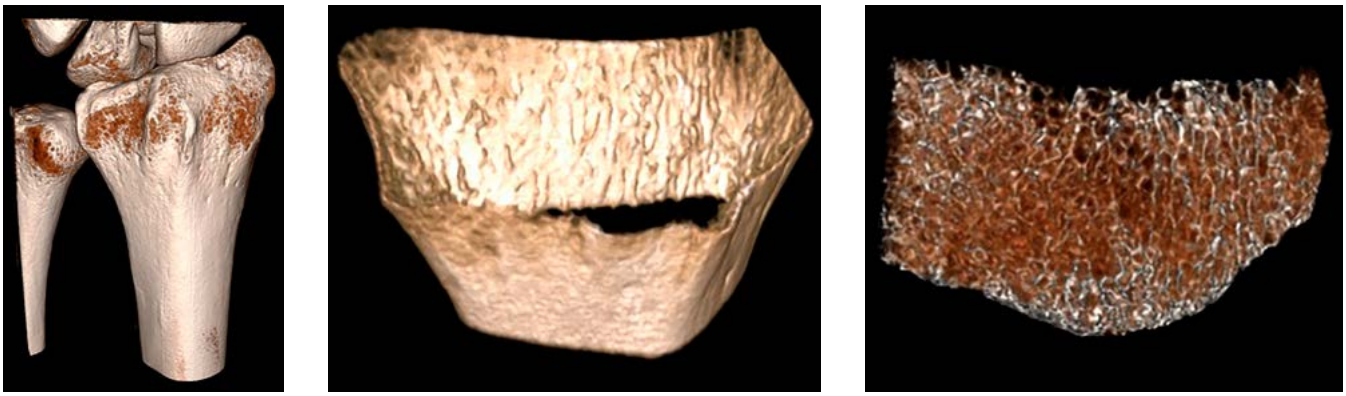
Klintström E, Smedby Ö, Moreno M, Brismar TB. Trabecular bone structure parameters from 3D image processing of clinical multi-slice and cone-beam computed tomography data. Skeletal Radiology, 2014 Vol. 43, nr 2, s. 197-204. DOI: 10.1007/s00256-013-1766-5.



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
Erik Tesselaar

Photon-Counting CT of the Wrist

Advancements in medical imaging are often spearheaded by the insatiable quest for better diagnostic accuracy and patient safety. One such frontier is computed tomography (CT), and the latest innovation comes in the form of Photon-Counting Detector CT (PCD-CT). In 2023, two studies explored PCD-CT's efficacy in evaluating wrist fractures and its interaction with metal artifacts compared to conventional Energy-Integrating Detector CT (EID-CT).

A Clearer View on Fractures: A common challenge in musculoskeletal radiology is the accurate assessment of small fractures, particularly in the scaphoid bone of the hand. Our group compared the performance of PCD-CT and EID-CT in identifying such fractures and monitoring their healing over time. Remarkably, radiologists found PCD-CT images significantly clearer and more reliable in diagnosing fractures. This advancement was not just in terms of qualitative assessments; the sharper cortical and trabecular bone structures were quantitatively confirmed, strengthening diagnostic confidence.

Notably, while EID-CT operates at a minimal slice thickness of 0.4 mm, PCD-CT makes it possible to reconstruct images at a reduced slice thickness of 0.2 mm – yielding superior image quality. Over time, follow-up scans exhibited the sustained superiority of PCD-CT in image quality, although the diagnostic confidence between the two technologies evened out. We have previously observed that, as a result of the new detector technology, radiation doses can be maintained, or even be lower, with PCD-CT.

The Challenge of Metal Artifacts: A second study addressed a persistent issue in CT imaging: metal artifacts. These artifacts, frequently seen in scans involving even relatively small orthopedic implants, can obscure vital clinical information. Until now, our understanding of these artifacts in PCD-CT has been limited.

The study used a phantom model with a titanium orthopedic screw to assess how various parameters, like tin prefiltration and reconstruction kernels, affected metal artifacts in PCD-CT and EID-CT. While PCD-CT exhibited more pronounced streak artifacts and slight increases in blooming effects compared to EID-CT, it also provided sharper implant-bone interface edges.

Encouragingly, certain parameters and techniques, such as tin prefiltration and high energy virtual monoenergetic images (VMI), reduced the metal artifacts significantly. Hence, although PCD-CT presented challenges in terms of metal artifacts, it also revealed paths to mitigating these issues, offering a sharper and potentially more accurate assessment of the area around metal implants.

In conclusion, these two pioneering studies confirm how promising the next generation of CT technology is with regards to musculoskeletal imaging. They affirm that PCD-CT provides significantly clearer and more accurate images for diagnosing and monitoring scaphoid fractures. Although it presents some challenges with metal artifacts, solutions are emerging to mitigate these issues effectively. As we advance towards increasingly accurate and safe methods of medical imaging, PCD-CT emerges as a promising tool, offering a more detailed window into the complexities of the human anatomy.

Computed Tomography | Musculoskeletal | Acquisition

Project information

PROJECT NAME
IMPACT and IMPACT-METAL.

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

MAIN PROJECT PARTICIPANTS
Nina Kämmerling, Ola Fredäng, Simon Farnebo, Mårten Sandstedt, Anders Persson.

GRANTS
RFOU Grants, Region Östergötland (2023)

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.

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Booij R, Kämmerling NF, Oei EHG, Persson 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. Eur J Radiol. 2023 Feb;159:110662. doi: 10.1016/j.ejrad.2022.110662. Epub 2022 Dec 20. PMID: 36565594.

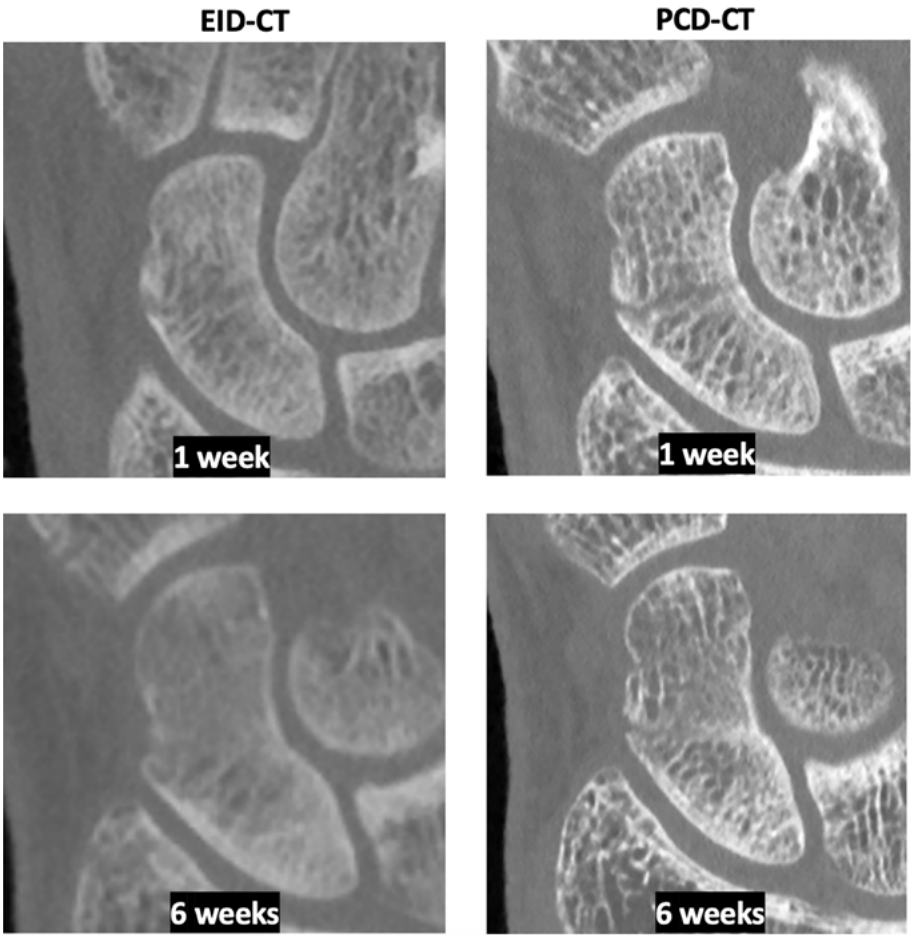

Figure 1. Wrist scaphoid fracture scanned using EID-CT (left) and PCD-CT (right) at 1 day and 6 weeks after injury. Note the better visibility of the fracture line and the trabecular structure on the inside of the bone.

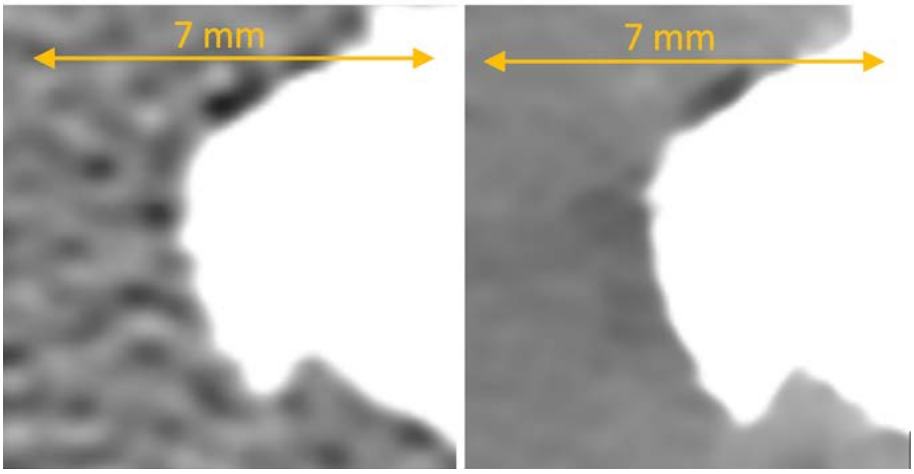

Figure 2. Phantom images showing the interface between bone and a small metal implant, obtained with EID-CT (left) and with PCD-CT (right). The noise level is notably reduced in PCD-CT, but certain metal artefacts are still affecting assessment of the interface.

POPULAR SCIENTIFIC SUMMARY
Björn Gerdle

Pain Mechanisms in Chronic Widespread Pain Including Fibromyalgia

Chronic widespread pain (CWP) including fibromyalgia (FM) is characterized by generalized musculoskeletal pain and often is associated with symptoms such as psychological distress, insomnia, fatigue, and cognitive difficulties. CWP affects not only patients but also their families and society, leading to significant suffering and high socioeconomic burden. Peripheral and central nervous system mechanisms are believed to contribute to the clinical picture in CWP, but an understanding of the activated pain mechanisms is mainly lacking.

In the first part of this project concerning CWP we have investigated the function (connectivity) of some of the networks in the brain with functional magnetic resonance imaging (fMRI) i.e. the default mode network (DMN) and the salience network (SN). An important result was that that the connectivity within the DMN was decreased and connectivity within the SN was increased for CWP. The anterior insula is part of the SN and plays a key role in switching between internal- and external-oriented tasks. Thus, the insula has a reflective role and can switch between monitoring subjective feelings such as emotions and paying attention to external events. In a second on-going part of the project the networks in the brain of fibromyalgia patients and healthy controls are investigated as well as clinical characteristics (e.g., pain intensity, psychological distress, quality of life etc.), fitness level, pain sensitivity and biochemical alterations in blood, muscles and fat tissues. The right intraparietal sulcus (IPS) node of the Central executive network (CEN) showed a higher level of connectivity strength with right insula in FM with higher pain intensity compared to controls. More anxiety symptoms in FM correlated with higher levels of connectivity strength between the ventromedial prefrontal cortex DMN node and right sensorimotor cortex. These findings support the theory of altered insular connectivity in FM and suggest altered IPS connectivity in FM.

A currently important research area is if there exist associations between peripheral biochemical tissue alterations (in saliva, blood and muscle), body composition aspects (including fat content and infiltration in different tissues) and alterations in the brain of FM. The results from this project will be clinically important both with respect to assessment and when designing and choosing interventions for these patients.

MRI | Neurology | Musculoskeletal | Acquisition | Imaging Biomarkers

Project information

PROJECT NAME

Pain Mechanisms in Chronic Widespread Pain Including Fibromyalgia.

PROJECT LEADER

Björn Gerdle, Pain and Rehabilitation Centre, and Department of Health, Medicine and Caring Sciences.

MAIN PROJECT PARTICIPANTS

Eva Lund, Peter Lundberg, Bijar Ghafouri, Helene van Ettinger-Veenstra, Håkan Olausson, Rebecca Boehme, Rikard K. Wicksell, Maria Engström, Ann Bengtsson, Mikael Forsgren, Olof Dahlqvist-Leinhard.

GRANTS

Swedish Research Council (terminated)
ALF Grant, Region Östergötland
ForSS (terminated)

KEY PUBLICATIONS

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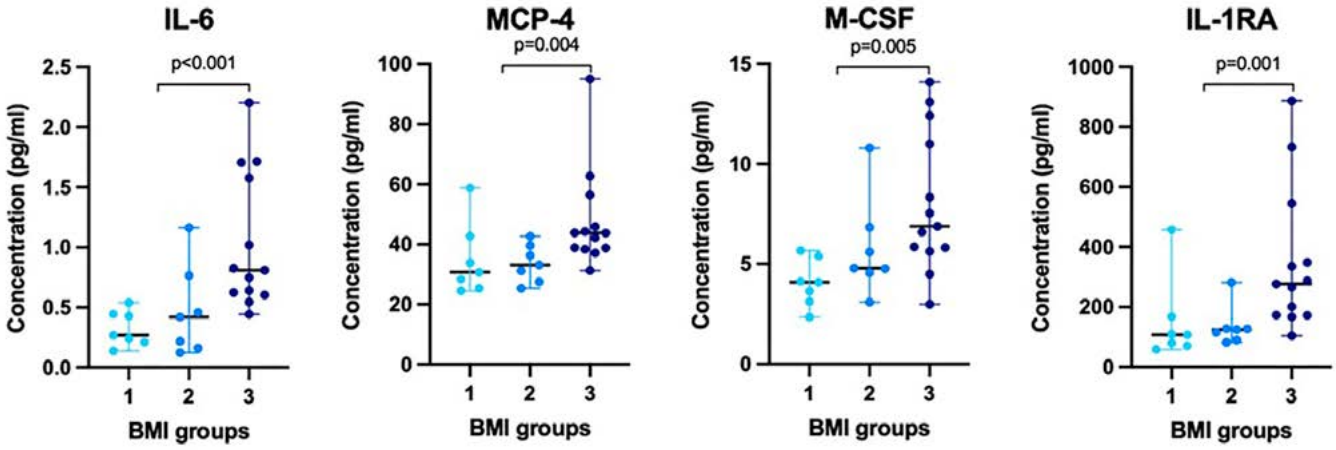


Plasma protein levels in different classes of BMI in patients with fibromyalgia. P-values were obtained from the comparison between nonobese (i.e., normal weight + overweight) and obese patients with FM through the Mann-Whitney U test. BMI group 1, group 2, and group 3 consist of subjects with normal weight, overweight, and obesity, respectively. The graphs present protein concentrations for the subjects as individual values and median with range. BMI= body mass index.

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. Treatment options are rehabilitation alone or combined with ACL-reconstruction. 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 and 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 15 publications and several analyses with specific interest on imaging have been done and are planned. Example:

- Diagnostic accuracy of dual energy CT (DECT) for detection of bone marrow lesions in the injured knee using MRI as reference method.

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, Sofi Sonesson, Anne Fältström, Melanie Svensson, Bashir Tajik Edwardsson, Angie Liu, Anders Persson, Ann-Sofi Björkman, Martin Englund, Richard Frobell, Miika Nieminen, Victor Casula, Seppo Koskinen, Nicola Giannotti, Riccardo Cristiani, Riccardo Gobbi.

GRANTS

Swedish Medical Research Council (2015-2024)
Swedish Research Council for Sport Science (2017-2024)
Medical Research Council of Southeast Sweden (2020-2024)
ALF Grants Region Östergötland (2018-2024)

KEY PUBLICATIONS

Kvist, J., H. Gauffin, H. Tigerstrand Grevnerts, C. Ardern, M. Hagglund, A. Stalman and R. Frobell (2018). "Natural corollaries and recovery after acute ACL injury: the NACOX cohort study protocol." BMJ Open 8(6): e020543.

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 Superficial and Deep Medial Collateral Ligament Injuries on Magnetic Resonance Imaging in Patients With Anterior Cruciate Ligament Tears. Arthroscopy 2023 doi: 10.1016/j.arthro.2023.05.029 [published Online First: 20230622].

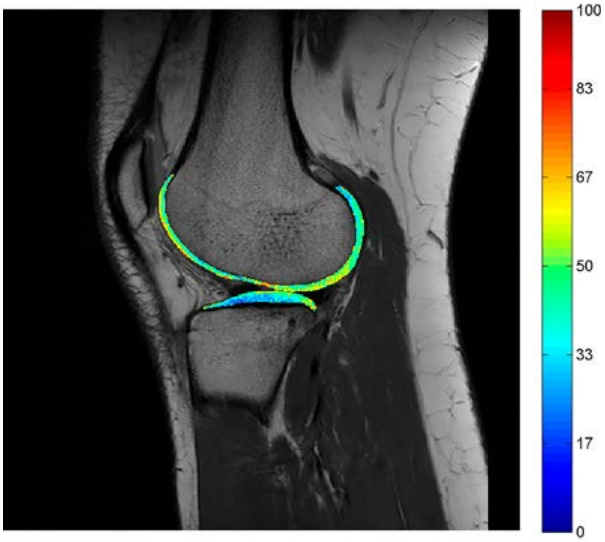


Figure 1. Figure from: Casula, V., Tajik, B. E., Kvist, J., Frobell, R., Haapea, M., Nieminen, M. T., Gauffin, H., Englund, M. (2022). Quantitative evaluation of the tibiofemoral joint cartilage by T2 mapping in patients with acute anterior cruciate ligament injury vs contralateral knees: results from the subacute phase using data from the NACOX study cohort. Osteoarthritis and Cartilage. doi:https://doi.org/10.1016/j.joca.2022.02.623.

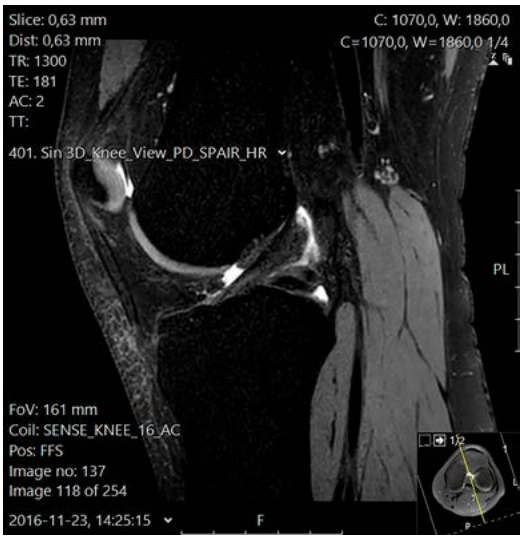


Figure 2. Normal ACL. Intact ligament structure and fiber structure. Normal thickness and length of the ligament.

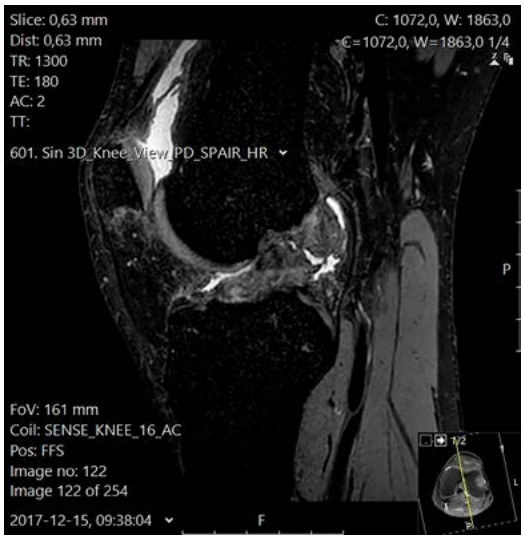


Figure 3. Ruptured ligament. Complete rupture of both ligament structure and fibers, with thickened ligament. Injury located in the middle third of the ligament.

- Quantitative MRT analysis of cartilage matrix organization, as measured by T2 relaxation time, of the tibiofemoral joint cartilage after acute ACL 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, some of them related to joint loading after the injury concomitant meniscus and cartilage injuries. Future longitudinal observations of the same cohort will allow for better understanding of early development of PTOA.
- Ongoing development of a classification score and review of the healing potential of the ACL fibers in the non-reconstructed knee, as well as for the concomitant meniscus injuries.

NACOX KNÄSTUDIE

POPULAR SCIENTIFIC SUMMARY
Jörg Schilcher

PCCT for Radiographic Assessment of Osseointegration

Implant survival of total joint replacement in the hip (THR) has long been an area of concern in orthopedic medicine. In Sweden alone, around 17,000 hip replacement surgeries are performed each year. Our research team has been exploring innovative diagnostic techniques to enhance the long-term success of these implants. Our study centers on the use of Photon-Counting Detector Computed Tomography (PCD-CT) for superior image resolution and assessment of osseointegration.

The crucial factor for the success of THR is the initial integration of the prosthesis in the bone, a process known as osseointegration. Inadequate osseointegration can lead to implant loosening, causing pain and discomfort to patients and often requiring complex reoperations. Unfortunately, current diagnostic tools, such as plain radiographs, are limited in their ability to reliably detect early loosening or other issues related to osseointegration.

Our research is focused on utilizing PCD-CT, a technology that holds promise for substantial improvements over traditional Energy-Integrating Detector CT (EID-CT). PCD-CT's innovative detector design allows for improved image resolution and can better accommodate the dense materials used in implants. These attributes potentially make PCD-CT a more precise tool for assessing osseointegration, thereby leading to earlier and more accurate diagnoses.

We investigated PCD-CT's effectiveness by examining extracted acetabular cups (the pelvic implant of a THR) removed from patients during surgeries where the old implant is replaced with a new one. In some cases, these implants show remnants of bone that has grown on the implant surface (osseointegration). Our multi-disciplinary team had radiologists evaluate the quality of the osseointegration under different scanning parameters. Additionally, we performed quantitative measurements, such as noise and sharpness levels, to objectively assess the technology's performance.

Our initial results show a marked improvement in image quality with PCD-CT compared to EID-CT, especially in visualizing the interface where the patient's bone has grown onto the implant. These advancements, recently published in the European Radiology Experimental journal, could pave the way for more accurate early diagnoses, thus preventing unnecessary surgeries and reducing patient suffering.

While the findings are encouraging, they are based on a limited sample – extracted implants from only two patients. Therefore, further research is required to assess how surrounding soft tissues might affect the imaging quality. Future projects will involve patients with suspected implant loosening to further substantiate the clinical efficacy of PCD-CT in assessing osseointegration.

Computed Tomography | Musculoskeletal | Acquisition | Visualization

Project information

PROJECT NAME

Photon-counting CT for Radiographic Assessment of Osseointegration.

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, Erasmus Medical Center, Rotterdam, The Netherlands.

KEY PUBLICATIONS

Woisetschläger M, Booij R, Tesselaar E, Oei EHG, Schilcher J. Improved visualization of the bone-implant interface and osseointegration in ex vivo acetabular cup implants using photon-counting detector CT. Eur Radiol Exp. 2023 May 1;7(1):19. doi: 10.1186/s41747-023-00335-y. PMID: 37121937; PMCID: PMC10149426.

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.

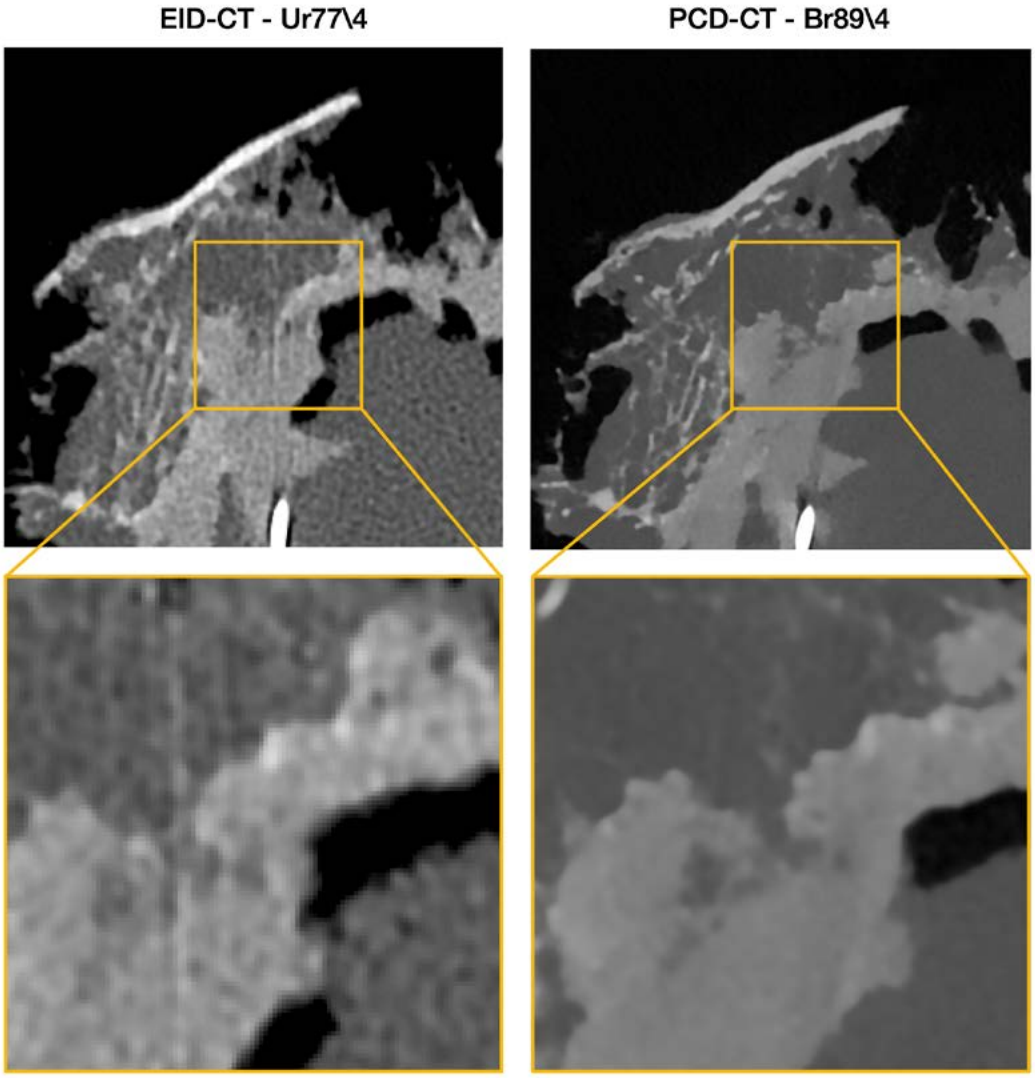


Figure 2. Example of images obtained with EID-CT (left) and PCD-CT (right). Differences in visualization quality of the cement-bone interface in the cemented cup can be clearly observed.

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

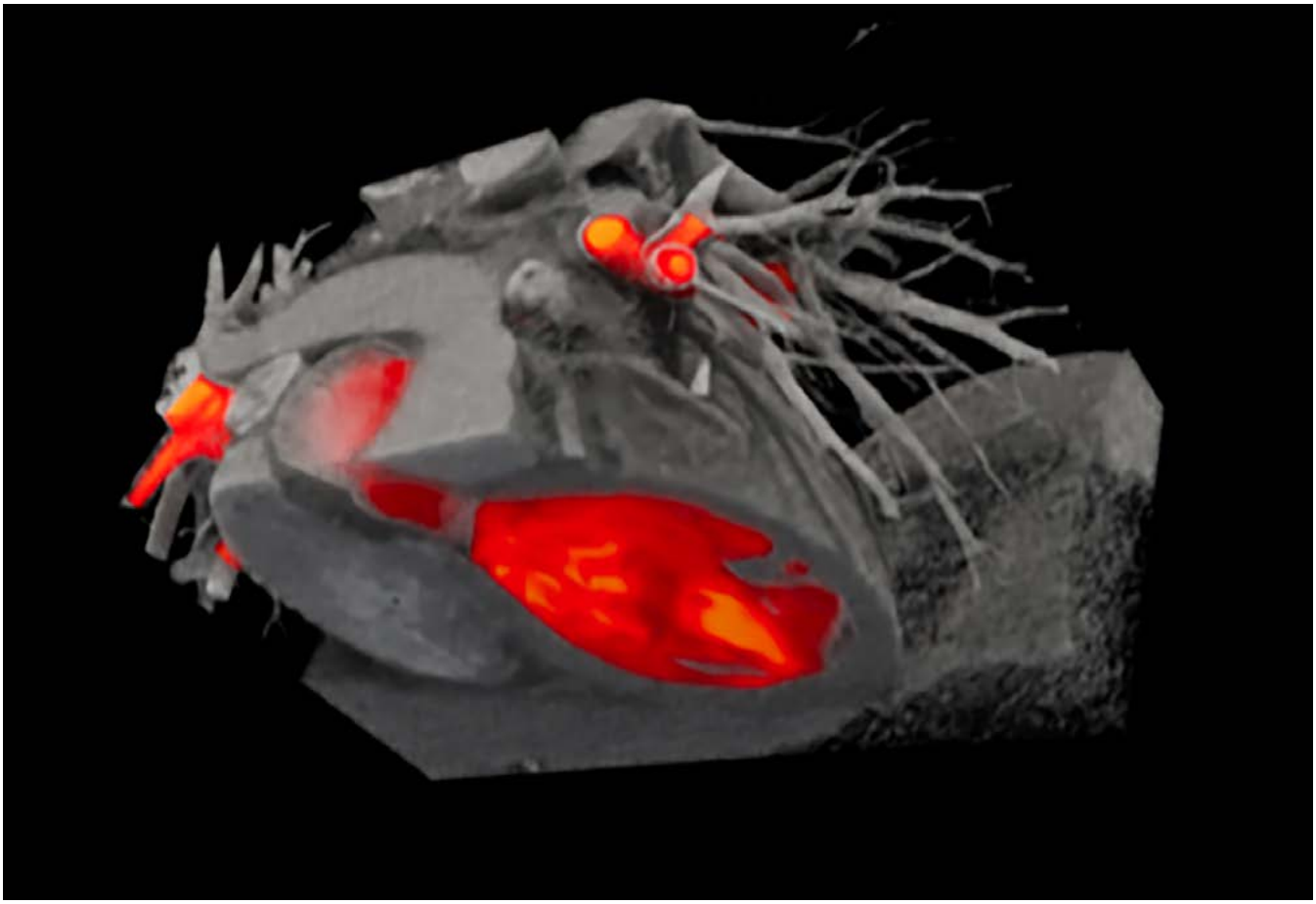
Swedish Heart Lung Foundation (2022-2023)
Visual Sweden / MeDigiT (2022-2025)
WASP/DDLS (2022-2024)
Swedish Research Council (2023-2026)

KEY PUBLICATIONS

Bäck S, Henrikson L, Bolger AF, Carlhäll CJ, Persson A, Karlsson M, Ebbers T. Assessment of transmitral and left atrial appendage flow rate from cardiac 4D-CT. Communications Medicine 3 (1), 22, 2023.

S Bäck, I Skoda, J Lantz, L Henriksson, LO Karlsson, A Persson, C-J Carlhäll, Ebbers T. Elevated atrial blood stasis in paroxysmal atrial fibrillation during sinus rhythm: a patient-specific computational fluid dynamics study. Frontiers in Cardiovascular Medicine 10, 2023.

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.



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

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

Petter Dyverfeldt , Carl-Johan Carlhäll, Jan Engvall, Sohaib Ayaz Qazi, Federica Viola, Chiara Trenti, Twan Bakker, Kajsa Tunedal, Tamara Bianchessi.

GRANTS

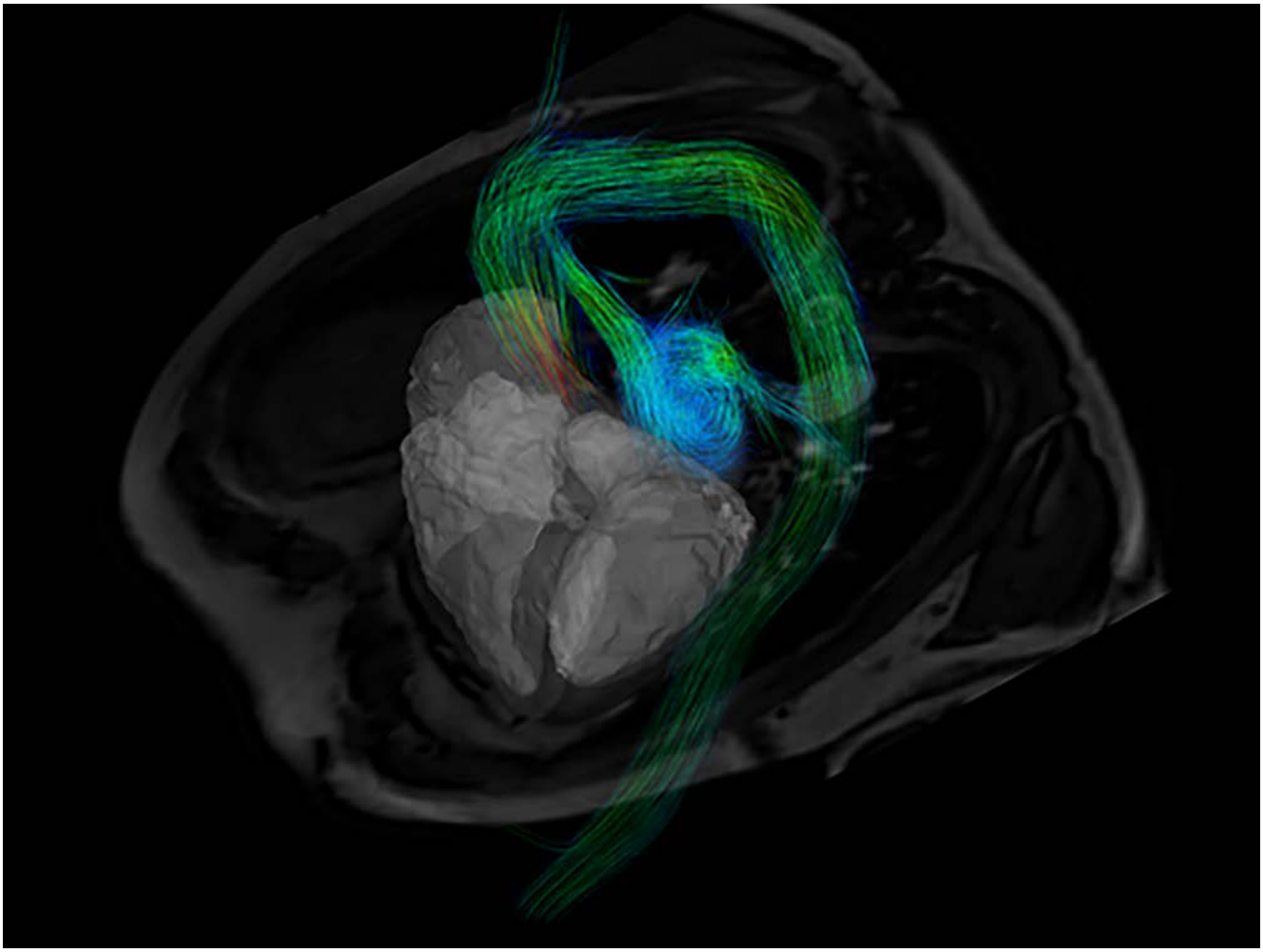
Swedish Research Council (2019-2022)
Swedish Research Council (2023-2026)

KEY PUBLICATIONS

MM Bissell, F Raimondi, L Ait Ali, BD Allen, AJ Barker, A Bolger, N Burris, C-j Carhäll, JD Collins, T Ebbers, CJ Francois, A Frydrychowicz, P Garg, J Geiger, H Ha, A Hennemuth, MD Hope, A Hsiao, K Johnson, S Kozerke, LE Ma, M Markl, D Martins, M Messina, TH Oechtering, P van Ooij, C Rigsby, J Rodriguez-Palomares, AAW Roest, A Roldán-Alzate, S Schnell, J Sotelo, M Stuber, AB Syed, J Töger, R van der Geest, J Westenberg, L Zhong, Y Zhong, O Wieben, P Dyverfeldt. 4D Flow cardiovascular magnetic resonance consensus statement: 2023 update. Journal of Cardiovascular Magnetic Resonance 25 (1), 40, 2023.

M Lindenberger, M Ziegler, N Bjarnegård, T Ebbers, P Dyverfeldt. Regional and Global Aortic Pulse Wave Velocity in Patients with Abdominal Aortic Aneurysm. European Journal of Vascular and Endovascular Surgery 2023.

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, 57 (1), 191-203 2023.



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
Jonas Holm

Evaluating Antithrombotic Treatment Post-Coronary Artery Bypass Grafting with CT

Coronary artery bypass grafting (CABG) is the most common cardiac surgery in Sweden. It is employed to restore circulation to the heart muscle in the presence of coronary artery disease. Typically, vessel bridges (grafts) are routinely used to bypass constrictions in the coronary arteries. Sustaining the patency of these grafts over time is crucial for prognostic benefits, preventing new heart attacks, and reducing the risk of heart failure.

Post-surgery, medications are administered to prevent blood clot formation and ensure the long-term functionality of the grafts. The optimal dosage of these drugs, providing effective protection without leading to severe bleeding complications, remains uncertain. Most patients receive one or two antiplatelet medications (ASA and/or ticagrelor).

By assessing the functionality of the grafts through coronary computed tomography angiography (CTA) one year post-operation and comparing it with the antithrombotic treatment the patient has received, we aim to gain insights into different treatment strategies. Through this, we hope to optimize the choice of antithrombotic treatment following CABG.

Analytical Method and Data Collection: Patients are evaluated using coronary angiography and coronary CTA according to a protocol developed for the study. Based on the patients' heart rate, the CTA examination is adjusted using "Flash technique" to limit radiation exposure, or spiral technique when Flash technique is not feasible. The radiation dose has been deemed reasonable in relation to the study following ethical approval. To optimize image quality, beta-blockers and nitroglycerin are administered before the examination. Initial assessments are conducted at respective radiology clinics to avoid missing any potential pathological findings. Subsequently, the images are transferred to Linköping US, serving as the core lab for the study. Image interpretation will be carried out by three thoracic radiologists.

Computed Tomography | Cardiovascular | AI/Data analytics | Visualization

Project information

PROJECT NAME

Coronary CT Angio Evaluating Graft Patency in ACS Patients Treated with DAPT or Single ASA after CABG (CoCAP).

PROJECT LEADER

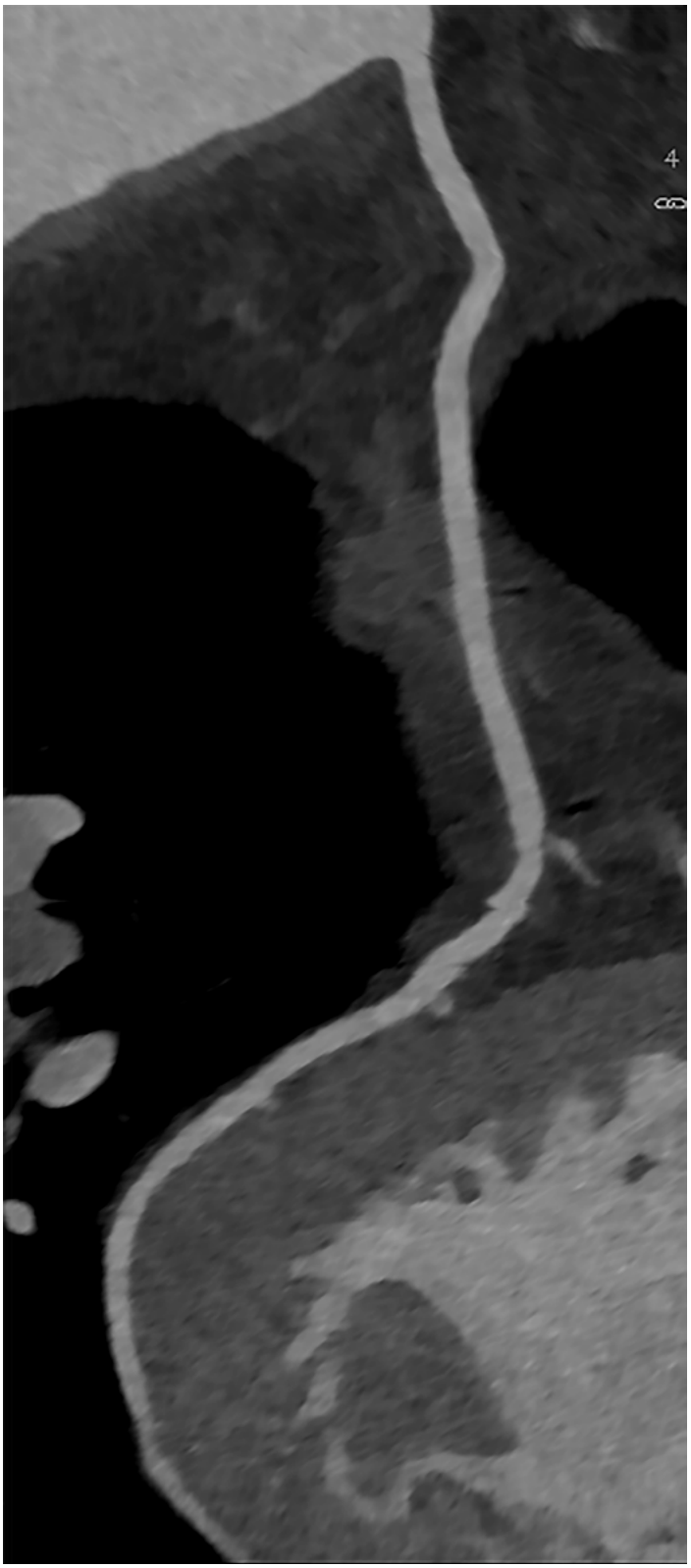
Jonas Holm, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine.

MAIN PROJECT PARTICIPANTS

Mårten Sandstedt, Lilian Henriksson, Sofia Sederholm Lavesson, Nina Hallsten.

GRANTS

HLF
ALF



The CT image shows a coronary venous graft that was anastomosed to the distal circumflex artery, segmented using curved multiplanar reconstruction.

POPULAR SCIENTIFIC SUMMARY
Jan Engvall

COSPRI

Chest pain is a frequent symptom in the population that may cause patients to seek medical attention. Due to the intensity of chest pain and accompanying symptoms, patients may seek attention at the emergency department to rule out a myocardial infarction, but with less intense symptoms, patients may also visit their primary care physician. General updated guidelines on the work-up and treatment of chest pain recommend a more frequent use of imaging methods. Guidelines tend to disqualify the use of functional testing, e.g. exercise bicycle testing, which previously was the primary method of investigation.

Based on the character of chest pain, age and sex, a pre-test probability (PTP) of the presence of coronary artery stenosis may be calculated. The new guidelines recommend acute inpatient investigation when a myocardial infarct is suspected and no investigation at all when the PTP is very low. But, most patients of middle age fall into a middle group with PTP in the range of 15–85%. For those patients, a step-wise outpatient investigation may take quite long time and the delay in arriving at a final diagnosis may cause unnecessary anxiety for the patient.

This study was designed to randomize 18 primary health care centres in Östergötland to use either a same-day application of exercise testing, myocardial perfusion, echocardiography, calcium scoring and microphone recording using wavelet analysis, or the standard step-wise investigation, in order to study the time delay from visit to a final diagnosis. The study is primarily a study of workflow in primary care, but also contains a broader application of investigative methods in primary care.

The technical developments utilized in this study are 1. calciumscoring of the coronary arteries to assess cardiovascular risk, 2. the standardized use of ultrasound to rule out other cardiac diseases and 3. the addition of sound analysis to calculate the likelihood of the presence of a coronary stenosis.

Computed Tomography | Ultrasound | Cardiovascular | Visualization | Imaging Biomarkers

Project information

PROJECT NAME

Chronic Coronary Syndrome in Swedish Primary Care.

PROJECT LEADER

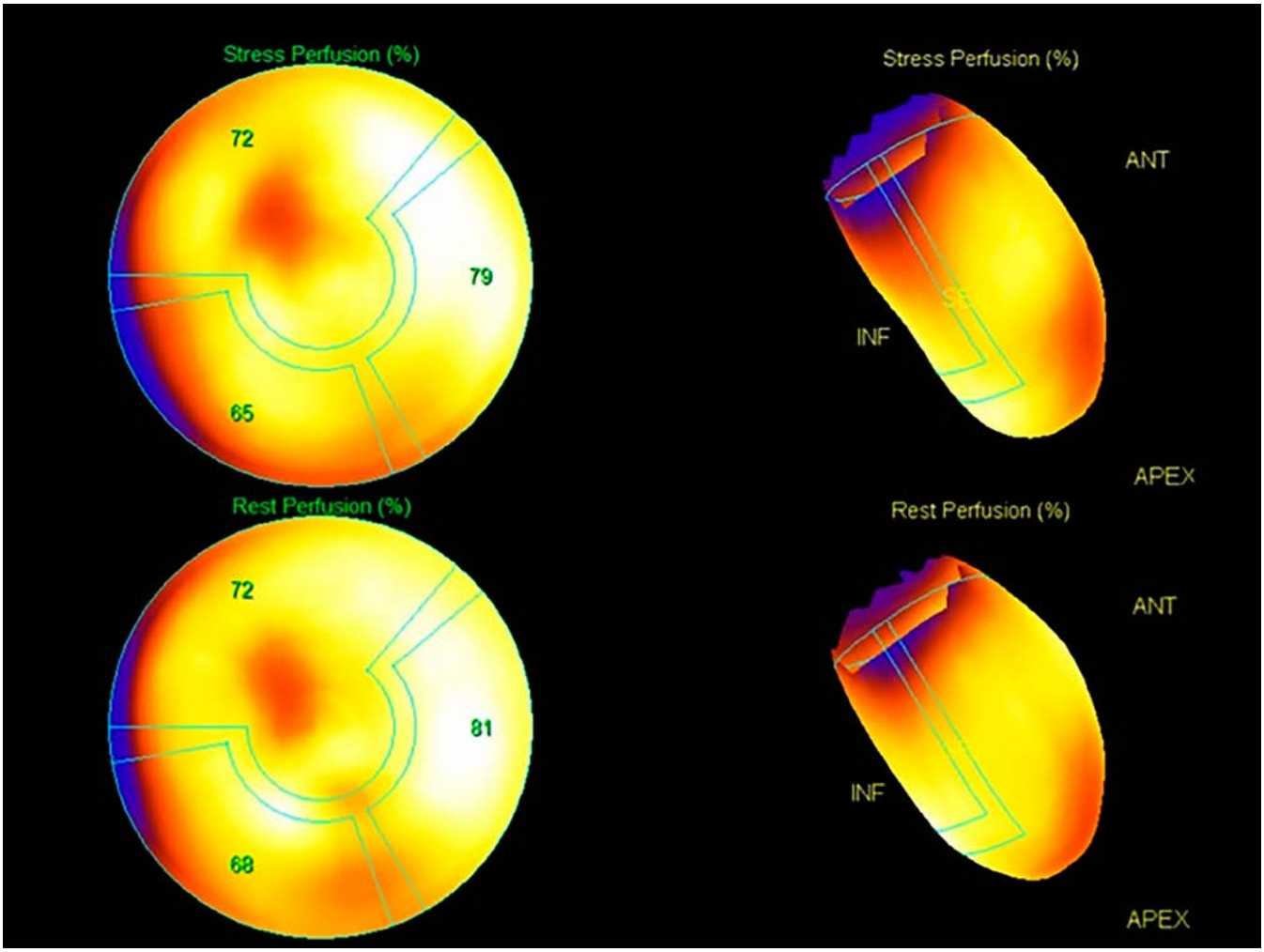
Jan Engvall, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine.

MAIN PROJECT PARTICIPANTS

Eva Olsson, Miguel Ochoa, Staffan Nilsson, Fredrik Iredahl, Sofia Sederholm Lavesson.

GRANTS

ALF/RÖ-991440 (to Staffan Nilsson for 3 years)
VR 2024 (to Fredrik Iredahl)



Myocardial perfusion displayed during stress (upper panel) and at rest (lower panel). The left ventricle is depicted in a polar plot, with the apex in the middle and the base at the periphery. The LV is divided into three perfusion territories, supplied by the three main coronary arteries. Perfusion is normal when yellow, reduced when red as in a small part of the LAD territory during stress. Perfusion remains reduced at rest, which suggests a permanent small myocardial scar without ischemia.

POPULAR SCIENTIFIC SUMMARY
Petter Dyverfeldt, Elin Good

Predictive Value of Carotid MRI

Atherosclerotic plaques 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 | AI/Data analytics | Imaging Biomarkers

Project information

PROJECT NAME

Investigating the predictive value of carotid plaque characteristics to evaluate cardiovascular risk in asymptomatic middle-aged individuals.

PROJECT LEADERS

Petter Dyverfeldt, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine
Elin Good, Department of Cardiology.

MAIN PROJECT PARTICIPANTS

Petter Dyverfeldt, Ebo de Muinck, Elin Good, Marcel Warntjes, Linda Bilos, Oscar Soto, Tamara Bianchessi.

GRANTS

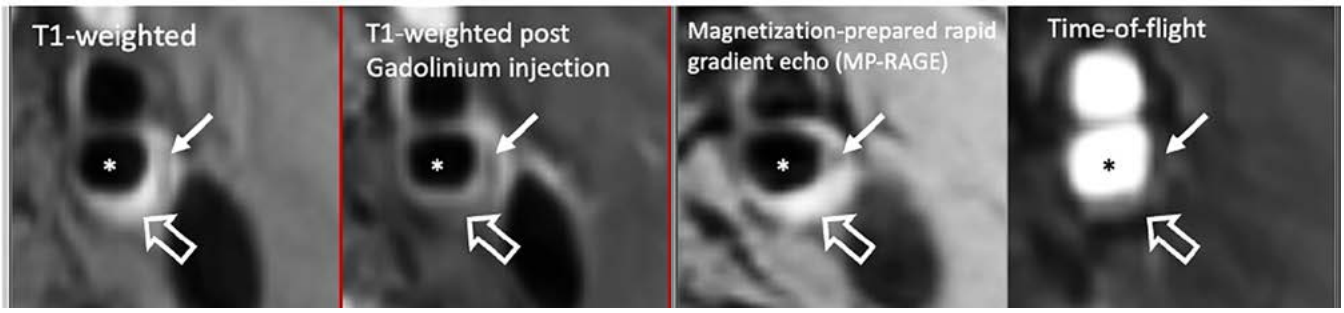
ALF Grant, Region Östergötland
Henry and Ella Margareta Ståhl foundation
Hälsofonden, Linköping University and Region Östergötland
Swedish Research Council, project grant

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

MR Turbulence Angiography

The heart's most important function is to pump blood out to the whole body. In healthy individuals, the blood flows in a well-organized and efficient way. When the heart valves that are located between the different parts of the heart become diseased, the flow is affected and transitions to a more chaotic, turbulent state. The presence of turbulent blood flow is therefore a clear characteristic of heart valve diseases. This is actually used during stethoscope examinations when the doctor listens for turbulence in the heart as a sign of heart valve disease. However, there is a lack of a clinical tool that can quantitatively image turbulence in the heart. Such a tool would enable completely new ways to diagnose heart valve diseases earlier and more accurately.

The goal of this project is therefore to develop a method that measures turbulence in the whole heart and with three-dimensional images shows where this turbulence is located.

To achieve this goal, we will develop an advanced method that uses magnetic resonance imaging to measure turbulence in the heart while the patient holds their breath (less than 20 seconds). Previously, similar measurements have taken 5–10 minutes. We will combine the fast image collection with image processing based on artificial intelligence, whereby a computer is trained to find the different parts of the heart. In this way, artificial intelligence can help us to automatically analyze turbulence in the collected images and visualize where and how much turbulence there is in different parts of the heart for each patient who undergoes the examination.

To evaluate and optimize the new techniques that we develop in the project, we will examine 200 patients with the two most common heart valve diseases. In these patients, we will perform several different variants of measurements with the new technique to determine how the technique should be used in the best way. Successful completion of this project will make it possible to evaluate heart valve diseases in a completely new way, by using a fast magnetic resonance imaging method to quantify and visualize turbulent blood flow. This will improve the diagnosis and affect the assessment of patients with heart valve diseases, with great positive social impact through reduced suffering and death as well as reduced costs for health care.

MRI | Cardiovascular | Acquisition | AI/Data analytics | Visualization | Imaging Biomarkers

Project information

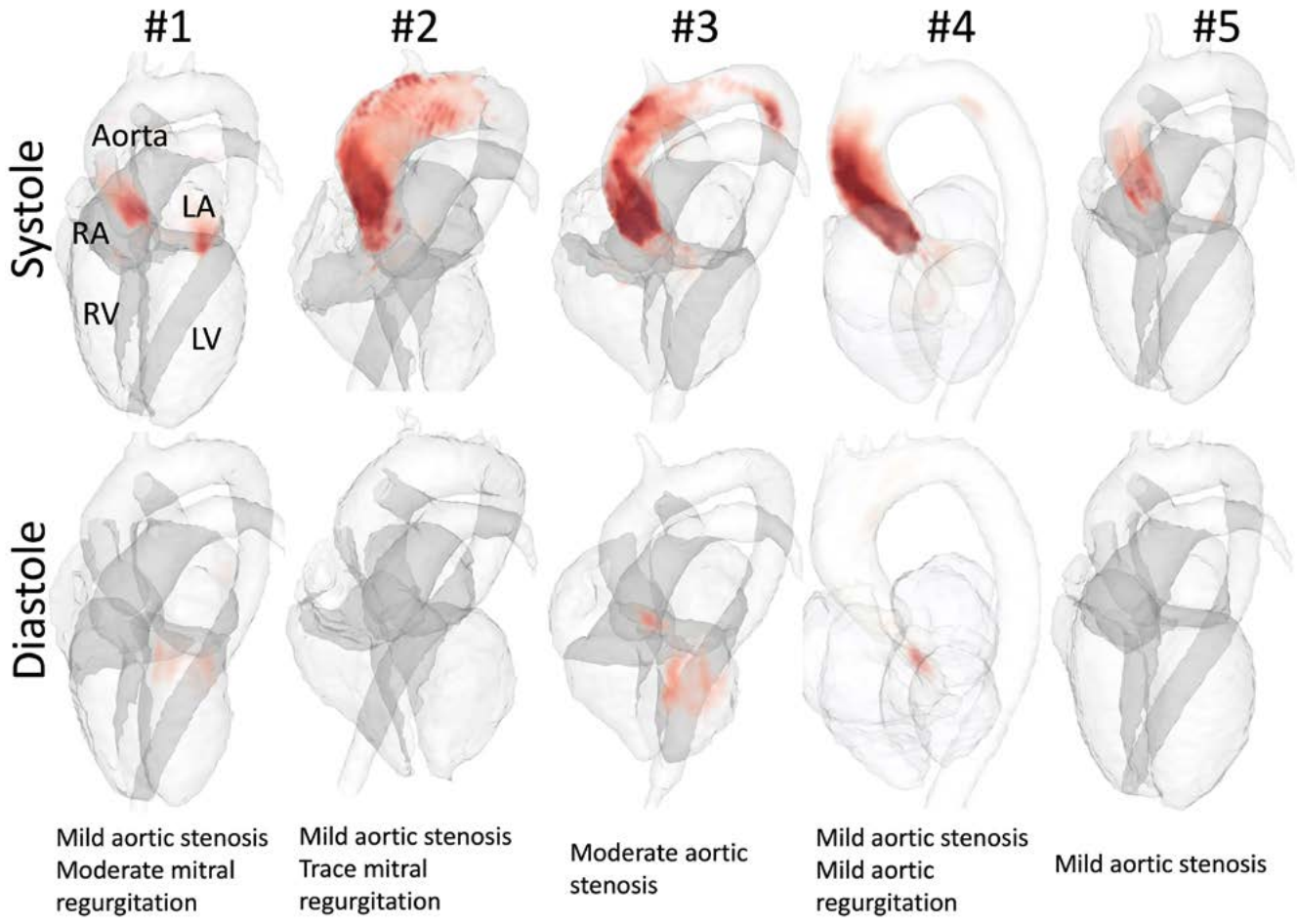
PROJECT NAME
MR Turbulence Angiography.

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

MAIN PROJECT PARTICIPANTS
Petter Dyverfeldt, Sohaib Ayaz Qazi, Tamara Bianchessi, Carl-Johan Carlhäll, Marcus Lindenberger.

GRANTS
ALF Grant, Region Östergötland (2024–2026)
Analytic Imaging Diagnostics Arena (AIDA) Innovation Grant (2023–2024
Swedish Research Council, project grant (2022–2025)
Linköping University Strategic Research Area in Circulation and Cardiovascular Metabolic Risk Factors, Visiting researcher grant (2022–2023)

KEY PUBLICATIONS
Dyverfeldt P, Trenti C, Ziegler M, Bjarnegård N, Lindenberger M. Helical flow in tortuous aortas and its relationship to turbulence: A whole-aorta 4D Flow MRI study. Frontiers in Cardiovascular Medicine 2023; 10:1124604.
Riva A, Eriksson J, Viola F, Sturla F, Votta E, Ebbers T, Carlhäll CJ, Dyverfeldt P. Impact of dobutamine stress on diastolic energetic efficiency of healthy left ventricle: an in vivo kinetic energy analysis. Frontiers in Cardiovascular Medicine 2023; 10:1103751.
Dyverfeldt P, Hope MD, Tseng EE, Saloner D. Noninvasive Magnetic Resonance Measurement of Turbulent Kinetic Energy for the Estimation of Irreversible Pressure Loss in Aortic Stenosis. J Am Coll Cardiol Img 2013; 6(1):64–71.



MR turbulence angiograms showing turbulent kinetic energy (TKE) in the whole heart and aorta at systole (top row) and diastole (bottom row). Valvular pathology for each patient is indicated in the bottom of the figure. LV, left ventricle; LA, left atrium; RV, right ventricle; RA, right atrium.

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 | Ultrasound | 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, HMV.

MAIN PROJECT PARTICIPANTS

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

GRANTS

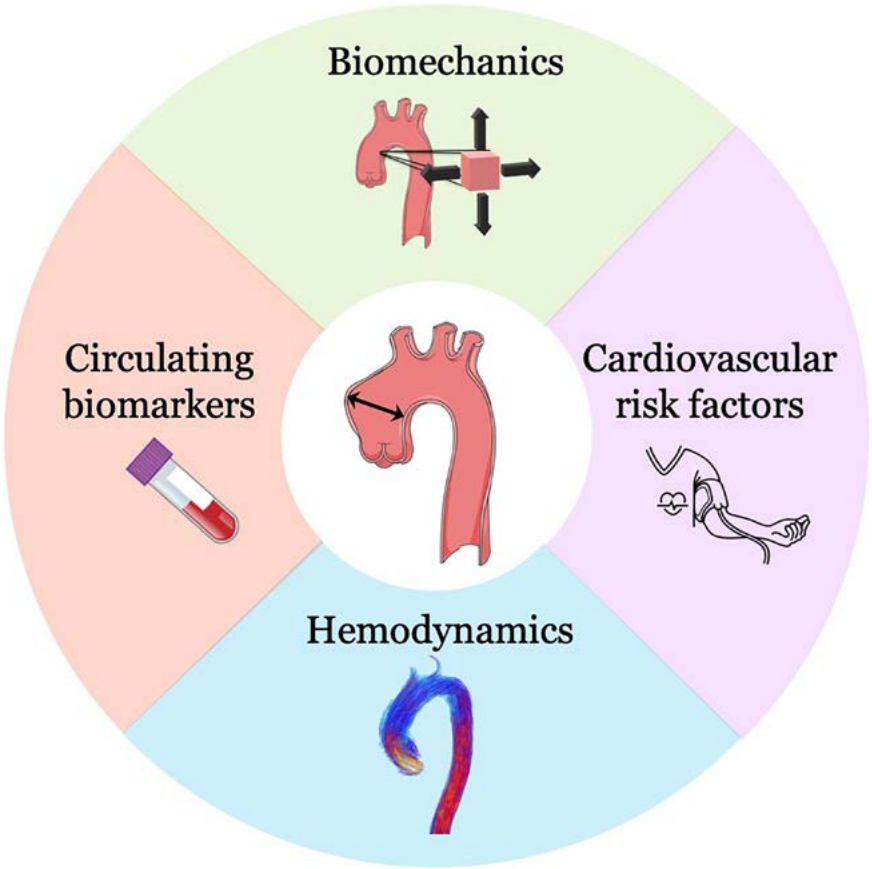
ALF Grant, Region Östergötland
Linköping University Strategic Research Area in Circulation and Cardiovascular Metabolic Risk Factors, seed grant
Medical Faculty at Linköping University, co-financing of PhD Student

KEY PUBLICATIONS

Trenti C, Fedak PWM, White JA, Garcia J, Dyverfeldt P. Oscillatory Shear Stress is Elevated in Patients with Bicuspid Aortic Valve and Aortic Regurgitation: A 4D Flow CMR Cross-Sectional Study. European Heart Journal - Cardiovascular Imaging 2023; In Press.

Lindenberger M, Ziegler M, Welander M, Ebbers T, Dyverfeldt P. Regional aortic pulse wave velocity in patients with abdominal aortic aneurysm. European Journal of Vascular & Endovascular Surgery 2023; In Press; https://doi.org/10.1016/j.ejvs.2023.09.040.

Swahn E, Lekedal H, Engvall J, Nyström FH, Jonasson L. Prevalence and determinants of dilated ascending aorta in a Swedish population: a case-control study. European Heart Journal Open 2023; 3: 1-8.



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

POPULAR SCIENTIFIC SUMMARY

Lene Rosendahl

Aortic Stenosis – Calcium Burden and its Impact on Left Ventricular Function

Aortic stenosis (AS) results in a reduction of the valve's opening area. Untreated, this leads to heart failure as the left ventricle (LV) is forced to pump against an increasingly higher pressure. Previously, the treatment of choice was surgical valve replacement. Presently, catheter-based valve replacement, "TAVI", has come to dominate and in 2023, 82% of all valve replacements for AS in the US were TAVI-procedures. Ultrasound is the method of choice to assess both the degree of AS and LV function. Ultrasound allows the calculation of valve area, assesses LV size and function and calculates the deformation of the heart muscle (strain). Computed tomography (CT) is a supporting technique which visualizes the aortic root, the coronary vessels and the aorta and also allows the calculation of the calcium burden of the valve. It is also possible to calculate LV size and function using the same parameters as ultrasound. The latest CT technology uses a photon counting detector which allows a higher spatial resolution and lower noise levels compared to previous multi-detector technology. The aim of the project is to increase our knowledge about the contribution of calcification to the severity of the aortic valve stenosis in order to improve the timing of catheter-based valve replacement. The goal is to reduce the risk of sudden death or irreversible heart damage through improved diagnostics and treatment, while postponing the risks of surgery and post-operative treatment to the future. We will include a total of 170 patients (study ASCORE 1, 100 + study ASCORE 2, 70) who, based on the recommendation of a multidisciplinary conference, will undergo further investigation in preparation of a possible TAVI procedure. Valve area obtained from the clinical ultrasound investigation is the ground truth to which the valve calcium burden calculated from CT will be compared. Furthermore, we will compare LV size and function obtained from the two modalities (study ASCORE 1). In a subgroup, the same parameters will also be studied with the new photon counter CT (study ASCORE 2).

We expect that assessment of calcium burden and LV function from CT, will improve timing for intervention in severe aortic stenosis.

Computed Tomography **Cardiovascular**

Project information

PROJECT NAME

Aortic stenosis – calcium burden and its impact on left ventricular function. A comparison between CT and ultrasound in TAVI patients.

PROJECT LEADER

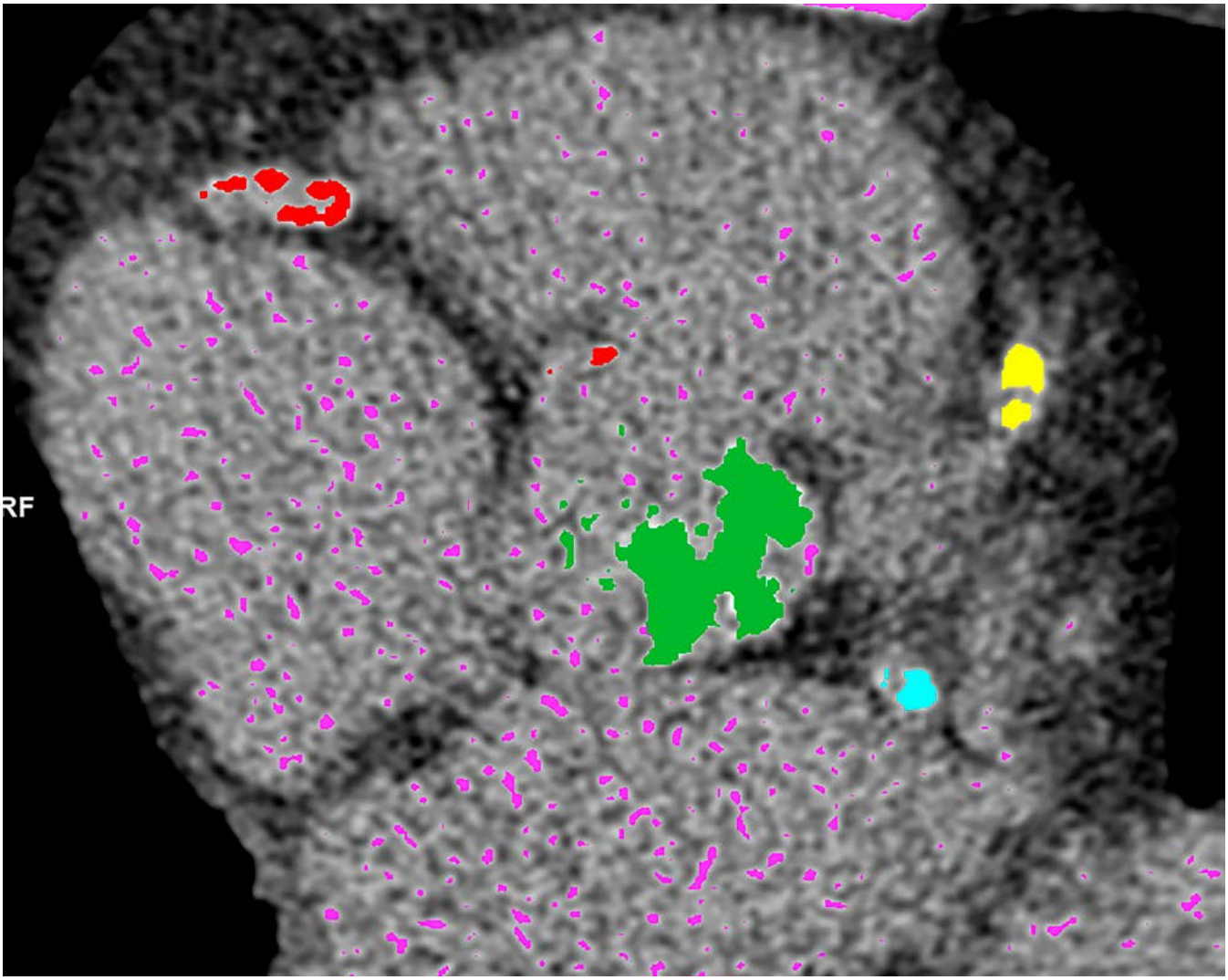
Lene Rosendahl, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine.

MAIN PROJECT PARTICIPANTS

Markus Irding, Peter Blomstrand, Jan Engvall, Mårten Sandstedt, Marcus Lindenberger.

GRANTS

FUTURUM – akademin för hälsa och vård (2022)



Severe aortic stenosis with atherosclerosis in the aortic valve. Calcifications in aortic valve and coronary arteries color coded to calculate Agatston score separately. Aortic valve color coded green, Right coronary artery red, Left Anterior descending artery yellow and Circumflex artery light blue.

POPULAR SCIENTIFIC SUMMARY
Bente Konst

Optimizing PCCT in Patients with Metal Devices

In medical imaging, precision and clarity are paramount for diagnosing and monitoring diseases. When a patient has implants, metal artifacts make it more challenging. Such artifacts can obscure important anatomical details and hinder diagnostic accuracy. To enhance the quality of cardiac imaging for patient with Left Ventricular Assitance Devise (LVAD), this study evaluated and optimized an imaging protocol using Photon Counting Computed Tomography (PCCT).

To achieve this, we examined various scan (kVp, and automated exposure control (IQ) settings) and reconstruction (kernels, slice thicknesses and iterative metal artifact reconstruction (iMAR)) settings on a phantom. The phantom comprised a Kyoto Multipurpose chest phantom, supplemented with lamb lungs and heart with an implanted LVAD, and iodine contrast, which mimic the conditions encountered in a real patient. We leveraged the PCCT's spectral capabilities to obtain virtual mono-energetic (VMI) and poly-energetic spectrum (T3D) reconstructions. Objective methods were employed to evaluate artifacts, including Hounsfield Unit/ Standard Deviation measurements in lung tissue, Fourier analysis for streak artifacts and depicted LVAD volume in the images for blooming artifact. In addition, radiologists visually graded the images using, focusing on the presence of metal artifacts and the interpretability of various structures, including the LVAD lumen, cardiac tissue, lung tissue, and spinal cord.

Identifying the best imaging settings through both visual grading and objective measurements, we applied the optimized protocol to a patient, whose scan was assessed similarly to the phantom. Additionally, we conducted regression and correlation analysis to determine the assessment method most closely associated with acquisition and reconstruction parameters, as well as the objective method demonstrating the highest correlation with visual grading.

Our research revealed that LVAD volume was the best objective method to assess metal artifacts, and its fluctuation emphasizing the significance of parameter selection .These artifacts is dependent on the following factors, ranked from the largest impact to the least impact: kVp, kernel, keV, and iMAR.

In conclusion, the optimal settings for third-generation LVAD imaging include 120 kVp, IQ level 80, 3 mm slice thickness, pacemaker iMAR preset, and T3D with BV56f kernel, along with VMI at 110 keV in conjunction with Qr40. These settings generate images suitable for follow-up LVAD therapy. Nevertheless, the pursuit of more effective methods to mitigate metal artifacts is underway, driving advancements in PCCT software. Future investigations may delve into metal artifact reduction using deep learning algorithms. However, a crucial prerequisite is understanding the variation of Hounsfield Unit (HU) numbers with different acquisition and reconstruction parameters, a key consideration for segmentation-based approaches that must be addressed upfront.

Computed Tomography | Cardiovascular | Acquisition

Project information

PROJECT NAME
Optimizing PCCT in Patients with Metal Devices.

PROJECT LEADER
Bente Konst.

MAIN PROJECT PARTICIPANTS
Linus Ohlsson, Lilian Henriksson, Mårten Sandstedt, Anders Persson, Tino Ebbers Erik Tesselaar.

GRANTS
CircM

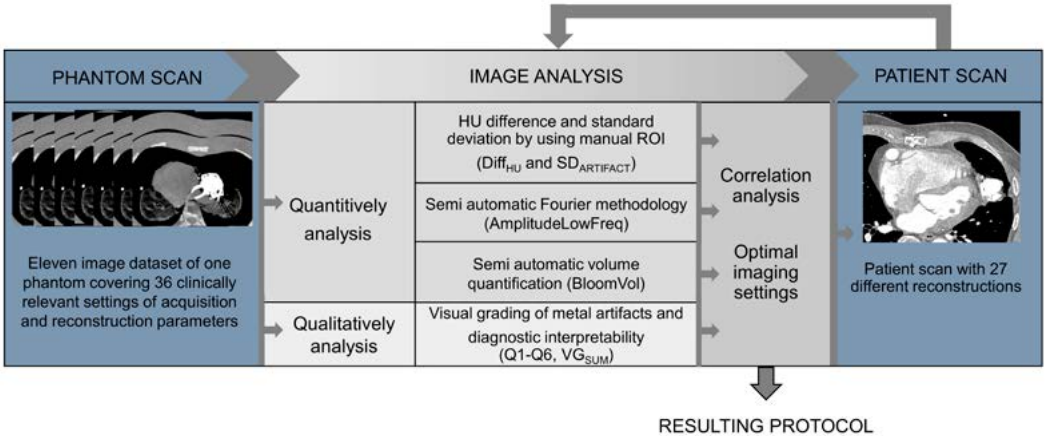


Figure 1. Flowchart of the study methodology.

Figure 2. A Multipurpose Chest Phantom N1, "Lungman", PH-1; Kyoto-Kagaku. The lung insert was replaced with lamb heart and lungs with an LVAD. Extra chest plates were added to simulate a standard patient size.

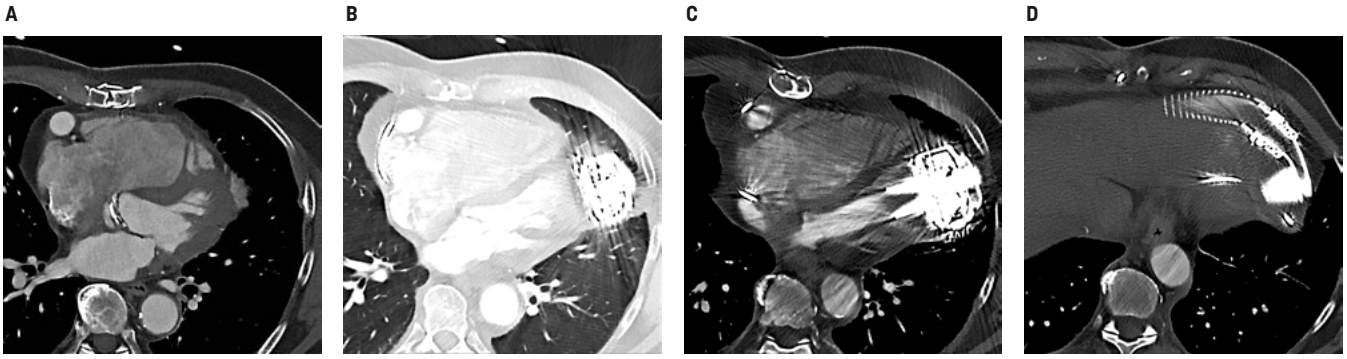


Figure 3. Shows an example of and highest image quality (T3D, Bv56f, 3 mm) of: A cardiac tissue, B lung tissue, C inflow cannula and D utflow cannula.

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 5058 study participants during 2015 and 2018 with a participation rate of 58%.

In addition to determining the traditional cardiovascular risk factors, the participants underwent extensive imaging, including non-contrast and contrast-enhanced computed tomography (CT) coronary angiography; CT scanning of the abdomen for the quantification of visceral and subcutaneous adipose tissue, liver fat; and ultrasound analysis for carotid artery atherosclerosis.

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 found that among Swedish middle-aged subjects, nearly two-thirds showed complete fatty degeneration of thymus on CT. This was linked to depletion of naïve CD8+ T cells indicating that CT scans of thymus might be used to estimate immunological aging (key publication 1).

SCAPIS 2: At national level we are currently planning for a physical follow-up and a re-examination of the SCAPIS cohort called SCAPIS 2. The re-examination will start March 13th 2024 at Linköping University Hospital and broadly follow the baseline protocol and include a 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.

Computed Tomography | MRI | Ultrasound | Cardiovascular | Pulmonary | Metabolism | 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 Diagnostics and Specialist 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

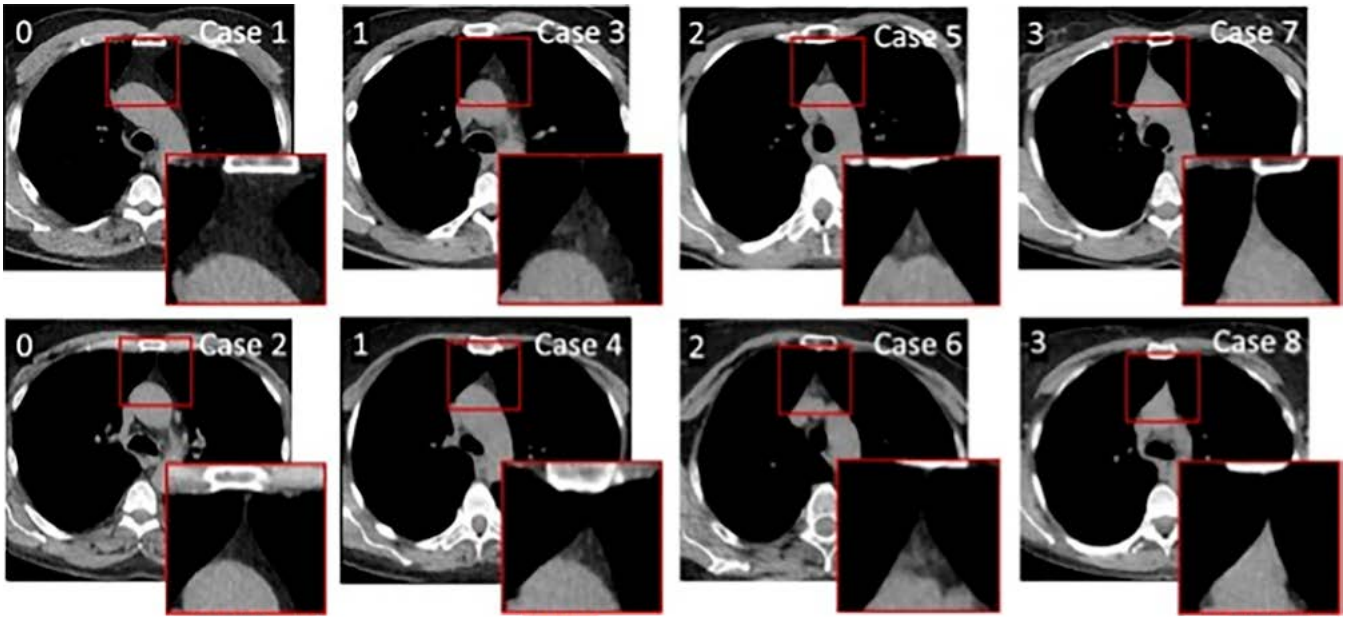
Vetenskapsrådet (2021-2025)
Hjärt-Lungfonden (2022-2024)

KEY PUBLICATIONS

Sandstedt M, Chung RWS, Skoglund C, Lundberg AK, Östgren CJ, Ernerudh J, Jonasson L. Complete fatty degeneration of thymus associates with male sex, obesity and loss of circulating naïve CD8$^+$ T cells in a Swedish middle-aged population. Immun Ageing. 2023 Aug 31;20(1):45. doi: 10.1186/s12979-023-00371-7. PMID: 37653480; PMCID: PMC10470174.

Östgren CJ, Otten J, Festin K, Angerås O, Bergström G, Cederlund K, Engström G, Eriksson MJ, Eriksson M, Fall T, Gummesson A, Hagström E, Hellman U, James SK, Jernberg T, Kihlberg J, Kylhammar D, Markstad H, Nilsson P, Persson A, Persson M, Pirazzi C, Renklint R, Rosengren A, Söderberg S, Sundström J. Prevalence of atherosclerosis in individuals with prediabetes and diabetes compared to normoglycaemic individuals-a Swedish population-based study. Cardiovasc Diabetol. 2023 Sep 27;22(1):261. doi: 10.1186/s12933-023-01982-6. PMID: 37759237; PMCID: PMC10537533.

Cederqvist J, Rådholm K, Muhammad IF, Engström G, Engvall J, Östgren CJ. Arterial stiffness and subclinical atherosclerosis in the coronary arteries at different stages of dysglycaemia. Diabet Med. 2023 Jul;40(7):e15102. doi: 10.1111/dme.15102. Epub 2023 Apr 8. PMID: 37004152.



Thymus fat and soft tissue content was visually analyzed and graded on a scale 0–3: grade 0, complete fatty replacement, no identifiable soft tissue in the thymic bed; grade 1, predominantly fatty thymus; grade 2, approximately one-half fatty and one-half soft tissue attenuation thymus; and grade 3, predominantly soft tissue attenuation thymus The image shows representative CT images of each thymic score. Each thymic score (indicated at top left in the image) is represented by two different cases. Cases 1 and 2: Score 0, complete fatty replacement, no identifiable soft tissue in the thymic bed, Cases 3 and 4: Score 1, predominantly fatty thymus, Cases 5 and 6: Score 2, approximately one-half fatty and one-half soft tissue attenuation thymus, and Cases 7 and 8: Score 3, predominantly soft tissue attenuation thymus (key publication 1).

POPULAR SCIENTIFIC SUMMARY

Peter Lundberg, Neda Haj 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 develops. This places great demands on the diagnostic tools in clinical pathology, that 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 Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine
Neda Haj Hosseini, Department of Biomedical Engineering, Division of Biomedical Engineering .

MAIN PROJECT PARTICIPANTS

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

GRANTS

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

KEY PUBLICATIONS

T Bianchessi, IE Tampu, I Blystad, P Lundberg, P Nyman, A Eklund, and N Haj-Hosseini, 'Pediatric brain tumor type classification using deep learning and MR-images from the children's brain tumor network' MedRxiv, 2023.

Christoforos Spyretos, 'Multiclass Brain Tumour Tissue Classification on Histopathology Images Using Vision Transformers', Master thesis, 2023.

C Spyretos, IE Tampu, A Eklund, N Haj-Hosseini- 'Classification of Brain Tumour Tissue in Histopathology Images Using Deep Learning', Medicinteknikdagarna 2023.

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

POPULAR SCIENTIFIC SUMMARY
Peter Lundberg

AI-Based Medical Record Screening for Patient-Safe MRI Examination

What we want to do? 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 an magnetic resonance imaging (MRI) scan. The method is based on automatic identification of "implant terms" through context processing of patient records.

Needs? When a patient today has, or is suspected of having, an implant, the procedure to obtain such is fact entirely manual, it is also laborious and involves a range of experts with specialized knowledge. It is therefore 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 himself usually does not know the model of implant or even the presence of one. In addition, even if implants has been removed, left-behind leads may be overlooked. About 30 000 MR-examinations are performed annually in Region Östergötland, and an increasing number of our patients have implants.

Challenge? 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 practioners, 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, David Abramian, Arne Jönsson Håkan Gustavsson, Tomas Bjerner, Emma Eneling, Magnus Stridsman, Oscar Jerdhaf.

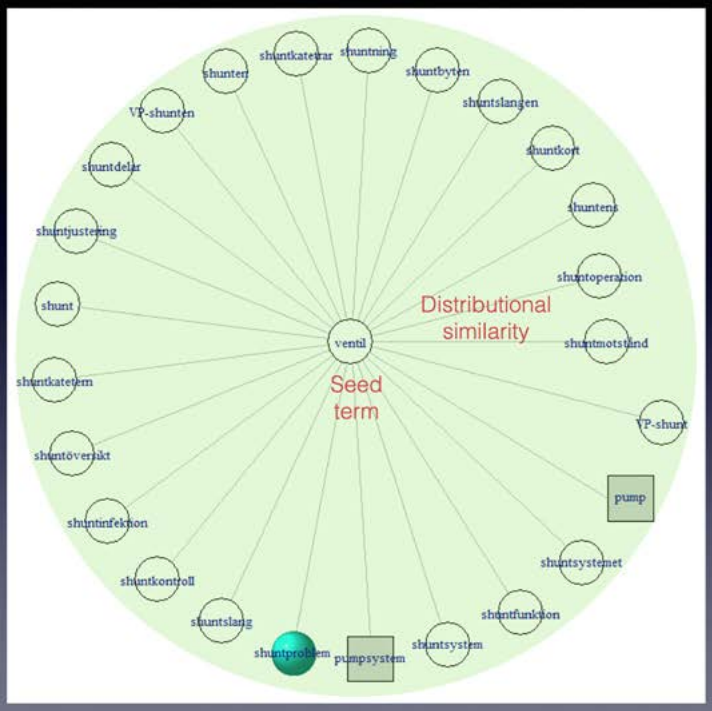
GRANTS
MedTech4Health
Vinnova
Socialstyrelsen
Nordic Innovation

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
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. The latter group can be further categorized into resectable, borderline resectable and locally advanced PDAC, mainly depending on extent of tumour vessel involvement (e.g. coeliac trunk, superior mesenteric artery and hepatic artery.

The assessment of these parameters is currently conducted using CT images captured at different contrast phases with conventional CT machines. However, the limited resolution of today's CT machines raises uncertainties in evaluating certain parameters, as for example the involvement of vessel structures uncertain. In this project, we aim to determine if the increased resolution of the photon counting CT can improve the reliability of overgrowth information, thereby enhancing the selection process for surgical or oncological therapy. Additionally, we will explore whether the increased quantitative information from the photon counting CT, combined with radiomics and AI information, can serve as an imaging biomarker for the predicting possible therapy outcomes.

The initial analysis comparing image quality between the Siemens Force system and the Siemens photon-counting Count system is currently underway.

Computed Tomography | Oncology | Gastrointestinal | Acquisition | AI/Data analytics | Imaging Biomarkers

Project information

PROJECT NAME

Photon Counting in Pancreatic Ductal AdenoCarcinoma.

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.

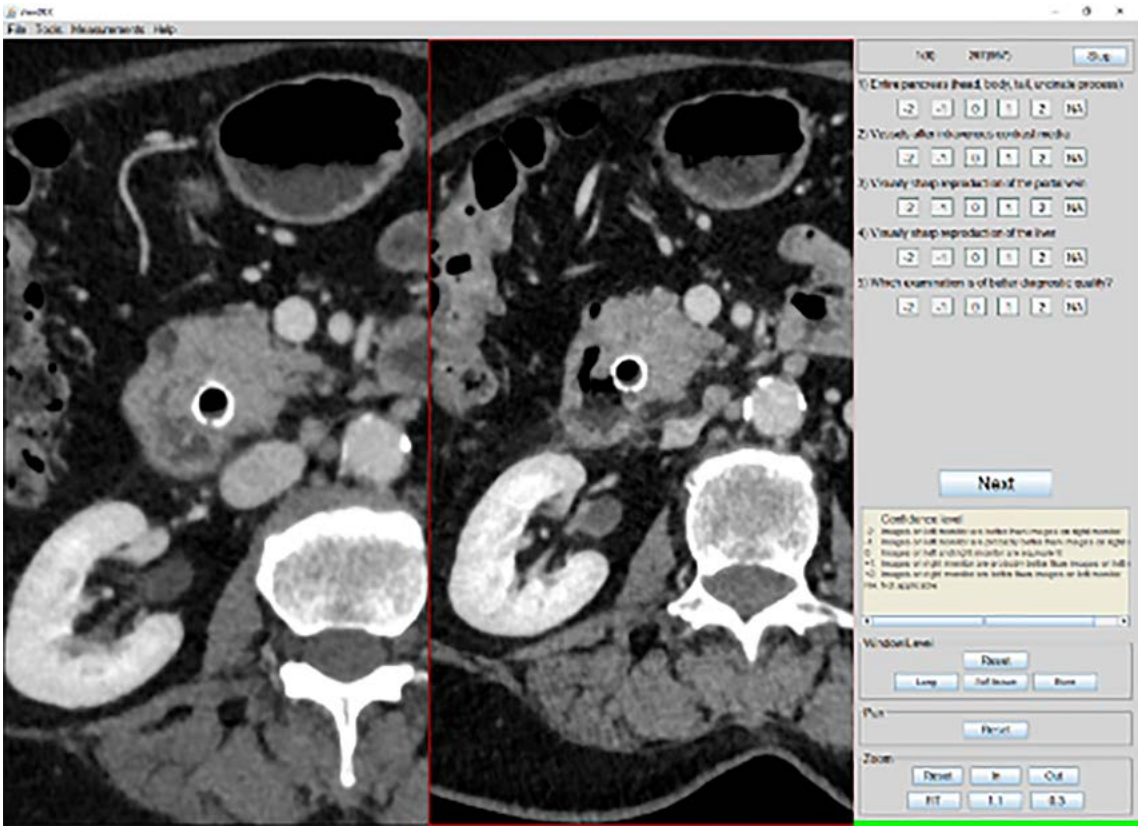


Figure 1. Comparison of EID-CT (right) and PDC-CT (left) in a a pancreatic cancer patient, analyzed regarding image quality parameters in ViewDex 3.0.

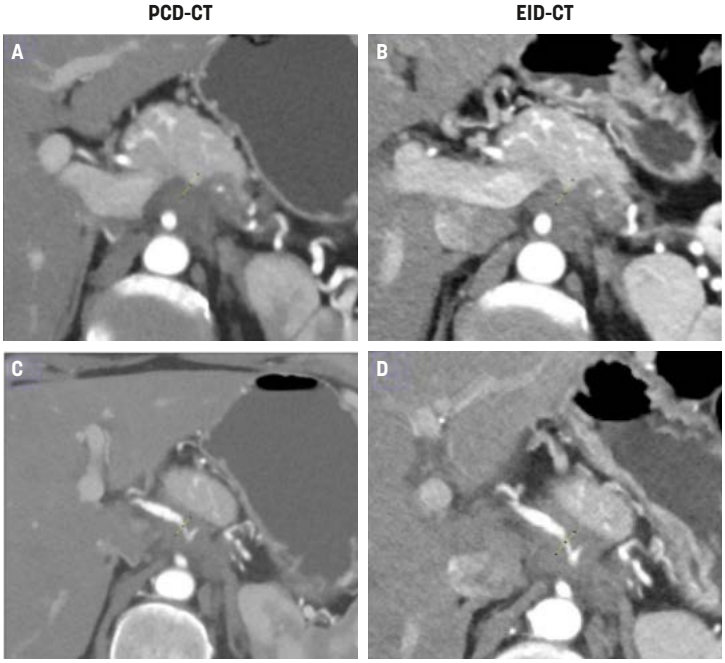


Figure 2. Zoomed images of EID-CT (right) and PDC-CT (left) in a pancreatic cancer patient, analyzed regarding image quality parameters in ViewDex 3.0.

	Arterial							Venous				
Pat.	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q1	Q2	Q3	Q4	Q5
1	0	-1	-1	0	-1	0	-1	-1	-1	-1	-2	-1
2	1	0	0	0	0	1	0	1	0	0	0	0
3	1	1	1	1	1	1	1	0	-1	-1	-1	-1
4	2	1	1	1	1	1	1	1	0	1	1	1
5	1	0	0	0	-1	1	0	1	0	1	1	0
6	-1	-1	-1	0	-1	0	-1	-1	-1	-1	-1	-1
7	0	0	0	1	1	1	1	1	1	1	1	1
8	1	0	1	1	2	1	1	1	0	0	0	0

-2	strong preference for PCD-CT
-1	slight preference for PCD-CT
0	no preference
1	slight preference for EID-CT
2	strong preference for EID-CT

Figure 3. Heatmap visualizing the results of the relative image quality assessment between EID-CT and PCD-CT pancreas protocols.

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. AIDA management resides at CMIV and CMIV is the main physical meeting place of AIDA.

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. It is, however, difficult for AI solutions to reach actual use in imaging diagnostics. The reason is that the step from experiments to clinical routine entails many challenges. Understanding the targeted clinical workflows and carefully designing user interaction are just as important as the predictive performance of the AI model.

AIDA's objective is to assist taking AI solutions for imaging diagnostics all the way to clinical use. An underpinning fundamental insight is that this complex challenge requires both interdisciplinary and cross-sectoral collaboration.

The AIDA program consists of many types of activities. Most resources are used for innovation projects developing AI methods. These are run by research groups in industry and academia across Sweden, in collaboration with healthcare providers. AIDA also supports clinical competence development in AI, through regularly organizing courses and through supporting clinical fellowship projects. A cornerstone of the program is the meeting place AIDA organizes, with frequent cross-disciplinary workshops and meetups, where knowledge is disseminated and experiences exchanged.

In a special initiative, AIDA acts as an incubator for national AI validation platforms for medical imaging. The aim is to help care providers to take their responsibility to control that the solutions used are safe and effective. Three pilot platforms are being developed, where the one targeting mammography screening, named VAI-B, is the largest and most advanced.

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 is a heavy-load computational system 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, and technical expertise to assist research efforts. Currently 24 datasets with 12 TB of such data is available, so far having been shared with researchers in 29 countries around the world.

AIDA is an initiative within the Strategic innovation program Medtech4Health, jointly supported by VINNOVA, Formas and the Swedish Energy Agency. The AIDA Data Hub is 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, ITN.

MAIN PROJECT PARTICIPANTS
Caroline Bivik Stadler, Joel Hedlund, Catrin Nejdeby, Håkan Gustafsson, Maria Kvist, Jonas Unger, Gabriel Eilertsen, Shreyas Shivakumara, Betül Eren Keskin, Emre Balsever, Varshith Konda, Pontus Freyhult, Erik Ylipää, Darren Treanor, Petter Dyverfeldt, Neda Haj-Hosseini, Anders Eklund, Tino Ebbers, Martin Lindvall, Karin Stacke.

GRANTS
VINNOVA Medtech4Health
SciLifeLab
VINNOVA Precision Health
VINNOVA Health Data Demonstrator

KEY PUBLICATIONS

Claes Lundström, Martin Lindvall. Mapping the Landscape of Care Providers' Quality Assurance Approaches for AI in Diagnostic Imaging. Journal of Digital Imaging (2023).

Fernando Cossío, Haiko Schurz, Mathias Engström, Carl Barck-Holst, Apostolia Tsirikoglou, Claes Lundström, Håkan Gustafsson, Kevin Smith, Sophia Zackrisson, Fredrik Strand. VAI-B: a multicenter platform for the external validation of artificial intelligence algorithms in breast imaging. Journal of Medical Imaging (2023).

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).

Panel debate at the Swedish Radiology Conference on clinical validation and implementation of AI with Peder Wiklund, Henriettae Ståhlbrandt, Johan Henriksson, and Sophia Zachrisson, moderated by Håkan Gustafsson.

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 was completed in October 2023 when 342 patients had been included. Of these, 303 patients had successfully completed all parts of the study. A sub study within EPSONIP, EPSONIP-SLEEP, has started with the aim to study sleep patterns in patients with type 2 diabetes with and without fatty liver disease. Two posters were presented at the Liver Meeting (AASLD) in Boston, 2023.

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 (DISP).

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, Shan Cai, Cecilia Jönsson, Karin Hedin, Markus Holmberg, Karin Rådholm.

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.

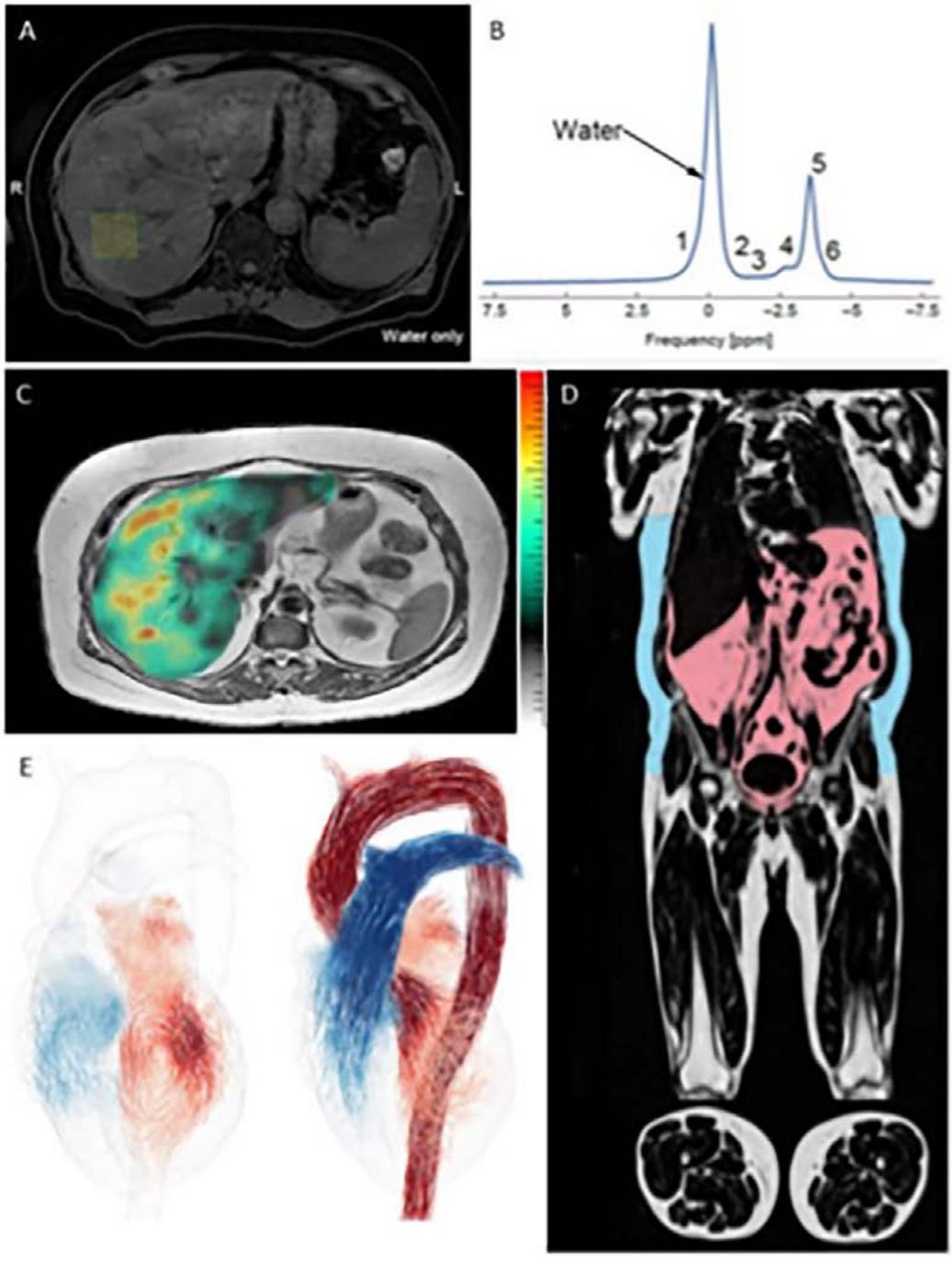


Image A shows the representative water MR image with 547 the placement of a proton magnetic resonance spectroscopy (^{1}H-MRS) voxel in the right hepatic lobe. Image B shows in vivo 1H-MRS spectrum for water and fat. Image C shows MRE for a cirrhotic NAFLD patient. Image E shows a whole-body water-fat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

POPULAR SCIENTIFIC SUMMARY
Mattias Ekstedt

The ACCESS-ESLD Study

The ACCESS-ESLD study is a giant leap towards early detection, and comprehensive understanding and prevention of complications associated with liver cirrhosis. By leveraging advanced MRI technology, this multi-center prospective cohort study is intended to bring forward profound insights into the changes that occur over time in patients with liver cirrhosis.

In the ACCESS-ESLD study, 150 patients with liver cirrhosis are monitored over a period of 18 months, with regular MRI examinations at 6-month intervals, allowing in-depth monitoring of temporal changes.

The primary aim of the study is to examine if changes in body composition, especially muscle volume and muscle fat, can be linked to the progression of end-stage liver disease complications, such as liver decompensation, hepatocellular carcinoma, and sarcopenia.

By combining multiple muscle groups, blood samples, and genetic composition we hope to improve the diagnostic yield and to identify those patients at highest risk of severe outcomes. ACCESS-ESLD is a prospective cohort study in which patients with liver cirrhosis, but without a previous diagnosis of hepatocellular carcinoma are included. All patients included will undergo a MR-based body composition profile utilizing the Muscle Assessment Score (MAsS), which includes fat-free muscle volume z-score (FFMV) and thigh muscle fat index (sex-adjusted MFI), using the AMRA® Researcher based on an 8-minute MRI on the same day as the clinical work-up. The clinical work-up includes: comprehensive blood panels, vibration-controlled transient elastography for liver stiffness assessment, questionnaires to ascertain health-related quality of life and physical fitness, hand-grip strength to gauge physical frailty, and an assessment of present and previous medical history as well as the absence or presence of liver decompensation and related morbidities.

The ACCESS-ESLD study stands at the frontier of liver cirrhosis research, paving the way for early detection, effective intervention, and improved patient outcomes. The study's holistic approach, from sophisticated imaging to physical assessments, promises a brighter, more informed future for those battling liver cirrhosis.

MRI | Musculoskeletal | Gastrointestinal | Metabolism | Visualization | Imaging Biomarkers

Project information

PROJECT NAME

A rapid, non-invasive, Clinical surveillance for CachExia, Sarcopenia, portal hypertenSion, and hepatocellular carcinoma in End-Stage Liver Disease.

PROJECT LEADER

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

MAIN PROJECT PARTICIPANTS

Mikael F Forsgren, Wile Balkhed, Patrik Nasr, Daniel Sjögren, Jennifer Linge, Anna Cederborg, Markus Holmberg, Nils Dahlström, Henrik Stjernman, Martin Rejler, Stergios Kechagias, Olof Dahlqvist Leinhard, Peter Lundberg, Wolf Bartholomä.

GRANTS

Region Östergötland ALF-grant
FORSS
Stiftelsen Ruth och Richard Juhlins Fond
Svenska läkaresällskapet (SLS)
SLS Gastroenterologisk forskningsfond
Magtarmfonden
Wallenberg centrum för molekylärmedicin (WCMM)

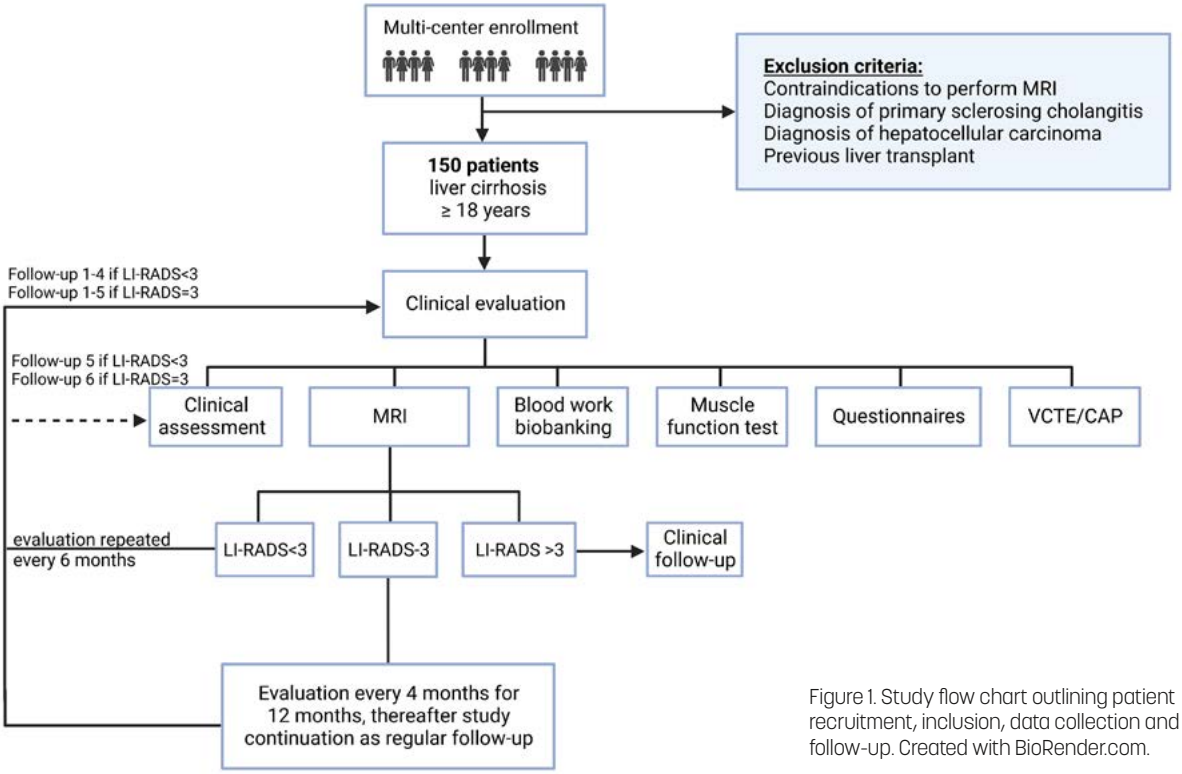


Figure 1. Study flow chart outlining patient recruitment, inclusion, data collection and follow-up. Created with BioRender.com.

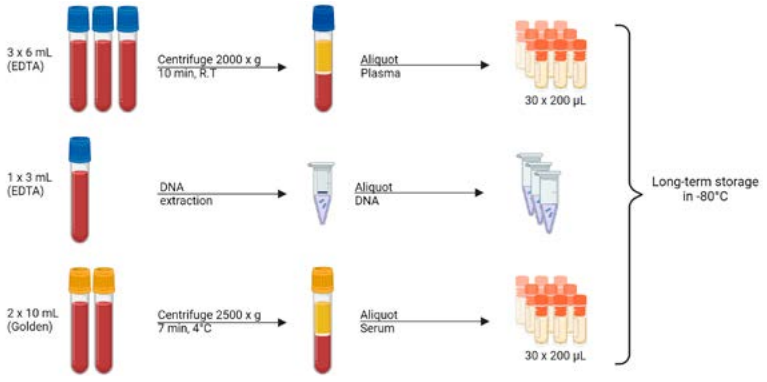


Figure 2. Overview of blood sample acquisition and biorepository. Created with BioRender.com.

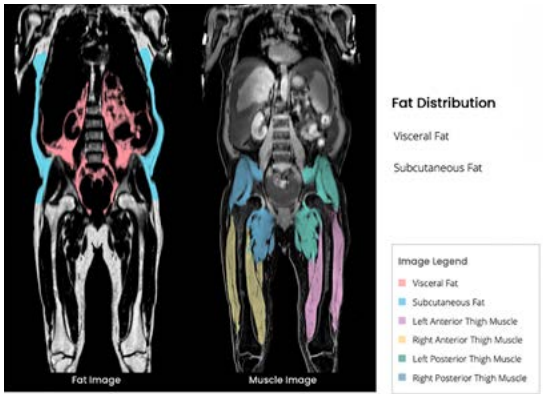


Figure 3. Example of whole-body water-fat separated images of fat distribution and muscle volume.

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 ^{192}Ir, emitting photons at an average energy of 350 keV is used. Brachytherapy is sometimes called interior radiation therapy. Invasively inserted catheters or anatomy shaped applicators are inserted and provides the possible positions to place the source in the patient. Advantages over external beam radiotherapy include the capacity to better conform the dose to the treatment volume (the target), lower doses to healthy tissue, and fewer issues with organ motion (as the catheters move with the target). Three-dimensional (3D) imaging with ultrasound, magnetic resonance, or computed tomography is used to assist catheter placement and to delineate the volume to be treated (the target) and the nearby healthy organs at risk. The dwelling time of the single 192-Ir source varies depending on the location in the patient to create the final dose distribution. Treatment planning involves deciding source positions and source dwelling times in a way that yields the best compromise between a high dose to the target volume and doses to organs at risk low enough to limit the risk of severe side effects. Manual methods or methods based on mathematical optimization are used. Benefits of the latter include that it proceeds faster (an advantage in brachytherapy as the patient awaits treatment under 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 them in clinical context. Automated treatment planning is prone to yield uneven distribution of dwelling times, giving rise to regions with high dose, often resolved by manual fine-tuning. We recently published (Dohlmar et al 2023) an oncologist's observer study on a cohort of prostate cancer treatment using visual grading methods with origin in radiology for the first time in radiotherapy. Our in-house developed algorithm to automatically improve clinical treatment plans on their spatial properties (Morén et al 2019) was chosen in the majority of cases. Our focus is on treatment planning for cervical cancer, for which a brachytherapy boost is state-of-the-art in curative treatment, and on treatment planning methods robust to uncertainties. The method Morén et al 2019 was also implemented in a research version of a clinical treatment planning system (Morén et al 2023).

MRI | Digital Microscopy | 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 Specailist Medicine.

MAIN PROJECT PARTICIPANTS

Frida Dohlmar, Michael Sandborg, Björn Morén, Torbjörn Larsson.

GRANTS

VR-NT (2020-2023)
Cancerfonden (2019-2021)
LiU Cancer (2020-2024)
Region Östergötland "student till docent" (2021-2022)

KEY PUBLICATIONS

Dohlmar F, Morén B, Sandborg M, Smedby O, Valdman A, Larsson T and Carlsson Tedgren Å 2023 Validation of automated post-adjustments of HDR prostate brachytherapy treatment plans by quantitative measures and oncologist observer study Brachytherapy 22 407–415.

Morén B, Bokrantz R, Dohlmar F, Andersson B, Setterquist E, Larsson T and Carlsson Tedgren Å 2023 Technical note: Evaluation of a spatial optimization model for prostate high dose-rate brachytherapy in a clinical treatment planning system Med Phys 50 688–93.

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.

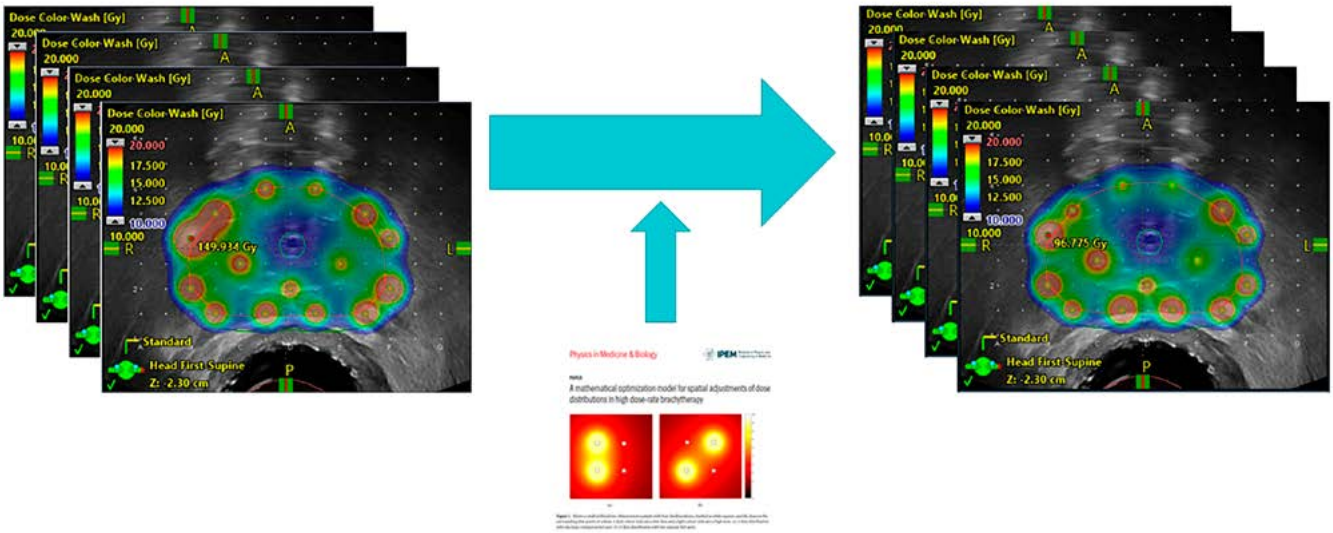


Figure 1. The principle underlying the qualitative assessment of our method in Dohlmar et al (2023) where eight oncologists were asked to blindly select among the original, clinically used treatment plan (left) and a version of the same plan that had been further adjusted on spatial 3D properties by the method developed in Morén et al (2019) (right).

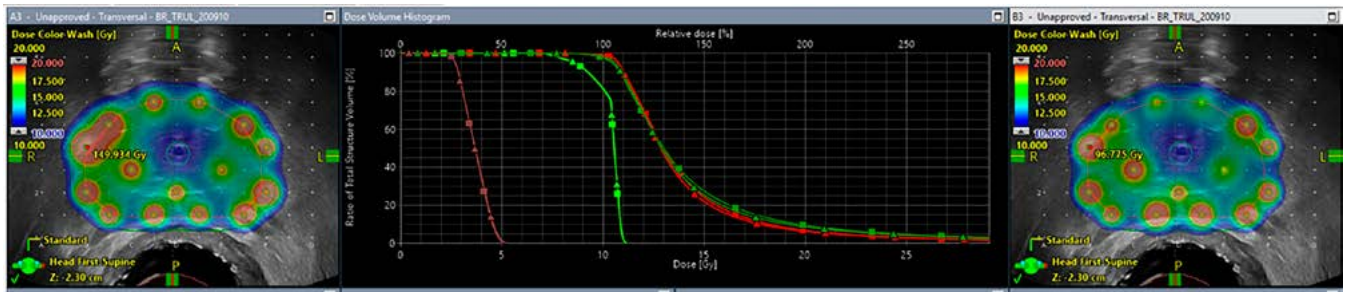


Figure 2. The observer study was setup for pairwise comparison of the two alternative plans in a clinical treatment planning system, then showing also the dose volume histograms of the two plans. Dose volume histograms represent a 2D way to judge a 3D plan and are assessed to judge clinical plans.

POPULAR SCIENTIFIC SUMMARY
Anders Eklund

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. Addressing this challenge requires more efficient planning and treatment strategies.

The main goal of the ASSIST project is to enhance healthcare efficiency by leveraging the advances in deep learning, where a computer is trained to perform various tasks. Radiation therapy is an effective treatment method for tumors, complementing surgery and chemotherapy. However, radiation therapy requires time-consuming preparations involving the acquisition of medical images, segmenting the tumor and risk organs, and developing a treatment plan to target as much of the tumor as possible without harming healthy tissue. Deep learning can be applied to all these steps to shorten the planning time, resulting in increased patient throughput and shorter queues.

To determine the most effective treatment plan for tumor patients, there is a 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 tumor border accurately, thereby aiding the machine learning algorithms to be employed for treatment planning. Of particular interest are advanced diffusion MRI methods due to their sensitivity to tissue microstructure. By applying several mathematical constraints, we obtain reliable estimates of microstructure-sensitive MRI 'biomarkers' from fewer images. Adapting machine learning methods further boosts the computational efficiency of such methods.

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 are developing methods for so-called 'federated learning,' where computers can be trained without sending medical images between hospitals. We have recently performed federated trainings for brain tumor segmentation between Linköping and Lund, using local data from the oncology department of each hospital.

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 LEADER

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

MAIN PROJECT PARTICIPANTS

Ida Blystad, Deneb Boito, Iulian Emil Tampu, Muhammad Usman Akbar, Neda Haj-Hosseini, Magnus Herberthson, Alfredo Ordinola.

GRANTS

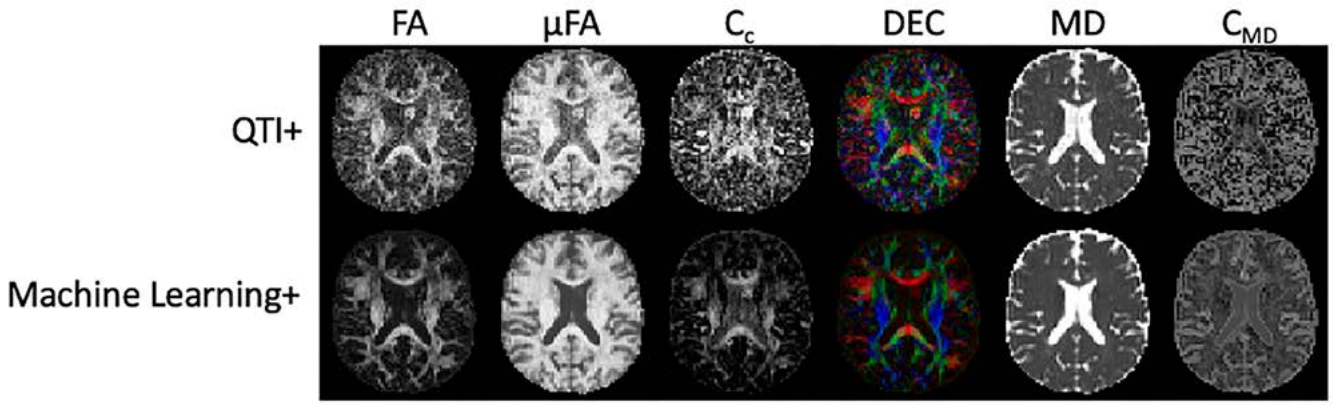
VINNOVA (2021-2024)

KEY PUBLICATIONS

Tampu, I., Haj-Hosseini, N., Blystad, I., Eklund, A., Deep learning-based detection and identification of brain tumor biomarkers in quantitative MR images, Machine Learning: Science and Technology, 2023.

Boito, D., Herberthson, M., Dela Haije, T. C. J., Blystad, I., Özarslan, E. (2023). Diffusivity-limited q-space trajectory imaging. Magnetic Resonance Letters; 3:187-196.

Boito, D., Özarslan, E., Q-space trajectory imaging with positivity constraints: a machine learning approach. Proc Intl Soc Mag Reson Med, 31, Toronto, 2023, p. 3780.



An example from a healthy volunteer comparing the state-of-the-art and the machine learning based estimates of diffusion MRI 'biomarkers'. From left to right: Fractional anisotropy (FA), microscopic FA, coherence (C_c), direction-encoded color (DEC), mean diffusivity (MD), and the covariance of MD.

POPULAR SCIENTIFIC SUMMARY
Åsa Carlsson Tedgren

Spectral Photon-Counting CT for Radiotherapy

Today's computed tomography (CT) images are affected by inaccuracies and artifacts caused by polyenergetic photon beams. Despite active research, 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, for instance, Alvarez-Macovski-based reconstruction in Figure 1.

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 to determine calcium content in the prostate gland. Such information is helpful 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 can also be helpful 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 2) and a method for determining the elemental composition of the segmented tissues using a neural network. We work on evaluating DIRA as a tool that increases the accuracy of radiation therapy planning. Also, we work on techniques allowing the use of raw data produced by clinical CT scanners in DIRA.

We have developed and tested techniques for the computation of absorbed dose distributions in proton therapy via the general-purpose Monte Carlo code TOPAS. These techniques allow us to quantify the improvement in dose distribution accuracy achieved by DIRA.

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

Project information

PROJECT NAME

Spectral photon-counting CT for more accurate radiotherapy.

PROJECT LEADER

Åsa Carlsson Tedgren, Institutionen för medicin, hälsa och vård (HMV), enhet för diagnostik och specialistmedicin (DISP).

MAIN PROJECT PARTICIPANTS

Alexandr Malusek, Maria Magnusson, Michael Sandborg.

GRANTS

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

KEY PUBLICATIONS

Magnusson, Maria, Gudrun Alm Carlsson, Michael Sandborg, Åsa Carlsson Tedgren, and Alexandr Malusek. "On the Choice of Base Materials for Alvarez-Macovski and DIRA Dual-Energy Reconstruction Algorithms in CT." In Photon Counting Computed Tomography: Clinical Applications, Image Reconstruction and Material Discrimination, edited by Scott Hsieh and Krzysztof (Kris) Iniewski, 153–75. Cham: Springer International Publishing, 2023.

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.

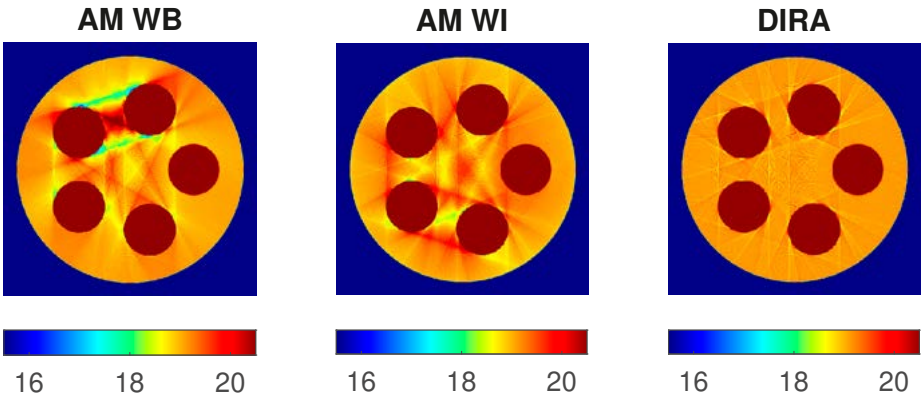


Figure 1. Images of a cylindrical protein phantom containing water, bone, and iodine solution inserts reconstructed at 50 keV by the Alvarez-Macovski method using (a) the (water, bone) and (b) (water, iodine) doublets. (c) A reconstruction by DIRA using the (water, bone) doublet in the bone and soft tissue regions, and (iodine, water) doublet in the iodine solution regions. Taken from Magnusson et al. doi.org/10.1093/rpd/ncab097 under CC BY.

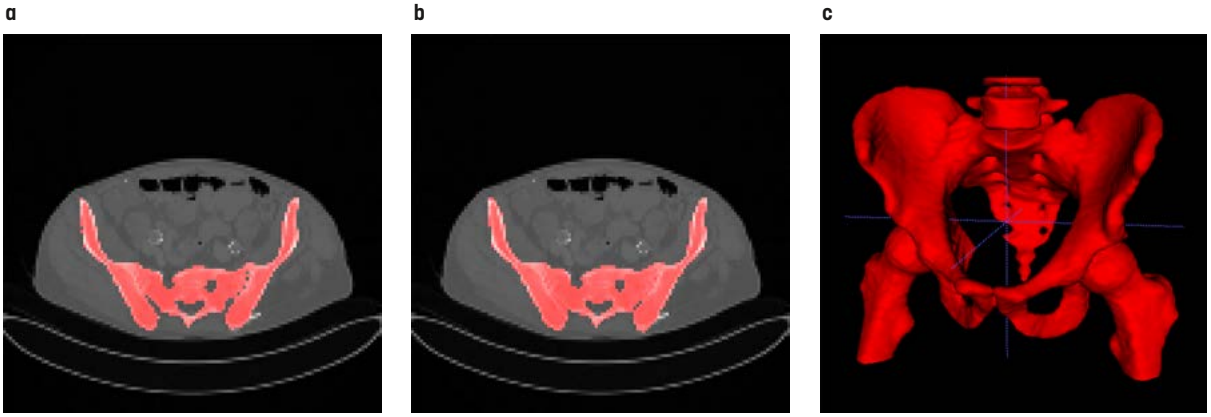


Figure 2. Segmentation of pelvic bones via the 3D U-Net architecture. (a) Ground truth. (b) Prediction of our algorithm. (c) 3D view of the prediction. Taken from (González Sánchez et al., 2020) under CC BY.

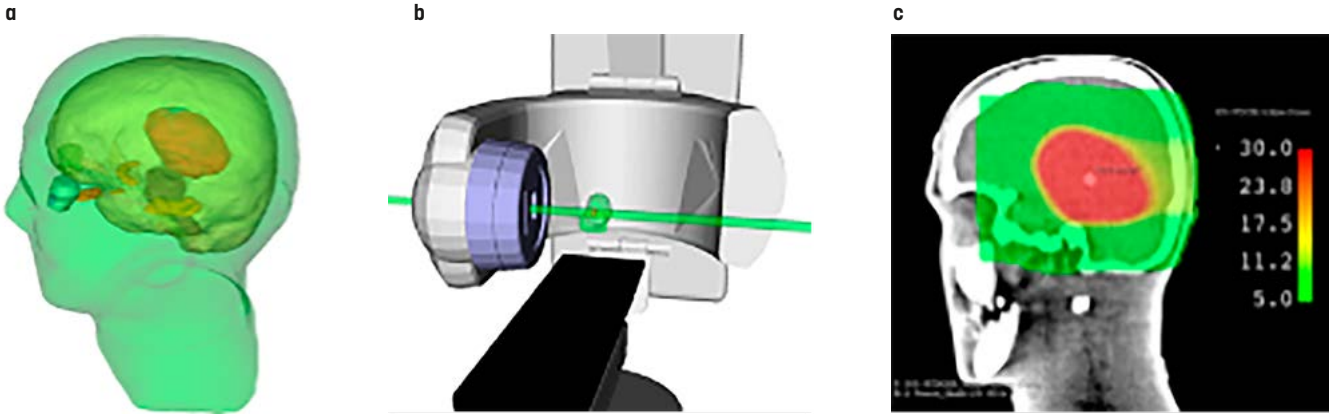


Figure 3. (a) Segmented organs and the tumour in a head phantom. (b) One proton field of a radiation treatment plan. (c) Spatial distribution of absorbed dose from protons in the tumour.

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. Furthermore intraabdominal and subcutaneous fat decreased significantly. Measurements of telomer length, change from white to brown fat are underway. Two PhD student have been graduated with projects from this study, another three are working with projects based on the study.

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

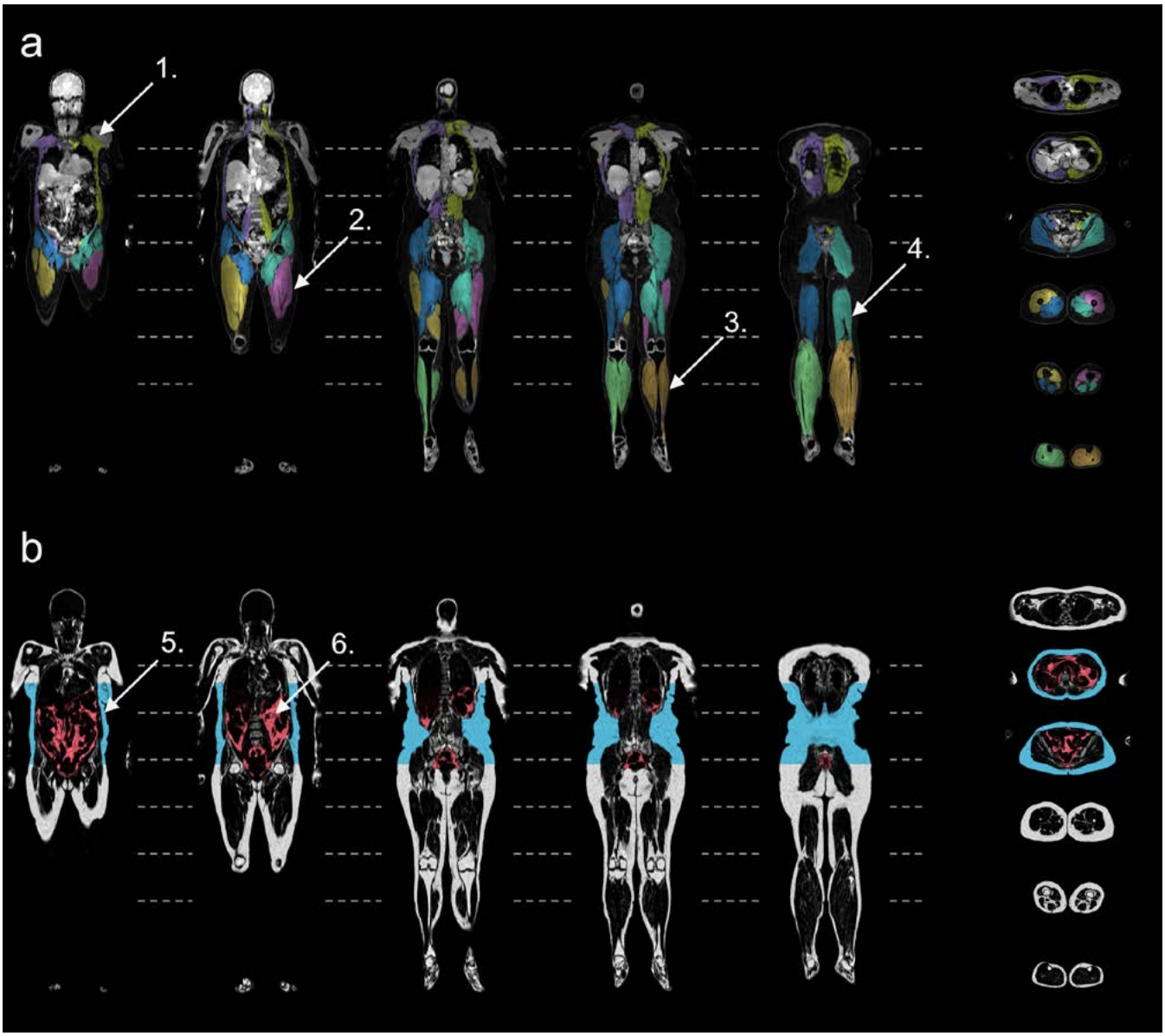
Vetenskapsrådet (ended 2022-12-31)
ALF grants (Anna-Clara Spetz Holm)

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.

Sigrid Nilsson, Mats Hammar, Janne West, Magnus Borga, Sofia Thorell, Anna-Clara Spetz Holm. Resistance training decreased abdominal adiposity in postmenopausal women. Maturitas, 2023; 176:1-7.



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
Marcel Warntjes

Automatic Ventricle Segmentation Using 3D Quantitative MR

Quantitative Magnetic Resonance Imaging has the ability to measure physical characteristics of the patient. Using absolute measures allows for robust segmentation of specific tissue types. This has been implemented, for example, to measure the volume of the brain or the amount of white matter and grey matter in the brain to monitor potential pathologies and brain atrophy. QMRI can also detect the volume of cerebrospinal fluid (CSF) in the brain. With brain atrophy the volume of the brain declines and is replaced by CSF. When a patient suffers from hydrocephalus, however, the amount of CSF inside the intracranial cavity increases as well. In this case, it is important to know how much of this CSF resides inside the ventricular system. The balance between the total amount of CSF and the ventricular volume provides an indication what part is due to atrophy and what part is due to hydrocephalus. When an operation is required, placing a drain in the ventricles to reduce the CSF, it is vital to monitor the effect of the drain.

With the advent of fast 3D MR quantification methods, it is now possible to acquire an isotropic high-resolution dataset in 6 minutes and process this automatically to detect the intracranial volume, the brain and CSF. An algorithm was developed to select the ventricles from all CSF, as exemplified in Fig. 1. The algorithm was trained on 45 manually segmented ventricles by a neurologist and a neurosurgeon. Segmentation is challenging due to thin membranes in the CSF between the ventricles and other cisterns, extreme shapes and image artifacts caused by drain placement. The Dice overlap scoring between manual segmentation and the current automatic segmentation is 98%. The automatic post-processing, however, is completed in 2 seconds, whereas manual segmentation requires more than 15 minutes.

SyntheticMR AB, a spin-off company from CMIV, was founded in 2007 to commercialize MR quantification. Their product, SyMRI, is sold worldwide on all MR vendors and today they have sales offices in the USA, India and Japan. So far, MR quantification has been performed based on a multi-slice TSE sequence with high in-plane resolution but relatively few slices. Recently, a full 3D quantification was released. The automatic ventricle segmentation is a further development on this approach, which may be an important tool for hydrocephalus patient monitoring in the future.

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

Project information

PROJECT NAME

Automatic Ventricle Segmentation Using 3D Quantitative MR.

PROJECT LEADER

Marcel Warntjes, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine.

MAIN PROJECT PARTICIPANTS

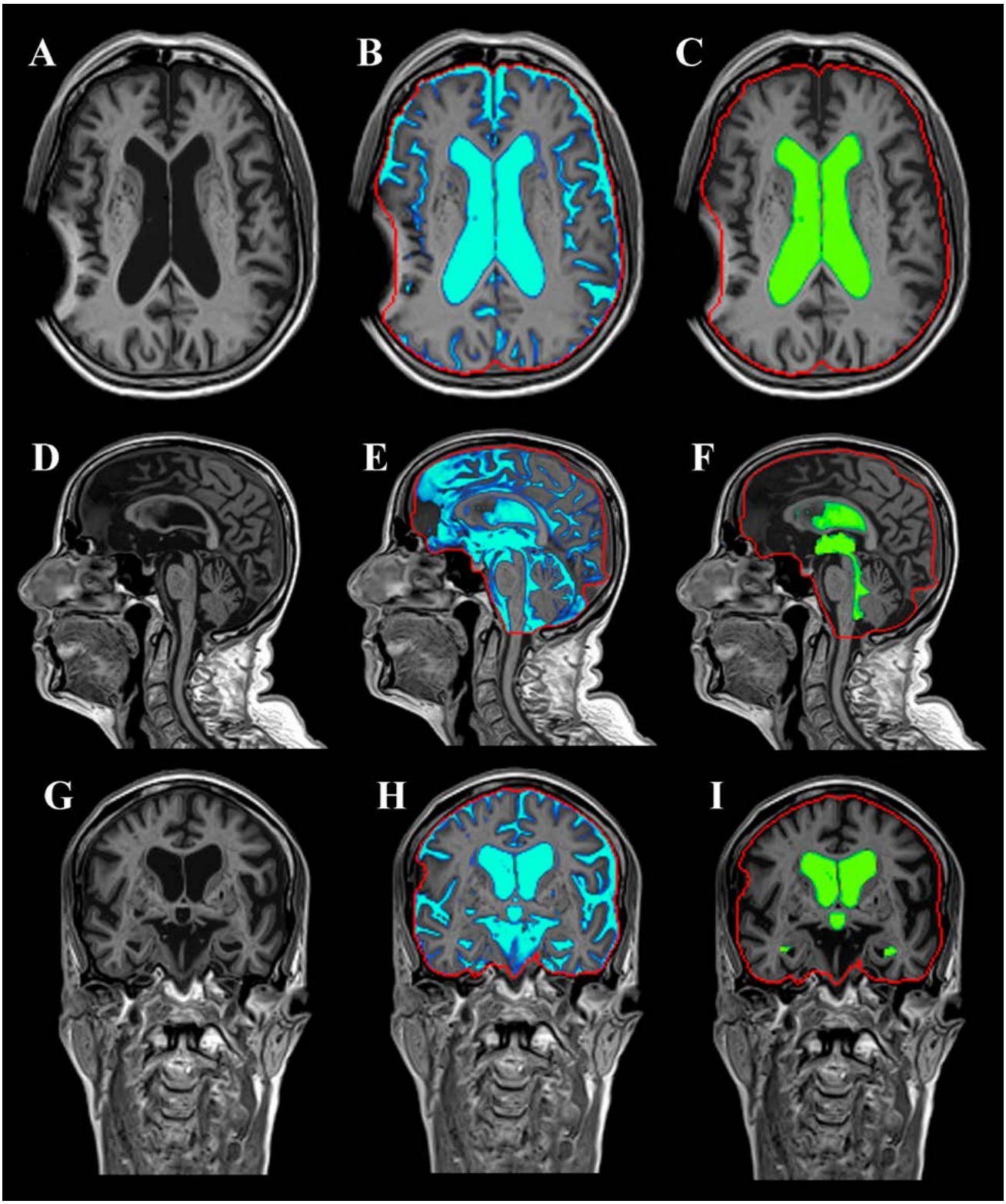
Rafael Holmgren, Charalampos Georgiopoulos, Anders Tisell.

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 ventricle detection using quantitative MRI. Based on the measured parameters a synthetic T1W image can be created in 3D (A). Note the image artefact on the left due to the drain. Using relaxation rates and proton density the partial volume of CSF is calculated (B). From all CSF the ventricular CSF is selected (C). D-F are sagittal reformats, G-I are coronal reformats.

POPULAR SCIENTIFIC SUMMARY
Tino Ebbers

Medical Digital Twin

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. An interactive software for visualization of moving joints and the heart, where the images are collected using advanced computed tomography (CT), has been developed. The solution has been evaluated in 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 for improving valve surgery and risk assessment of blood clot formation in atrial fibrillation. Other parts 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 metabolics and cardiovascular physiology of the whole body, which is of interest for amongst others AstraZeneca. In collaboration with AMRA, a usability study is conducted to investigating 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 | 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 , Jonas Lantz, Anders Persson, Nils Dahlström, Gunnar Cedersund, Kajsa Tunnedal, Sophia Bäck, André Da Luz Moreira, Linus Ohlsson, Federica Viola, Twan Bakker, Several participants from companies.

GRANTS

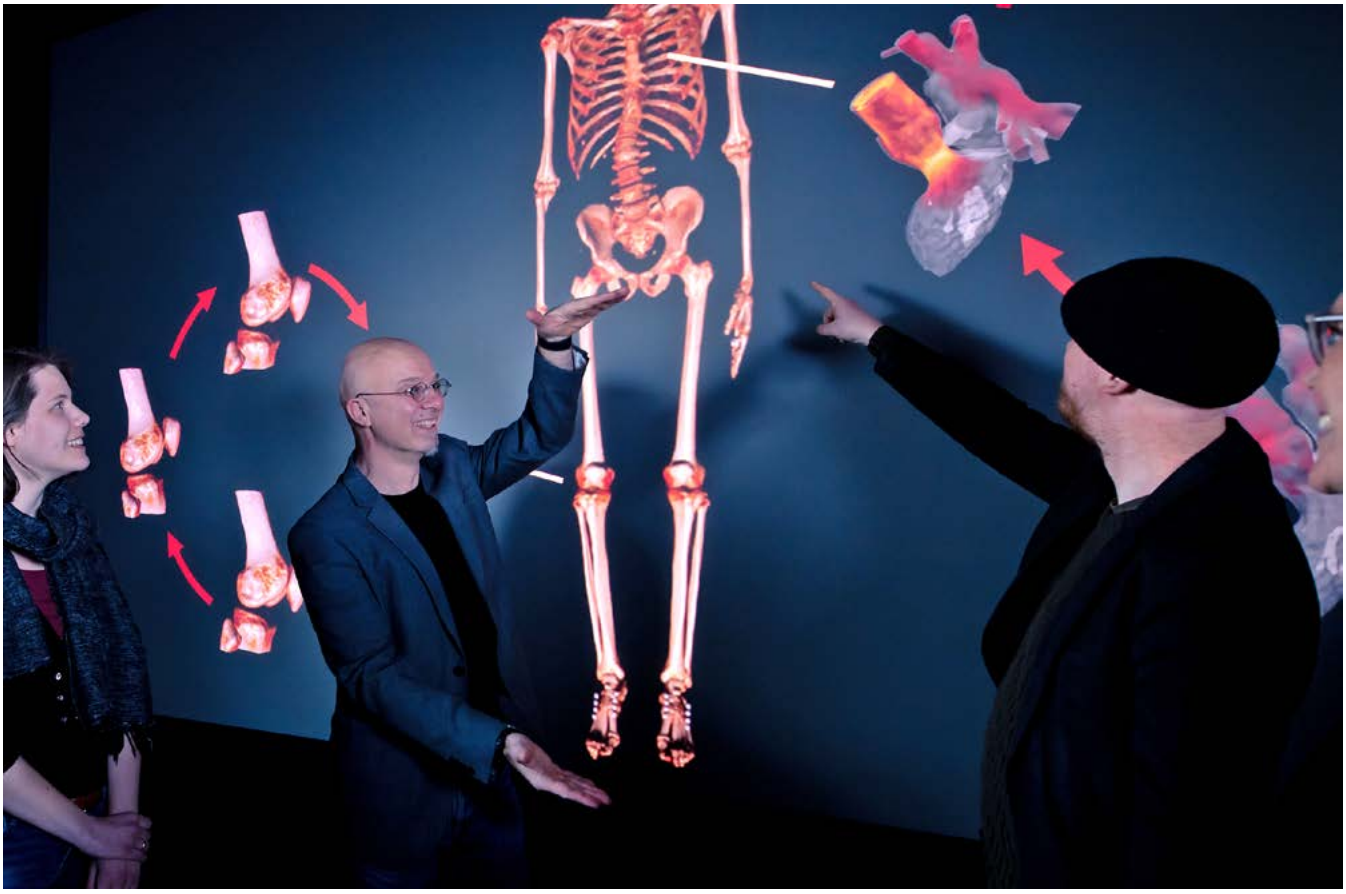
Visual Sweden (2022-2025)
In-kind contributions from several companies

KEY PUBLICATIONS

K Tunedal, F Viola, BC Garcia, A Bolger, FH Nyström, CJ Östgren, J Engvall, P Lundberg, P Dyverfeldt, CJ Carlhäll, G Cedersund, T Ebbers. Haemodynamic effects of hypertension and type 2 diabetes: Insights from a 4D flow MRI-based personalized cardiovascular mathematical model. The Journal of Physiology 601 (17), 3765-3787, 2023.

L Ohlsson, ADL Moreira, S Bäck, J Lantz, CJ Carlhäll, A Persson, K Hedman, MS Chew, N Dahlström, T Ebbers. Enhancing students' understanding of cardiac physiology by using 4D visualization. Clinical Anatomy 36 (3), 542-549, 2023.

T Herrgardh, C Simonsson, M Ekstedt, P Lundberg, KG Stenkula, E Nyman, P Gennemark, G Cedersund. A multi-scale digital twin for adiposity-driven insulin resistance in humans: diet and drug effects, in press Diabetology & Metabolic Syndrome 2023.11.



Sophia Bäck, Tino Ebbers and Gunnar Cedersund.

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 focused on the future refinement of LI-RADS, aiming to improve the treatment of HCC patients and surveillance of patients at risk to develop HCC. One example of such refinement is the ability to use alternative diagnostic criteria (other than those presently used) to diagnose earlier stages in this pathway from benign to malignant.

In the long term, the clinical aim of the proposed line of investigation is to contribute to improved diagnostics of all liver malignancies through the 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 datasets 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 collected in the integrated diagnostics panorama include in-vivo radiology, ex-vivo radiology, pathology, and genomics, with high-resolution photon counting CT being a particularly important resource. In this proof-of-concept phase, the computational research track focuses on upstream enrichment AI, i.e., improving radiology precision through insights gained from downstream data sources. 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

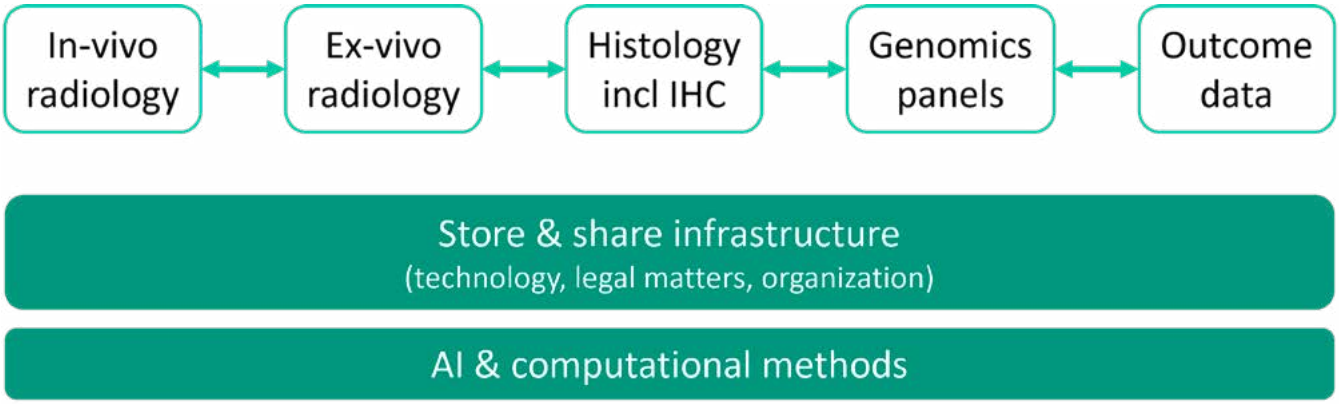
Claes Lundström, Darren Treanor, Per Sandström, Bergthor Björnsson, Caroline Bivik Stadler, Simone Ignatova.

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
Markus Heilig

The Behavioral and Neural Mechanisms of Alcohol Choice Preference

Both animals and humans are continuously and concurrently presented with several reward-predictive stimuli, and complex decision-making underlies the pursuit of the preferred reward. In substance use disorders (SUD), choices among prospective rewards available in the environment progressively shift in favor of drugs over non-drug alternatives (Ahmed, Lenoir et al. 2013). This tendency to prefer drugs occurs despite the devastating consequences of drug use, making it a central feature of the disorder (American Psychiatric Association 2013, Heilig, Augier et al. 2019). Currently, there are two behavioral economic theories on the mechanisms behind this feature. One theory posits that this feature results from attributing greater expected value to alcohol, surpassing the negative consequences associated with its use. The other posits that it results from a devaluation of the negative consequences or insensitivity to costs.

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 (Fig.1). In the task, participants choose to accumulate points associated to pictures depicting an alcoholic drink or a snack. Depending on the accumulated points, participants received either of the rewards at the end of the session. Pictures were tailored to individual preference. To assess cost sensitivity, the paradigm included a relative cost manipulation, where each image was associated with points that could be the same for the two rewards, favoring alcohol or favoring the snack. The relative cost of choosing alcohol was highest in the latter condition, as alcohol choice here was associated to maximal "loss" toward anticipated earning of the alternative snack reward.

In a population of both light and heavy, non-treatment seeking drinkers, we recently showed that choice preference for alcohol vs. a concurrently available snack reward was sensitive to the relative cost of alcohol and was associated with alcohol use severity (Fig.1). We replicated the relative-value-dependent behavioral finding in a follow-up study in the Magnetic Resonance Imaging (MRI) scanner in a separate population of light and heavy drinkers (Fig.2). We found brain correlates of this behavioral pattern in both groups. We identified that activity in regions involved in value-based estimation and salience processing, including orbitofrontal cortex and insula, was modulated by relative cost of alcohol, when choosing alcohol (Fig.2). Overall, these findings suggests that the higher alcohol use in real life in heavy drinkers compared to light drinkers does not seem to be associated to insensitivity to costs but might be more the result of greater value attribution to alcohol compared to alternative rewards.

MRI Neurology

Project information

PROJECT NAME

The Behavioral and Neural Mechanisms of Alcohol Choice Preference.

PROJECT LEADER

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

MAIN PROJECT PARTICIPANTS

Irene Perini, Hanna Karlsson, Sarah Gustavson, María del Carmen Cortes Molina.

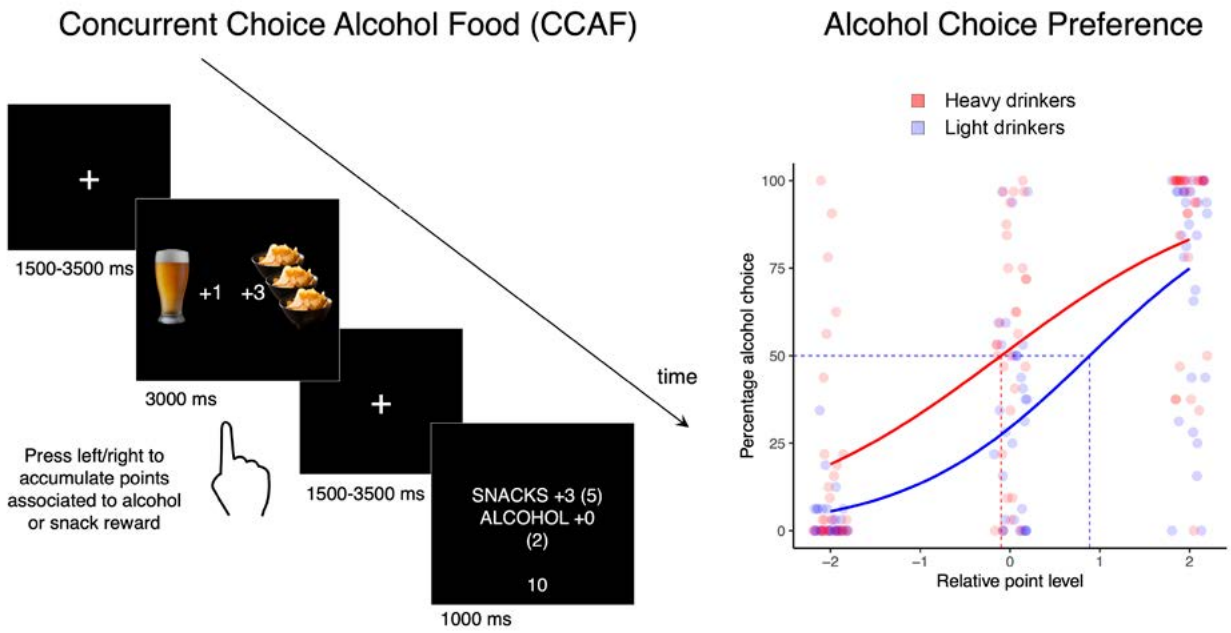


Figure 1. Behavioral experiment. Left. Concurrent Choice Alcohol Food (CCAF) task design. In this task, participants were instructed to accumulate points associated with alcohol or snacks, which could then be redeemed at the end of the session with the respective reward. Each alcohol and snack picture 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. In both groups, increased choice preference for alcohol was observed when relative point level was in favor or alcohol.

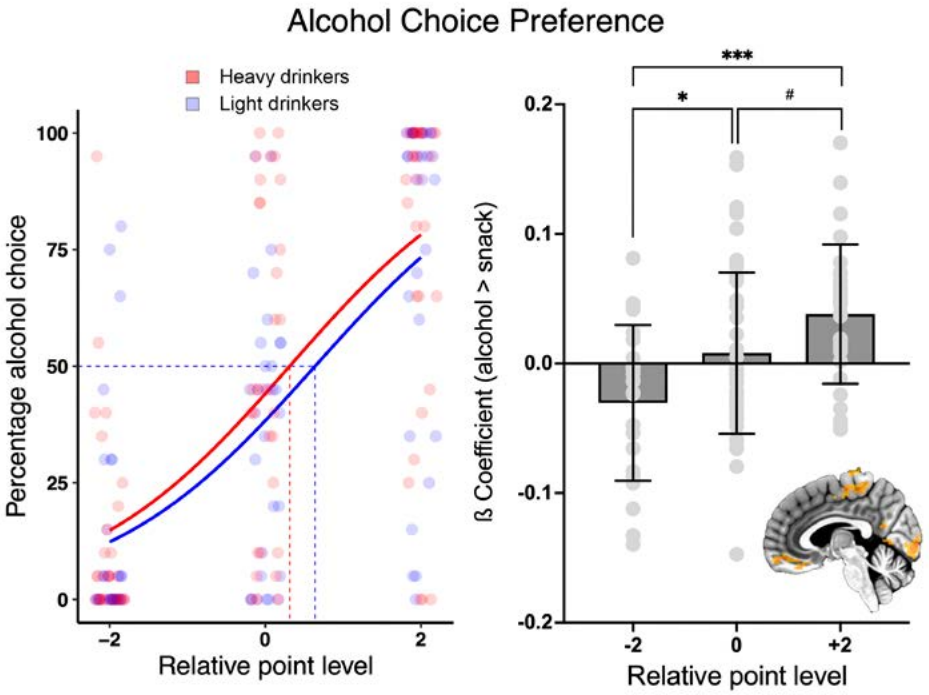


Figure 2. MRI results. Left. As in the behavioral experiment, in both groups, increased choice preference for alcohol was observed when relative point level was in favor or alcohol. Right. Brain findings showed increased activity for alcohol choice as a function of relative value.

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 purporse 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

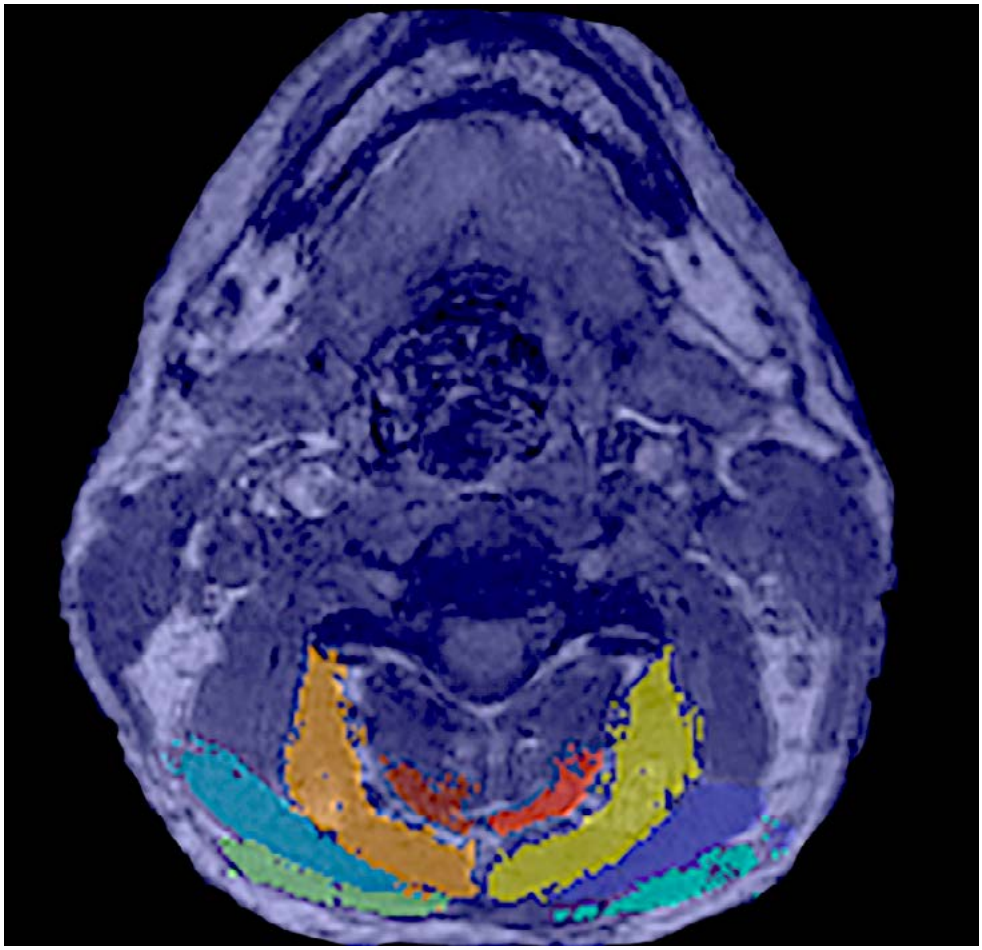
Anneli Peolsson, Department of Health, Medicine and Caring Sciences, Division of Prevention, Rehabilitation and Community Medicine.

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



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

Ida Blystad, Kristin Zeiler

PoCo-19: a Multidisciplinary Study on Fatigue in Patients with Post-Covid Condition

In the aftermath of the COVID-19 pandemic, it has become clear that the infection caused by the coronavirus can result in long-term sequelae for some patients. The underlying causes of these lingering problems are not clear, and the symptomatology is diverse, often suggesting brain involvement. Patients can, for example, experience cognitive impairment, fatigue, depression, and anxiety.

In this multidisciplinary project, researchers from rehabilitation medicine, neuropsychology, neuroradiology, biomedical engineering, pre-clinical sciences, qualitative research in medical humanities, and phenomenological philosophy of medicine have come together to explore the patients' experience of fatigue in post-COVID syndrome and its underlying characteristic disease mechanism. Patients who have post-COVID syndrome and suffer from fatigue are investigated with brain MRI, as well as clinical examinations, neuropsychological tests, cytokine profile analysis, and qualitative phenomenological philosophy analysis.

Previous studies have shown that the MR images of post-COVID patients are unspecific in their pattern, and to deepen our knowledge about the structure and function of the brain in this patient group we are now using advanced quantitative MR sequences to be able to measure changes that are not visible in the ordinary MR images. With these quantitative techniques, we can detect changes in the microstructure of the brain tissue, as well as investigating functional aspects, such as connectivity, i.e., how the different parts of the brain communicate with each other. Using an advanced diffusion MR-technique, we have been able to show in a previous analysis that there are changes to the microstructure of the white matter of the brain in patients who were hospitalized for COVID-19 and have persisting symptoms at follow-up.

In this ongoing study, we are now in the final phase of collecting data on patients with post-COVID and fatigue, as well as healthy controls for comparison. The data collection is going to be complete during winter 2023, and then the analysis phase ensues. As this is a multidisciplinary project, the different analytic steps will also be cross-read and triangulated to gain an understanding of the research questions on different levels and from different angles.

MRI | Neurology | Imaging Biomarkers

Project information

PROJECT NAME

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 LEADERS

Ida Blystad, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine.
Kristin Zeiler, Professor, Department of Thematic Studies, Technology and Social Change.

MAIN PROJECT PARTICIPANTS

Anders Tisell, Evren Özarslan, Deneb Boito, Anders Eklund, Muhammad Usman, Richard Levi, Anestis Divanoglou, Ulrika Birnberg Thornberg, David Engblom, Eleanor Byrne, Sofia Jämterud Morberg, Felipe León.

GRANTS

Vetenskapsrådet (dnr 2021-01245)

KEY PUBLICATIONS

MRI with generalized diffusion encoding reveals damaged white matter in patients previously hospitalized for COVID-19 and with persisting symptoms at follow-up. Boito D, Eklund A, Tisell A, Levi R, Özarslan E, Blystad I. Brain Communications, 2023, DOI: 10.1093/braincomms/fcad284.

Brain MRI and neuropsychological findings at long-term follow-up after COVID-19 hospitalisation: an observational cohort study. Hellgren L, Birberg Thornberg U, Samuelsson K, Levi R, Divanoglou A, Blystad I. BMJ Open. 2021 Oct 27;11(10):e055164. doi: 10.1136/bmjopen-2021-055164. PMID: 34706965; PMCID: PMC8551746.

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

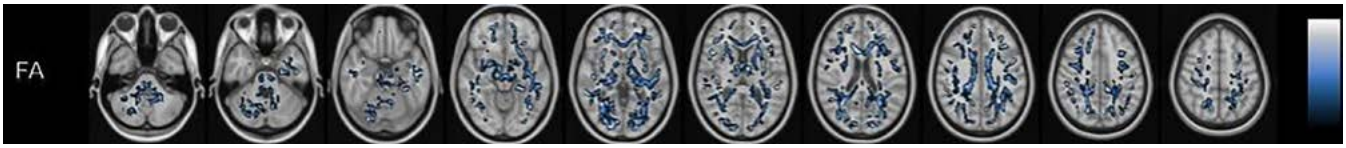


Figure 1. This is an example of how an advanced MR diffusion sequence can detect differences in fractional anisotropy (FA) in patients with remaining symptoms at follow-up after hospitalization for covid-19 compared to a control group.

Figure 2. The research group uses MR to investigate the diffusion metrics of the brain.

POPULAR SCIENTIFIC SUMMARY
Maria Engström

Image-Based Biomarkers of Brain Disorders

The research project focuses on the interpretation and modeling of blood oxygen level-dependent (BOLD) responses in functional MRI (fMRI) and cerebrovascular reactivity (CVR) imaging. The research aims to deepen the knowledge about how changes in cerebral blood flow, influenced by neurovascular coupling dynamics, shapes BOLD responses measured by MRI.

To achieve this goal, we develop mathematical models where different hypotheses describing e.g., excitatory and inhibitory neurons, are translated to mathematical equations (= models). The 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. In recent work, we have included neurovascular data from different species so that qualitative insights from animals are preserved in the quantitative analysis of human data (Sten et al. 2023). We have also developed a metabolic model based on MR Spectroscopy (MRS) that can describe time-series data for glucose, lactate, aspartate, and glutamate. The metabolic model is connected to a detailed mechanistic model of the neurovascular coupling, and the interconnected model can simultaneously describe BOLD data and predict expected metabolic responses in experiments where metabolism has not been measured (Sundqvist et al., 2022). In collaboration with partners in New Zeeland we have also made a reproducibility study for our neurovascular model (Dempsey et al., 2022).

Ongoing research aims to: 1) further investigate the role of inhibitory neurons in neurovascular coupling (Sundqvist et al., manuscript), 2) combine the neurovascular model with a model for spiking neural network dynamics (Podéus et al., manuscript), 3) develop a mathematical model of thought processes, and 4) develop a mechanistic model that describes changes in BOLD responses to hypercapnia challenge in CVR measurements (in collaboration with partners in New Zealand).

MRI | Neurology | Acquisition | Modeling | AI/Data analytics | Visualization | Simulation | Imaging Biomarkers

Project information

PROJECT NAME

Image-Based Biomarkers of Brain Disorders.

PROJECT LEADER

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

MAIN PROJECT PARTICIPANTS

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

GRANTS

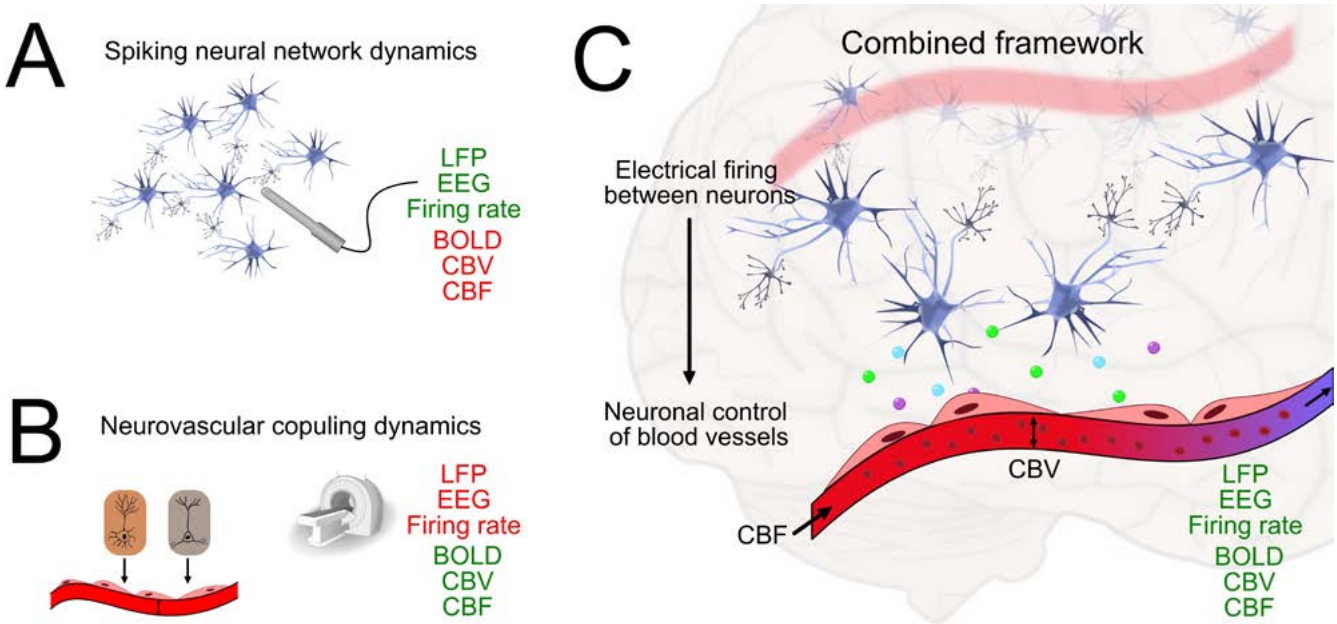
Swedish research council (2019-2022)
Swedish Brain Foundation (2022-2023)

KEY PUBLICATIONS

Sebastian Sten, Henrik Podéus, Nicolas Sundqvist, Fredrik Elinder, Maria Engström, Gunnar Cedersund. A quantitative model for human neurovascular coupling with translated mechanisms from animals. PLOS Computational Biology, 2023; 19(1): e1010818. doi: 10.1371/journal.pcbi.1010818.

Nicolas Sundqvist, Sebastian Sten, Peter Thompson, Benjamin Jan Andersson, Maria Engström, Gunnar Cedersund. Mechanistic model for human brain metabolism and its connection to the neurovascular coupling. PLOS Computational Biology, 2022; 18(12): e1010798. doe: 10.1371/journal.pcbi.1010798.

Sergio Dempsey, Gunnar Cedersund, Maria Engström, Gonzalo Maso Talou, and Soroush Safaei. Reproducibility study for a computational model of the neurovascular coupling unit. Physiome 2022. doi: 10.36903/physiome.21714863.



Graphical abstract describing dynamics in spiking neural networks and the neurovascular coupling. A) Illustrates that spiking neural network dynamics, measured by local field potentials (LFP), EEG, and spiking rates, influence the neurovascular coupling, measured by blood oxygen level dependent (BOLD) responses, cerebral blood volume (CBV), and cerebral blood flow (CBF). B) Illustrates how the neurovascular coupling dynamics is dependent on neural activity. C) Illustrates the combined framework that constitute the basis of a mechanistic mathematical model. Image courtesy: Henrik Podéus.

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/m^3) 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/m^3.

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

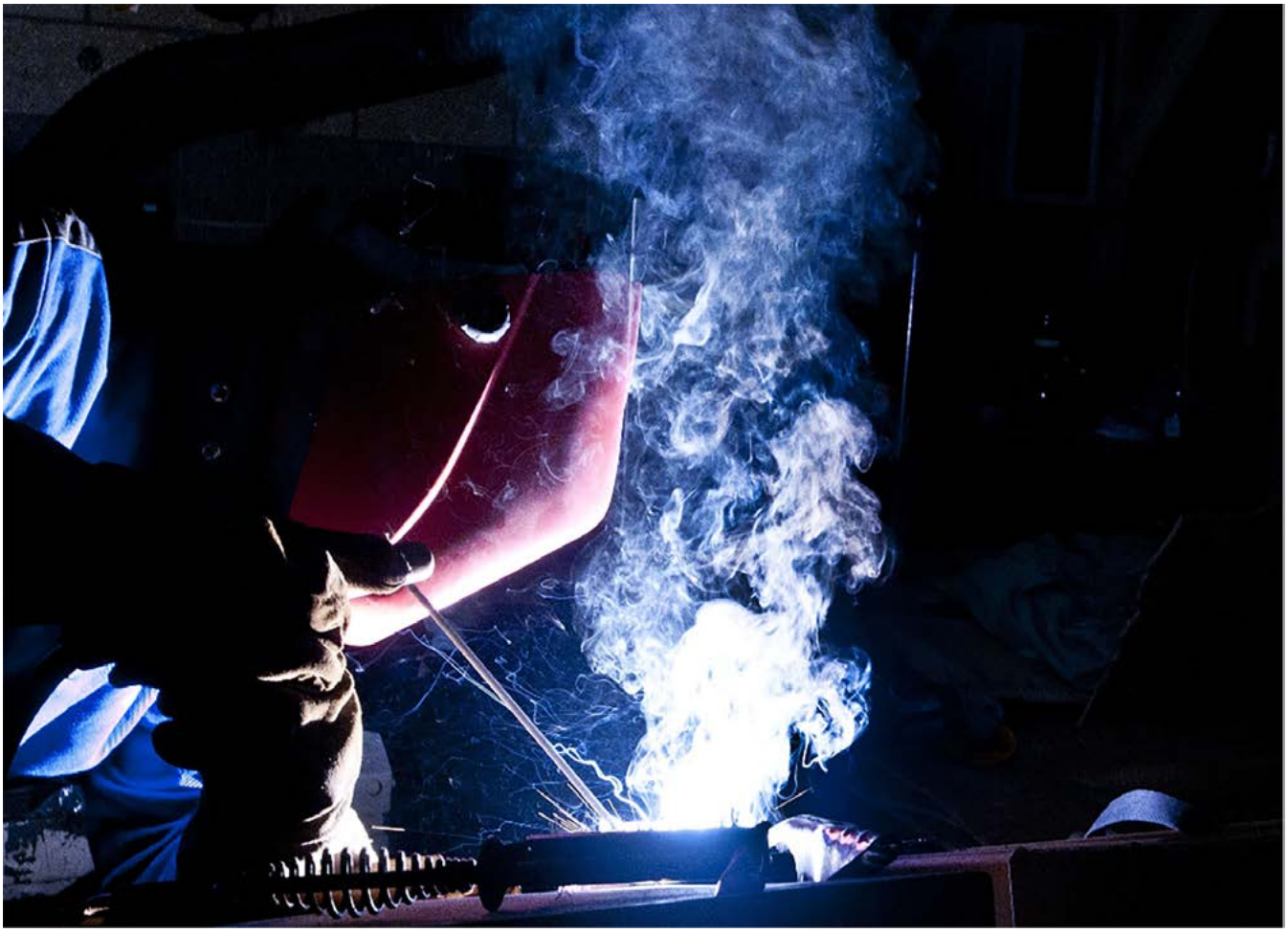
Peter Lundberg, Department of Health, Medicine and Caring Sciences, Division of Diagnostics and Specialist Medicine.

MAIN PROJECT PARTICIPANTS

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

GRANTS

FORTE



Welding in progress.

POPULAR SCIENTIFIC SUMMARY
Bharti Kataria

Evaluation of Reconstruction Methods in CT

In all diagnostic x-ray examinations using ionising radiation, it is imperative to produce images of good diagnostic quality while simultaneously keeping the radiation dose to human organs as low as reasonably achievable (the ALARA principle) to minimise detrimental radiation effects. Abdominal and thoracic computed tomography (CT) are common examinations that lead to the irradiation of radiosensitive tissues in humans.

Image quality in CT is related to radiation exposure. A reduced exposure can lead to an increase in 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 compromising 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.

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 the computation of potential patient dose reductions from the regression coefficients of the statistical model. Another study explored the possibility of a learning curve for image quality produced by ADMIRE over time. To study the change in radiologist evaluation of image quality over time, a re-analysis of the data from two studies (Kataria et al, 2018, 2020) was conducted, incorporating the time variable in the logistic regression models. In both materials, the 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).

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.

Computed Tomography **Gastrointestinal** **Pulmonary** **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, Jonas Nilsson Althen, Mischa Woisetschläger.

GRANTS

ALF (2017, 2018, 2021)
FoU (2017-2024)
Patientsäkerhetsforskning (2018-2019)
RFoU (2017-2023)

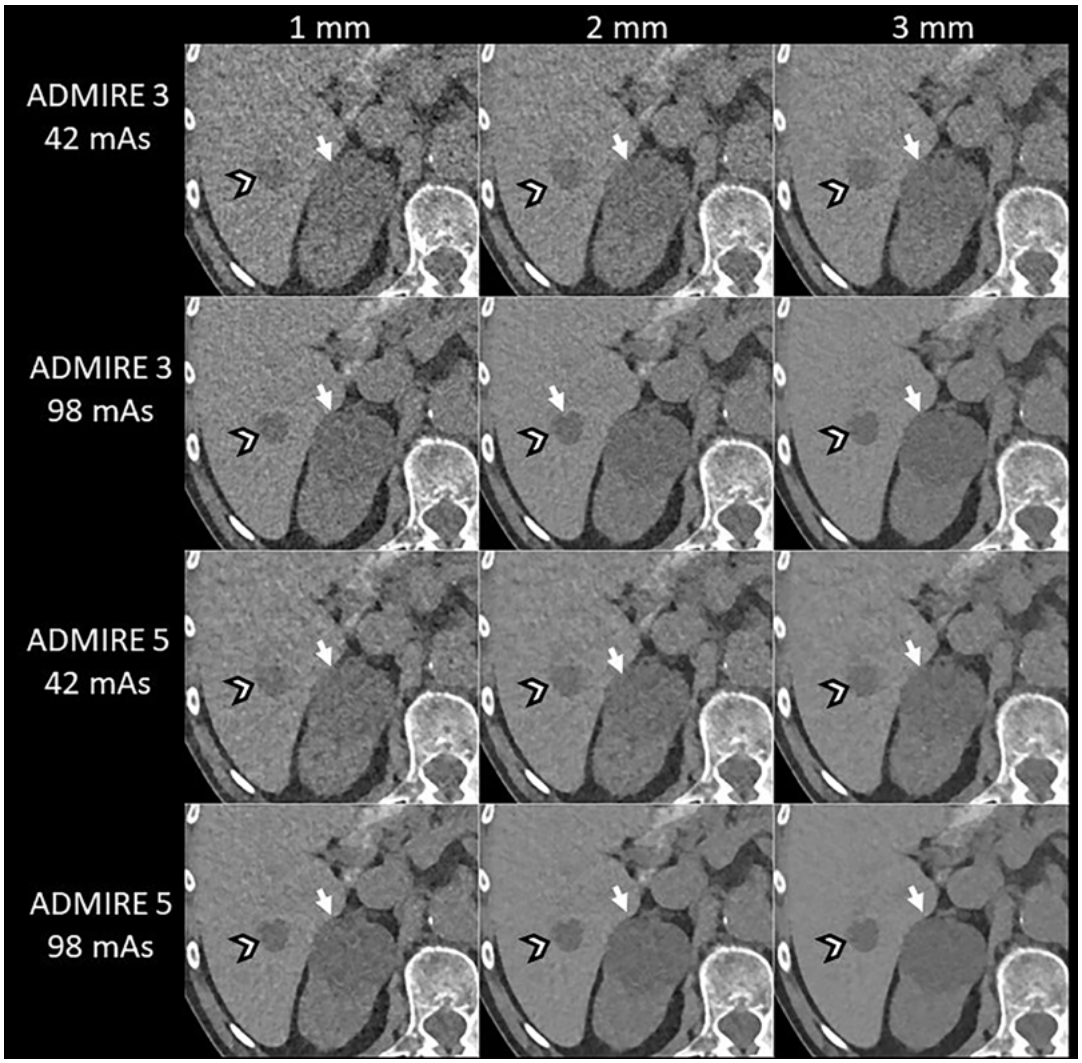
KEY PUBLICATIONS

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. https://doi.org/10.1007/s00330-017-5113-4.

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. https://doi.org/10.1016/j.ejrad.2019.108703.

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, Radiat Prot Dosimetry 195 (3-4) (2021) 177-187, https://doi.org/10.1093/rpd/ncab020.

Kataria B, Woisetschläger M, Nilsson Althén J, Smedby Ö and Sandborg M. Image quality assessments in abdominal CT: Relative importance of dose, iterative reconstruction strength and slice thickness. (2023, Under peer review, submitted for publication in Physics in Medicine & Biology).



Images from an 88-year old male patient at dose levels 42 mAs and 98 mAs (quality reference, Qref) were reconstructed with an iterative reconstruction algorithm ADMIRE with strengths 3 and 5 at slice thicknesses of 1mm, 2 mm, and 3mm (Kataria et al., 2023). Image quality represents liver parenchyma with a benign liver cyst (black/white arrowhead) and renal parenchyma with a cystic lesion in the right kidney (white arrowhead).

Objective quantitative measurements in anthropomorphic phantoms do, to some extent, support our results from the qualitative subjective assessment by radiologists, but subtle changes in noise texture owing to the IR algorithm indicate that phantom measurements alone are not sufficient and need to be complemented with evaluations in human subjects.

Our experimental design has been successful, and the novel statistical analysis was used to estimate the potential dose reduction in thoracic and abdominal CT with a change in dose, algorithm and slice thickness. ADMIRE 3 alone allows for significant dose reductions and further dose reductions are possible when combining ADMIRE strength 5 with thin-slices. 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.

The important conclusion is that the model-based reconstruction algorithm ADMIRE improved image quality in thoracic and abdominal CT, allowing for significant dose reductions (30%) in abdominal CT that have been implemented clinically. Higher strengths of ADMIRE combined with thin-slice imaging also allow for dose reductions and may be beneficial in thin-slice imaging protocols in abdominal CT. Potential dose reduction can be estimated using ordinal regression models, as they also allow for simultaneous analysis of several parameters.

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 of in the liver and abdomen, however, it is limited to be used in clinical setting due to the long acquisition time. Compressed sensing (CS) is a method for image acquisition acceleration that is gaining in popularity in abdominal imaging.

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, Shan Cai, Christian Simonsson, Frederik Testude, Ralph Sinkus, Marcel Warntjes, Magnus Borga, Karin Markenroth Bloch.

GRANTS

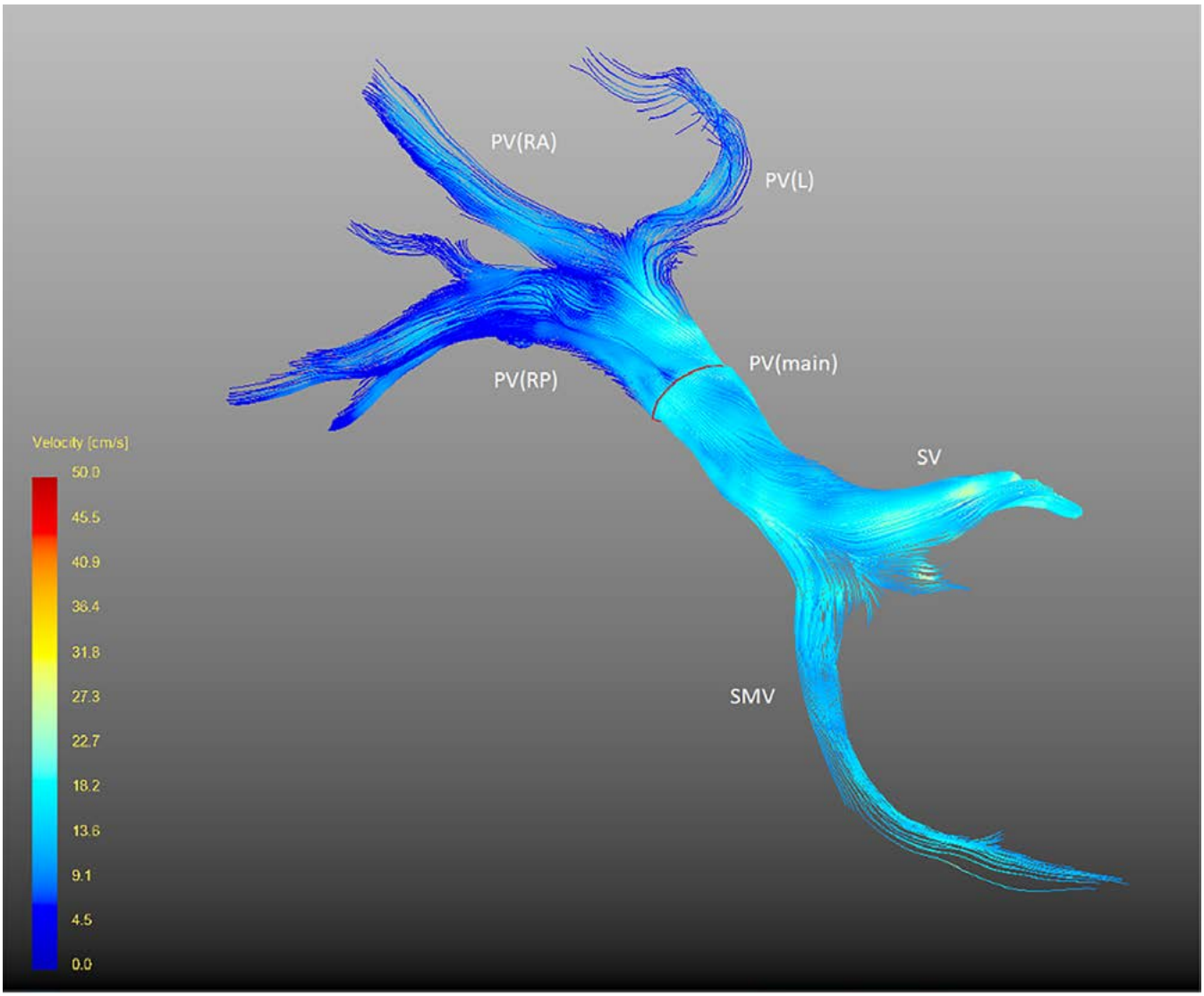
Swedish Research Council (VR/NT) (2021-2024/2025 etc)
ALF (2019-2022)

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
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 is developed.

One of the MR methods used is elastography. The examination shows fibrosis, formation of connective tissue, in the liver. The connective tissue makes the liver less flexible and impairs its normal elasticity. During MR mechanical vibrations are sent into the patient´s body. The vibrations are propagated differently depending on the flexibility of the tissue. Through registration of the different vibrations the MR-scanner can separate healthy from diseased tissue regions.

MRI | Gastrointestinal | Acquisition | Modeling | Imaging Biomarkers

Project information

PROJECT NAME

Liver Function Evaluation.

PROJECT LEADER

Peter Lundberg, Department of 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, Markus Karlsson, Patrik Nasr, Johan Kihlberg, Marcel Warntjes, Gunnar Cedersund, Bengt Norén, Bergthor Björnsson, Jens Tellman.

GRANTS

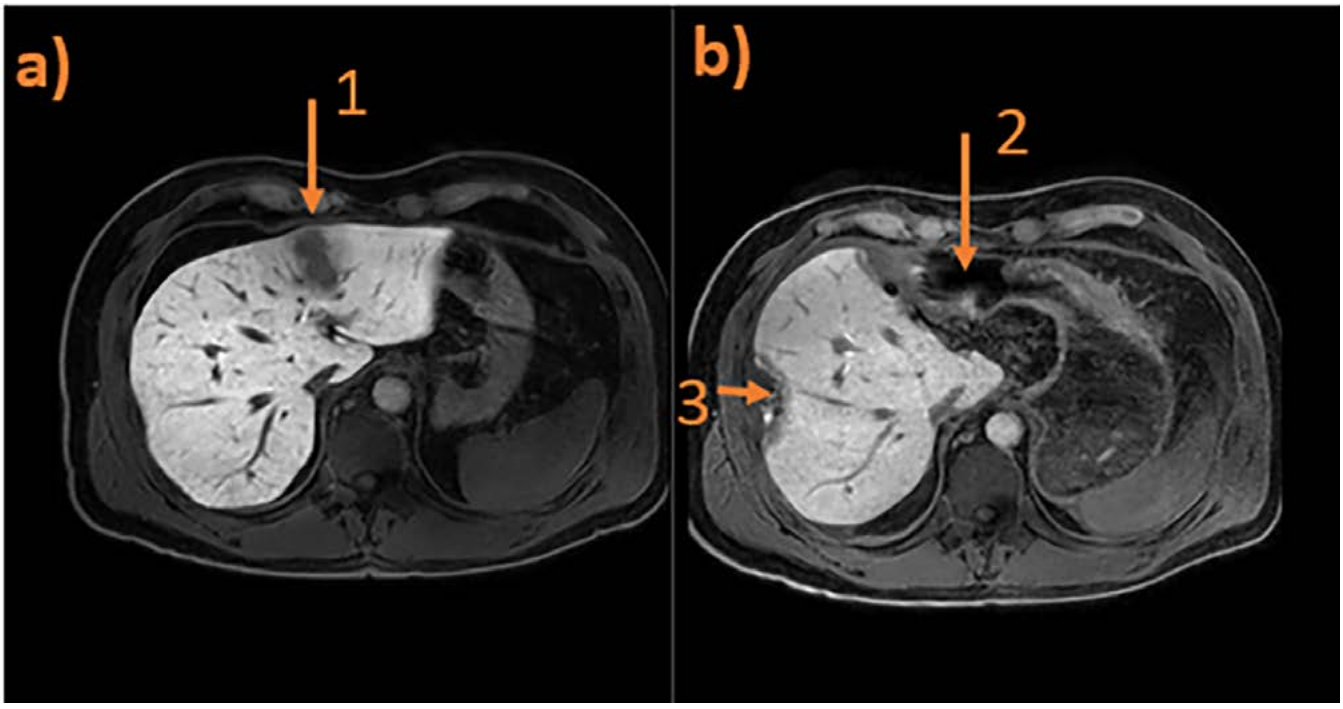
Swedish Research Council (VR/NT) (2021-2024/2025 etc)
VINNOVA (2013-2017)
Swedish Research Council (VR/NT) (2015-2018/2019 etc)
ALF (2019-2022)

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
Mischa Woisetschläger

Implementation of Synthetic MRI in the Abdomen

Background: Synthetic MRI is an innovative method for generating MRI images, where T1, T2, and PD weighted images can be derived from a single MRI acquisition, eliminating the need for three separate acquisitions as currently done. The method also enables the quantification of T1, T2, and PD relaxation times, tissue-specific parameters that theoretically allow the differentiation of various tissues in the body. This technology may thus potentially enable quantitative differentiation between tissues (tissue characterization) and pathology (healthy or diseased tissue).

In this project, we aim to investigate whether synthetic MRI can enhance the detection capabilities for specific cancers within the abdomen. We also explore whether synthetic MRI can enhance confidence in treatment results after various chemotherapies and local treatments (RF and TACE treatments) and whether it can improve 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 tumour 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 proves to be stable and reliable, it could potentially be utilized in radiation planning, predicting treatment results, detecting and segmenting MRI images, and providing a more secure differentiation between healthy and 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, Department of Health, Medicine and Caring Sciences.

MAIN PROJECT PARTICIPANTS

Nils Dahlström, Marcel Warntjes, Bengt Norén Mohammed Mahran.

GRANTS

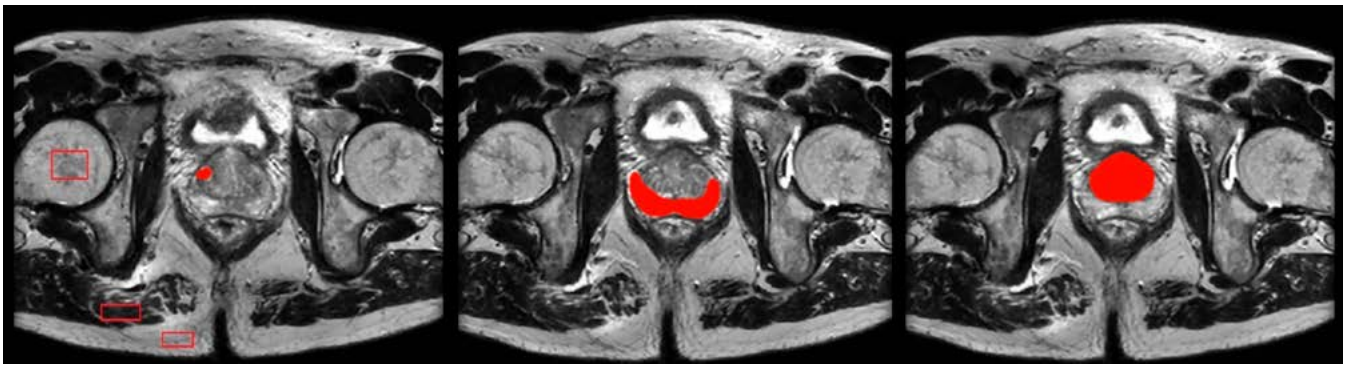
Percy Falk Stiftelse
Forsknings- och stipendieförvaltningen

KEY PUBLICATIONS

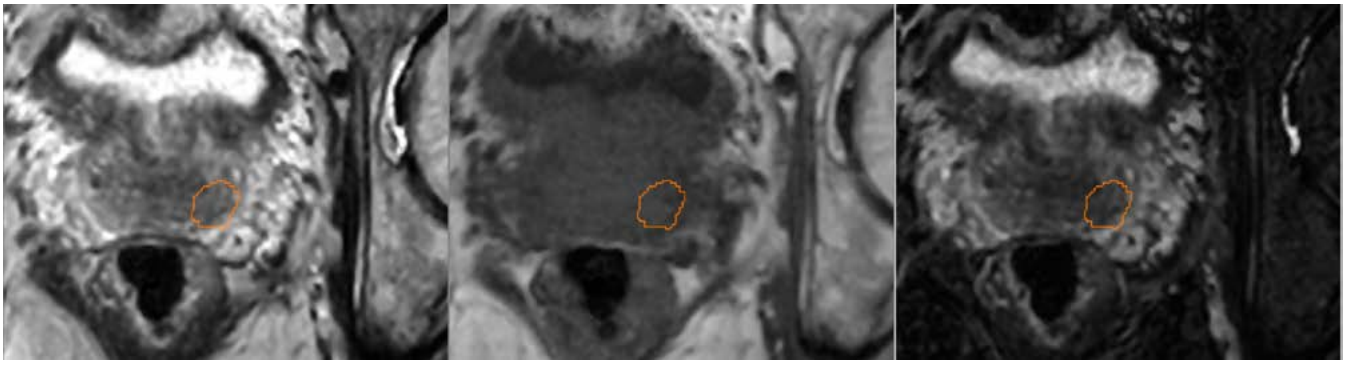
Warntjes JB, Dahlqvist O, Lundberg P. Novel method for rapid, simultaneous T1, T2*, and proton density quantification. Magn Reson Med. 2007;57(3):528-37.

Blystad I, Warntjes JBM, SmedbyÖÈ, 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.

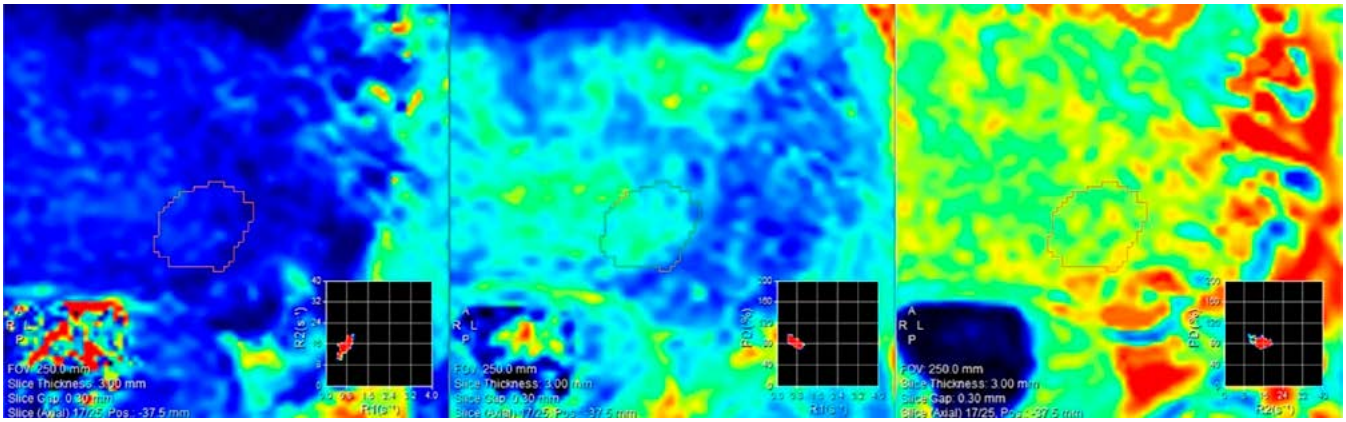
Synthetic MRI of the Knee: Phantom Validation and Comparison with Conventional MRI, Neil M. Kumar, Benjamin Fritz, Steven E. Stern, J. B. Marcel Warntjes, Yen Mei Lisa Chuah, Jan Fritz, Radiology 2018; 289:465-477.



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



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



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

The Scientific Council and CMIV Research School listening to research pitches.

The CMIV Retreat

As previous years, we had a kick-off for the research school, the scientific council together with the management group. We spent two great days in Vadstena.

Mattias Ekstedt, Eva Klintström and Catrin Nejdeby.

Tino Ebbers, Lee Jollans and Iulian Emil Tampu.

Petter Quick.

Chiara Trenti,
Iulian Emil Tampu,
Twan Bakker and
Sohaib Ayaz Qazi.

Kajsa Tunedal.

Mårten Sandstedt.

Marcelo Pereira Martins, Tino Ebbers and Tomas Bjerner.

André Da Luz Moreira.

Tamara Bianchessi.

Lee Jollans.

Twan Bakker, Tamara Bianchessi, Chiara Trenti, André Da Luz Moreira, Lee Jollans, Sophia Bäck, Bente Konst, Kajsa Tunedal, Linus Ohlsson.

Milda Pocevičiūtė, Shan Cai, Anna Ljusberg, Federica Viola, Marcelo Pereira Martins, Muhammad Usman Akbar, Frida Dohlmar.

Ann-Sofi Björkman, Sohaib Ayaz Qazi, Gustav Magnusson, Iulian Emil Tampu.

The CMIV Research School

A basic principle for our doctoral program is the translational approach, where we encourage projects to have a close connection to the clinic.

CMIV Research School's Year in Review

During the past year, the CMIV Research School has witnessed significant progress and achievements. We are pleased to announce the inclusion of Carl Edin, Tamara Bianchessi, and Twan Bakker as new PhD-students within the research school. Additionally, we have celebrated the successful defenses by David Abramian, Elin Good and our former chairman, Milda Pocevičiūtė. Our seminar Mondays have been a hub of new discoveries within the research school, sparking discussions on future projects, concepts, and research ideas.

Another notable development this year is the appointment of a study director to our research school. The primary role of the study director will be to support us in the operational management of the school and address long-term issues such as grant opportunities, collaborations, and expansion, all while maintaining the current bottom-up, student-led approach. We are fortunate that Ida Blystad, a neuroradiologist and CMIV-affiliated researcher, has accepted the role of interim study director.

In addition to formal seminars and defenses, informal gatherings play a pivotal role in our community. Events such as our festive Christmas gathering, ice hockey games, barbecues, and our annual CMIV retreat, this year held at Vadstena Klosterhotel, have been highlights. At the annual retreat, where the scientific council and the research school connect through both formal and informal sessions, we had the pleasure of hosting pitches from the research school, engaging with the team from Visualize Your Science, and witnessing the brave souls who dared to take a dip in the chilly waters of Lake Vättern. Impressively, we achieved a record number of participants, with over twenty PhD-students, and for the first time, together and mixed with Postdoctoral researchers as well. We believe it's crucial for CMIV affiliated Postdocs to have a sense of community and a strong connection to the upcoming younger researchers. This not only fosters new collaborations but also offers insights and inspiration for PhD students considering their next career steps.

The retreat in Vadstena also marked the conclusion of Gustav Magnusson's period as chairperson, for which we are warmly grateful. Gustav was subsequently succeeded by former vice-chairman Linus Ohlsson, junior physician, and PhD student from the department of Thoracic and Vascular Surgery. Furthermore, joining the leadership of the research school during the autumn was Anna Ljusberg, medical physicist and PhD student within the department of medical radiation physics, delightedly assuming the role of the new vice chairman of the research school.

Linus Ohlsson
CHAIRMAN OF THE RESEARCH SCHOOL

Bente Konst, Anna Ljusberg, Sophia Bäck, Chiara Trenti and Federica Viola.

The CMIV Research School provides a doctoral program encompassing both medical and technological perspectives, offering a cohesive research education. A fundamental principle guiding our doctoral program is the translational approach, wherein we encourage projects to establish a close connection to clinical applications. Presently, the research school hosts approximately 35 PhD students from 8 different nationalities. Within these diverse backgrounds, a selection of students will showcase their research endeavors.

Twan Bakker

Assessment of Blood Flow in an Artificial Heart

The heart functions as the pump for the cardiovascular system, providing the circulation of blood through the body and its organs. Patients experiencing heart failure are, to some extent, unable to provide proper perfusion of the vascular system. The last treatment option for patients with severe conditions on both sides of the heart is a complete heart transplant. However, due to a scarcity of suitable donor hearts, patients often face critical time constraints. To extend this window, a total artificial heart emerges as a crucial interim solution.

Mechanical assist devices generally suffer from secondary problems when integrated into the biological circulatory system, including concerns such as blood clot formation and hemolysis from a fluid flow perspective. At CMIV, our task is to evaluate the flow in a total artificial heart prototype by Scandinavian Realheart AB, aiming for a comprehensive understanding of blood flow dynamics and the aforementioned risks. During this research we utilize 4D flow Magnetic Resonance Imaging (MRI), which allows us to measure the flow inside the prototype throughout the cardiac cycle.

With 4D flow MRI we were able to evaluate the complex flow patterns and calculate velocities and turbulence, that have been linked to blood damage. The results from these acquisitions can later be used as a validation for predictive simulation models, and to identify locations where the prototype needs to be improved.

Looking ahead, we will evaluate the blood damage employing various techniques and compare them with blood lab experiments that were performed this year. All this data will be used to achieve a more complete understanding of the flow dynamics within the total artificial heart. We aim to help reduce the risk of blood damage for the individuals awaiting such a life-saving device.

PROJECT INFORMATION

Project

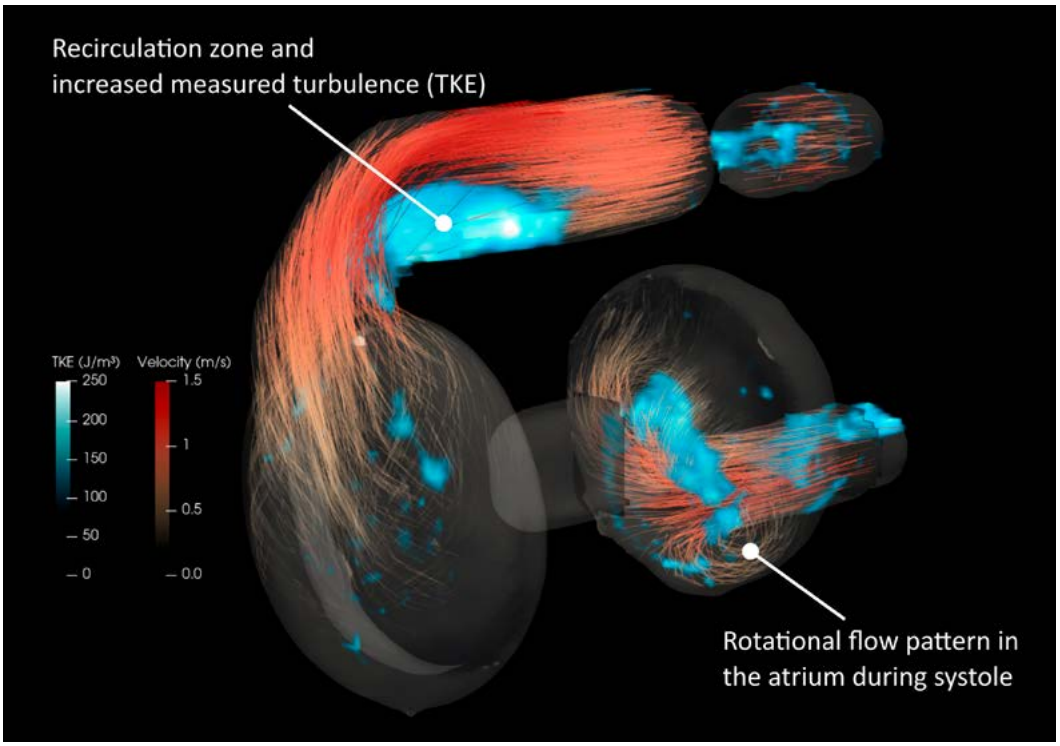
Assessment of Blood Flow in an Artificial Heart.

Supervisors

Jonas Lantz, Tino Ebbers, Ina Laura Perkins.

Short CV

PhD student Linköping University, since September 2023.
Research Engineer at CMIV, 2022-2023.
MSc. Mechanical Engineering, Linköping University, 2022.
BSc. Aeronautical Engineering, Inholland University of Applied Sciences, 2017
Design Engineer at Airbus Defence and Space, 2017-2020.



Visualization of the measured velocity and turbulence with 4D flow MRI in the total artificial heart.

Wolf Claus Bartholomä

LIFE 2 and ACCESS ESLD

Posthepatectomy liver failure (PHLF), a perilous outcome of liver surgery, remains a potential threat to patients undergoing liver resection. When the remaining liver tissue, following surgery, fails in essential functions like detoxification, synthesis, and metabolism, PHLF can emerge. The risk of PHLF hinges on factors such as the extent of liver resection and overall liver health. Compromised liver function from underlying diseases escalates the risk.

Studies indicate that PHLF occurs in 0–6% of cases when the Future Liver Remnant (FLR) volume exceeds a threshold, soaring to 20–90% when it falls below. This poses a serious challenge for hepatobiliary surgeons, as causative treatment of liver failure is not possible – all that can be done is to support the patient until liver function hopefully returns to normal. If this fails, liver transplantation is the sole cure. Hence, precise preoperative assessment and meticulous candidate selection are imperative to prevent PHLF and enhance outcomes.

A primary trigger for PHLF lies in an inadequately sized or poorly functioning FLR. In current practice, the minimum safe Future Liver Remnant (FLR) volume is determined by a standardized fraction of the total liver volume, typically 30%, or higher in cases of cirrhosis and steatosis. The liver volume itself is usually estimated based on patient weight and height using a mathematical formula such as Vauthey's formula. Obviously, this approach falls short of tailoring to individual patients.

Here, MRI with liver-specific contrast could offer a considerable improvement. This advanced technology allows, through the use of liver-specific contrast media, insight into the functionality of the liver remnant. It enables the identification of preexisting issues, such as undiagnosed diffuse liver disease, enhancing precision in FLR estimation. By individualizing FLR estimates based on direct and localized measurements of actual liver function, the project could help shift preoperative planning from a one-size-fits-all to a personalized, precision-based strategy.

Our study, spanning 300 patients across university hospitals in Linköping, Stockholm, Gothenburg, Copenhagen, and Helsinki, compiles extensive clinical data on liver function and posthepatectomy liver failure. Leveraging preoperative imaging with liver-specific contrast medium (Primovist, Bayer Healthcare), the Hepatic Uptake Index (HUI), derived from liver parenchyma signal intensity and FLR volume, functions as a surrogate for liver function. The aim is to explore if HUI, alongside other clinical data, can reliably predict posthepatectomy liver failure. Success in this effort could empower hepatobiliary surgeons to better select suitable candidates for liver surgery, diminishing patient mortality and morbidity post-resection.

With all data acquired and measurements performed, data evaluation has begun. Preliminary data using 182 patients shows a significant difference in Hepatic Uptake Index between patients experiencing posthepatectomy liver failure and those who do not. In the next step, we need to calculate if HUI can be used to better predict PHLF using more complex statistics and the entire dataset. Hopefully, the overall data will allow us to create a model to improve patient survival and well-being post hepatectomy by enabling a more individualized and exact method of assessing the future liver remnant.

PROJECT INFORMATION

Project

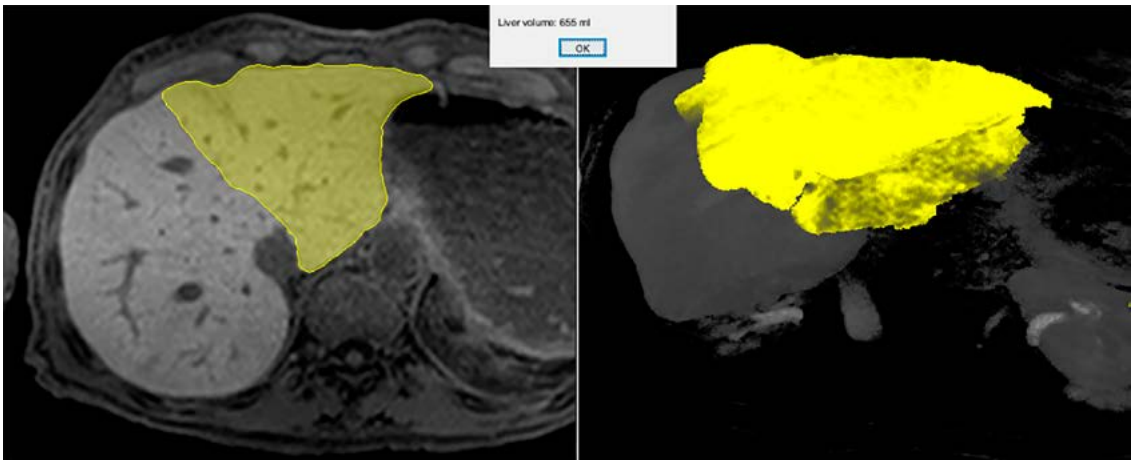
Applications of MR Contrast in Liver Diagnostics.

Supervisors

Peter Lundberg, Nils Dahlström, Per Sandström, Mischa Woisetschläger.

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.



FLR (Future Liver Remnant) calculation.

Tamara Bianchessi

Image Processing for Improved Utility of Cardiovascular MRI

In healthy subjects, cardiovascular flow is considered mainly laminar; however, its values are near the turbulence threshold. These conditions change when age- or pathology-related processes occur either in the valves, vessels, or heart chambers, leading to regions of turbulent flow during the cardiac cycle. This indicates that turbulence is a hallmark of several cardiovascular diseases. Turbulent Kinetic Energy (TKE) can be computed from 4D flow MRI, which refers to three-dimensional and time-resolved phase-contrast MRI with three directional velocity encoding. It offers insight into cardiovascular physiology with the ability to quantify advanced hemodynamic parameters such as flow velocity, pressure gradients, helicity, and TKE. In particular, TKE computed from 4D flow MRI describes the kinetic energy of the fluctuating velocity field and quantifies the inefficiencies of the energetic transfer in blood flow.

This project aims to establish, in an automatic manner, reference values for TKE and identify its determinants in the whole heart, ascending aorta, and pulmonary artery. 3D turbulence angiograms will be created to visualize and quantify TKE on previously acquired 4D flow MRI data in subjects with valve diseases, other cardiac pathologies such as heart failure, and healthy controls. TKE will be computed at relevant time frames in the cardiac cycle for each cardiac chamber and vessel. Velocities magnitude and geometric parameters, like the diameter, characterizing each chamber, will be computed and compared against the TKE values to establish correlations and possible differences between the different groups present in the dataset.

PROJECT INFORMATION

Project

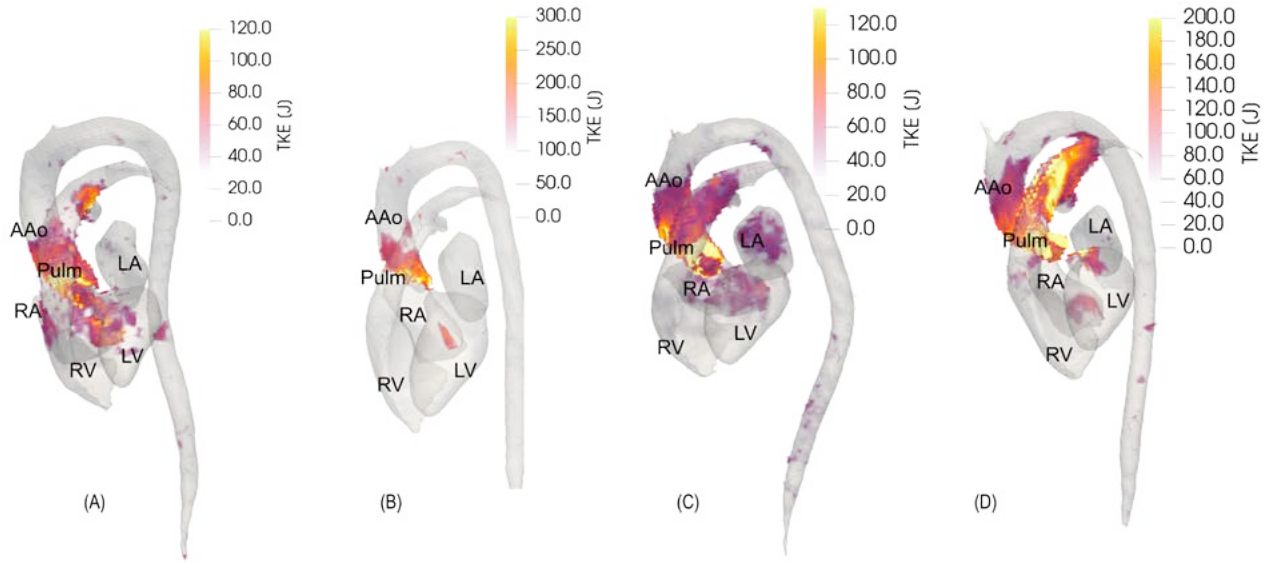
Image Processing for Improved Utility of Cardiovascular MRI.

Supervisors

Petter Dyverfeldt, Carl-Johan Carlhäll, Elin Good.

Short CV

PhD Candidate at the Unit of Cardiovascular Science at Linköping University Hospital, July 2023-Present.
Research engineer at the Unit of Cardiovascular Science at Linköping University Hospital, January 2023-June 2023.
Research preparatory course, Department of Health, Medicine and Caring Sciences at Linköping University Hospital, June 2022-December 2022.
Master of Science, Biomedical Engineering, Linköping University, Sweden, August 2020-June 2022.
Bachelor of Science, Biomedical Engineering, Politecnico di Milano, Italy, October 2016-March 2020.



3D turbulence angiograms at peak systole in a selection of subjects from the study. Deep learning-based segmentations of the heart, the aorta, and the pulmonary arteries provide anatomical orientation. (A): control healthy subject, (B) subject with aortic stenosis, (C) subject with mitral insufficiency, (D) subject with pulmonary valve stenosis. LA: left atrium, LV: left ventricle, AAo: ascending aorta, RA: right atrium, RV: right ventricle, Pulm: pulmonary arteries.

Ann-Sofi Björkman

Spectral CT for the Musculoskeletal System

Imaging of musculoskeletal tissues, such as bones, joints, and soft tissue can be achieved using different techniques. 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 excellent for fracture detection, fast, widely available, and suitable for almost all patients; however, the visualization of soft tissues is limited.

In musculoskeletal imaging, the presence of metal implants, such as prostheses and plates, and screws is common and leads to metal artifacts that impair image quality in both MRI and CT.

Technical advancements within computer tomography, particularly dual energy CT (DECT) and, more recently, photon counting detector CT (PCD-CT), have the potential to improve image quality and, for some patients, replace the need of an MRI examination. The common property of these techniques is that they make use of energy separation of X-ray photons, known as Spectral CT. In DECT, X-ray photons with two different mean energies are used, while the detector functions similarly to conventional CT. In PCD-CT, the detector is different: X-ray photons are directly converted to an electrical signal and counted, as opposed to the conventional detector where photons are first converted to visible light before generating the electrical signal. This leads to increased spatial resolution, reduced image noise, and the ability to lower the radiation dose. Recent studies also suggest that PCD-CT might reduce the problem of metal artifacts.

The aim of the PhD project is to use Spectral CT to enhance imaging of the musculoskeletal system, with focus on knee imaging.

In the current study, the FORT study, patients with fractures to the knee or ankle requiring surgery with metal plates and screws are imaged using PCD-CT, in addition to the conventional CT examination performed after surgery. The objective is to determine the optimal settings for the PCD-CT to reduce metal artifacts and provide better image quality, as well as to compare it to the conventional CT. Patient recruitment is complete, and data is being analysis is underway.

PROJECT INFORMATION

Project

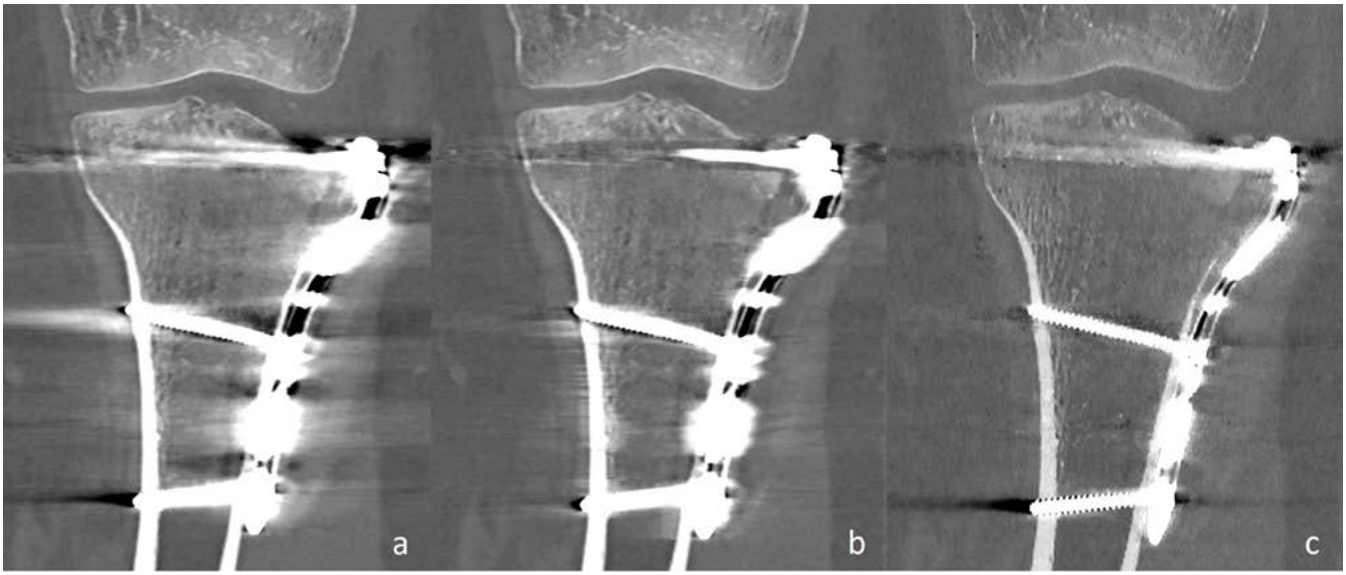
Spectral CT for the Musculoskeletal System.

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- .



Images from the PCD-CT showing a knee with a metal plate and screws. Metal artifacts are seen as bright and dark streaks in the image and make metal parts look larger than they really are. In image (b) compared to image (a) a metal artifact reducing algorithm has been turned on, markedly reducing the artifacts. In image (c), instead of using the algorithm, the artifacts have been reduced by using a high monoenergetic level of 110 keV.

Anna Bodén

Enhancing Digital Pathology for Visual Precision

Pathology, a discipline devoted to the microscopic study of tissue, commonly uses different stains for observations and diagnosis. Some stains also predict which drug cancer will respond to and hence decide the treatment of patients. The review of a stain is performed in the case context; however, the slide is screened manually and involves two dominating activities: navigating and searching. Depending on the stain, cells and tissue render different observed features and patterns, revealed at different magnification levels. Digital pathology, the digitization of tissue samples through high-resolution scanning (0.23–0.50 µm/pixel), enhances pathologists' overview and orientation of tissue at the slide level. Additionally, novel reviewing strategies are adopted. This study intends to explore new visualization methods to aid pathologists in improving efficiency and accuracy.

The Feature-Enhancing Zoom (FEZ) method demonstrates the potential to reshape review patterns. In a previous study titled 'Scale Stain: Multiresolution Feature Enhancement in Pathology Visualization,' two common clinical tasks were explored: the detection of Helicobacter pylori and the estimation of KI67 expression. Results from this study indicated a reduction in pathology time spent on navigating and searching (pan and zoom) when the FEZ method was applied for detecting Helicobacter pylori or localizing a KI67 hot spot. A 15% efficiency gain was revealed.

In this study, we have adapted the Feature-Enhancing Zoom to be operable in the clinical environment. Our aim is to further explore the visual search for diagnostic features on the most frequent and critical stains per different diagnostic areas, based on real case scenario statistics. Critical questions are explored regarding the usability of this tool, such as interoperability, presentation of different stains, artifacts, pathologists' adaptability to this innovative working strategy, and the level of trust and interpretability of Feature-Enhancing Zoom results.

PROJECT INFORMATION

Project

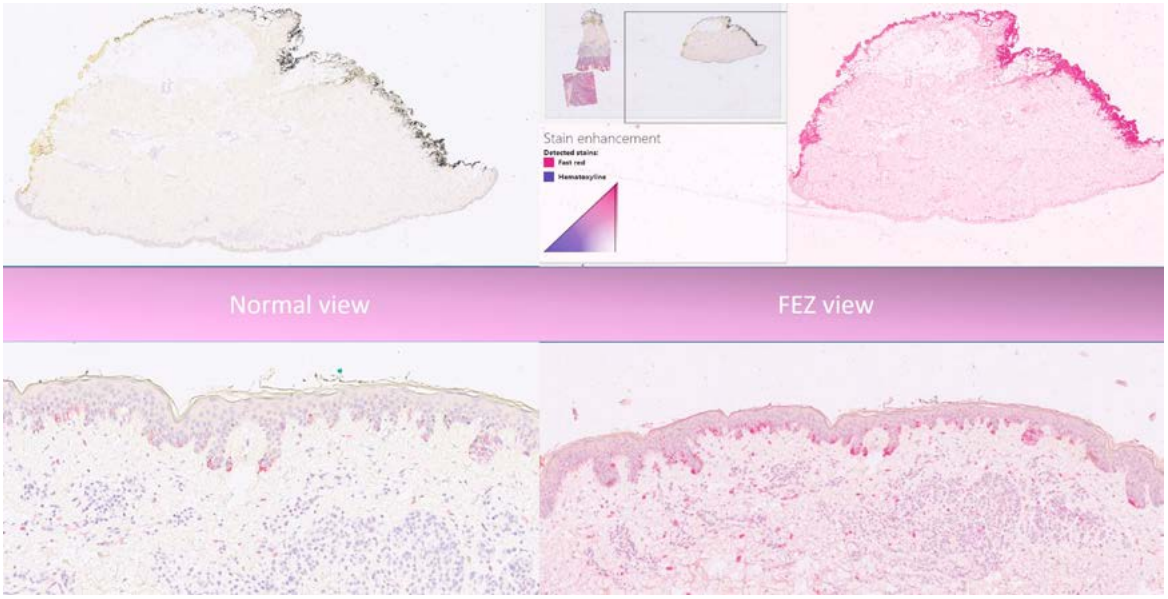
Feature-Enhancing Zoom for Enhanced Diagnostic Precision and Efficiency – a visual aid tool for digital pathology.

Supervisors

Darren Treanor, Claes Lundström, Martin Hallbeck.

Short CV

Consultant pathologist in clinical pathology, subspecialized in breastpathology, Linköping University hospital, 2010-present.
Medical degree, Karolinska Institute, 2000
Half time seminar, 2021
PhD student at Department of Biomedical and Clinical Sciences, 2015.



Combined figure illustrating a skin sample from a lesion diagnosed as dysplastic nevi, colored by the stain HMBRÖD (Human Melanoma Black, stained with fast red), an IHC marker used by dermatopathologist to differentiate malignant melanocytic lesion, melanoma, versus benign melanocytic lesions, nevi. The stain enhancement in the FEZ viewer are used to confirm negative stain in melanocytes located in dermis as well as positive stain in melanocytes located in epidermis. Normal presentation of the stain to the left and enhancement to the right.

Sophia Bäck

Blood Flow and Stasis in Atrial Fibrillation

Atrial fibrillation (AF) is a very common heart disease characterized by the irregular contraction of the atria. This changed motion can lead to blood coagulation, which can cause stroke. In this project, our goal is 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.

In the current study of the project, we developed a new way of analyzing blood flow in the left atrium. This approach, called "flow component analysis," was originally developed for the left ventricle, and in this study, we applied it to the left atrium. To derive the flow components of the left atrium, the path particles taken in the left atrium are being analyzed. Based on when a particle enters and leaves the left atrium, it is assigned to a specific component. Most interesting for the left atrium are the components conduit and reservoir, which describe the amount of blood that passes through the left atrium quite quickly, as well as the residual volume, which contains the particles that stay in the left atrium for at least 2 heartbeats.

With the left atrial flow component analysis, we could identify different blood flow patterns in patients with atrial fibrillation compared to controls. The AF patients generally had larger atrial volumes, leading to larger residual volumes, but similar conduit and reservoir flow. The increased residual volume could highlight patients with an increased risk for stroke.

Left atrial flow component analysis is a comprehensive tool to better understand the blood flow in the left atrium. In the future, this could help clinicians better identify AF patients who have a higher risk of stroke and prescribe medication on a patient-specific basis.

PROJECT INFORMATION

Project

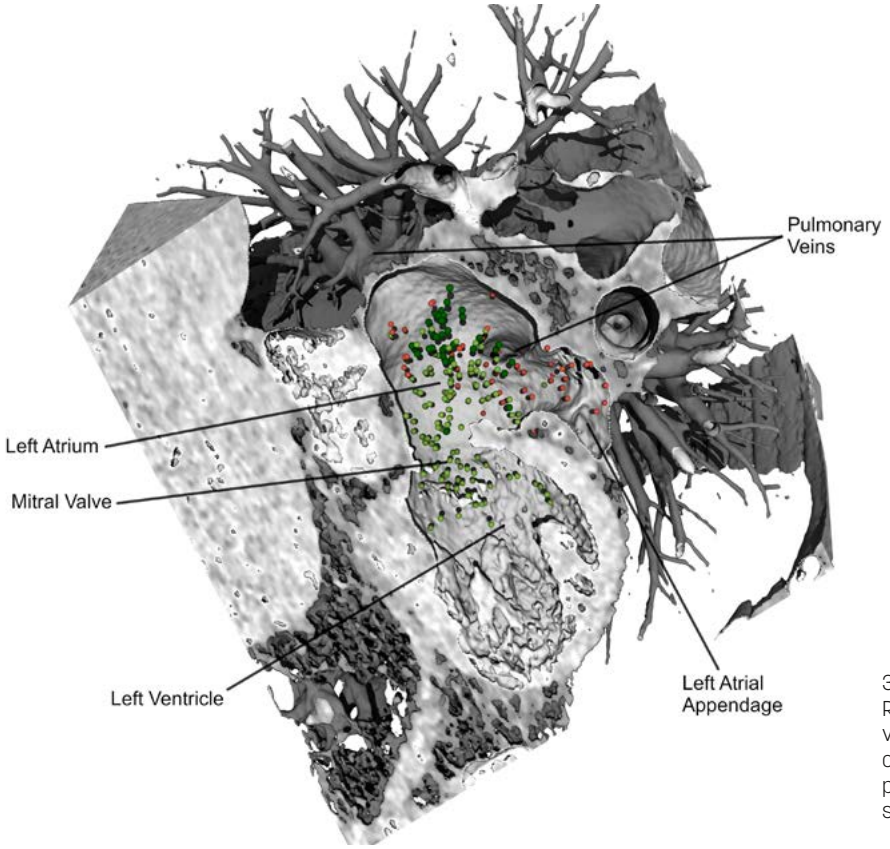
Assessment of Blood Flow and Stasis in Atrial Fibrillation.

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 rendering of the left heart based on a CT image. Red spheres represent particles from residual volume, that stay in the left atrium for at least 2 cardiac cycles. Bright green spheres represent particles from reservoir flow and dark green spheres represent particles from conduit flow.

Shan Cai

Multimodal Magnetic Resonance Measurements of Diffuse Liver Disease

Diffuse liver disease, which can be caused by infections, inherited conditions, immune or autoimmune disorders, and vascular injuries, is a growing public health problem worldwide. Non-alcoholic fatty liver disease (NAFLD) is the most common form of diffuse liver disease, with around 20–30% of the world's population affected. Diffuse liver disease can result in inflammation, fibrosis, and ultimately develop into cirrhosis and liver failure. However, the early symptoms of diffuse liver disease are nonspecific, and it is usually diagnosed at advanced stages when the conditions are not reversible. Although a liver biopsy is considered a "gold standard" for the diagnosis, this procedure is invasive with low repeatability and limited by sample errors. Thus, there is a significant demand for specific and noninvasive approaches for diagnosing diffuse liver disease.

Magnetic Resonance Imaging (MRI) is a noninvasive technique, considered the most promising imaging modality for quantitatively assessing diffuse liver disease. However, further development of multimodal MRI tools is still needed in this field. In this research project, we aim to investigate and develop novel quantitative MRI methods, in combination with image processing and mathematical modeling, to evaluate and stage diffuse liver diseases. The goal is to identify and quantify a range of signs, such as inflammation, fibrosis, and portal hypertension in the liver, and assess liver function, as well as their spatial distribution, to achieve a spatially resolved assessment. These multimodal MRI methods are expected to provide potential clinical biomarkers that can significantly impact the diagnosis, treatment, and management of diffuse liver disease. We believe that these methods will offer a specific and comprehensive evaluation, allowing for a more reliable diagnosis.

In our recent study, we explored quality assurance measures for a three-dimensional (3D) MR-elastography (MRE) research system. MRE is a powerful tool for grading liver fibrosis by measuring wave propagation in the liver. In comparison with the commercially available 2D-MRE systems, 3D-MRE can provide additional biomechanical parameters for evaluating liver inflammation and fibrosis but lacks a well-developed quality assurance protocol. Based on the quality assurance parameters investigated in this study, we proposed a method that can be used to generate a confidence map (Figures A and B) for 3D-MRE to indicate reliable data areas for measuring liver tissue biomechanical properties.

PROJECT INFORMATION

Project

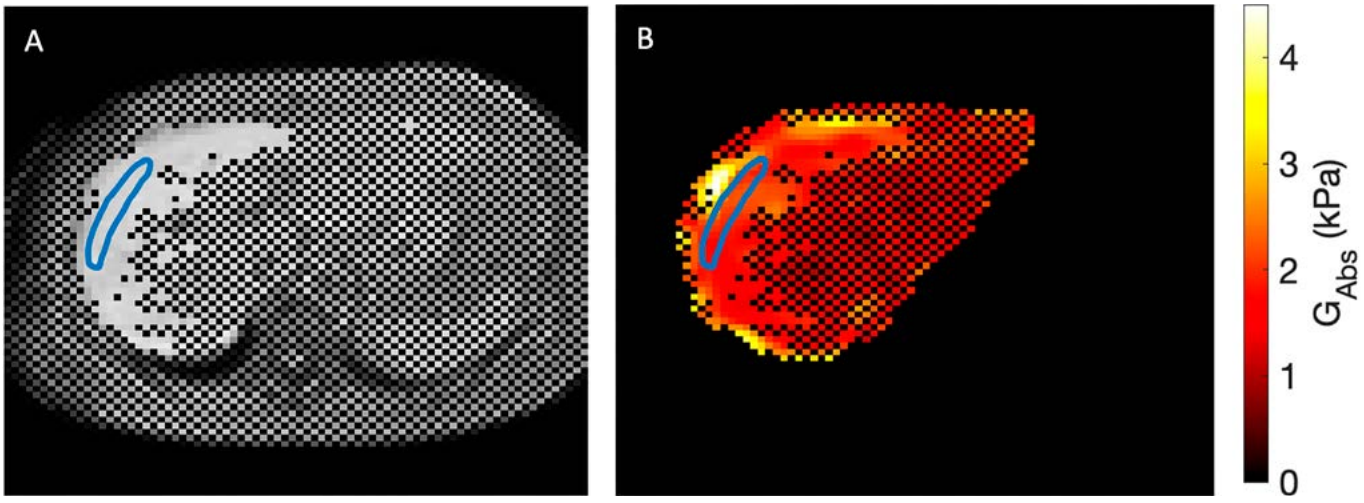
Multimodal Magnetic Resonance Measurements of Diffuse Liver Disease – Technological Developments and Novel Imaging Biomarkers.

Supervisors

Peter Lundberg, Stergios Kechagias, Karin Markenroth Bloch, Magnus Borga, Nils Dahlström.

Short CV

Master of Science (MSc), Biomedical Engineering, Linköping University 2020–2022.



An example of performing quality checking with a confidence map created using the quality parameters (unpublished). Regions-of-interest (ROIs) can be placed in the unmeshed area. The confidence map is superimposed over an anatomical image (Figure A) and the shear stiffness map, GAbs (Figure B).

André Da Luz Moreira

Parametric Modelling of the Mitral Valve

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.

We have developed a framework for mitral valve modelling, which we are currently refining and improving for testing. It is based on both MRI and CT images taken during a full cardiac cycle. The framework relies on mathematical models for specific structures of the valve, namely the mitral annulus and leaflets. Our goal is to reproduce the mitral valve geometry with sufficient accuracy to represent is effects in cardiac hemodynamics. This would allow us to study how changes in mitral geometry impact blood flow, and hopefully becomes a tool to assist clinicians in the future.

PROJECT INFORMATION

Project

Modelling and Simulation of patient specific mitral valve function and cardiac hemodynamics.

Supervisors

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

Short CV

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

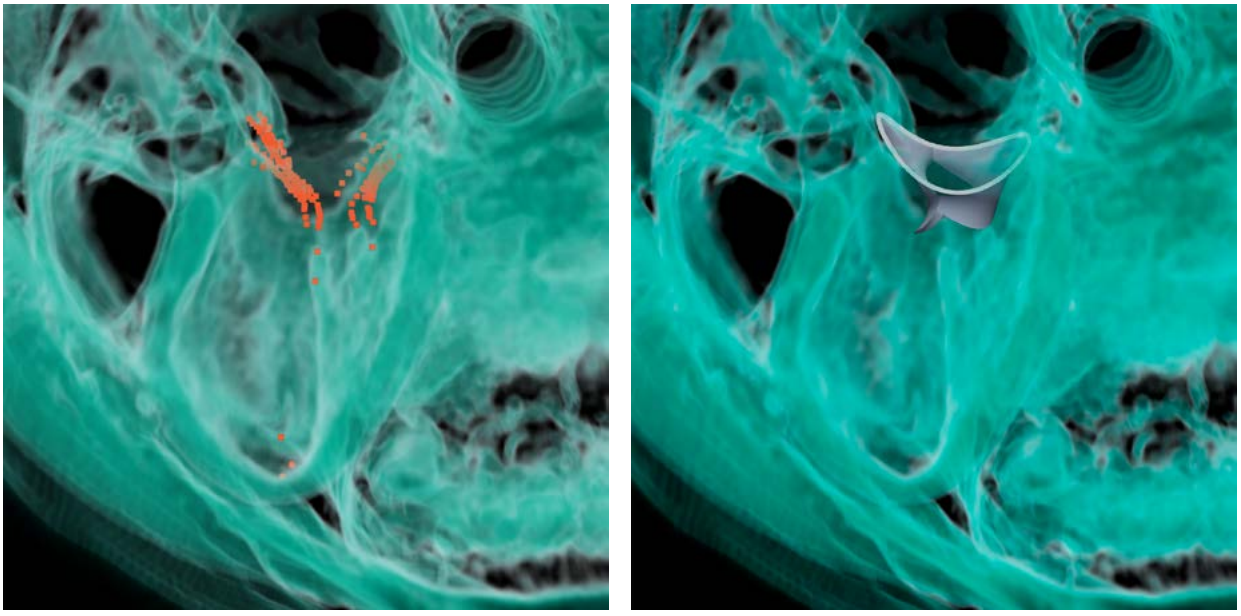
Linköping University, MSc. in Aeronautical Engineering with specialization in aircraft aerodynamics, 2017–2019.

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

PhD Student, Linköping University, 2022–Present.

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.



Examples of tracked points and modelled mitral valve.

Frida Dohlmar

Automated Treatment Planning for Brachytherapy

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. This is referred to as an implant, and an example for cervical cancer is seen in Figure 1. The source stops at predefined positions in the implant for a certain time to deliver the prescribed absorbed dose. It is commonly used for prostate and cervical cancer in combination with external beam radiation therapy.

My project focuses on the treatment planning of brachytherapy, which involves deciding the dwell times for different positions in the implant. International recommendations for treatment planning for cervical cancer treatments suggest doing this manually, meaning deciding the individual dwell times in a trial-and-error manner until a satisfactory dose distribution is achieved. There are recommendations for both the desired dose distribution and the dwell distribution. Concerning the dose distribution, the goal is to achieve a high dose to the target volume and as low a dose as possible in the surrounding organs.

In the clinical treatment planning systems, there are tools to perform the treatment planning in an automated way using optimization tools. The treatment planner then set up dose aims for the target volume and dose constraints on the organs surrounding the target volume. This method is fast and could be easier to implement for new clinics, but unfortunately it has been shown that the distribution of the dwell times does not comply with the recommendations for this method. Therefore, a method for automated treatment planning using pseudo-structures to steer the dwell time distribution has been invented. This method is tested on cervical cancer patients previously treated in Linköping. The method was compared with the manual method and optimization just on the clinical structures. The results shows that it is possible to achieve treatment plans with dose distribution and dwell time distribution that comply with the recommendations, an example of the dose distribution can be seen in Figure 2. Future work is to test the method with pseudo-structures in different treatment planning systems.

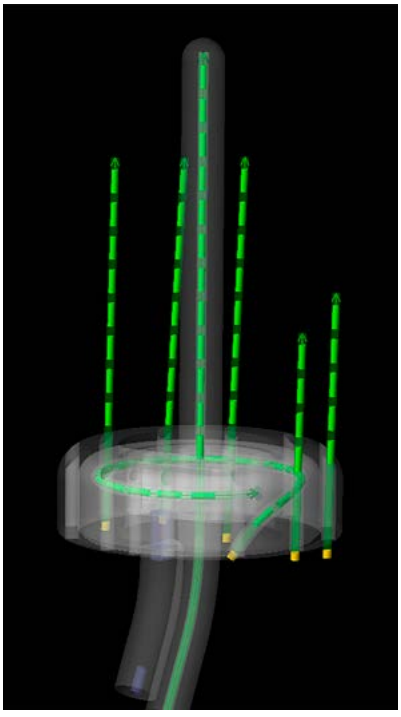


Figure 1. An example brachytherapy implant used for the treatment of cervical cancer. The implant consist of one intra-uterine tandem, a ring and two needles.

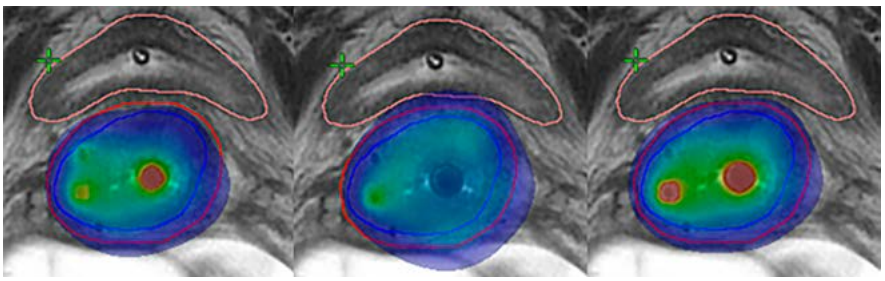


Figure 2. An axial MR-image of a cervical cancer patient. The colors representing the high dose volume (blue: 7 Gy and red: 30 Gy), left the clinical (manual) treatment plan, middle the automated with pseudo-structures and to the right the automated only with clinical structures.

PROJECT INFORMATION

Project
Dosimetric evaluation and development of new methods for automated brachytherapy treatment planning.

Supervisors
Åsa Carlsson Tedgren, Torbjörn Larsson, Michael Sandborg, Björn Morén.

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

Anna Ljusberg

Myelin Changes after Brain Cancer Treatment

In Sweden, approximately 1400 patients are diagnosed with brain tumors each year. "Brain tumor" is an umbrella term encompassing various types of cancer. The specific tumor type is contingent upon the cells of origin, and diverse types are prevalent at different life stages. Some are more frequently observed in children, while others manifest in adults.

In the case of children, one-third of all cancer instances involve tumors in the brain or central nervous system. Despite approximately 80% survival rates, cancer remains the leading cause of death for younger children.

Cancer treatment is typically based on three primary categories: surgery, chemotherapy, and radiation therapy. For adults, most cases involve a combination of all three, while treatment for children varies depending on tumor type and malignancy grade. All treatments are rigorous and can induce severe side effects. Monitoring treatment efficiency and side effects is crucial.

The primary imaging tool for evaluation and treatment planning is magnetic resonance imaging (MRI). In our group, we strive to incorporate quantitative MRI (qMRI) as a complement to conventional MRI. QMRI allows for the quantification of differences in tissue relaxation over time, moving beyond visual assessment alone.

In a prior study conducted on adults, we observed a reduction in myelin in the white matter after radiation therapy. A higher absorbed dose was correlated with increased damage. Myelin serves as a protective sheath around neurons, and impairment to this structure can lead to interruptions in nerve signals, resulting in neurological symptoms.

Currently, our focus is to include qMRI and other advanced MR-sequences in examinations performed on children diagnosed with brain tumors. One study focuses on children recently diagnosed with a brain tumor and referred for surgery, where qMRI will be used before, during and after surgery and for follow-up, with the aim to improve tumor and side-effects identification. Another study involves 18-year-olds who have previously been treated for brain tumors in their childhood. The aim here is to compare the qMRI-data with a group of healthy volunteers in the same age and investigate if the myelin concentration has been affected by treatment. Findings will also be compared with neurocognitive test results.

PROJECT INFORMATION

Project

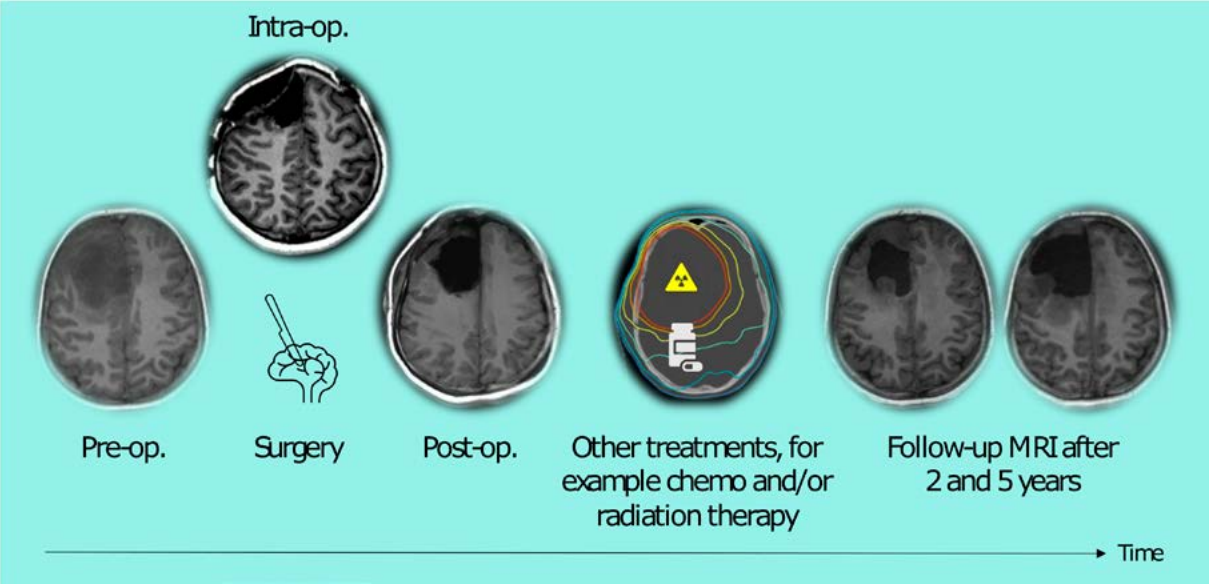
Quantitative MR for diagnosis and treatment follow-up of brain tumors.

Supervisors

Anders Tisell, Ida Blystad, Emelie Adolfsson, Peter Lundberg.

Short CV

Vice chairman of CMIV research school, Sep 2023- .
Medical physicist, radiation therapy, Linköping University hospital, 2015-present.
Master of science in medical physics, 2013 Lund University.



Schematic overview of time points for MRI-examinations for children diagnosed and treated for brain cancer.

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. Multiple systems to perform CVR measurement this way have been proposed in the literature, none however, works together with a ventilator. Therefore, a large group of patients that are being ventilated and might benefit from CVR measurement have 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 below. We have systematically tested our system in a ventilator utlizing a test-lung, as well as in healthy, free breathing, volunteers.

PROJECT INFORMATION

Project
Magnetic Resonance Imaging studies on Cerebrovascular Reactivity.

Supervisors
Anders Tisell, Maria Engström, Charalampos Georgiopoulos, Gunnar Cedersund, Lovisa Tobiesson.

Short CV
Bachelor's and master's degree in engineering physics from Chalmers University.
Research assistant at Gothenburg University.
Research engineer at Linköping University Chair CMIV Research School.

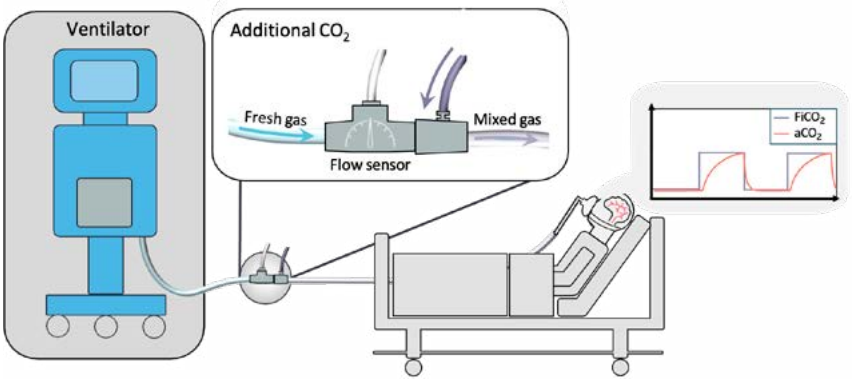


Figure 1. Illustrating the Additional CO_2 method: It introduces high-concentration CO_2 intermittently into the breathing circuit, modulating the composition of inhaled gases. The flow of fresh gas from the ventilator is continuously measured through a flow sensor, while a mass-flow controller (not shown) regulates the admixture of CO_2 to maintain a predetermined target CO_2 concentration in the inhaled gas.

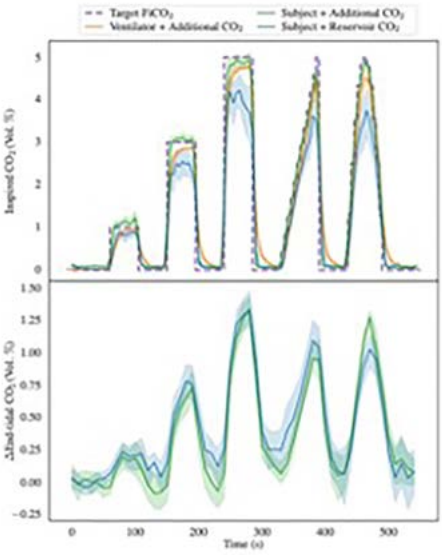


Figure 2. Upper graph illustrating the precision of the Additional CO_2 method, in both ventilator and free breathing subjects, in achieving different fractional concentration of CO_2 ($FiCO_2$) in the inhaled gas. Also shown is the precision achieved with a reference system, Reservoir CO_2, which, in contrast to the Additional CO_2 method, administer CO_2 with the help of a reservoir. The bottom graph shows the resulting end-tidal CO_2 response in the free breathing subjects.

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. 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 investigating the true true 3D aspect of morphological thoracic and respiratory obstruction using 3D reconstructed computed tomography scans. We want to see if there is a difference in results depending on type of surgical approach. We also aim to establish the morphological relationship between the vertebral body/disc deformation and the thoracic asymmetry.

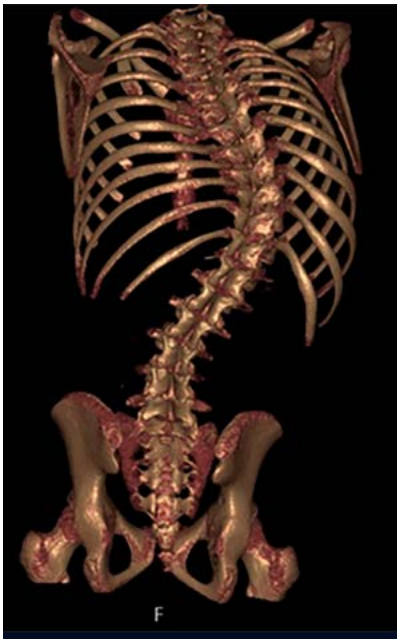


Figure 1. A 3D reconstruction of the scoliotic spine.

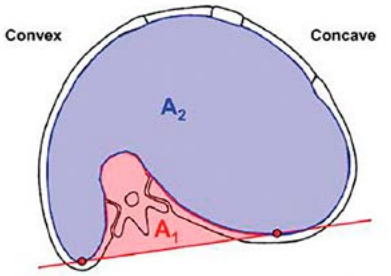


Figure 2. An axial illustration of the scoliotic thorax.

PROJECT INFORMATION

Project
Idiopathic scolioisis - patomechanism and morphology.

Supervisors
Hans Tropp, Ludvig Vavruch.

Short CV
Medical School, Linköping University, 2014-2019.
Assistant Physician, Linköping University Hospital, 2020-2022.
PhD Student, 2020-present.
Resident in Orthopedics, Linköping University Hospital, 2022-present.

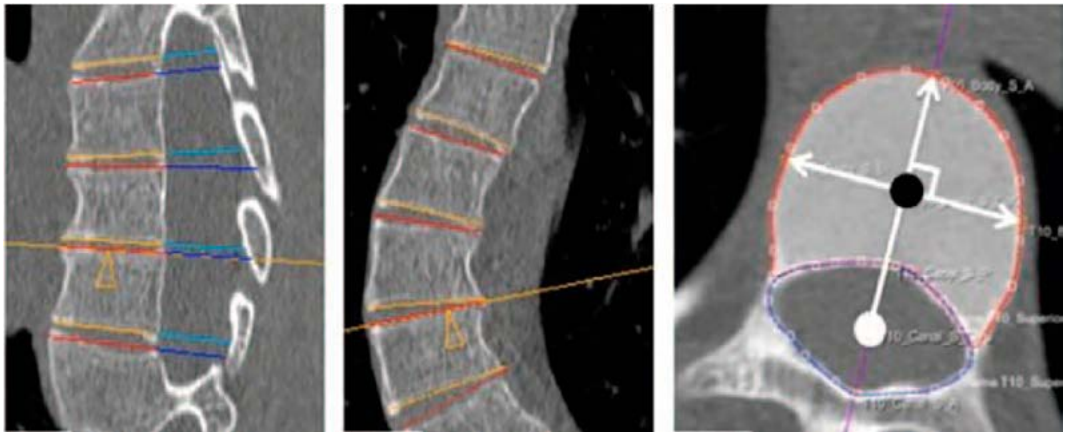


Figure 3. Measuring vertebral body/disc deformation.

Linus Ohlsson

Intracardiac Geometry and Hemodynamics during Left Ventricular Assist

Heart failure is one of our most severe common diseases, where progression to advanced failure leads to a low prognosis and few treatment options. Recent advancements in the use of a left ventricular assist device, HeartMate 3 (HM3), have shown significant benefits in advanced heart failure therapy, with improved survival rates compared to previous devices. The transition is particularly significant as HM3 is likely not only to serve as a bridge to heart transplantation but is increasingly being discussed as an effective destination therapy.

Despite these advancements, the need for meticulous hemodynamic monitoring remains during all types of mechanical circulatory support. While ultrasound remains the primary hemodynamic imaging method, its effectiveness is limited. The introduction of photon-counting computed tomography (PCCT) offers time-resolved cardiac imaging with reduced metal artifacts. This, combined with computational modelling, potentially presents a novel approach to understand intracardiac hemodynamics during this therapy. The aim of my research is accordingly to investigate and describe both intracardiac geometry and hemodynamics in patients with ongoing therapy and correlate potential findings with device settings.

The overall project employs an explorative cross-sectional design including patients within the Swedish Southeastern healthcare region. We have conducted several phantom and optimization studies, and a PCCT protocol has now been developed for time-resolved computed tomography of patients with these types of mechanical heart pumps. Therefore, research subjects are currently invited to undergo PCCT scans along with selected ultrasound imaging. The assist device is connected to software that allows for setting variations in between the scans. Analyzed variables includes three-dimensional geometry, and computed parameters such as intracardiac blood flow velocity maps, pressure maps, turbulence maps, and risk of blood stasis. The variables are related with device settings and, alongside, selected echocardiographic measurements and patient details.

Initial image quality from the photon-counting computed tomography has shown promising results. If the resulting flow simulations and hemodynamic models provide valuable information, and the method is deemed robust and reproducible, we may approach additional centers to expand the research project's data collection, analyses, and opportunities.

PROJECT INFORMATION

Project

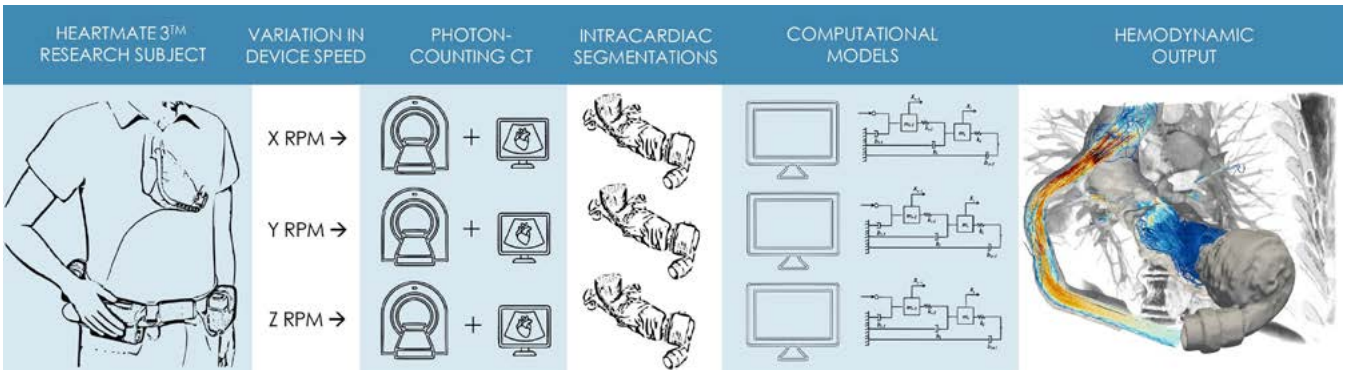
Exploring the impact of HeartMate 3 on intracardiac geometry and hemodynamics using time-resolved photon-counting CT.

Supervisors

Tino Ebbers, Hans Granfeldt, Jonas Lantz, Éva Tamás.

Short CV

PhD student, Department of Cardiothoracic and Vascular Surgery, Region Östergötland, 2022-present.
Chairman, CMIV Research School, Linköping University, 2023-present.
Teaching Assistant, Anatomy, Linköping University, 2020-present.
Junior Doctor, Department of Clinical Physiology in Linköping, Region Östergötland, 2023.
Research Assistant, Linköping University, 2022.
President, Medical Faculty Student Union, Linköping University, 2021-2022.
President, Medical Association, Linköping University, 2020-2021.



The figure exhibits the overall setting within the project. The hemodynamic output example shows blood flow velocities within the left ventricle and outflow graft in one research subject.

Marcelo Martins

Close-to-Bedside MRI in Neurosurgical Critical Care

In the realm of neurosurgery, patients in the neurosurgical critical care unit (NCCU) often require repeated diagnostic imaging. Yet, intrahospital transport for imaging poses risks, as even minor physiological fluctuations can lead to secondary brain injury.

To address this critical concern, among other, a Magnetic Resonance Imaging (MRI) scanner was installed in our NCCU for intraoperative use. With this, we've developed a preparation and transportation approach that we believe minimizes the impact on patients' vital signs when imaging with MRI is necessary. Unlike traditional intrahospital transfers to the Radiology department, our new method, that we refer as "close-to-bedside MRI", allows us to conduct all necessary preparations within the patient's own care room.

This approach is carried out by a highly skilled core staff. They utilize comprehensive checklists and specialized transportation techniques to ensure the safety of both the patient and the MRI procedure. Most notably, the MRI scanner is situated within the ward itself, reducing transportation time to a mere couple of minutes.

Our first project is dedicated to evaluating the effectiveness of the close-to-bedside MRI approach in preserving critical physiological parameters, as compared to the traditional practice of transporting patients outside the NCCU to the Radiology department. This will help us understand if this new approach is as safe and effective as we believe it to be. Furthermore, we aim to investigate the impact of different professional constellations on patient and MRI safety. In contrast to standard practice, where radiographers collaborate closely with external anesthesia teams, our approach involves intensive care nurses from the NCCU working alongside radiographers to ensure safety during MR scans.

If our approach proves successful in maintaining patient and MRI safety, we can foresee integrating MRI as a repeatable imaging tool for NCCU patients. This would open up new avenues for studying patient groups that often lack access to MRI scans due to their instability.

One of the exciting possibilities is the daily measurement of cerebral blood flow, which could be invaluable in detecting vasospasm – an all-too-common complication following subarachnoid hemorrhage. Early detection and treatment of vasospasm can make a life-saving difference for patients, and we believe our close-to-bedside MRI approach can play a pivotal role in achieving this. We believe this approach in the NCCU promises to improve patient care by making MRI scans safer, more accessible, and offering invaluable insights into the well-being of critical care patients.

Bringing the MRI table into the patient's own care room enables safe and efficient imaging within the Neurosurgical Critical Care Unit.

PROJECT INFORMATION

Project

Magnetic Resonance Imaging as a Monitoring and Diagnostic Method in Neurosurgical Care.

Supervisors

Peter Zsigmond, Anders Tisell, Johan Kihlberg, Charalampos Georgiopoulos.

Short CV

MRI Radiographer, Linköping's University Hospital, 2016-present.
Modality Leader MRI 6, CMIV, 2020-2023.
Master of Science (1 year) in Medical Sciences (Radiography), Karolinska Institute, Sweden, 2018-2021.
General Radiographer, Nyköping's Regional Hospital, 2014-2016.
Bachelor of Science, Radiography, Coimbra Health School, Portugal, 2009-2013.

Milda Pocevičiūtė

Explainable AI Applied to Histopathology Image Analysis

Digital pathology has enabled research on Artificial Intelligence (AI) systems 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 understandability, transparency, and reliability of AI systems developed to assist pathologists. 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. In my work, I have explored utilisation of this type of algorithm called attention-based Multiple Instance Learning. An example of a generated in-built attention map is provided below. Here, the areas in a H&E stained lymph node section that are 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

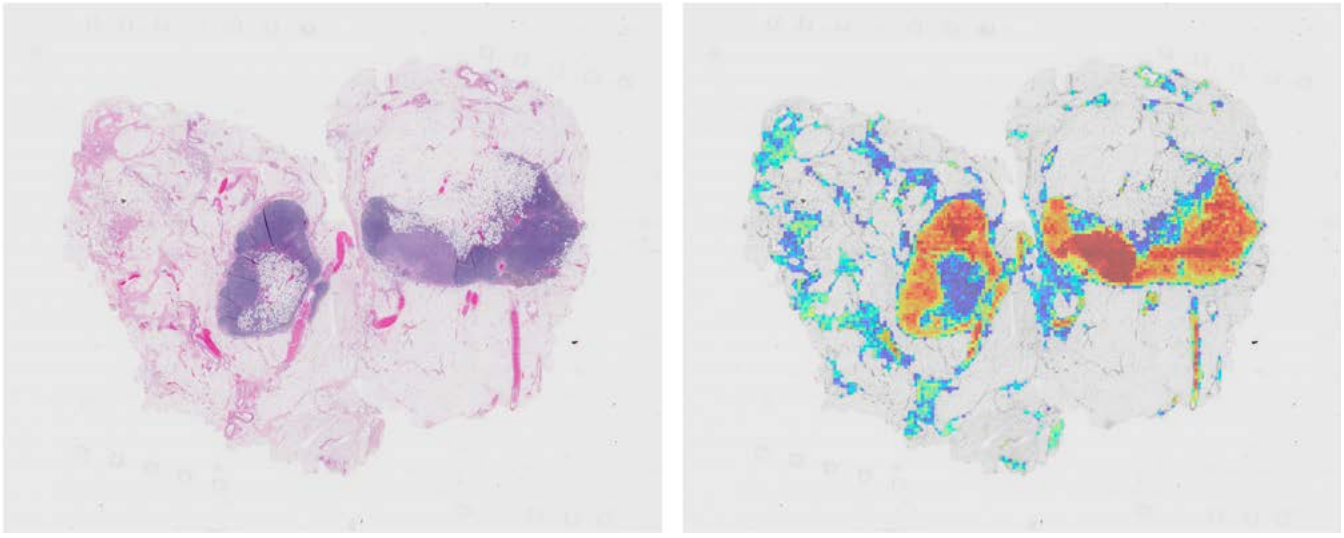
Explainable AI Applied to Histopathology Image Analysis.

Supervisors

Claes Lundström, Gabriel Eilertsen and 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.



The left image is an original WSI of an H&E stained lymph node section. The right image visualises an attention-based heatmap generated by a Multiple Instance Learning algorithm for the WSI. The areas that are most likely to contain tumour cells are marked in red.

Christian Simonsson

Combining Systems Biology and MRI to Characterize Liver Function

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.

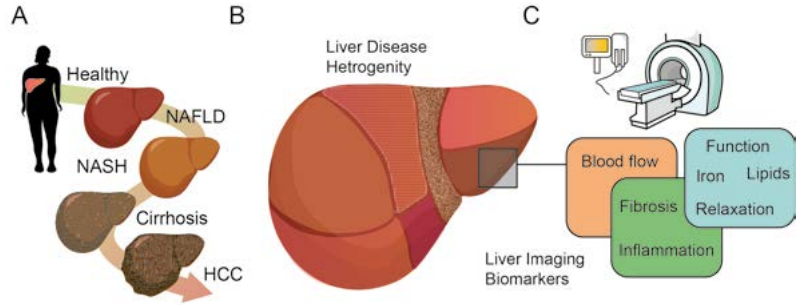


Figure 1. A) Progression of NAFLD. B) Heterogeneity of liver disease C) imaging bio markers used in our multi-modal MRI examinations.

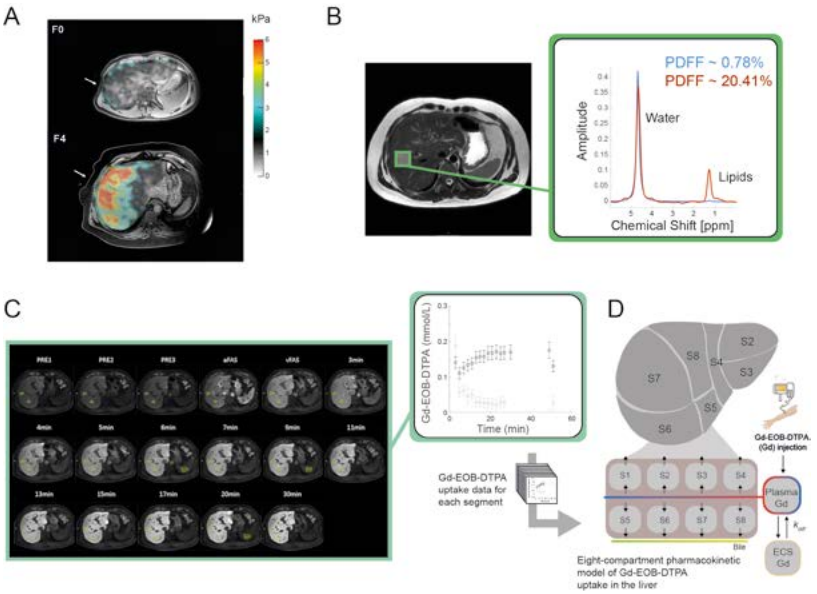


Figure 2. Example of images and methods from the multi modal MRI examinations. A) Elastogram from MRE, showing the liver stiffness for two different patients, one healthy (F0) and one with severe fibrosis (F4). B) Example of ^{1}H-MRS spectra to measure PDFF for two different cases, one healthy and one 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 focus on collecting imaging data from patients from the whole spectrum 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 ^{1}H-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 a few 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, Peter Gennemark.

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 (CVD) stands as the leading global cause of mortality.

Computed tomography (CT) assessment plays a pivotal role in this risk evaluation.

Coronary artery calcium scoring (CACS) is an examination designed to detect coronary artery calcifications (CAC). Since the 1990s, it has been used for risk assessment in asymptomatic patients.

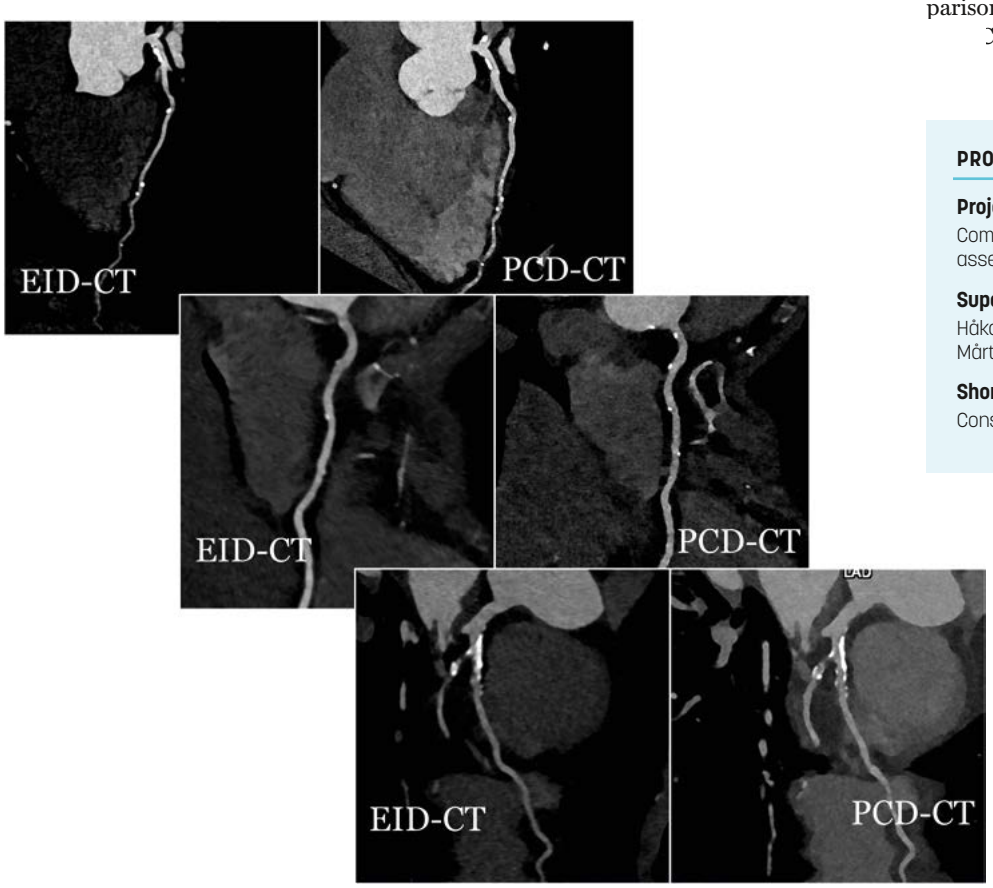
While CACS offers a quantitative assessment of calcified burden in the coronary arteries, CCTA enables visualization of coronary artery plaques in relation to vessel lumens, thus enabling evaluation of stenosis.

Conventional energy integrated detector computed tomography (EID-CT) demonstrates high sensibility in detecting coronary artery stenosis and excellent negative predictive value. However, this method tends to overestimate CAD, leading to moderate specificity and positive predictive value. A recent advancement in CT technology is photon counting detector computed tomography (PCD-CT). This innovation offers several technical benefits. Of particular relevance to this project are the potential implications for coronary artery diagnostics, including how the heightened spatial resolution and reduced blooming artifacts could enhance diagnosis.

When introducing a new clinical examination technique, it is imperative to determine whether established scoring methods, such as the AS, remain reliable for early CAD detection and risk stratification.

Additionally, a comprehensive exploration of PCD-CT applications in coronary artery diagnostics is crucial for a thorough understanding. The primary interest and potential advantage of this project is that if the PCD-CT technique demonstrates a high positive predictive value, it could refine the diagnostic process and improve the selection of patients referred to invasive coronary angiography (ICA), ultimately reducing complications associated with invasive examinations and lowering costs.

The aim of my thesis is to evaluate the new CT technology (PCD-CT) in comparison to well-established techniques,
CT and ICA.



Example of coronary arteries with calcifications, from tree different patients. Images from EID-CT to the left and PCD-CT to the right. (Fig 2)

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.

Iulian Emil Tampu

Deep-Learning Biomarker Detection in qMRI Images of Brain Tumors

Summary of results: Deep-learning explainability methods applied on models trained for tumor detection identify brain regions outside the visible tumor which have tumor-like behavior in quantitative values, but which are invisible to the eye. This suggests the presence of infiltrative tumor regions detectable through deep-learning but invisible to radiologists.

Background: 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 is visible in conventionally acquired MR images (cMRI), which can be the source of tumor regrowth if left untreated.

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 trained deep learning models for tumor detection using either cMRI or qMRI as input data. Deep learning explainability methods were then applied on the trained models to visualize what regions are used by the algorithm for the detection task. Finally, the change in relaxation values after contrast injection were analyzed for the regions inside and outside the visible tumor region.

PROJECT INFORMATION

Project

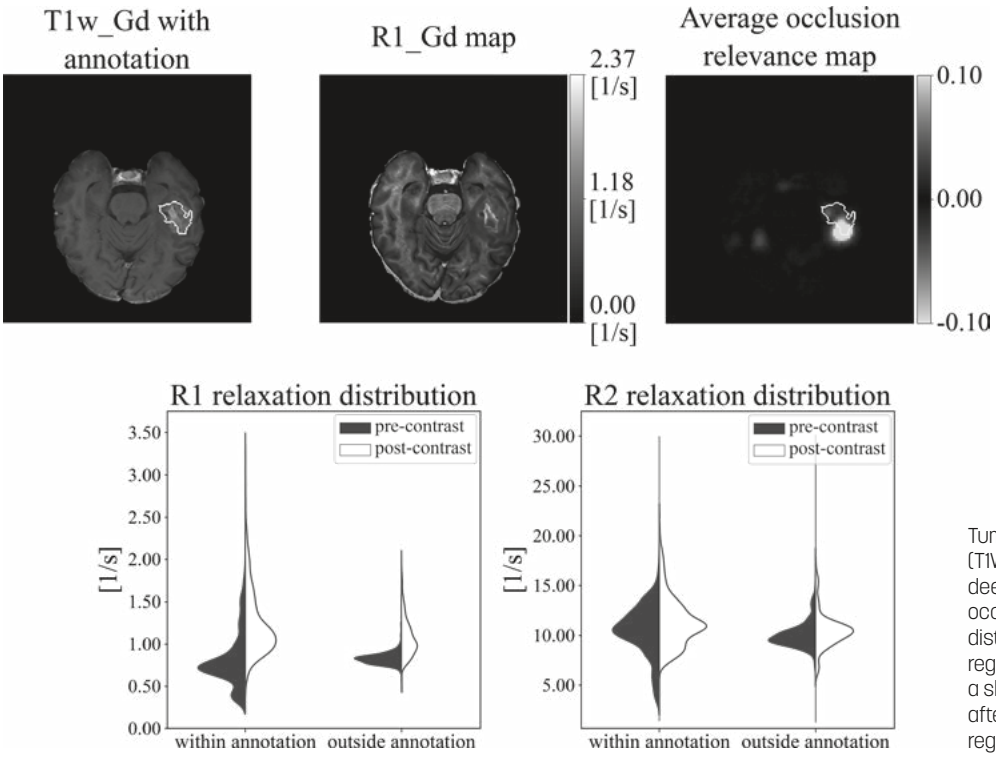
Brain tumor biomarker detection using deep learning and quantitative MRI-images.

Supervisors

Neda Haj-Hosseini, Anders Eklund, Oliver Gimm, Ida Blystad.

Short CV

University of Padova, BSc in Biomedical Engineering, (2013-2016).
Linköping 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).



Tumor region as seen by conventional MRI (T1W_Gd), quantitative MRI (R1_Gd map) and deep-learning model explainability (Average occlusion relevance map). The relaxation distribution analysis shows that identified regions outside the tumor annotation have a shift in quantitative relaxation values after contrast injection comparable to the regions inside the annotation.

Chiara Trenti

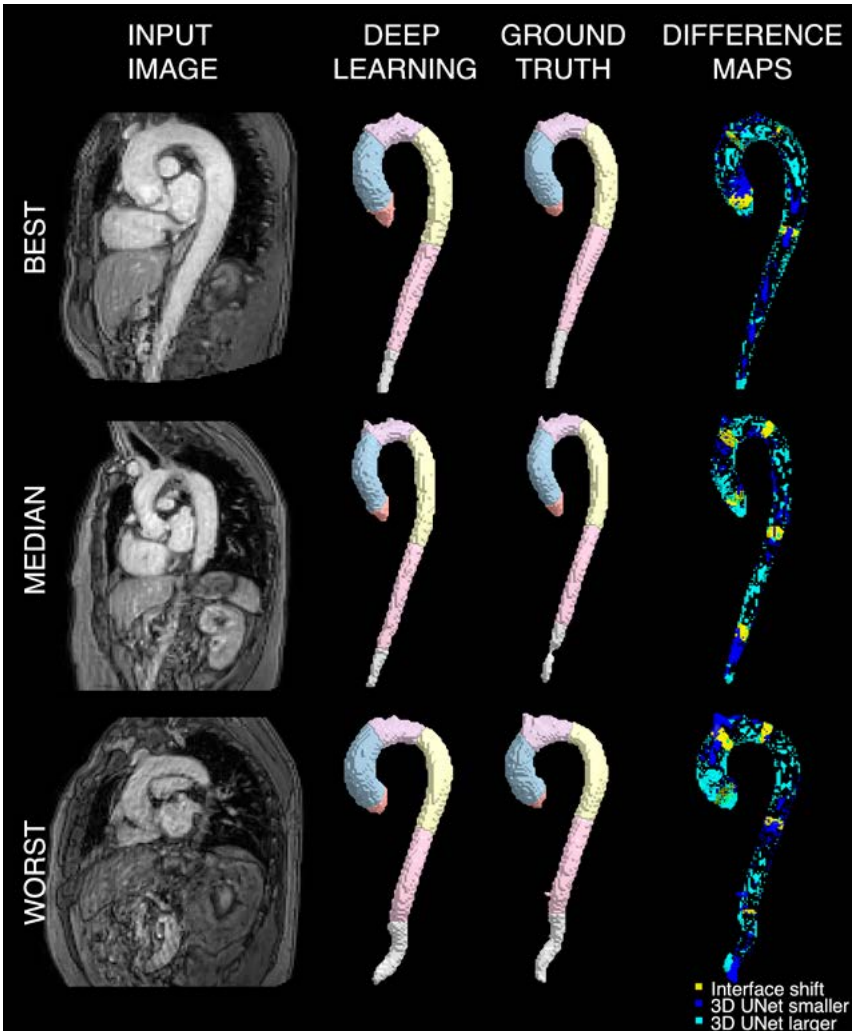
Nonsize Factors in Aortic Dilation

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 measuring the aortic size for stratification towards surgical intervention. However, size alone is not a sufficient predictor for complications. For example, most patients with ascending aorta dissection present with small aneurysms and thus do not fall within the current guidelines for 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 if artificial intelligence can be used to perform segmentation of the aorta on the imaging in a completely automatic manner. Image segmentation is the process of delineating a region of interest, for example the aortic lumen, on the CMR images. This is mainly done manually or with semi-automatic methods that are time consuming and rely heavily on anatomical similarities between images. Automatic segmentation of the aorta on CMR images would greatly simplify and accelerate the time-consuming image processing.

A deep learning neural network (3D Unet) was adopted and optimized to output four labels: the ascending aorta, aortic arch descending aorta suprarenal abdominal aorta (see the figure). The data used for training included CMR images of 106 patients, around half of them with aortic dilation. The magnitude volumes, representing the chest' anatomy, were used as input to the network. The results demonstrate that segmentation of the aorta with deep learning is feasible. Most differences were found in the aortic branches and in the interface between the segments, however accurate segmentation of these regions is difficult and not needed for most applications.



From the left to the right: input magnitude images, the output of the deep learning model (3D UNet), ground truth images and the difference maps the best (top), median (middle) and worst (bottom) subject. Visual inspection reveals a difference in the segmentation of the supra-aortic branches and distal part of the abdominal aorta. Moreover, most differences are found in the interface between adjacent segments. Different colors correspond to different labels: AAo = Ascending aorta, AoA = Aortic arch, DAo = Descending aorta, SAo = Suprarenal Aorta.

PROJECT INFORMATION

Project

Novel assessment of aortic function in health and disease.

Supervisors

Petter Dyverfeldt.

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.

Kajsa Tunedal

A Cardiovascular Model for Blood Pressure Regulation

A too high blood pressure, hypertension, is one of the main risk factors for cardiovascular diseases such as stroke, coronary artery disease, or heart failure. The current treatments for hypertension include both lifestyle changes and a choice of a range of blood pressure-lowering drugs. However, the treatment choice is often based on general guidelines rather than patient-specific factors, and a trial-and-error approach where different drugs are tested until an optimal effect is reached. A more comprehensive and patient-specific understanding of blood pressure regulation is needed to improve the treatment and outcome of hypertensive patients. In this project, we are developing mathematical models to understand the patient-specific mechanisms of both short- and long-term blood pressure regulation in health, disease, and during treatment.

Using 4D flow magnetic resonance imaging and blood pressure data, patient-specific mathematical models can be created – from detailed lumped parameter models of blood flow and blood pressure during one heartbeat to exercise effects during minutes or hours and models of long-term blood pressure changes over several years. With the lumped parameter models, we have showed that we can comprehensively analyze and estimate hemodynamic variables and find differences between groups that otherwise cannot be derived non-invasively. Together, these models create a digital copy of each patient's hemodynamics, a multi-timescale digital twin, that can describe, explain, and predict the mechanisms of patient-specific changes in blood pressure and blood flow both today, within a few hours, and several years into the future.

To facilitate the development of a multi-timescale cardiovascular digital twin and further investigate the patient-specific effects of anti-hypertensive treatment, we collect detailed data on cardiac- and vessel function before, during, and after the start of anti-hypertensive treatment as well as during both rest and exercise. These new data and models can be used to gain insights into the complex mechanisms of cardiovascular function, which could lead to a more personalized understanding and targeted approaches to prevention, diagnosis, and treatment of hypertension.

PROJECT INFORMATION

Project

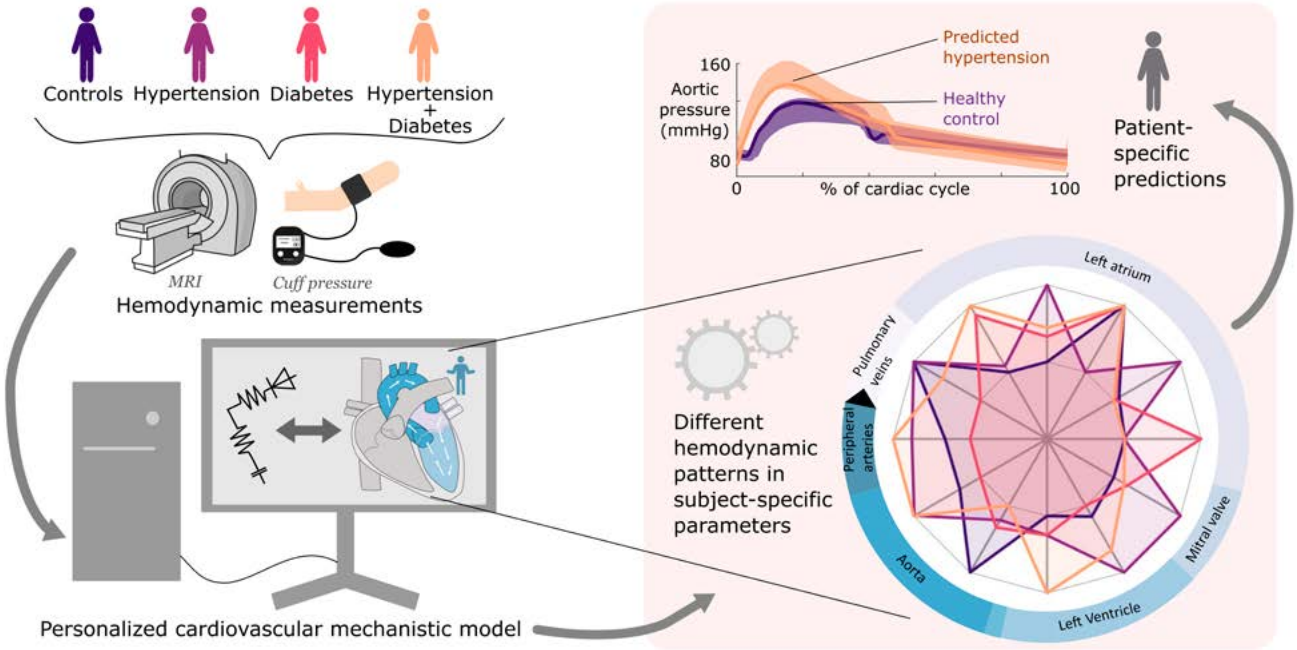
A cardiovascular mechanistic avatar for blood pressure regulation

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.



Using detailed measurements from 4D flow MRI and blood pressure, personalized cardiovascular models can be created. These models can describe and predict the blood pressure and blood flow on several timescales: from one heartbeat to exercise during several minutes, to drug treatments during months or years.

Federica Viola

Diastolic Function Assessment with 4D Flow CMR

Diastolic left ventricular dysfunction is a powerful contributor to the symptoms and prognosis of patients with heart failure. In patients with depressed left ventricular systolic function the ratio between the peak velocities of the early (E) and late (A) mitral inflow, known as the EA ratio, is the first step in the clinical algorithm defining the grade of diastolic dysfunction and the presence of elevated left atrial pressure. Doppler echocardiography is currently the preferred imaging technique for diastolic function assessment, due to its accuracy, safety, availability, and cost efficiency, while cardiovascular magnetic resonance (CMR) is less established as a method. As CMR and echo are both commonly used in patients with cardiovascular disease, it is of utmost importance to make comparable measurements, and to define and minimize differences between these methods.

Comparisons of 2D Phase Contrast-CMR and 4D Flow measurements of clinical diastolic function parameters have demonstrated the superior correlation of 4D Flow with Doppler echocardiography results in studies on healthy subjects and patients with mild to severe diastolic dysfunction. The CMR methods usually rely on manual data post-processing, however, this requires operator expertise, is time-consuming, and is associated with intra- and inter-observer variability.

In this study, we compare one automated, deep learning-based, and two semiautomated approaches for 4D Flow CMR-based EA ratio assessment to conventional, gold standard echo-based methods.

4D Flow-based EA ratio values were computed using three different approaches; two semi-automated, assessing the EA ratio by measuring the inflow velocity and the inflow volume at the mitral valve plane, and one fully automated, creating a full LV segmentation using a deep learning-based method within which the EA ratio could be assessed without constraint to the mitral plane.

We found that the EA ratio measured with all three 4D Flow methods was strongly associated with the gold standard Doppler echocardiography, while the absolute peak E and A velocities were underestimated. The automatic, deep learning-based method performed best, with the most favorable runtime of ~40 seconds. As both semiautomatic methods were very strongly associated to the automatic one, they could be employed as an alternative for estimation of EA ratio if the segmentations are not available.

PROJECT INFORMATION

Project

Diastolic Function Assessment with 4D Flow CMR using Automatic Deep Learning EA Ratio Analysis.

Supervisors

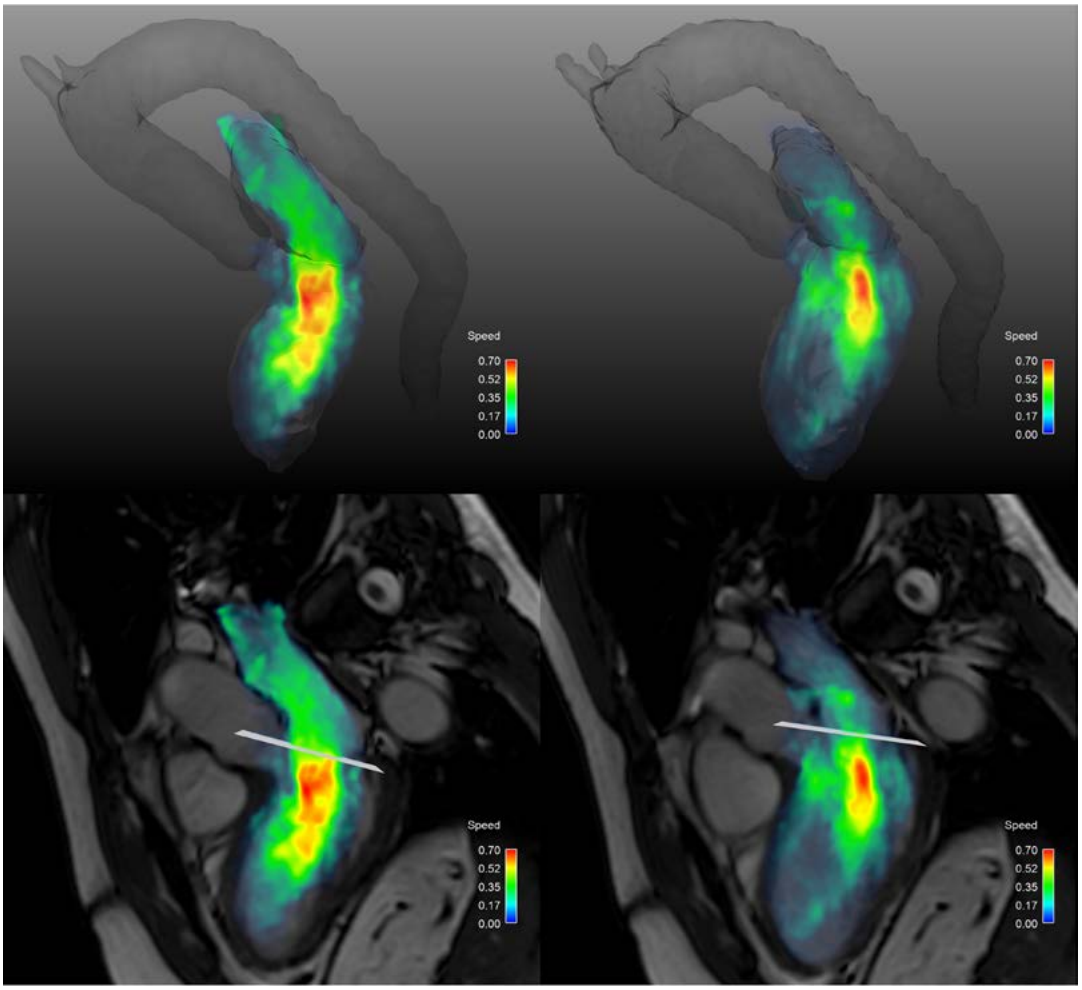
Tino Ebbers, Petter Dyverfeldt, Carl-Johan Carlhäll, Farkas Vanky.

Short CV

Research Engineer at the Unit of Cardiovascular Science at the Linköping University Hospital, November 2014-Current.

MSc in Biomedical Engineering, Linköping University of Technology, Linköping, Sweden, Sept 2012 -Sept 2014.

BSc in Electronic Engineering with highest honors; 110/110 cum laude, Università degli studi di Palermo, Palermo, Italy, October 2002- July2007.



The automatic approach, LVvel, and the semi-automatic methods, MVvel and MVflow, during early and late filling. (A–B): In LVvel the cardiovascular deep learning-based segmentations were used to mask the velocity inside the left ventricle. (C–D): in Mvvel and MVflow the mitral valve plane position was tracked from the three-chamber image, and velocity reformatted over a plane. The speed at early filling (A–C) and late filling (B–D) is shown as the maximum intensity projection.

Milda Pocevičiūtė is nailing her thesis three weeks before the dissertation. This is a Swedish tradition which makes it publicly available.

Dissertations

During 2023 three of the CMIV PhD students have finished their studies and defended their theses. The PhD students and the research school are an important part of CMIV, and we are proud to present their theses here.

Elin Good
LINKÖPING UNIVERSITY, DEPARTMENT OF HEALTH, MEDICINE AND CARING SCIENCES

Interrogating Atherosclerotic Plaque Biology Through Responses to Cardiovascular Risk Management and Imaging

DEFENDED ON FEBRUARY 17, 2023

Atherosclerosis causes more deaths than any other disease worldwide, and the cause of death is most commonly a rupture of a vulnerable atherosclerotic plaque, resulting in a thrombotic event in the heart or brain. The major risk factors for plaque progression are well known, but all the mechanisms that drive atherosclerotic plaques towards catastrophic events are not yet fully elucidated.

The thesis that was defended on February 17, 2023, revolved around the atherosclerotic plaque; how plaques can be analysed using cardiovascular magnetic resonance imaging and the study of biological responses to cardiovascular risk management. In Study I we interrogated the quality of cardiovascular risk management in patients diagnosed with high-grade carotid stenosis and found that cardiovascular risk management was deficient in all aspects, despite the very high risk for events in these patients. Thus, we designed the next two studies to address the unmet clinical need for improved cardiovascular risk management in patients with carotid atherosclerosis while at the same time asking mechanistic questions about the effect of this approach on lymphocyte phenotypes (Study II) and on plaque composition (Study III).

In Study II, the effect of cardiovascular risk management on Natural Killer cell, Natural Killer T cell and T lymphocyte subpopulations were studied in patients with carotid atherosclerosis. Our results show a polarisation away from a senescent phenotype towards more naïve i.e., juvenile cell types suggesting a transition towards a possibly less pro-inflammatory lymphocyte profile.

In Study III, we applied a newly developed quantitative Dixon MRI technique to the quantification of lipid rich necrotic core and hemorrhage inside atherosclerotic plaques. Employing this technique, we explored the relationships between these high-risk plaque compositional features and circulating lipoproteins as they changed over time in response to cardiovascular risk management. In the current study there was no evidence for such a linear relationship.

To further study the associations between inflammation and quantitative plaque measurements we explored in Study IV the relationship between inflammation in atherosclerotic plaques as measured by ^{18}F-FDG uptake and features of high-risk plaque as measured by quantitative Dixon MRI.

To facilitate the use of carotid MRI in larger cohorts we developed in Study V a technique for the segmentation of the carotid artery using supervised machine learning.

Taken together these studies describe the importance of cardiovascular risk management, the complexity of atherosclerotic plaque biology and they propose new strategies for quantitative plaque imaging.

Dr Elin Good at the Academic Celebration at Linköping University, where she received her doctor's hat and diploma.

David Abramian
LINKÖPING UNIVERSITY, DEPARTMENT OF BIOMEDICAL ENGINEERING

Modern multimodal methods in brain MRI

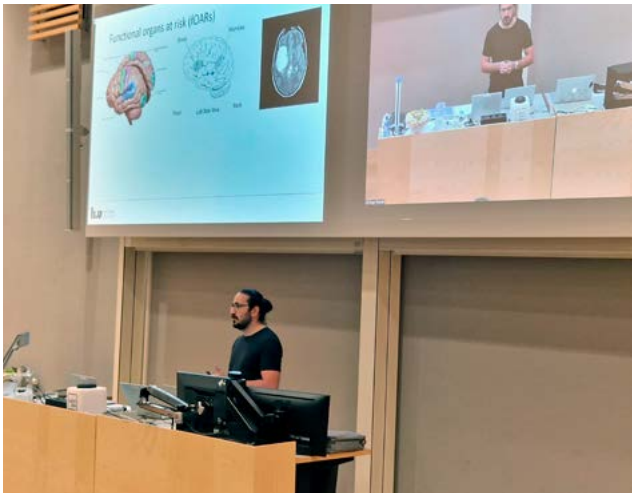
DEFENDED ON MAY 5, 2023

Magnetic resonance imaging (MRI) is one of the most important methods in medical imaging. By measuring changes in the magnetic properties of tissue, three-dimensional images of the human body can be created. MRI is a flexible technique, and different modalities can be used to measure different physiological properties. For studies of the brain, the most important modalities are structural MRI, which provides images with high resolution and good contrast between different tissue types, functional MRI, which can be used to study which parts of the brain are engaged during various experiments, and diffusion MRI, which is mainly used to study the microstructure of neuronal axons.

This thesis presents several advanced methods for analyzing MR images which fulfill two primary aims. The first is exploring how images from different MRI modalities can complement each other and lead to better to better results. The second is using modern tools in mathematics and computational science, such as artificial intelligence, Bayesian statistics and signal processing on graphs, to analyze MR images.

The publications in this thesis cover several different topics in brain imaging. The first two papers present methods to improve the analysis of functional MRI using information from structural MRI and diffusion MRI. The third article presents a method for locating active

areas of the brain with functional MRI, and how this information can be used when a brain tumor is removed using radiation (so as not to damage these important areas). In the fourth article, artificial intelligence is used to increase the spatial resolution in diffusion MRI, which can improve the analysis of the orientation of nerve fibers in brain white matter. Finally, the fifth paper shows that structural MR images that have been anonymized by removing the subject's face can be partially recreated using artificial intelligence. This illustrates that, while artificial intelligence has great potential to improve medical imaging and diagnostics, it also carries some dangers.



David Abramian at the defense of his thesis.

Milda Pocevičiūtė

LINKÖPING UNIVERSITY, DEPARTMENT OF SCIENCE AND TECHNOLOGY

DEFENDED ON NOVEMBER 3, 2023

Generalisation and reliability of deep learning for digital dathology in a clinical setting

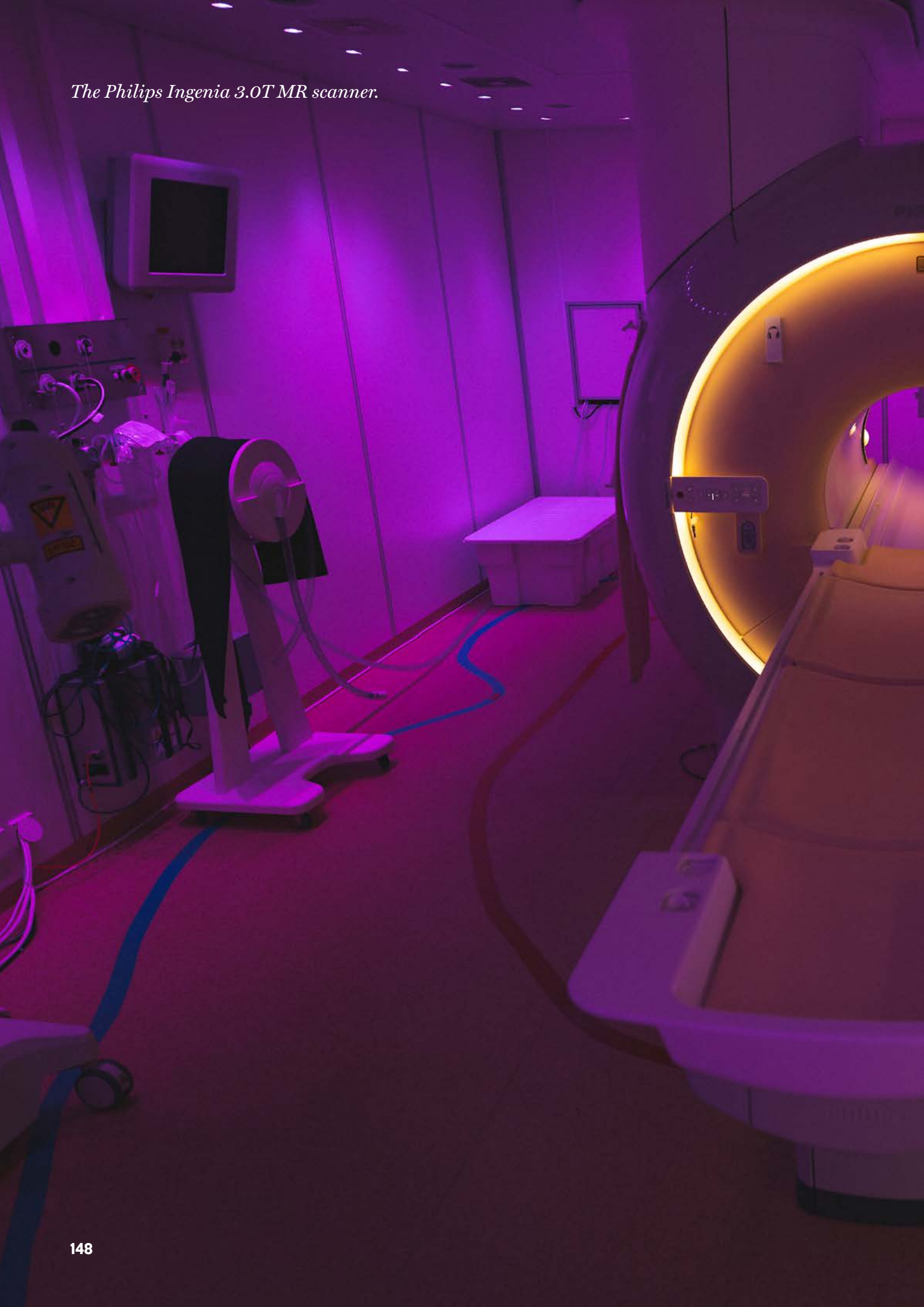
Imagine a future where pathologists can rely on AI to detect breast cancer metastases and grade prostate cancer, streamlining routine tasks and potentially saving lives. Unfortunately, the journey to widespread adoption of DL in pathology labs has been slow, facing hurdles that demand innovative solutions. A major obstacle is the variability in deep learning (DL), a type of AI model, performance across different medical centers, patient subgroups, and even within the same center over time. A seemingly simple fix of collecting more data and retraining the algorithms often is not feasible due to associated costs and constraints of the regulatory approvals. Additionally, DL models often provide predictions without a measure of confidence, leaving users uncertain about their reliability. This thesis proposes several possible solutions to the presented generalisation and reliability problems of DL for digital pathology.

To tackle the issue of performance variations, an unsupervised approach to quantify expected changes in a model's performance between datasets is proposed. It may serve as a cost-effective and time-efficient initial validation step before deploying DL systems in clinical practice. In addition, the reliability of DL algorithms may be enhanced substantially by identify out-of-distribution (OOD) samples that DL model should not be processing since it has not encountered such cases during the training. This is achieved by utilising generative model called Generative Adversarial Networks (GANs).

The thesis also dives into uncertainty estimation, a crucial element in bolstering the overall performance and reliability of DL systems. Various uncertainty estimation approaches are evaluated to identify the most suitable for digital pathology application. Another study investigates the benefits of spatial uncertainty aggregation, showing its potential in boosting tumor segmentation performance. By evaluating the detection of false negatives, this approach could potentially reduce the risk of missing crucial tumor cells. Finally, the importance of close collaboration between researchers, pathologists, and DL vendors for developing and bringing the most valuable AI systems to pathology labs is emphasised.

In conclusion, the thesis discusses multiple approaches that promise to aid the adoption of DL systems in clinical practice, addressing issues of reliability, generalisability, and clinical needs. With these innovative solutions, we can envision a future where pathologists gain access to trustworthy AI tools, empowered to make more accurate and timely diagnoses.

Milda Pocevičiūtė at the defense of her thesis in Wranne theatre at CMIV. Senior Lecturer Mattias Rantalainen from KTH, Associate Professor Oleg Sysoev from LiU, and the opponent Professor Nasir Rajpoot from Warwick University.



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.

The 4K projector room.

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.

Postdocs participating at the CMIV Retreat: Bente Konst, Lee Jollans and Muhammad Usman Akbar.

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.

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PhD students Ann-Sofi Björkman, André Da Luz Moreira and Marcelo Pereira Martins during one of the team building activities at the CMIV Retreat.

Publications

The CMIV research efforts lead to a steady stream of scientific publications. An overview of the 2023 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, 2019-2023

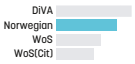
The analysis is based on sources [1]–[4], listed below. Different sources are used for different parts of the analysis. A criterion for inclusion is that publications have been registered in DiVA for the time period covered in the analysis. Publication types that are included in the analysis are:

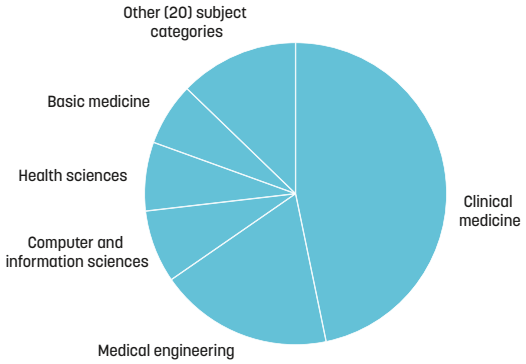
- Refereed journal articles and reviews
- Scholarly book chapters
- Scholarly books
- Refereed conference publications

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

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

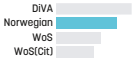
2. Subject categories, 2019-2023





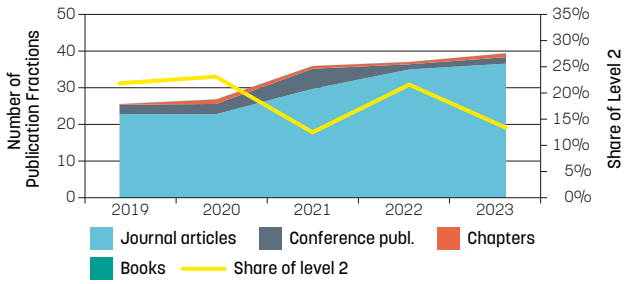
Displayed subject categories are those registered with each publication in DiVA, and are based on Standard för svensk indelning av forskningsämnen 2011 (Swedish Research Subject Standard 2011), updated 2016, SCB/UKÄ. In the compilation, subject categories at the three-digit level have been used.

3.a Norwegian model, 2019-2023

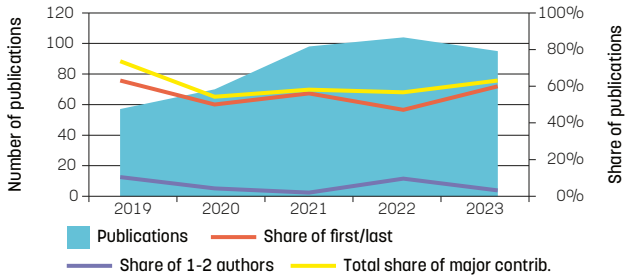


Publications published in journals and by publishers in the Norwegian list	Number of publications	Number of publication fractions	Share of level 2
Journal articles	388	146.3	20 %
Conference publications	27	13.9	0 %
Chapters	9	3.6	5 %
Books	0	0.0	0 %

Share of level 2, total: 18 %



3.b Author position, 2019-2023

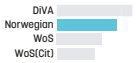


Publication fraction refers to the share of a publication originating from the department. For example, if two out of four authors are affiliated with the department, the fraction is 0.5.

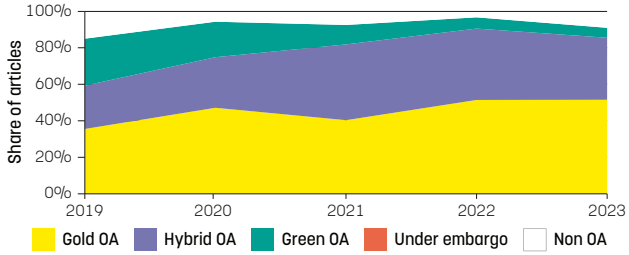
In the Norwegian model, the included publication channels are divided into two levels – 1 (scientific) and 2 (scientific and leading in its field of research). Level 2 publication channels comprise a maximum of 20 percent of channels in their research field.

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.

4. Open access, 2019-2023

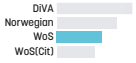


Share of open access publications (incl. OA after an embargo period):	
Journal articles	92 %
Conference publications	37 %
Chapters	22 %



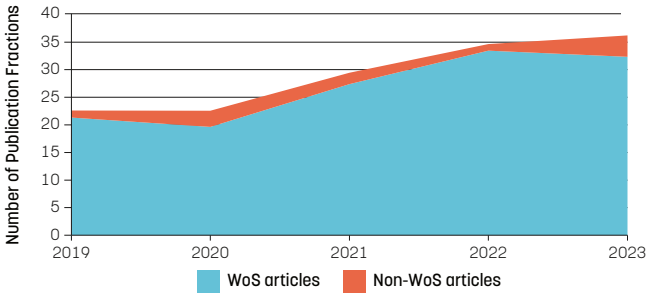
Open Access (OA) publications have been identified with the help of data from Unpaywall (unpaywall.org). The diagram shows articles according to Open Access type. OA data for articles has been supplemented with data from our own customized algorithm. Gold Open Access is defined as articles published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

5. Coverage in Web of Science, 2018-2022



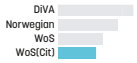
	Number of publications	Number of publication fractions
Journal articles and conference publications *	383	145
Coverage		
Journal articles: 92 %		
Conference publications: 73 %		

*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.

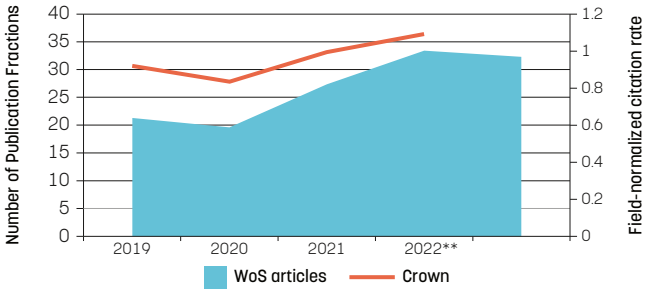
6. Citation analysis, 2019-2023



	Number of publications	Number of publication fractions
Journal articles *	271	99.6

Results, field-normalized

Field-normalized citation rate (crown): 0.98
Share of highly cited articles (top 10 %): 10 %
Share of uncited articles: 18 %
Number of articles in Q1-journals (2019-2023): 157
Share of articles in Q1-journals (2019-2023): 45 %

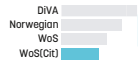


When publication fractions are less than 10, the citation indicators are not displayed. If the basis is small, individual items can have a high impact on averages.The indicators have been calculated with a modified method for normalization. The normalization is now done on publication level, in previous analyses it was done on journal level

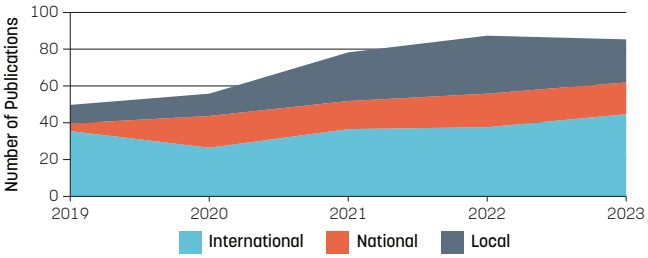
- Field-normalized citation rate (Crown): a measure of impact of articles included in the analysis that provides acomparison with the international average for the same subject area, year and type of article, where 1 is the globalaverage. Field normalized rate of citation is fractionalized, i.e. the 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. The calculation of top 10% has been changed according to e.g. the method used by VR. Now top 10% is based only on the share of thepublication which is top 10%, which generally results in lower values compared to the previous method. As a result ofthis the value of the indicators can be difficult to compare with equivalent values in previous analyses.
- Share of uncited articles: indicates how citations are distributed, i.e. if citations are evenly distributed amongarticles, or if a small number of articles account for the majority of citations.
- Quartile ranking of journals based on Journal Impact Factors (JIF) ranking within a subject category in Web ofScience. Q1 includes journals with a JIF within the top 25% in at least one subject category.

The citation rate for newer articles is generally low, leading to individual items causing high impact on the average rate.

7. Co-authorship - geographical, 2019-2023

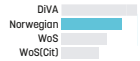


Share of articles with international co-authorship	51 %
Share of articles with national co-authorship	20 %
Share of articles with local co-authorship	29 %



Share of publications in WoS where department authors have co-authored with international, national or localcollaborators (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.

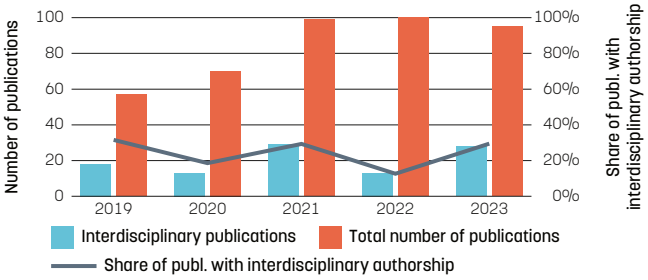
8. Interdisciplinary authorship, 2019-2023



Publications with interdisciplinary authorship*

Number	101
Share	24 %

*Publications with authors from more than one faculty



9. Altmetrics

	Scientific blogs	News media	Patents	Policy documents	Open syllabi	Twitter	YouTube	Wikipedia
Number of referenced publ.	21	43	8	1	0	305	2	3
Share of referenced publ.	5 %	10 %	2 %	0 %	0 %	69 %	0 %	1 %
Total number of references	38	445	9	1	0	3600	2	3

The analysis is based on publications in DiVA in 2019-2023 with a digital object identifier (DOI) or an ISBN. 96 % of publications have any of these identifiers.

Alternative metrics (or altmetrics) is a new way of measuring the impact of scholarly publications and shows the dissemination and impact of publications in social media and other channels.

The company Altmetric has developed tools to identify references to research publications in online channels, such as social media (blogs, Twitter, Facebook, discussion forums etc.), news media, patent databases etc. See www.altmetric.com for further information regarding methods and content.

Some publications can share identifiers (such as ISBN for individual chapters published in the same book). In such cases, all references to each publication are included.

Publications 2023

CMIV affiliated researchers are written in bold.

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LÄNK-B

Frida Dohlmar, Anna Ljusberg, Shan Cai and Anders Tisell.

Annual accounts

In 2023, CMIV achieved a turnover exceeding 58 million SEK. However, the financial result for CMIV in 2023 amounted to a deficit of SEK -310 thousand.

Throughout the fiscal year 2023, CMIV was actively involved in various grant-funded research projects. The AIDA – Analytic Imaging Diagnostics Arena, supported by VINNOVA, continued its operations. Six projects, funded by AIDA, along with three clinical fellowship and two clinical evaluation projects, commenced during the year.

SciLifeLab extended its funding for the AIDA data hub in 2023. Ongoing research projects such as SCAPIS, SCAPIS2 (Swedish Heart-Lung Foundation), and MeDigiT (Visual Sweden) continued their work.

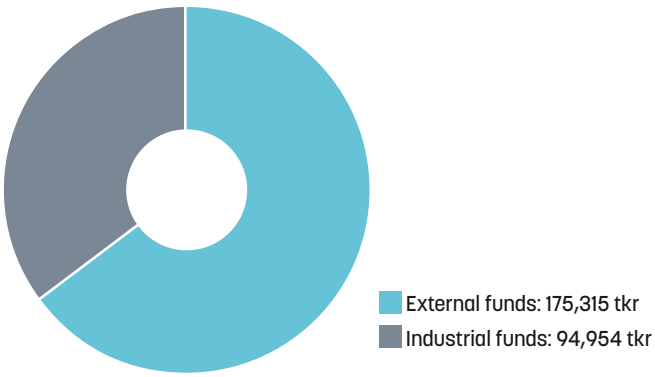
The EUCAIM project, funded by the Digital Europe Programme and VINNOVA, initiated in 2023, and the EU Horizon 2020-funded project Bigpicture sustained its progress. Additionally, the project "Incubator for national AI validation platforms in diagnostic imaging (VAI-x)" persisted with funding from VINNOVA.

Both the Faculty of Medicine and Health Sciences and the Faculty of Science and Engineering continued their support for CMIV's endeavors in the Digital Pathology area.

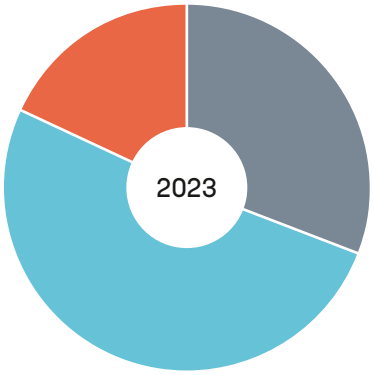
ECONOMIC SUMMARY	2019	2020	2021	2022	2023
Total revenue	**56,266**	**55,007**	**57,384**	**58,794**	**58,306**
EXPENSES					
Staff expenses	-20,390	-22,480	-23,660	-23,907	-23,973
Cost of premises	-5,752	-6,647	-6,474	-6,372	-6,727
Misc. Operating expenses	-18,848	-17,928	-19,551	-20,489	-22,667
Depreciation expenses	-8,440	-7,848	-6,878	-6,897	-4,564
Financial expenses	-126	-11	-4	-10	-685
Total expenses	**-53,556**	**-54,913**	**-56,568**	**-57,675**	**-58,616**
Result of operations	**2,710**	**95**	**815**	**1,119**	**-310**

Research funding at CMIV 2010-2023

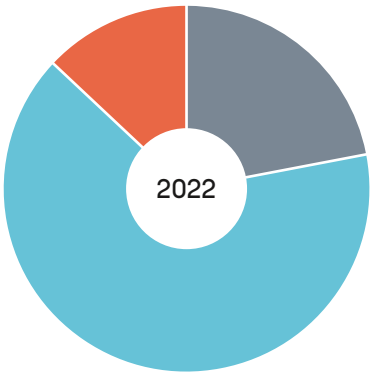
CMIV receives funding from research funds and the industry both directly to the R&D platform and to specific research projects. In addition, the affiliated researchers have their own funding; these grants will, however, not be presented here.



CT Research and Clinic (%)

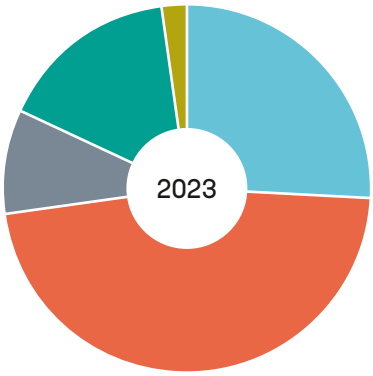


Research, 31
Clinic, 51
Special exams only at CMIV CT, 18

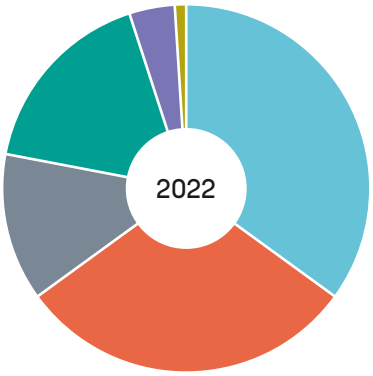


Research, 22
Clinic, 65
Special exams only at CMIV CT, 13

Distribution on Research on the MR Scanners (%)



Neuro, 26
Gastro, full body, 16
Musculoskeletal, 47
Pediatric, 2
Cardiovascular, 9



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


squash
circuito mineiro

CMIV PhD Students Racing Towards Bold New Frontiers in Science!

André Da Luz Moreira, Anders Tisell, Frida Dohlmar, Gustav Magnusson, Kajsa Tunedal, Anna Ljusberg, Ann-Sofi Björkman, Iulian Emil Tampu and Twan Bakker.

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