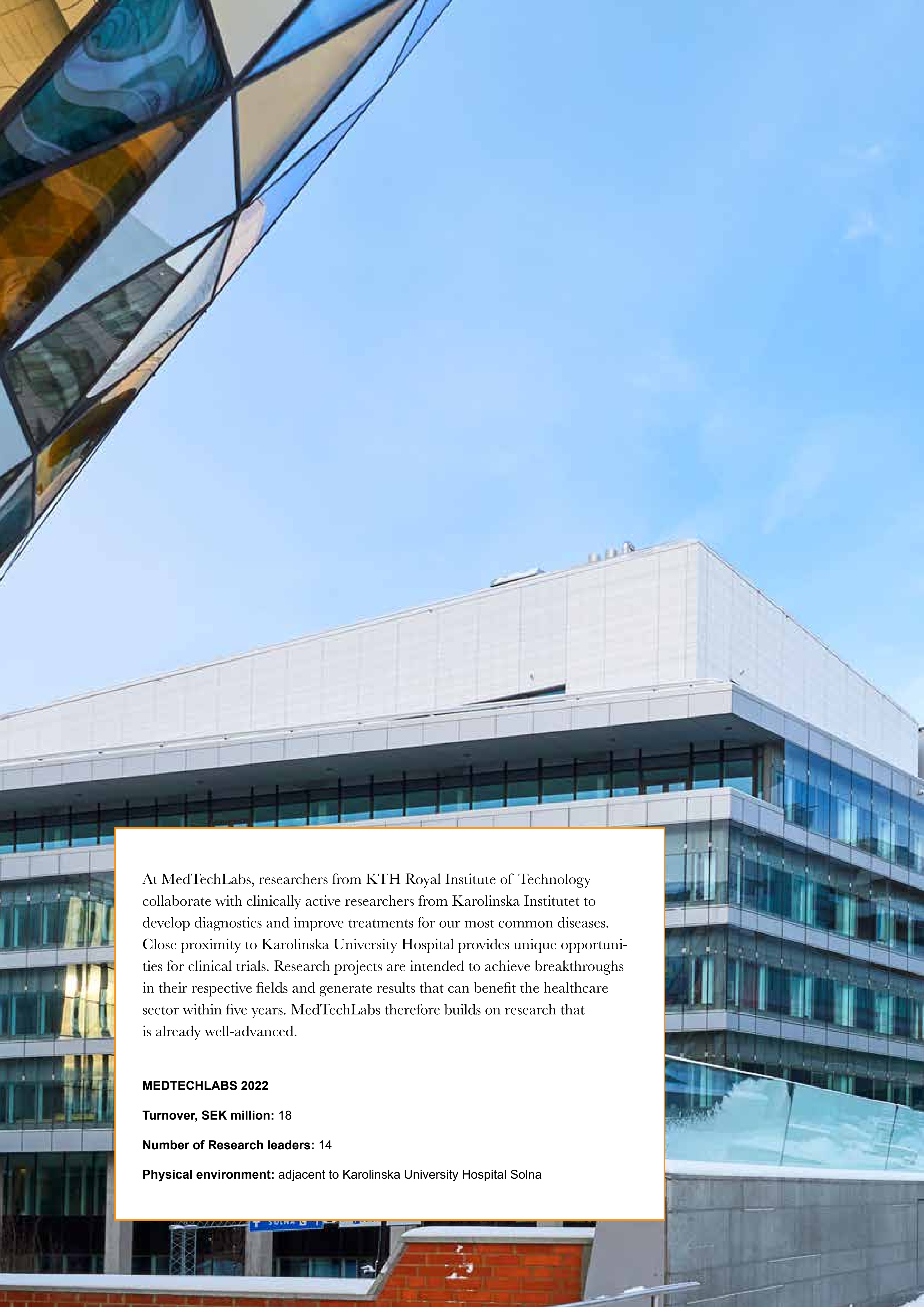
With focus on our most common diseases

ANNUAL REPORT 2022

MedTechLabs | Karolinska Institutet | KTH | Region Stockholm



At MedTechLabs, researchers from KTH Royal Institute of Technology collaborate with clinically active researchers from Karolinska Institutet to develop diagnostics and improve treatments for our most common diseases. Close proximity to Karolinska University Hospital provides unique opportunities for clinical trials. Research projects are intended to achieve breakthroughs in their respective fields and generate results that can benefit the healthcare sector within five years. MedTechLabs therefore builds on research that is already well-advanced.

MEDTECHLABS 2022

Turnover, SEK million: 18

Number of Research leaders: 14

Physical environment: adjacent to Karolinska University Hospital Solna

CONTENTS

"Swedish innovations such as the pacemaker, the Gamma Knife, the ultrasound and the Seldinger technique were all developed to meet the needs of healthcare. MedTechLabs manages and develops our proud heritage of innovation."

Johan Schuber

Johan Schuber, Executive Director

Håkan Sandberg, Communication Officer

MedTechLabs is an interdisciplinary centre for medical technology research that carries on this proud legacy to create better conditions for patient survival and improved quality of life for those with cancer, cardiovascular and other non-communicable diseases. We create the conditions for healthcare to offer patients much more secure diagnoses and better treatment, at a lower cost.

The centre is a long-term investment initiated in 2018 and managed by KTH, Karolinska Institutet and Region Stockholm with the intention of contributing to the development of medical technology from a national and international perspective. New knowledge and implementable solutions also contribute to the development of the Stockholm region's life science ecosystem, making the region an attractive investment for global companies. The centre's research programmes are intended to achieve breakthroughs in their respective fields and generate results that can benefit the healthcare sector within five years. The programmes therefore build on research that is already well-advanced.

The hallmarks of MedTechLabs should be quality, excellence and innovation. Our wish is to attract the best researchers who want to collaborate on translational research. The fact that our research takes the needs of the healthcare sector as its point of departure provides Region Stockholm with excellent conditions for offering the very best care to tomorrow's patients.

Clara Hellner, Director of Research and Innovation at Region Stockholm, and Chair of MedTechLabs Board.

GOALS, WAYS OF WORKING AND GOVERNANCE

GOALS

1. To become among the top 10 interdisciplinary centres worldwide for medical technology research where we develop instruments and methods that will benefit large patient groups.
2. To provide a stimulating environment and seed funding for creating new interdisciplinary research projects attracting significant external financial support from national and European funding agencies, philanthropists and private foundations.
3. To establish MedTechLabs as a facilitator combining research and medical technology trials, by providing a holistic process for how clinical studies can be conducted attracting both researchers and global companies.
4. To enable high-impact technology transfer for implementation in healthcare, demonstrated through start-up companies, patents, industrial collaborations, events, and online education.

WAYS OF WORKING

MedTechLabs consists of an infrastructure for translational research, an educational part for rapid implementation of research results in healthcare and the research areas: Imaging and minimally invasive methods, Artificial intelligence in healthcare and Bioelectronic medicine. Each research area has one or more research programs with five-year funding. Research projects that have funding other than from MedTechLabs can also apply for affiliation and thus benefit from networking, visibility and facilitation.

We work systematically to create conditions for new constellations through, among other things, an annual research day - MedtechLabs Research Day – as well as recurring network-building activities.

One prerequisite for research results to achieve their potential for implementation in healthcare is that it is easy to conduct translational research, all the way from initial experiments on animals to human clinical studies. And then, that the technique is verified with clinical trials. The collaboration at MedTechLabs provides excellent opportunities to achieve this.

Niclas Roxhed, Director, Associate Professor at Division for Micro and Nanosystems, KTH.

GOVERNANCE

Board: Clara Hellner, Region Stockholm, Martin Bergö, KI, Amelie Eriksson Karlström, KTH, Helena Erlandsson Harris, KI, David Konrad, Karolinska Universitetssjukhuset, Linda Lindskog, Karolinska Universitetssjukhuset, Peter Savolainen, KTH, Birgitta Janerot Sjöberg, Karolinska universitetssjukhuset.

Management: Niclas Roxhed, KTH, Staffan Holmin, KI, Lena Lewin, KI, Elisabet Rendahl, Region Stockholm, Johan Schuber, KTH.

Patient Council : Barbro Wong, Rheumatism Association Stockholm, Elisabet Schesny, Swedish Breast Cancer Association, Sara Norman, Swedish Kidney Association and Lennart Håwestam, Stockholm Disability Rights Federation, Stockholm Stroke Association.

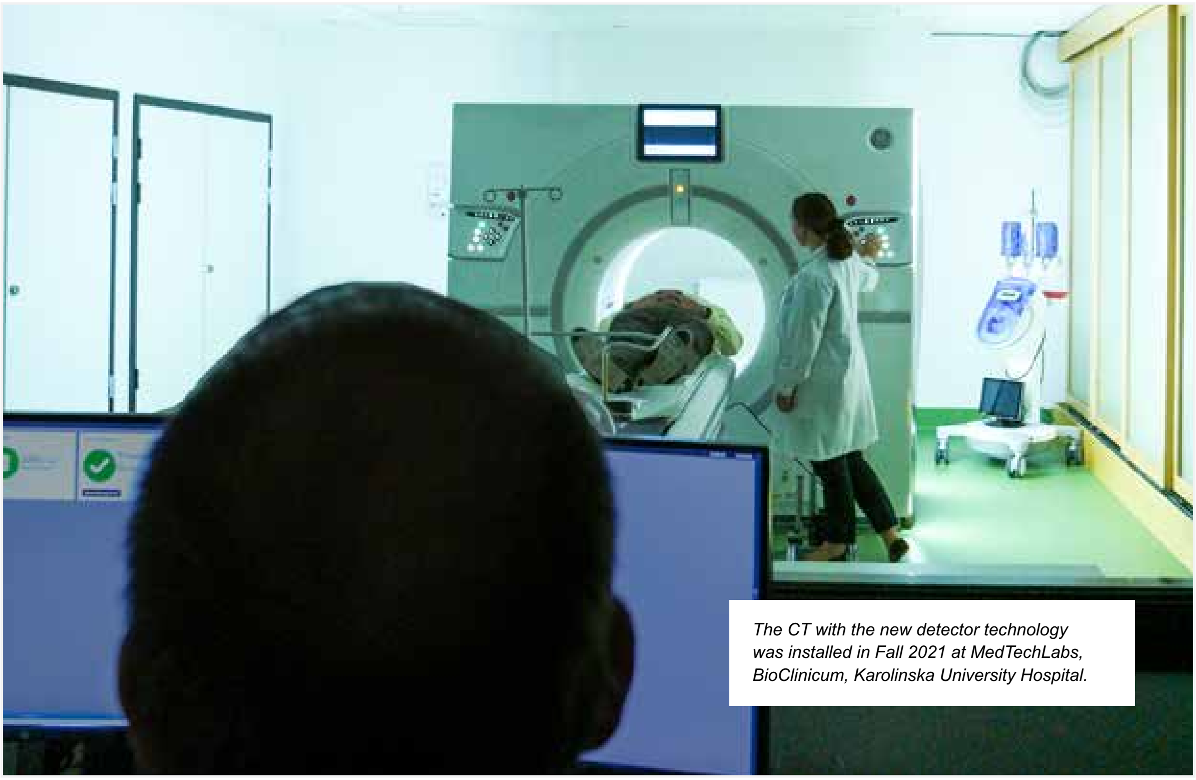
INFRASTRUCTURE FOR TRANSLATIONAL RESEARCH

COMPUTED TOMOGRAPHY LABORATORY (CT LAB) IN BIOCLINICUM

MedTechLab's infrastructure in BioClinicum is part of Karolinska University Hospital. Companies can hire to test and develop prototypes in early product development in a fully equipped hospital environment where clinical studies are an important part of the development process of a new technology. MedTechLab's model creates the opportunity for the company's development engineers to work with the prototype on site. We also offer office spaces to collaboration partners as well as opportunities to demonstrate technology and results. MedTechLabs hosts workshops and other important events, which are needed to achieve the best project results. Cooperation with industry takes place in project form.

Photon-counting detector technology for CT (PCCT)

In 1979, Godfrey Hounsfield and Allan Cormack received the Nobel Prize for their work with CT technology, which today has become one of the most common routine examinations worldwide.



The CT with the new detector technology was installed in Fall 2021 at MedTechLabs, BioClinicum, Karolinska University Hospital.

"The CT technology that became available during the 1970s opened up a whole new world for us doctors. This, the next stage in development, offers unbounded possibilities. Here at Karolinska University Hospital, in various ways we treat over one million patients every year. Our aim is that the hospital should constantly progress and provide better care and treatment and I believe that we have demonstrated that we can do so. The fact that we are now the first in the world with this new technology also affirms both that Karolinska Institutet is ranked among the best environments for clinical research in the world, and that Karolinska University Hospital is advancing as one of the best hospitals in the world. Our machinery and its relationship to how we work as Europe's smartest hospital means that we must constantly move forwards. To do so together with others is a success factor, and the CT laboratory is an excellent example of this. The strength in working together has been made particularly apparent during the pandemic. It means a great deal to the hospital and the hospital's patients that clinical studies are now underway to ensure that the next generation of computed tomography benefits patients and the health service.

Speech by **Björn Zoëga,** CEO Karolinska University Hospital, at the inauguration of the CT lab in 2021.

Clinical studies

In 2021, a clinical study began on behalf of GE Healthcare to verify the new PCCT technology.

– We are the first in the world to test this technology, which we are very proud of. The international competition from the best universities is tough and many were interested in conducting the study. The pilot study will be followed by another clinical trials with greater number of participants and further optimization of the image quality before the technology can be introduced in healthcare, says Staffan Holmin, clinical trial leader at Karolinska University Hospital. The technology has a wide range of application areas where several different organ systems can be imaged. In the study we compare the images from the participants' surveys with images taken with standard CT´s. The study also provides a larger image material that is used for further image processing optimization.

IMPLEMENTATION

ACUTE STROKE TREATMENT WITHIN 24 HOURS – DECISION SUPPORT WITH PERFUSION

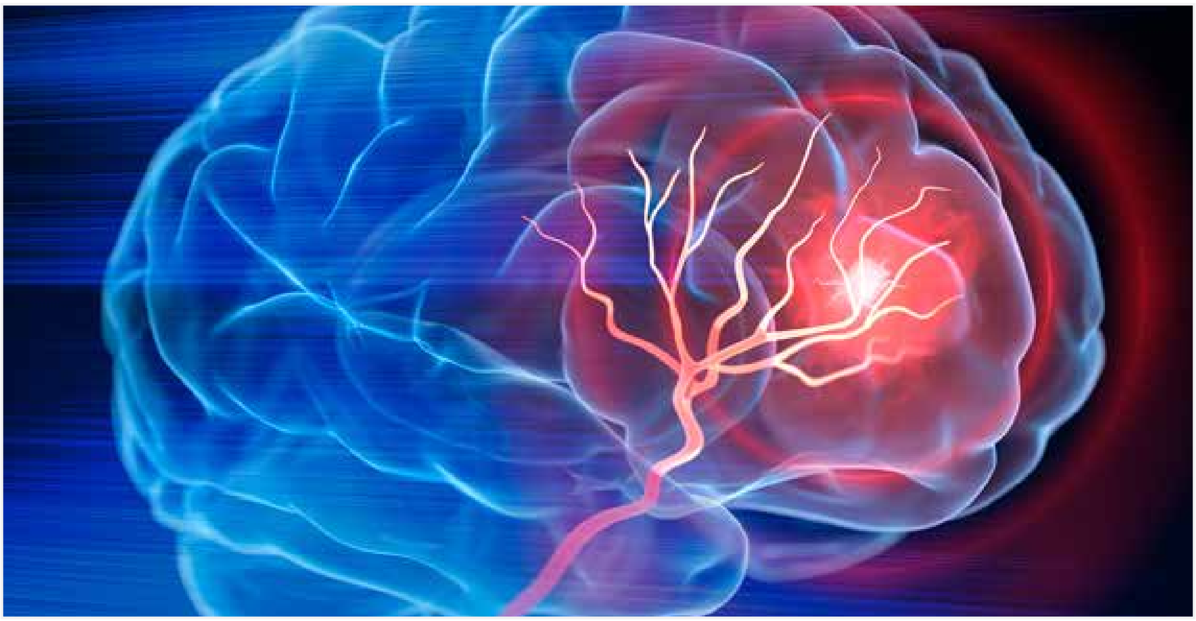
The aim of this on-line training is to inform and educate about the value of perfusion in the investigation of stroke up to 24 hours from onset after several studies were published in 2018. This will put a strong focus on rapid clinical management and advanced neuroradiology of acute stroke even by those who wake up with a stroke or are searched late. The training should lead to cost-effective and rapid dissemination of new verified methods for treatment and diagnosis.

In the late 1990s, several studies were conducted on the value of intravenous thrombolysis as a clot-dissolving treatment. The EU required treatment to be conditional on a safety study, which led to an observational study in 2002 - 2006 that proved it was a safe treatment in the time window within 3 hours of illness. In 2008, the time window was extended to 4.5 hours. In 2015, evidence finally came for the value of intra-arterial treatment with thrombectomy, with verified large-vessel occlusion, for up to 6-12 hours from onset of illness. In autumn 2017, a central triage system for patients with severe stroke started at Karolinska Solna. In 2018, the value of late thrombectomy came based on the selection based on a so-called mismatch based on perfusion.

The work model has led to that employees at Karolinska University Hospital are able to provide patients with acute stroke with refined diagnostics and better treatment than before. Knowledge of these methods and techniques is now effectively spread to other hospitals within the Stockholm region, through MedTechLab's developed online training "Acute stroke treatment within 24 hours – decision support with perfusion"

The training is made up of text with information, questions and short films (1-12 min long) and is available 24/7. The idea is that when you have time, you can do a small part at a time in about 15-30 minutes out of a total of about 4 hours. The training is aimed at ST doctors in radiology, X-ray nurses and other healthcare personnel in the management of acute stroke. It aims to provide knowledge about how the care chain and investigation with perfusion should be done in order to provide the patient with care based on the latest evidence.

The training is available on Region Stockholm's training portal Lärtorget.



RESEARCH PROGRAMS

SPECTRAL CT-IMAGING AND ENDOVASCULAR TECHNIQUES

MedTechLab's first program started in 2018 and is based on the world-leading X-ray technology developed at KTH and top-notch research in the field of endovascular techniques. The work to refine and implement the new x-ray technology in healthcare requires both research and development and constitutes a significant part of the research program. This includes both issues around pattern recognition (AI) and data management, as well as what type of visual information the radiologist needs when assessing disease states for various parts of the body.

"researchers from KTH and Karolinska Institutet can study patients in a hospital environment with the capacity for advanced care when required."

Higher image resolution and lower doses of radiation provide healthcare with many benefits when diagnosing and treating. It makes it easier to distinguish between different tissues and materials. Early-stage tumours and inflammatory conditions will become easier to detect. Greater detail may make it possible to avoid invasive procedures and we hope to be able to more effectively diagnose strokes in the cerebellum and brain stem. This is the underlying strategy of MedTechLabs, where researchers from KTH and Karolinska Institutet can study patients in a hospital environment with the capacity for advanced care when required.

Endovascular techniques, which uses X-rays to navigate inside the body's vessels in order to, for example, extract blood clots or treat vasoconstriction. The technology also makes it possible to take samples and inject or deposit drugs locally in organs that are otherwise difficult to reach. It is also possible to use these techniques to diagnose and treat cancer and cardiovascular diseases, including strokes. The program will contribute to Stockholm becoming a node for the development of next-generation technology for photon-counting computed tomography to the benefit of millions of patients worldwide.

FACTS

Funding 2019 - 2023: 35 MSEK

Program Directors:

Mats Danielsson, Professor of Medical Imaging at KTH

Staffan Holmin, Professor of clinical neuroimaging at Karolinska Institutet, Consultant neuroradiologist at Karolinska University Hospital

BREAST CANCER IMAGING POWERED BY ARTIFICIAL INTELLIGENCE DIAGNOSTICS

The main objective of the program is to develop and test AI-based models for radiological and histopathological image analysis. The research program contributes to faster and better diagnosis and thus the possibility of detecting cancer earlier in the course of the disease and curing more patients. Thanks to Sweden's unique access to comprehensive and quality-assured patient data, the program can use decoded data (images and samples) from all patients diagnosed with breast cancer through mammography in the Stockholm region between the years 2005 and 2019.

Radiological image analysis

Within the sub-area of radiological image analysis, two clinical studies are ongoing since 2021. The first study, ScreenTrust MRI, is performed at Karolinska University Hospital with magnetic resonance imaging (MRI). There, a commercial AI model is combined with two in-house developed models to select a group of women who, after an unobjectionable screening mammography, are offered to supplement with a magnetic camera. The goal is to minimize the percentage of undetected cancer. The second study, ScreenTrust CAD, is performed at Capio St Göran Hospital using the best commercial AI model. We want to investigate the possibility of supplementing or replacing one of the two radiologists who review each screening mammogram.

The goal is to develop computational methods that automatically analyze and understand images of biological processes, using microscopic images as the primary source of information. We use methods from machine learning, statistics and bioinformatics to quantify image data. The methods we develop must be scalable in order to handle very large data sets.

Pathological examination

Through careful analysis by a pathologist, a breast cancer can be divided into three groups; grade 1 with the lowest aggressiveness, grade 3 with the highest aggressiveness and grade 2 as a gray area in between. Patients with grade 3 tumors often benefit from adjunctive chemotherapy. We have created an AI model that can detect cancer in the images and stratify tumors of intermediate grade (NHG2) into high or low grade. In the program, an own AI model is developed that will serve as decision support for the pathologist. Today there is great variation in the assessments of images because pathologists assess differently. An AI must be able to find information in the images that we humans cannot detect. This will lead to more patients receiving a clearer diagnosis and thus the right treatment.

We have developed a system for breast cancer detection and grading (submitted manuscript) based on AI image analysis. We have created digital histopathology images by digitizing microscope slides from the hospital archives in Stockholm. All images undergo rigorous quality assurance, processing and normalization. This constitutes a clinically important task that can contribute to reduced gray areas and to identify patients who need additional treatment with chemotherapy after surgery.

FACTS

Funding 2019 - 2023: 20 MSEK

Program Directors:

Johan Hartman, Professor of Pathology at Karolinska Institutet, Pathologist at Södersjukhuset

Kevin Smith, Associate professor in Computer vision and Biomedical image analysis, KTH

BIOELECTRONIC MEDICINE

Inflammatory diseases cause a great deal of suffering for patients all over the world, as well as creating challenges for healthcare. Stimulation of the vagus nerve may be the anti-inflammatory treatment of the future.

The focus of the programme is on being able to monitor and stimulate the vital vagus nerve with short electrical pulses in order to treat inflammatory diseases in a targeted manner. This is the first programme in the world to clinically implement bioelectronic medicine to treat inflammatory diseases at the point of care. Beginning in January 2020, this interdisciplinary collaboration brings together physicians, immunologists, engineers and mathematicians. Research is primarily focused on studying how signals are transmitted between nerves and immune cells at a molecular level and which parts of the long vagus nerve communicate with the immune system, because, even if clinical data is available to demonstrate the potential of the method.

Bioelectronic medicine could reduce the use of anti-inflammatory drugs and also direct the treatment directly to the part of the body where the inflammation is located.

New technology for minimally invasive nerve stimulation

There is currently no atlas of the neurophysiology of inflammation regulation – something that is needed if we are to study these mechanisms in detail, understand them and, eventually, target treatment with more precision. We are developing a method for wirelessly activating specific, small peripheral nerves in experimental inflammation and creating an atlas of the functional anatomy of neuroinflammation.

Automated inflammation intensity monitoring

By analysing large amounts of data from the vagus nerve during experimental inflammation, we can identify signal patterns representing inflammation intensity. The aim is to create a lexicon of signal patterns from which to extract detailed information on inflammation. We use data available in the literature, as well as our own data, to develop methods in the field of machine learning, based on autoencoders and clustering, in order to identify nerve signals that can be linked to cytokines. Proinflammatory cytokines are produced by the immune system and secreted in the event of injury, stress or inflammation. Although results demonstrate that the new technologies are effective at identifying relevant signal types, especially tumour necrosis factor (TNF), there are also considerable variations between recordings. It is therefore very important that controlled experiments with improved signal quality are conducted.

Longitudinal patient monitoring

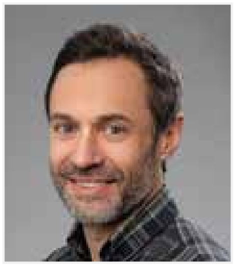
Clinical data, measurements and patients' own reports are collected longitudinally over the course of inflammatory bowel disease. We plan to use mathematical modelling to attempt to predict the course of inflammation. We anticipate that, through improved prognostication of relapses in inflammatory diseases, we will be able to optimise treatment, alleviate symptoms and shorten the episodes of the disease.

FACTS

Funding 2019 – 2023: 15 MSEK

Program Directors:

Peder Olofsson, Head of Division of Cardiovascular Medicine, Department of Medicine at Karolinska Institutet



Henrik Hult, Professor in Mathematical Statistics at KTH

OPTICAL 3D-MICROSKOPY FOR MORE EFFECTIVE DIAGNOSIS OF KIDNEY DISEASES

Chronic kidney disease is a growing global threat to public health. About 10% of the world's population is affected, but in the elderly and people with high blood pressure, cardiovascular disease and diabetes, over 35% are affected. The proportion of people who die from chronic kidney diseases is expected to increase in the coming years, unless more countries invest in preventive measures and early treatment. With an early diagnosis of the development of kidney disease, one can stop or reverse the course of the disease, and prevent costly kidney dialysis or kidney transplantation.

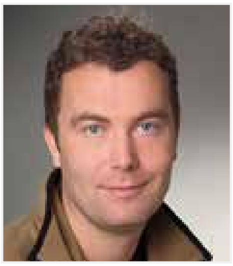
Our method will deliver both 2D and 3D images of kidney biopsies and through image analysis ('machine learning', 'deep-learning', AI) we intend to develop support for more efficient diagnosis and earlier detection of common kidney diseases. Automatic image analysis of morphological changes in the kidney will provide a faster, safer and quantitatively improved analysis of the development of kidney diseases. Through 3D microscopy, the filter structures of the kidney can be visualized with light microscopy. It enables a simple automatic analysis and quantification of the health status of the kidney. Introduction of super-resolution optical pathology will make it possible to replace today's electron microscopy analysis, which takes place in extremely thin layers, to 3-D morphologically follow the development of kidney diseases in situ.

The project is a collaboration between pioneers in super-resolution optical microscopy at KTH and clinical kidney researchers at Karolinska University Hospital and Danderyd Hospital.

FACTS

Affiliation to MedTechLabs from 2021, other funding

Program Directors:



Hans Blom, Docent in Biophysics at KTH

Sigrid Lundberg, Research leader at Department of Nephrology, Karolinska Institutet, Consultant, Kidney Medicine, Danderyd University Hospital

IMPACT

The analyzes carried out since 2020 show that MedTechLab's research leaders are world class. Our goal, that the research should be useful in healthcare already within five years, gives us reason to work systematically so that the ecosystem with education, innovative startups and industrial collaborations works well.

For academic research, two main aspects of impact are relevant: the scientific impact, the impact of our work in terms of citations and similar accepted indicators, and the societal benefit, i.e. the extent to which the scientific results are brought to health care, through training and patents that can lead to new products and services. Analyzes of research quality and impact for research leaders associated with MedTechLabs show high values that stand up well in international competition. The innovation analysis from 2020 of patents that can have a technical and economic impact, shows a high probability that the patents will be important for the healthcare system's opportunities to develop diagnostics and better treatments for our most common diseases. Overall, the analyzes show that MedTechLabs has succeeded well in attracting excellent researchers who are motivated by the fact that their research will benefit healthcare and patients. The researchers are doing well in the international competition and the relative value is increasing at all levels.

MONITORING THE QUALITY AND IMPACT OF RESEARCH

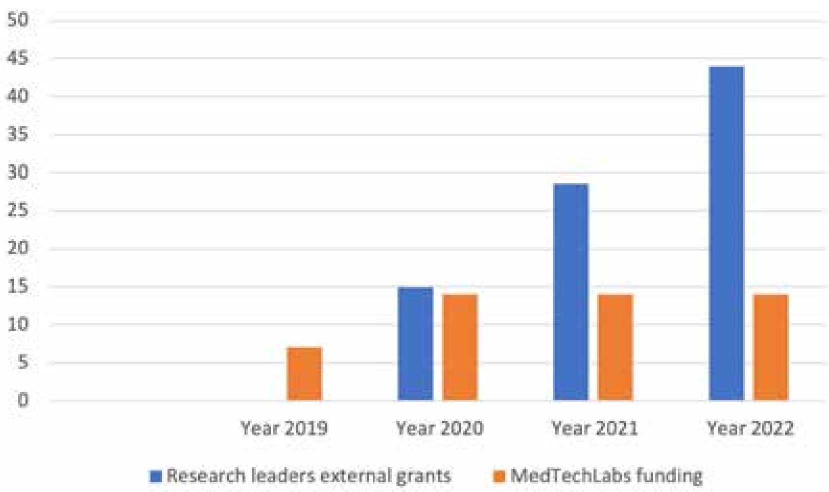


Figure 1: *The external funding raised by MedTechLab's research leaders has increased from SEK 14.9 million in 2020 to SEK 44 million in 2022. That is an exchange of more than 3:1 of the funding from MedTechLabs (SEK 14 million for 2022)*

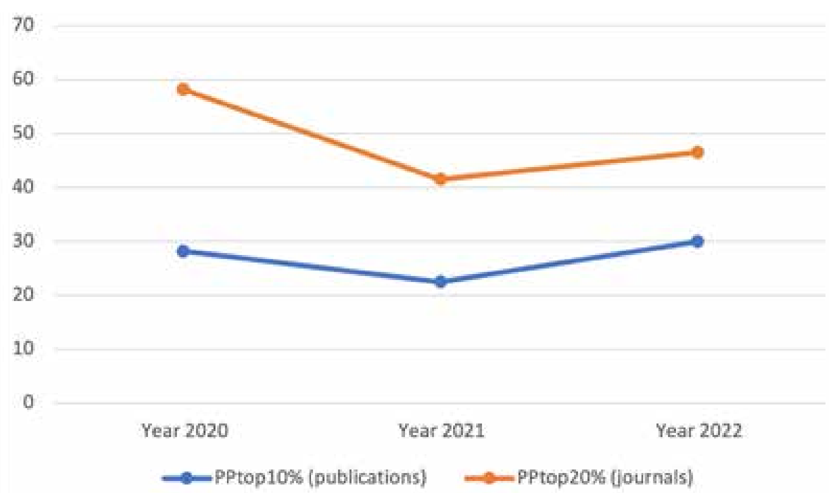
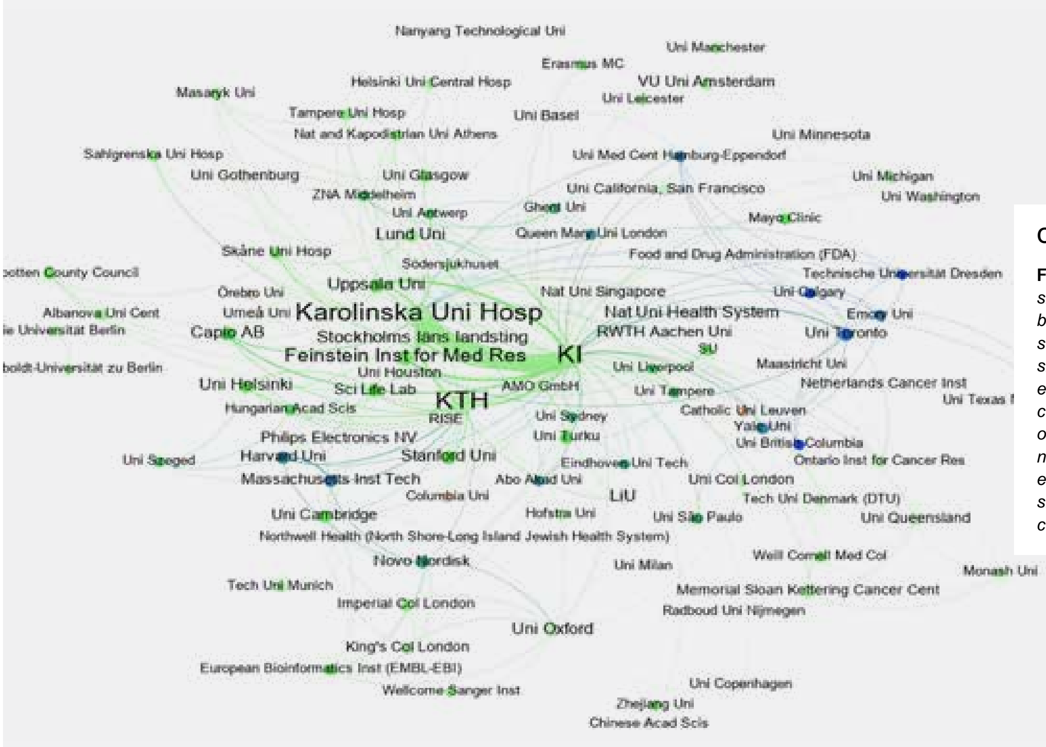


Figure 2: *Figure 2 MedTechLab's research has an excellent scientific impact. The number of (peer-reviewed) publications since the start of the center is indicated, both per year and cumulatively, together with distribution percentages. PPtop10% indicates the percentage of publications as the 10% most cited publications in a WoS category, compared to publications in the same category and year. Self-citations are excluded. Only articles and reviews are considered. PPtop20% indicates the share of publications in the 20% most cited journals in a WoS category, compared to publications in the same category and year. Only articles and reviews are considered. The swings are due to a few extremely impactful papers.*



Collaboration between institutions

Figure 3: *A collaborative analysis that shows how scientific work has been cited between different actors, which means both scientific and societal impact. The figure shows organizations (nodes) with at least eight articles and linked by at least three co-authors. Publications with more than 25 organizations are excluded. The size of the nodes indicates the number of papers in each organization and the size of the lines shows the extent to which the organization collaborates. Analysis by KTH Library.*

In 2022, we generated 31 papers. The proportion of publications accepted into the most prestigious (top 20%) journals was 46.5 percent. The field-standardized citation rate, Cf, reflects an article's citation rate compared to the citation rate of comparable publications, i.e. publications of the same document type, from the same year and within the same subject. For all articles by the research leaders associated with MedTechLabs. The Cf amounted to 2,22 in 2020. Share of publications that, compared to other publications in the same field and in the same year, belong to the top 10% most often cited in 2020 was 30,2 percent. This result can be compared with the values of PP(top10%) and Cf that researchers at some of the top universities in the world produce, according to the CWTS Leidenrankingen for the years 2017-2020, see table.

Ranking based on the dissemination and impact of research results, sorted by Cf	PP(top10%) 2017-2020 Biomedical and health science	Cf 2017-2020 Biomedical and health sciences
MIT	31,6 %	2,54
MedTechLabs	30,2 %	2,22
University of Oxford	23,2 %	2,13
Stanford University	23,1 %	2,09
University of Cambridge	23,6 %	2,05
Harvard University	22,0 %	1,92
Johns Hopkins University	19,1 %	1,79
Karolinska Institutet	17,2 %	1,69
KTH	14,0 %	1,27

Definitions of bibliometric terms

Volyme: All types of documents published in Web of Science are counted (e.g. articles and reviews).

Scientific impact: PP (top 10%): Percentage of a university's publications that, compared with other publications in the same field and in the same year, belong to the top 10% most frequently cited.

Field normalised citation score (Cf): The average number of normalised citations of a publication. Cf > 1 means that a publication has been cited more often than the worldwide average for comparable publications; i.e., publications of the same document type, published in the same year and on the same subject.

Source: CWTS Leiden Ranking

INNOVATION ANALYSIS BASED ON PATENT INDICATORS

The analysis was executed 2020 by Cascelotte AB on behalf of MedTechLabs. It is based on data on patents granted to research leaders affiliated to one of the research programs.

The majority of applications and patent families originate from research leaders affiliated to the programme Spectral CT-imaging and Endovascular Techniques. The selection does not include any patent applications or patent families from research leaders affiliated to the programme Breast Cancer Imaging Powered by Artificial Intelligence Diagnostics. This is because the software and AIs are protected or commercialised through intellectual property rights other than patents. There is one patent family included for research leaders in the Bioelectronic Medicine programme.

Cascelotte's analysis results indicate that patent applications from MedTechLab researchers within the Spectral CT and Endovascular techniques program are on the same level as patent applications from the corresponding technology area at the Mayo Clinic, (CT Clinical Innovation Center) and at Johns Hopkins University (I-STAR Labs) – recognized world-leading research environments – with a significantly higher probability of technical and financial impact than the world average in the reference group medical technology and i3 Institute for Innovation in Imaging, Harvard University Boston USA.

According to the model, patent applications with a TBI value above 70 have a statistical probability of having an economic impact.

Research centre	Share of TBI > 70	Share of TBO > 90
Mayo	75 %	21 %
MedTechLabs	63 %	35 %
I-Star Labs	55 %	36 %
i3	32 %	16 %
SE1	39 %	18 %
WW1	26 %	9 %

Table 1. This table shows the percentage of patent applications with a TBI value above 70 and 90 respectively, and the average TBI value for all included research centres and for reference groups.

About the analysis

The analysis is based on 76 (67 unique) patent families in which research leaders affiliated to MedTechLabs are registered as inventor or applicant. A significantly higher percentage of applications from researchers affiliated to MedTechLabs have a Technology Business Index (TBI) value above 70.

In Table 1, all unique patent applications submitted after 2010 where the researcher is registered as an applicant and/or inventor have been included for each researcher. Patent applications where then grouped in the relevant research team.

Two reference groups have been included to make it easier to analyse the results. The reference groups consist of patent applications in the fields of medical technology, measuring instruments and pharmaceuticals during the period from 2010 onwards.

Reference groups:

SE1: All Swedish patent applications within the aforementioned fields.

WW1: All patent applications worldwide within the aforementioned fields.

TECHNOLOGY BUSINESS INDEX

Created by Cascelotte, the Technology Business Index (TBI) is a composite index in which the impact of all of the constituent indicators on the economic value of a patent application is scientifically confirmed through several different studies. TBI is also based on advanced cohort analyses and weighting of indicators. TBI values are between 0 and 100, where a higher value is linked to a higher probability that a patent will have a technical and economic impact. TBI is not a normalised value, both the outcome and the spread are skewed, but TBI provides the following three important thresholds:

TBI > 70: it is statistically probable that a patent with a TBI greater than 70 will have an economic impact.

TBI 30–70: the model cannot determine with statistical certainty whether or not the patent will have an economic impact.

TBI < 30: it is statistically improbable that a patent with a TBI below 30 will have any economic impact.

Cascelotte uses data from all patent applications worldwide that have a registered search report. The database CascelotteDB contains approximately 25 million patent applications registered over the period 2000–2021. As it takes around 18 months for a patent to be published, the dataset for 2019 onwards cannot be assumed to be complete. Even data for 2018 should be approached with caution and assumed to be incomplete. This implies that TBI values are not statistically relevant to applications submitted from 2019 onwards. Learn more about the methodology at www.cascelotte.com

RESULTS 2022

HIGHLIGHTS

- Staffan Holmin was awarded the Karolinska Institutet newly instituted Prize for Innovation and Utility.
- Mats Danielsson was awarded the Hans Wigzell Foundation Science Prize.
- Niclas Roxhed received a grant of SEK 8 million from Erling Persson's foundation.
- Erik Fredenberg, GE Healthcare, was affiliated to MedTechLabs as a new adjunct professor at KTH.
- Stratipath, a startup founded by Johan Hartman and Mattias Rantalainen was awarded the Athena prize.
- Fredrik Strand and Mattias Rantalainen both recieved starting grants from the Swedish Research Council

EXTERNAL RESEARCH FUNDING

We have offered the research leaders application support for EU calls within Horizon Europe - EIC Pathfinder Open, Marie Sklodowska-Curie Actions (MSCA) Doctoral Networks and ERC Advanced Grant.

EXTERNAL EVALUATION

In accordance with the main agreement, an evaluation of the center was carried out in the spring of 2022. The panel consisted of Thomas Laurell, Professor of Biomedical engineering, Lund University, Hans Enocson, former CEO GE Healthcare Sweden, Lisa Ekselius, professor of psychiatry, Uppsala University, Angelica Fritihof, Chairman of the Strategic patient and relatives Council, Karolinska University Hospital. A self-evaluation report was conducted by the Program Directors. The evaluation came out well.

Norway's business delegation visits MedTechLabs HRH The Crown Princess.

INCREASED AWARENESS

During the year, we worked systematically to increase awareness of the center and its activities. This has happened by communicating results from MedTechLab's research and research leaders in the form of news feeds on Linked In and website as well as through interview reports. We work continuously to improve our communication channels in order to reach relevant target groups. During the spring of 2022, MedTechLab's management contributed to the application for Stockholm to host the world congress in medical technology (2028 IUPESM World Congress for Medical Physics and Biomedical Engineering) by participating in the construction of campaign kits. Stockholm came second but was encouraged to apply again. MedTechLab's hosted a number of international delegations being a part of the visiting program at KI and Karolinska University Hospital.

OUTREACH

	2022	**2021**	2020
Social media: LinkedIn			
Followers	749	445	205
Post views	67 492	43 998	n/a
Clicks	3 775	6 338	n/a
Social media: Youtube			
Number of videos	15	15	1
Views	1 476	1 160	148
Viewing hours	76,5	49,5	24
Newsletter			
Subscribers	248	251	101
Mailshots	8	11	3
External publicity			
Newspapers articles, editorial	16	10	1

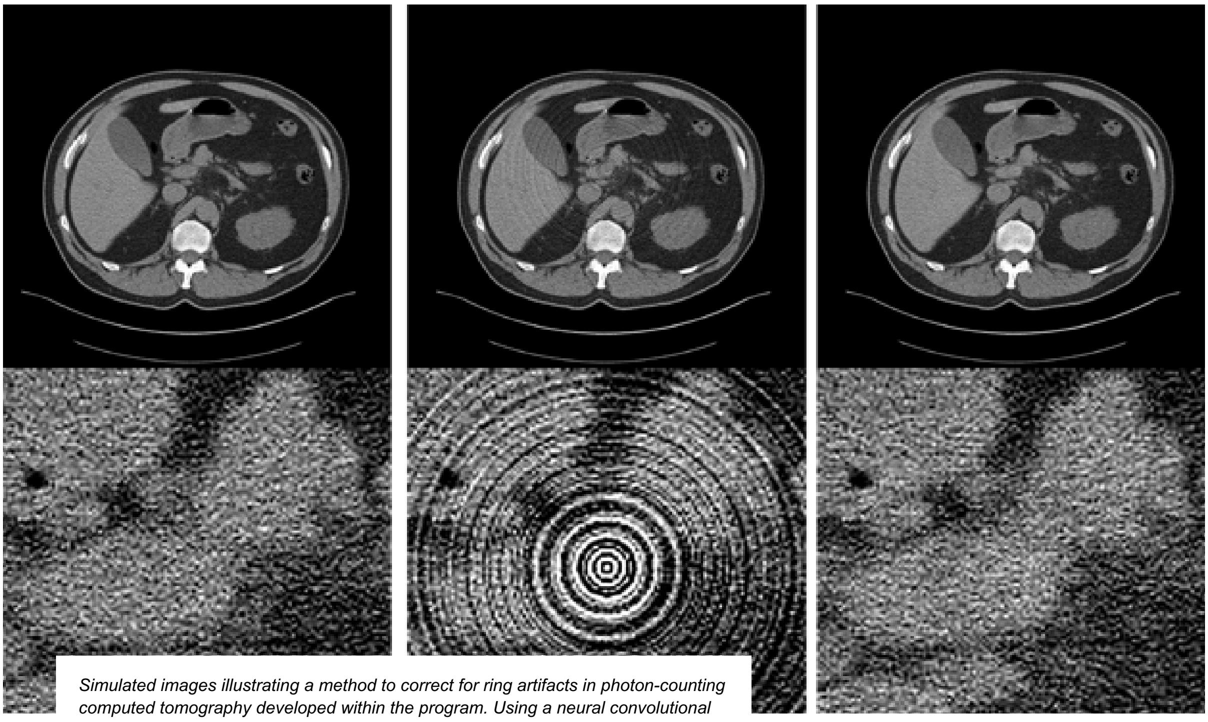
Articles, editorial 2022:

Life Science Sweden/MedTechMagazine: 4
Dagens Industri: 1
Smålands Dagblad: 1
Neurologi i Sverige: 1
Forte: 1
Onkologi i Sverige: 1
Lif: 1
Pharma industry: 1
Karolinska Sjukhuset: 1
Karolinska institutet: 4

RESULTS OF RESEARCH PROGRAMS

SPECTRAL CT-IMAGING AND ENDOVASCULAR TECHNIQUES

With the aid of this technology, significantly improved diagnoses and treatments will be available to patients with cancer and cardiovascular disease, including stroke.



Simulated images illustrating a method to correct for ring artifacts in photon-counting computed tomography developed within the program. Using a neural convolutional network, the observed image (middle) can be transformed into a corrected image (right) that is very similar to the true image (left), with no visible artifacts. This type of artifacts, which can occur if a CT scanner is not calibrated often enough, strongly negatively affects the diagnostic value of the image, and the proposed correction method can therefore reduce the need for frequent time-consuming calibrations.

PROJECTS WITHIN SPECTRAL CT IMAGING AND ENDOVASCULAR TECHNIQUES

ANALYSIS OF LUNG CHANGES IN POST-COVID PATIENTS USING COMPUTED TOMOGRAPHY AND AI.

Research leader: Mats Persson.
Chest x-rays and computed tomography play a major role in the care of patients with covid-19 and the follow-up of patients who have residual problems after the disease. At the same time, knowledge of how the X-ray images should be interpreted is still limited. Together with Karolinska University Hospital, we are developing an AI tool based on deep neural networks to automatically classify computed tomography images with regard to different types of lung damage. In a first step, we train neural networks to distinguish between healthy lungs, two different types of pulmonary fibrosis and other lung changes. In the next step, we will apply these networks to computed tomography images of patients with lung damage from covid-19. In this way, we will be able to compare lung damage from covid-19 with fibrosis diseases, which can provide information on long-term prognosis and treatment methods for patients with remaining symptoms after the covid-19 examination.

NEW IMAGE RECONSTRUCTION METHODS FOR PHOTON-COUNTING COMPUTED TOMOGRAPHY

Research leader: Mats Persson.
In order for the new photon-counting computed tomography technology to reach its full potential, the

This project has been made possible by donaions to Professor Mats Danielsson from Einar Mattsson, the Allba Foundation and the Stockholm Pandemic Resilience foundation.

newly developed hardware needs to be supplemented with improved data processing algorithms so that the measured data is fully utilized and provides the best possible image quality. Within this project, we are developing next-generation image reconstruction methods for photon-counting computed tomography and evaluating the resulting image quality. In collaboration with the Department of Mathematics at KTH, we have developed an image reconstruction method based on deep neural networks, deep learning, which can greatly reduce the noise in the images, especially in images that show the material composition of the tissue. We have also developed methods to use deep learning to remove image errors arising from physical imperfections in image acquisition, which can reduce the requirements for frequent and time-consuming calibrations of scanners in clinical operation. In a few years' time, the combination of photon-counting computed tomography with next-generation image reconstruction can take image quality in computed tomography to a completely new level.

NEW PERFORMANCE MEASURES AND VIRTUAL CLINICAL TRIALS FOR EVALUATING IMAGE QUALITY IN PHOTON-COUNTING COMPUTED TOMOGRAPHY

Research leaders: Mats Persson and Erik Fredenberg.
As photon-counting computed tomography begins to be used clinically, the need to be able to compare the image quality that can be obtained with different techniques or imaging protocols increases. We develop simulation models for different detector technologies and develop methodology to calculate how the image quality in a reconstructed image depends on properties of the detector and image acquisition parameters, based on the framework based on linear system theory that Mats Persson developed as a postdoctoral fellow at Stanford University.

A closely related project has been started in 2022 by Erik Fredenberg, who is an adjunct professor at KTH on a part-time basis. In close collaboration with Mats Persson and with Prismatic Sensors AB (part of GE Healthcare) where Erik Fredenberg works in parallel with the position at KTH, he develops a methodology for virtual clinical trials of photon-counting computed tomography.

With this technology, in the future it will be possible to use advanced simulation models to evaluate the performance of an imaging system for various imaging tasks, which reduces the need for costly and ethically sensitive clinical studies.

AN ULTRA-HIGH RESOLUTION PHOTO-TRACKING DETECTOR

Research leader: Mats Danielsson.
The central component of the photon-counting spectral computed tomography technique is a newly developed photon-counting silicon detector. Even the version of the detector that is currently being evaluated in a computed tomograph represents a major improvement compared to previously used detector types, but at the same time it represents only a first step towards the full potential of silicon detector technology. In this project, which is a collaboration with Linköping University, we are developing a new detector version with micrometer resolution and the ability to not only count but also track the photons as they move through the detector. In addition to significantly higher resolution, this detector technology can provide lower noise and better sensitivity to the spectral composition of the X-ray radiation. A potential application is also the ability to efficiently image with phase contrast, an imaging technique that can provide new types of information about imaged tissues. During the year, a first prototype detector was developed and characterized at the MAX IV synchrotron light facility. Work is now underway to partly compare the measurement results with simulations, and partly to evaluate the new detector's ability to take images with micrometer resolution.

TISSUE ACCESS USING ENDOVASCULAR TECHNIQUES

Research leaders: Staffan Holmin and Johan Lundberg.
We have continued with the development of the concept of placing a thin instrument (so-called Extruder) inside the vessels and now have, among other things, managed to create access to the brain parenchyma in pigs via veins. This enables studies around transplantation of cells and potentially around sampling. We have published results of heart and kidney access as well as modified technique for access to the pancreas. We have further developed, tested and patented a microbiopsy tool to enable minimally invasive cardiac sampling for all parts of the heart and developed and verified tissue handling protocols for analysis of RNA in these small

samples. Ongoing tests of the heart biopsy instrument for verification in human tissue take place in collaboration with Sahlgrenska University Hospital. A new company, Microcardix AB, has been formed around the technology and it has been accepted as a DRIVE project at Karolinska Institutet Innovations. We are conducting a study with the technology together with the microarray analysis company One Lambda. Development and testing of a microbiopsy tool for use inside the Extruder is ongoing. We have applied for a patent for the technology. We have recently developed and are testing a new instrument dedicated to sampling endothelial cells in various disease states. We have applied for patent protection for the technology. Furthermore, we have published results of clinical studies of dual energy CT scanning after thrombectomy (where blood clots are removed with thin tools via blood vessels) and during thrombolysis (dissolution of blood clots). We have also done a data analysis and published the results from the Stockholm Triage Study, which meant that patients with suspected blood clots in the large vessels of the brain were transported directly to Nya Karolinska. In addition, we have published new experimental MR and PET-based concepts to identify threatened brain tissue in acute ischemic stroke.

ENDOVASCULAR TECHNIQUE – CELL TRANSPLANTATION

Research leaders: Staffan Holmin, Johan Lundberg. We have also worked on four additional projects in endovascular technology. First, we focused on endovascular delivery of non-enhanced mesenchymal stem cells (MSCs) to the heart. Four pigs were administered 24 million cells each and sacrificed at 24 hours post injection (n = 2) and 72 hours post injection (n = 2). To understand and measure the retention of the transplanted cells to the heart, we compared injections with a larger (OD = 0.450 mm) or smaller (OD = 0.194 mm) device. Six pigs were administered 15 million Zr89 radiolabeled cells each and imaged with a PET/MRI camera two hours after injection. Finally, we compared vascular endothelial growth factor (VEGF) protein expression in the heart after injection of naïve MSCs (n = 2), MSCs genetically modified to express VEGF (n = 2), or modified mRNA encoding VEGF (n = 2). In parallel, we developed a myocardial ischemia model. We injected microspheres at various concentrations into the coronary arteries of 7 pigs and assessed ejection fraction and infarct size using cardiac MRI to develop the model. Tissue processing is nearing completion and articles will soon be submitted as one or more manuscripts to peer-reviewed journals.

Beyond the endovascular techniques, we have developed a pulse sequence and post-processing for dynamic susceptibility contrast magnetic resonance imaging (DSC-MRI). We have scanned 80 patients in Solna, of which 10 were healthy controls and one subarachnoid hemorrhage patient. We have procured a model-based oxygen extraction fraction calculation within a 10-year innovation collaboration between the neuroradiology department and Cercare A/S where intellectual property rights developed in this joint venture will be owned by the commercial partner and they will manufacture CE-marked Products.

ENDOVASCULAR TECHNIQUE REMOTE CONTROLLED DRUG CAPSULES

Research leader: Niclas Roxhed.
The blood-brain barrier is one of the most challenging aspects of drug delivery to the brain. With the Extruder technology, we can bypass the barrier, but the procedure is difficult to do several times. Therefore, we want to use the Extruder technology to achieve remote, sequential and selectively triggered drug release in the brain using ultrasound. The goal is to develop an ultra-miniaturized controllable drug delivery system (microcapsules) in size 100um*100um*1mm that can be selectively triggered using different ultrasound frequencies.

Two main methods have been used by our team to manufacture and control this process. Initially, we investigate the biocompatibility of the microcapsules by implanting them in the brain of mice and assessing their effect on the brain. Magnetic Resonance Imaging (MRI) and a number of histological/cell marker stains (astroglial etc.) have been performed which do not show no effect of these microcapsules in mouse brain (=negative control), supporting the notion of biocompatibility of these microcapsules. In addition to biocompatibility studies, marker-filled microcapsules have also been implanted in mice and we have been able to selectively release the drug with external ultrasound signals well below regulatory limit values.

These initial results present a non-surgical approach to the treatment of brain diseases. Biocompatible microcapsules containing drugs can now be implanted in the brain through the vascular system and opened on command via remote control.

MOLECUALAR IMAGING/ RADIOCHEMISTRY

Research leaders: Staffan Holmin, Jeroen Goos. In recent years, cell-based therapies have been emerging as innovative tools to treat tumours or regenerate damaged tissues. Prime examples that are demonstrating great effectiveness in the clinic include immune cell and stem cell therapies. A great challenge of current cell-based therapies, however, is that their fate after injection is still largely unknown. Do the cells reach the target site? And do they stay there? This uncertainty makes it nearly impossible to assess at an early stage if the therapy is working or if treatment needs to be adjusted, risking an undesired continuation of ineffective therapy for months. We have greatly optimised current procedures and developed novel strategies for the labelling of immune cells and stem cells with clinically interesting isotopes, with increased specificity and improved target-to-background ratios. This has allowed us to follow human decidual stromal cells, rat macrophages, natural killer cells, human peripheral blood mononuclear cells and mesenchymal stem cells in the body of small and large animals using positron emission tomography (PET) up to two weeks after injection. Moreover, we were able to confirm the retention of stem cells in heart tissue after their endovascular implantation using the transvessel wall technique.

In addition to the molecular imaging of transplanted cells, we are developing novel methodology for the delivery of radiopharmaceuticals to brain tumours. We demonstrated that a brain tumour-specific scorpion venom peptide was able to cross an artificial blood-brain barrier to reach the core of a three-dimensional in vitro brain cancer model. Furthermore, we developed a novel bispecific antibody and demonstrated its high affinity for brain tumour cells. Currently, we are setting up a sophisticated murine model of brain cancer to validate these results. Ultimately, we expect that these novel theranostic agents could lead to improved, minimally invasive therapy strategies that effectively and selectively target brain tumours, with minimal side effects.

SCIENTIFIC PROGRESS UNTIL 2022

- Staffan Holmin recipient of the Hans Wigzell research foundation's scientific prize 2020
- Mats Persson was selected together with 24 young researchers from all over the world to give a talk at Online Science Days 2020, organized by The Lindau Nobel
- Mats Persson was awarded Göran Gustafsson's big prize for young researchers in 2021 (a total of SEK 2.75 million over three years) from Göran Gustafsson's Foundation
- Mats Persson was awarded the Swedish Research Council's establishment grant in 2021 for the project "Photon-counting computed tomography with high accuracy for improved cancer diagnostics"
- Jereon Goos was awarded the Swedish Research Council's establishment grant in 2021 for the project "Development of a non-invasive treatment therapy against brain cancer in children".
- Staffan Holmin was awarded by Karolinska Institutet the newly instituted Prize for Innovation and Utilization in 2022
- Mats Danielsson was awarded the Hans Wigzell Foundation Science Prize in 2022
- Erik Fredenberg, GE Healthcare, was appointed in 2022 as adjunct professor at KTH.
- Mats Danielsson and Mats Persson are members of a consortium that has been awarded SEK 8 million over four years for the project "Emerging CT technology for advancing proton therapy". Within this project, which is led from Umeå University, spectral computed tomography and deep learning will be used to improve dose planning for proton therapy.
- Jeroen Goos was awarded a Starting Grant from StratNeuro (Strategic research area neuroscience at Karolinska Institutet, Umeå University and KTH) in 2022 for the project ”Tearing down the walls of brain cancer: delivery of radiopharmaceuticals across the blood-brain barrier” (”Hitta vägen till hjärntumören: transport av radiofarmaka över blod-hjärnbarriären”)
- Jeroen Goos was awarded KID funding from Karolinska Institutet in 2022 for the partial financing of a doctoral student on the project ”Tearing down the walls of brain cancer: delivery of radiopharmaceuticals across the blood-brain barrier” (”Hitta vägen till hjärntumören: transport av radiofarmaka över blod-hjärnbarriären”)

SIGNIFICANT PUBLICATIONS

Ström, M. Persson, A. Eguizabal and O. Öktem, *"Photon-Counting CT Reconstruction with a Learned Forward Operator"*, IEEE Trans. Comput. Imaging, Vol. 8, pp. 536-550 (Jun. 2022)

C. Sundberg, M. Danielsson and M. U. Persson, *"Compton coincidence in silicon photon-counting CT detectors"*, Journal of Medical Imaging, Vol. 9, Issue 1, 013501 (Feb. 2022)

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H. Karlsson, V. Moro, A. Eguizabal, M. Eriksson, A. Ågren, D. Åkerström, and M. U. Persson, *"Deep-learning-based denoising for photon-counting CT: image domain or projection domain?"*, Proc. SPIE 12031, pp. 120312S 1-18 (2022)

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CLINICAL STUDIES/ COLLABORATION WITH HOSPITALS AND COMPANIES

- A prototype of a photon-counting CT scanner has been installed at the BioClinicum at Karolinska University Hospital and a clinical study has been conducted in collaboration with GE Healthcare to evaluate its image quality. The study was completed in the fall of 2022 and underwent monitoring without comment.
- Mats Persson is the project manager for a recently started research collaboration with GE Healthcare: "Improved photon-counting CT performance modeling for comparing silicon and CdTe detectors". This project aims to develop mathematical models for image quality for photon-counting computed tomography to and evaluate the image quality from photon-counting CT scanners. This collaboration further strengthens the contact between GE Healthcare and MedTechLabs and facilitates the translation of research results into practical patient benefit.
- Cooperation with SmartCella AB is ongoing regarding the Extruder technology and a strategic research and commercialization agreement for the technology exists between SmartCella AB and Astra Zeneca AB.
- We have IP-protected a cardiac microbiopsy tool and the company Microcardix AB that commercializes the technology has been accepted as a DRIVE project at Karolinska Institutet Innovations AB. A study together with the microarray analysis company OneLambda is ongoing.
- Model-based calculation of oxygen extraction fraction calculation has been procured within a ten-year innovation partnership between the Department of Neuroradiology and Cercare A/S where intellectual property rights developed in the partnership will be owned by the commercial partner that manufactures CE-marked products.
- In 2022, we have completed a prospective study on GE Healthcare MR equipment with time-domain normalized (TDN) calculation of dynamic contrast-enhanced magnetic resonance imaging (DCE-MR) in patients with post-COVID. We were able to show that a group of post-COVID subjects lacked focal perfusion defects but that both mean TDN time to peak (TDN-TTP) and TDN-TTP ratio were higher in post-COVID men compared to control groups. Furthermore, mean TDN-TTP and TDN-TTP ratio correlated with clinical dyspnea. In 2022, the inclusion of patients with brain hemorrhages in a study with dynamic susceptibility contrast (DSC-MR) has also been ongoing.

OTHER SOCIETY BENEFITS

- The Extruder biopsy tool has been patented.
- Biopsy tools for endothelial cell sampling have been patented.
- A new way of using imaging technology to implement cell tracking techniques is being patented.
- Staffan Holmin and Mats Danielsson invited to represent MedTechLabs at the Winter Minglet February 2023 under the auspices of Wallenberg and FAM.

THE PROGRAMME'S RESEARCHERS MEDTECHLABS AFFILIATES

Mats Danielsson, Program Director and research leader, KTH

Mats Perssson, research leader, KTH

Dennis Hein, doctoral student, KTH

Christel Sundberg, doctoral student, KTH

Erik Fredenberg, adj. professor, KTH

Håkan Almqvist, doctoral student, KI, KUH

Alma Eguizabal, postdoctoral fellow, KTH

Fredrik Grönberg, doctoral student, KTH

Staffan Holmin, Program Director and research leader, KI, K

Jeroen Goos, research leader, KI

Stefan Milton, post-doc, KI

Iman Zafar, PhD student, KI

Johan Lundberg, research leader, KI, KUH

Niclas Roxhed, research leader, KTH

Jonathan Al-Saadi, PhD student, KI

Arvin Chireh, affiliated PhD student, KI

Rikard Grankvist, affiliated doctoral student, KI

Theocharis Iordanidis, doctoral student, KTH

Mikael Sandell, affiliated doctoral student, KTH

Göran Stemme, professor, KTH

Argyris Spyrou, postdoctoral fellow , KTH

KI = Karolinska Institutet.
K = Karolinska University Hospital.

RESULTS OF RESEARCH PROGRAMS

BREAST CANCER IMAGING POWERED BY ARTIFICIAL INTELLIGENCE DIAGNOSTICS

Every year around 1,500 women in Sweden die from breast cancer. More and more cases are being discovered, while the relative mortality in the disease has decreased.

PROJECTS WITHIN BREAST CANCER IMAGING POWERED BY ARTIFICIAL INTELLIGENCE DIAGNOSTICS

Research leaders: Johan Hartman, Mattias Rantalainen, Kevin Smith and Fredrik Strand.
The radiology part of the program has so far developed an AI pipeline that is now used for all women undergoing mammography screening at Karolinska University Hospital. This is done within the framework of a clinical study and means that the women whose mammograms have been assessed as normal by radiologists but who still have a high AI score are invited to participate in a study with a magnetic resonance imaging (MRI) camera. About 30 percent of the women questioned wish to participate, and among these, a lottery is taken to either undergo supplementary screening with MRI or to have only had a mammogram. Of approximately 520 examinations carried out to date, at least 23 women's breast cancer has been detected in this way (ie, cancer in 44 out of 1000 examinations compared to 5 out of 1000 examinations for the general mammography screening). The goal is to achieve 1,000 completed MR examinations before the study is closed and analyzes begin. In addition, Fredrik Strand has been appointed scientific leader for a national platform for the validation of AI for the detection of breast cancer. This is a collaboration between Stockholm, Linköping and Malmö and aims to create a technology platform on which different hospitals can upload images and different AI companies can install their algorithms - so that the accuracy and reliability of the algorithms can be evaluated in historical material. Currently, three regions and three AI companies have chosen to join. Images and clinical data are transferred. The pilot phase is expected to be completed in February 2023, and after that the hope is to connect more hospitals and AI companies.

The histopathology part of the program has continued to focus on building large-scale digitization of microscope slides, hardware for computing power and training of AI models in-house. The research has focused on predicting gene expression and risk stratifying breast cancer patients directly from microscopy images.

SCIENTIFIC PROGRESS

- Fredrik Strand invited speaker at the RSNA annual meeting in Chicago 2022, at the Cambridge Conference on Breast Cancer Imaging 2022 and the European Society of Breast Imaging annual meeting 2022

CLINICAL STUDIES/ COLLABORATION WITH HOSPITALS AND COMPANIES

- Johan Hartman and Mattias Rantalainen are co-founders of Stratipath AB, a KI spin-out company. The first product for AI-based image analysis received CE-IVD approval in May 2022 to subsequently be used in routine healthcare. The product is expected to reduce the time to final cancer diagnosis and lower the costs of healthcare.

THE PROGRAMME'S RESEARCHERS MEDTECHLABS AFFILIATES

Johan Hartman, Program Director and research leader, KI, SS

Kevin Smith, Program Director and research leader, KTH

Mattias Rantalainen, research leader, KI

Fredrik Strand, research leader, KI, K

Balazs Acs, MD, PhD, KI, SS

Karin Dembrower, Consultant, CStG

Bojing Liu, postdoc, KI

Yue Liu, PhD student, KTH

Lea Cornelia, research engineer KTH

Fernando Cossío Ramirez, research engineer, K, KI

Stephanie Robertson, MD, PhD, KI, SS

Mattie Salim, PhD student, KI, K

Abhinav Sharma, PhD student, KI

Moein Sorkhei, research engineer, KTH

Shirin Olyaei Rasoul, R&D nurse, MR, K

Lisa Viberg, research coordinator, KI

Yanlu Wang, MR-physicist, K

Yinxi Wang, PhD student, KI

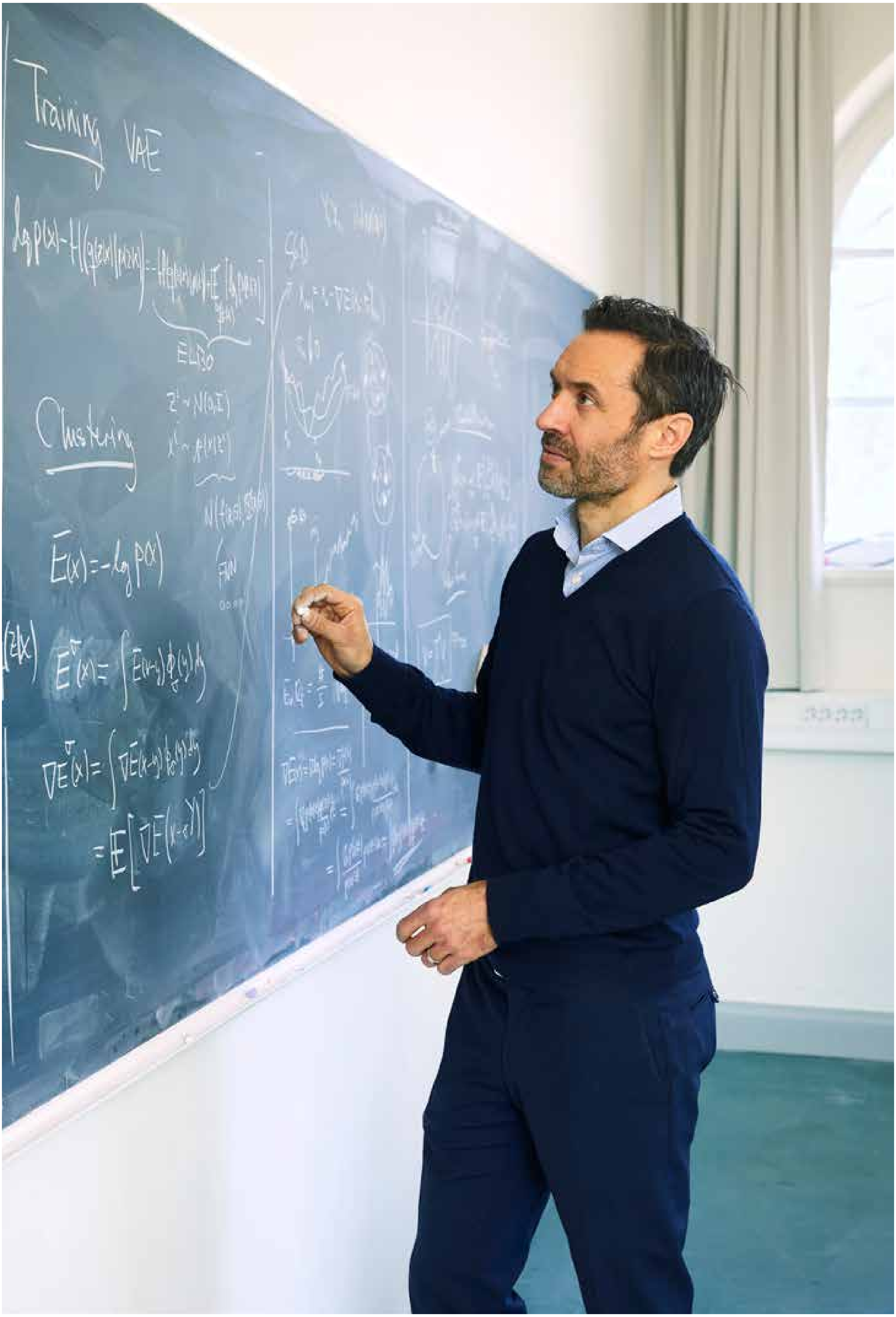
Philippe Weitz, PhD student, KI

KI = Karolinska Institutet. SS = Södersjukhuset.
K = Karolinska Universitetssjukhuset.
CStG = Capio Sankt Görans Sjukhus

RESULTS OF RESEARCH PROGRAMS

BIOELECTRONIC MEDICINE

Inflammatory diseases cause a great deal of suffering for patients all over the world, as well as creating challenges for healthcare. Stimulation of peripheral nerves, including the vagus nerve, may be the anti-inflammatory treatment of the future.


Training VAE
ELBO
Clustering
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PROJECTS WITHIN BIOELECTRONIC MEDICINE

DEVELOPMENT OF AUTONOMIC NERVE STIMULATION FOR INDIVIDUALIZED TREATMENT OF INFLAMMATORY DISEASES

Research leaders: Peder Olofsson and Henrik Hult.

To realize individualized treatment optimization in inflammatory disease, detailed knowledge of how autonomic nerve signals regulate inflammation, a stable interface with the vagus nerve, and automated signal analysis are needed.

New technology for minimally invasive nerve stimualtion

There is a lack of an atlas of the neurophysiology of inflammation regulation – something that is needed to study and understand mechanisms in detail and eventually be able to target treatment better.

We are developing a method to wirelessly activate specific, small peripheral nerves in experimental inflammation and create an atlas of the functional anatomy of neuronal inflammation regulation.

Automated monitoring of inflammation intensity

By analyzing large amounts of data from the vagus nerve during experimental inflammation, we identify signal patterns that represent inflammation intensity. The goal is to create a lexicon of signal patterns to extract detailed information about the inflammation. We use data available in the literature and our own data to develop methods in machine learning, based on auto-encoders and clustering, for the identification of nerve signals that can be linked to different cytokines. Proinflammatory cytokines are produced by the immune system and secreted in the event of injury, stress or inflammation, among other things. The results show that the new techniques are effective for the identification of relevant signal types, especially for TNF, but also that he variation between different recordings is large and it is of great importance to be able to do controlled experiments with improved signal quality in the future.

Longitudinal patient monitoring

Clinical data, measurements and patients' self-reports are collected longitudinally over the course of the disease in inflammatory bowel disease. We plan to use mathematical modeling to try to predict the course of inflammation. Through better prognostication of relapses in inflammatory diseases, we anticipate that treatment efforts can be optimized and disease episodes alleviated and shortened.

RESULTS SCIENTIFIC PROGRESS

- Henrik Hult cluster leader for application clusters within WASP.
- Henrik Hult, director of Brummer & Partners MathDataLab.
- Henrik Hult receives a 4-year project grant from SeRC, SEK 3.2M, November 2022.
- Henrik Hult arranges conference: "Mathematics for Complex Data" with 110 participants, KTH, June 2022.
- Peder Olofsson's doctoral student Alessandro Gallina completed his dissertation in April 2022.
- Peder Olofsson is working with KI Innovations to prepare a clinical study based on an invention/patent application from 2021.
- Peder Olofsson received a project grant from the Heart-Lung Foundation and others.
- Peder Olofsson co-published the discovery that nerve signals regulate atherosclerosis (Nature, 2022) and small intestinal inflammation (Frontiers in Neuroscience, 2022).
- Peder Olofsson & Henrik Hult published a mechanism for neural regulation of inflammation healing (PNAS, 2022).

SIGNIFICANT PUBLICATIONS

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Caravaca AS, Levine YA, Drake A, Eberhardson M, Olofsson PS. *Vagus Nerve Stimulation Reduces Indomethacin-Induced Small Bowel Inflammation.* Front. Neurosci. 2022 Jan 12;15:730407.

CLINICAL STUDIES/COLLABORATIONS WITH HOSPITALS AND COMPANIES

Planning for a clinical study of non-invasive vagus nerve stimulation is underway in collaboration with Tema Hjärta-Kärl, Karolinska University Hospital, Emune AB and KI Innovations.

THE PROGRAMME'S RESEARCHERS MEDTECHLABS AFFILIATES

Peder Olofsson, Program Director and research leader, KI, K

Henrik Hult, Program Director and research leader, KTH

April Caravaca, postdoctoral fellow, KI

Michael Eberhardson, consultant, researcher, KI, K

Laura Tarnawski, assistant professor, KI

Fredrik Viklund, professor, KTH

Adam Williamson, researcher, KI

Diego Ignacio Roy Hierro, degree project, spring semester 2022

Vladimir Shavva, post-doc, KI

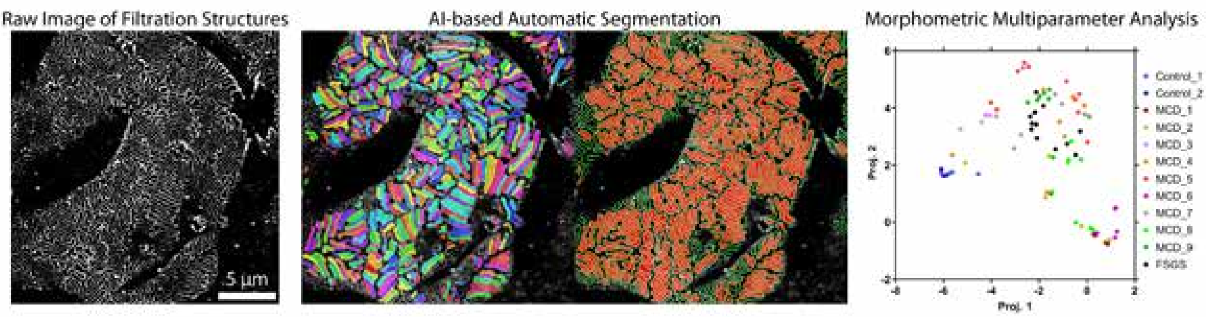
Wanmin Dai, PhD student, KI

KI = Karolinska Institutet.
K = Karolinska University Hospital.

RESULTS OF RESEARCH PROGRAMS

OPTICAL 3D-MICROSKOPY FOR MORE EFFECTIVE DIAGNOSIS OF KIDNEY DISEASES

Chronic kidney disease is a growing global threat to public health. About 10% of the world's population is affected, but in the elderly and people with high blood pressure, cardiovascular disease and diabetes, over 35% are affected.



Imaging, segmentation and quantification of filtration structure pathology in kidney samples. Images of nanometer-scaled kidney filtration structures are generated using new sample preparation and optical imaging methods (left panel). A trained deep learning network is used for automatic segmentation of structures (middle panel). Several quantitative parameters are extracted which describe pathological alterations in the kidney filter, and a multi-parameter umap projection reveals morphometric grouping of human patients with minimal change disease (MCD) and focal segmental glomerulosclerosis (FSGS) (right panel).

PROJECTS IN OPTICAL 3D MICROSCOPY FOR MORE EFFICIENT DIAGNOSIS OF KIDNEY DISEASES

Research leaders: Sigrid Lundberg and Hans Blom.

As an affiliate of MedTechLabs, the project has had the following focus during its first year:

A. Molecular and renal morphological sample preparation of clinical material.

B. Further development of image analysis support with AI for kidney morphological analysis.

C. Clinical validation of optical 3D renal pathology using AI-assisted diagnostics.

IIn project part A, marking and imaging in three-dimensional kidney biopsies is optimized for all structures that are currently used in practice in renal pathology. In published article (i), we have developed labeling and imaging for most of the molecular and morphological parameters investigated in current practice. Within project part A, we have further developed sample preparation and high-resolution 3D imaging of biobank samples in published article (ii).

Project part B aims to deliver AI-supported image analysis for all molecular and morphological parameters with diagnosis-specific categorization of kidney disease (cf. project idea Image 15). Last year we developed AI-supported image analysis for single morphological parameters in published article (iii) together with academic and clinical collaboration partners in Cologne, Germany.

Within project part C, we have initiated clinical validation of three-dimensional digital renal pathology with AI-supported image analysis for quantification and stratification of renal disease. The work takes place in collaboration with the Renal Medicine Clinic at Danderyd Hospital and the pathology department at Karolinska University Hospital. Ethical application and consent from participating patients and agreement for withdrawal of biological material from the biobank have been drawn up within Region Stockholm.

SCIENTIFIC PROGRESS

- Labeling and imaging for most of the molecular and morphological parameters investigated in current practice developed and published.
- Sample preparation and high resolution 3D imaging of biobank samples developed and published.
- Image analysis support with AI for renal morphological analysis of single parameters developed and published.
- Project support from Torsten Söderberg's foundation for the development of automated quantitative optical kidney pathology.
- Project support from the Swedish Kidney Association for further development of analysis of disease mechanisms in intact kidney with optical microscopy and deep learning for precision diagnostics.
- Project support from Stig and Gunborg Westman's foundation for research into kidney diseases, organ transplantation and organ donation with 3D kidney biopsy analysis.

SIGNIFICANT PUBLICATIONS

4. **D. Unnersjö-Jess et al (2021).** *A fast and simple clearing and swelling protocol for 3D in-situ imaging of the kidney across scales.* Kidney International 99(4):1010–1020.
5. **D. Unnersjö-Jess et al. (2022).** *Three-Dimensional Super-Resolved Imaging of Paraffin-Embedded Kidney Samples*. Kidney360 3(3):446–454.
6. **L. Butt et al (2021).** *Deep learning-based segmentation and quantification of podocyte foot process morphology.* BioRxiv doi.org/10.1101/2021.06.14.448284.

CLINICAL STUDIES/COLLABORATIONS WITH HOSPITALS AND COMPANIES

- Clinical demonstration and validation of optic kidney pathology initiated with DS, and K.
- AIDA clinical fellowship for developing optical kidney pathology with AI-supported diagnostics established.

THE PROGRAMME’S RESEARCHERS MEDTECHLABS AFFILIATES

Sigrid Lundberg, Program Director and research leader, DS, KI

Hans Blom, Program Director and research leader, KTH

David Unnersjö-Jess, post-doc, KTH, UiK

Robin Ebbestad, PhD student and MD, KI, DS.

Hannes Olauson, MD, Clinical patology, KI, K

Hjalmar Brismar, Professor, KTH, KI

Jaakko Patrakka, Adjunct Professor, clinical patologi KI, K

Annika Östman Wernerson, Professor Kidney and transplant science KI, K

DS = Danderyds hospital. KI = Karolinska Institutet.
K = Karolinska University hospital. UiK = Universityt in Cologne, Germany.

Analytic Imaging Diagnostics Arena (AIDA) is a national arena for research and innovation around artificial intelligence between academia, healthcare and industry. To translate technological advances in AI technology into patient benefit in the form of clinically useful tools, https://medtech4health.se/aida/fellowships/

FINANCIAL RESULTS

ECONOMIC OUTCOME IN 2022

Accrued unspent funds at the start of the year are largely due to the recruitment of the three assistant professors. It took longer than expected. This was regulated for 2020 and 2021 through a lower contribution from the parties than what the actual business requires. From 2022, the business will have a turnover of SEK 18 million per year. The administration costs for the center amounted to 8,3% of the total costs.

Opening balance 2022	1 345 000
Revenue 2022	
Region Stockholm	12 000 000
Karolinska Institutet	3 000 000
KTH Royal Institute of Technology	3 000 000
Costs 2022	
Research area Imaging and Minimally Invasive methods	
Clinical infrastructure	**1 434 000**
Rental costs for lab and workplaces	544 000
Research engineer 40%	240 000
Research nurse	600 000
Operating costs	50 000
Research programme Spectral CT-imaging and Endovascular Techniques	**7 000 000**
Research area Artificial Intelligence in Healthcare	
Research programme Breast Cancer Imaging Powered by Artificial Intelligence Diagnostics	**4 000 000**
Research area Bioelectronic Medicine	
Research programme Bioelectronic Medicine	**3 000 000**
Projects 2022	**1 374 000**
Uppdate Online course Acute stroke treatment within 24 hours	800 000
Increased awareness of MedTechLabs *1)*	374 000
External evaluation of MedTechLabs	200 000
Administration	**1 495 000**
Payroll Director, Deputy Director, Executive Director	1 209 000
Meeting costs	26 000
Communication Officer	200 000
Other Costs	60 000
Total Costs	**18 303 000**
Closing balance 2022	1 042 000
All figures in SEK	

1) Projects that create awareness of MedTechLabs research areas for relevant target groups

MedTechLabs

MedTech Labs is an interdisciplinary centre for medical technology research that develops diagnostics and improved treatments for our most common diseases. The objective is also to develop MedTechLabs into a leading centre of excellence internationally.

In this Annual Report, you can read about MedTechLabs' partners and researchers, our ongoing and completed research, governance and finances. We also present a unique innovation analysis of the patents generated by researchers affiliated to MedTechLabs, as well as an analysis of the quality and impact of our research.

www.medtechlabs.se