MedTechLabs

Karolinska Institutet | KTH | Region Stockholm

FROM BASIC RESEARCH TO SOCIETAL BENEFIT:

Better diagnostics with silicon-based photon-counting CT

Foreword

Swedish innovations such as the pacemaker and the the Gamma Knife all arose from the needs of healthcare. Mats Danielsson's pioneering research has resulted in an imaging method that provides more accurate diagnostics, demonstrating how adequate funding for basic research brings real benefit to society. Also, it highlights that there is no contradiction between research excellence and societal benefit, quite the opposite. Recent studies show both that 40 per cent of projects funded by the European Research Council (ERC) are named in patents and that 400 new companies have been created as a result of ERC projects. Perhaps Mats Danielsson's research group will generate another new start-up thanks to their new ERC grant.

Success requires highly motivated interdisciplinary teams in which each member contributes their expertise. Testing and developing prototypes in fully equipped hospital environments is also vital, as clinical trials are important in the development of new technologies. MedTechLabs creates excellent conditions for leading researchers to work together on translational science, providing the best possible care for tomorrow's patients.

We hope this brochure provides inspiration and guidance on how new technologies can develop from basic research and bring direct benefit to society.

Liz Adamsson
Executive Director
MedTechLabs

Aiming for better and safer diagnostic imaging

In 1979, the Nobel Prize was awarded to the two scientists who developed computed tomography. Further development is underway, and researchers led by Mats Danielsson have developed a photon-counting computerised tomography scanner in which the detectors are based on silicon. Their aim is to achieve better image resolution and lower radiation doses than with current technology.

IN SWEDEN ALONE, around one and a half million CT scans are performed every year. In the US, this number exceeds one hundred million. *Mats Danielsson*, professor of medical imaging physics at Stockholm's KTH Royal Institute of Technology, highlights the satisfaction that comes from developing new and improved medical technology.

— Visiting a hospital where you can see the doctors examining the images and discussing them is very rewarding, the realisation that we made some of that. It's great to feel part of that system — incredibly fulfilling, he says.

Previously, Danielsson developed successful mammography equipment, but his focus is now an advanced form of computed tomography, which aims to improve image quality with a lower dose of radiation. One of the world's three existing prototypes for this type of computer tomography can be found at Karolinska University Hospital, in MedTechLabs' premises. MedTechLabs is a centre that was founded in 2017 by Danielsson, among others, and that receives funding from Region Stockholm, KTH and Karolinska Institutet (KI). He describes how, when testing new equipment on patients, it must be located near the technically skilled engineers who need to make any necessary adjustments, while also being close to the hospital's resources.

— Integration has to be possible; your test equipment cannot be somewhere a kilometre away. This may sound like common sense, but you need to plan for it. We achieved this at MedTechLabs, which is fantastic, Danielsson says.

But let's start at the beginning. In 1979, researchers *Allan M Cormack* and *Godfrey Newbold Hounsfield* received the Nobel Prize in Physiology or Medicine for the development of computer-assisted tomography. This technique involves exposing the patient to X-rays from different directions. A computer can then be used to reconstruct a three-dimensional image of the body. At that time, according to the press release issued by the Nobel Assembly at KI, the technology was revolutionary; it allowed the imaging of things that were previously impossible to see, such as a tumour in a living person's brain. Mats Danielsson was 14 when the prize was awarded — is this something he remembers?

— I come from a small village in Småland, in the south of Sweden, where we didn't discuss the Nobel Prize at the kitchen table, he says

Instead, what interested him in physics was the chance to explore its boundary with philosophy.

— Understanding the universe, as well as understanding what researchers had concluded. That was what really appealed,' he says, and continues. Also, from the age of 15, going to CERN was my dream. Getting to CERN — that was my thing, it really stuck in my head.

The route there went via his education in engineering physics at KTH.

— I was awarded a book about rocks for achieving top marks, but hard work and inspiration are my formula for success, says Danielsson.

Once he arrived at CERN, he researched symmetry breaking, which is when time flows in reverse. He describes an experiment that took place in 1995, in what is called the antimatter factory, as being very concrete.

— In the control room, they spoke in French over a crackling loudspeaker, 'we're now delivering three million antiprotons'. Sitting there in the control room was great fun, with loads of computer screens showing what was

The first prototype for silicon-based photon-counting CT was installed at MedTechLabs in September 2021.

happening in all the subdetectors, he says.

He also enjoyed working in shifts, like people do in industry.

— I was used to shift work from Småland. They ran this experiment in the summer, when electricity was cheap, and it pretty much turned down the lights all over Geneva, Danielsson recalls.

In 1996, he defended his thesis, titled First Direct Measurement of T-violation, Based on the First Measurement of Violation of the Time Symmetry. Although particle physics and astronomy still appealed, he longed for something that would have a greater impact in the real world.

— Medicine was interesting — the directness of being able to help a fellow human being in a positive way, such as through earlier and better diagnoses, he says.

At CERN, silicon detectors were used to capture single charged particles and helped in the successful detection of the top quark. This type of detector was the origin of the technology underlying the abovementioned mammography equipment.

Between 1996 and 1999, Danielsson was a postdoc at Lawrence Berkeley National Laboratory in the US, where they research detectors and integrated electronics in X-ray imaging — a vital element in development. When the researchers started the project, X-rays were only available on film, so instead they developed digital detectors, which could count individual photons. In 2000, Danielsson founded a company called Mamea Imaging AB and developed the technology in close cooperation with a Swedish company from Linköping, Sectra. Eleven years later, Sectra Mamea AB, which had resulted from their work together, was bought up by Philips, which ensured that the mammography equipment was launched on a large scale.

The low-dose radiation mammography machine, which produces 40 per cent less radiation than conventional digital mammography, is now used in around a thousand hospitals in some 40 countries.

Mats Persson has worked on the project with Mats Danielsson since his time as a doctoral student. Today, his focus is on improving image quality, including the use of deep learning, AI.

— When mammography was unpopular, I had friends who said 'they found this breast cancer on your machine, but now I've had treatment and I'm fine'. The risk is significantly lower when a tumour is found and removed early, so that feels great,' says Danielsson.

The mammography machine was the first photon-counting imaging system to be approved by the US Food and Drug Administration (FDA). The idea of improving computed tomography in a similar manner to mammography equipment was raised back in the early 2000s.

— We wanted to obtain better image resolution with this technology, while also reducing radiation, says Danielsson.

Better image quality ensures clearer and earlier diagnostics, while a low radiation dose is important during screening, as well as when examining children, who are even more sensitive than adults. *Nature Medicine* published an article on the subject in November 2023. In over 900,000 Europeans who had at least one CT scan before the age of 22, researchers found a slight increase in the risk of some types of blood cancer. He also emphasises that computed tomography is broader than mammography.

— Instead of "just" finding and curing breast cancer, you can diagnose and guide treatment for a wide range of conditions, such as cancers and cardiovascular issues, he says.

In 2008, he received SEK 23.7 million from the Erling-Persson Foundation to develop detectors for use in a computerised tomography scanner. The technology is like that used in the mammography machine, which also counts individual photons. However, because radiation must be more intense in computer tomography, the technology had to be completely redesigned.

— Higher energy levels and more photons per second to keep track of created other kinds of problems. It took a while before I understood how we could make it work, says Danielsson.

Instead of 'just' finding and curing breast cancer, you can diagnose and guide treatment for a wide range of conditions, such as cancers and cardiovascular issues.

He describes how he solved one of the problems.

— Photons are scattered by something called the Compton effect. If they are not captured after detection, they destroy the image. But then I realised, we can use thin tungsten sheets to absorb them — that was an early idea, he says.

The idea was hatched on a rainy drive to Småland, as the windscreen wipers moved backwards and forwards, repetitively and meditatively.

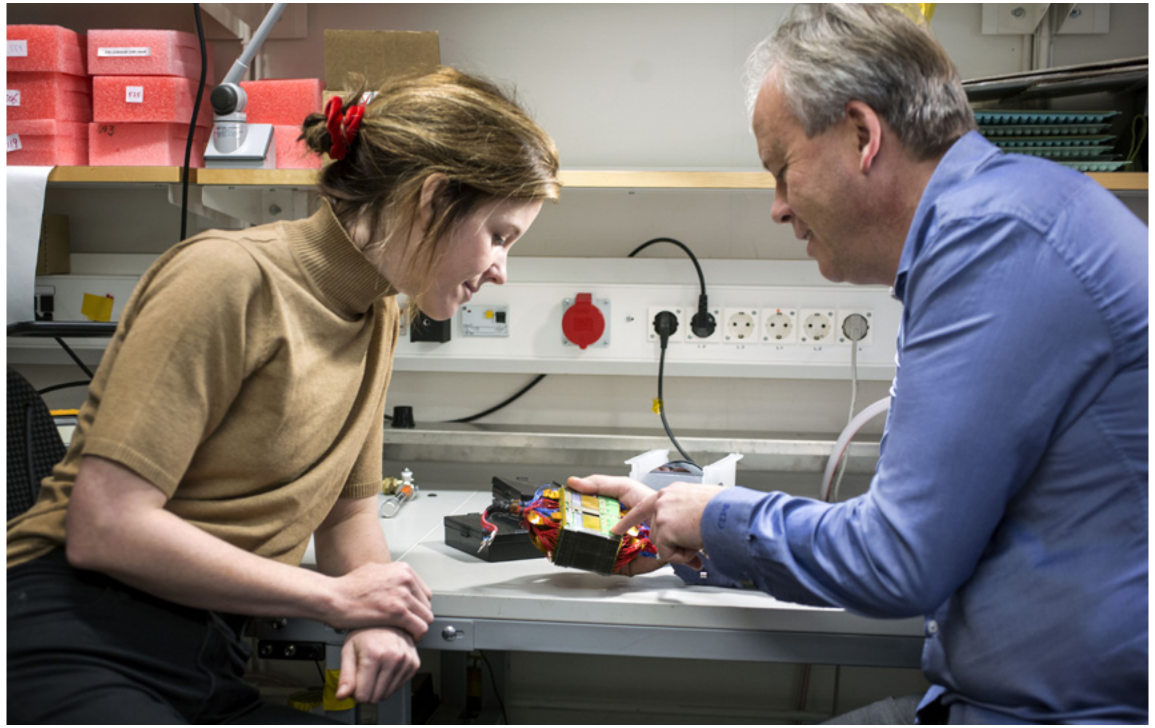
— But you don't have to drive a car to come up with ideas or solve problems. Cycling or running, or doing the gardening works just as well — as long as it's somewhat monotonous, says Danielsson.

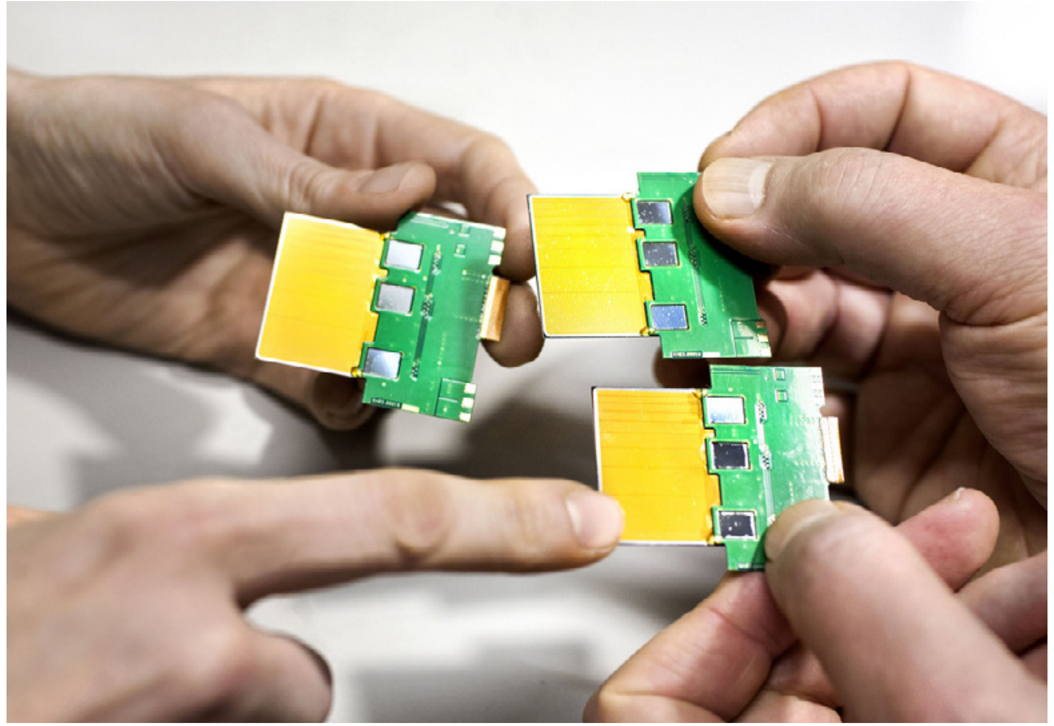
He founded Prismatic Sensors AB in 2012 to develop the technology.

— Initially, the company was dormant, and we mostly collected patents, he says.

He emphasises the importance of support from the Erling-Persson Foundation in the project's development.

— They have been absolutely vital. They believed in us all along and supported the project through their long-term investments, up until 2020 when GE HealthCare bought Prismatic, says Danielsson.





Moa Tamm Yveborg and Mats Danielsson with the photon-counting silicon-based detectors, which provide better images using lower doses of radiation. She is now head of engineering at Prismatic Sensors AB.

The acquisition was by mutual agreement, and he describes how the researchers and the American company had long worked together and knew each other well.

— With only four companies developing and selling CT scanners globally, there was no point in trying to manufacture and launch the new CT scanner ourselves, says Danielsson.

He also decided at an early stage to base the photon-counting CT's detectors on silicon.

— We are now competing with another system, where the detectors are based on cadmium. I don't like it because it is toxic and banned in the EU, but exemptions can be applied for and granted, he says.

He believes that exemptions unnecessarily extend the period in which hazardous materials can be used.

— Tell companies that 'it will be banned in ten years' and they'll come up with something else. It's as easy as that. I think the example with ozone, when they phased out freon, shows it is possible.

He clarifies that the problem is not that cadmium would be released during scanning in hospitals, but that cadmium is mined and there is a risk of it spreading as soon as the metal leaves the ground.

— Perhaps a CT scanner catches fire somewhere, spreading cadmium through the area. Nor is it found naturally in the body. Many substances are present in tiny, tiny quantities, but there shouldn't be a single cadmium atom in a healthy person, says Danielsson.

IN ADDITION TO SILICON NOT POSING A HEALTH RISK it can also create sharper images that can differentiate between tissue types. Mats Persson, associate senior lecturer at KTH's unit for the Physics of Medical Imaging, part of the Department of Physics, is now developing these technologies.

He started working on the project during his time as a doctoral student at KTH, where Mats Danielsson was his supervisor. Similarly to Danielsson, Persson was also interested in theoretical physics at the beginning of his research career. He describes how, in high school, he enjoyed reading popular science books about quantum physics, the universe and superstrings.

— I started studying engineering physics at KTH and wanted to be a theoretical physicist, but after a couple of years, I felt that doing something more applied would probably suit me better, so I could see a clear societal benefit to what I was doing. Then I discovered medical imaging — which is a subject where you need to know lots of maths and physics, says Persson.

He received his PhD in 2016 and then did a postdoc at Stanford University for two years. This was followed by another year at General Electric's research division in Niskayuna, New York. He was recruited by KTH in 2020, and his focus is now the computed tomography project.

— During my PhD, I was involved in hardware development and building a new detector. Now I've moved more towards thinking about what to do with the information that's produced — how do we obtain a good image?

Silicon-based photon-counting computed tomography enables much higher resolution than current technology. Basically, you can go from pixels of one millimetre to about half a millimetre, so you can see details that are half the size than was previously feasible. It is also possible to differentiate between materials.

— You can distinguish between soft tissue and calcium. In some cases, you can also see the differences between three materials,' says Persson, and shows a picture of a slice from a deceased person's heart **(image 1).**

— This was scanned with a tabletop version of our detector on a lab bench, and builds upon information found in the distribution of the photons we measure in the detector, he says.

The image was first presented in 2020, in an article published in European Radiology.

Persson describes how the information that iodine and →

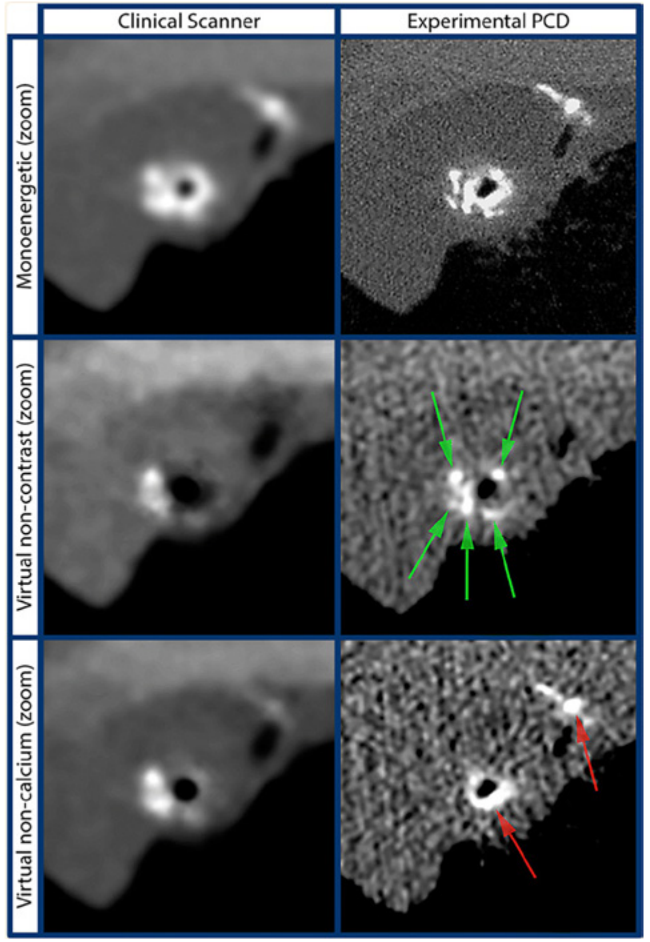


Image 1. This shows an image of heart tissue. The pictures on the right were taken with the experimental scanner that can differentiate between materials. They show iodine, a contrast agent injected into the patient (green arrows) and plaque (red arrows).

calcium have different spectral shapes can be used to distinguish between the materials.

— Today's computerised tomography technology can differentiate between two materials, but if you want to separate iodine and calcium from the background, which is soft tissue, and from each other, it is difficult to separate three materials with just two measurements, which is what computer tomography previously used, says Persson.

One reason for working with photon-counting computed tomography is that electronic noise can be reduced. The old CT technology, called energy-integrating CT, measures the sum of everything over a given period. There, it is not possible to distinguish between high and low pulses. Instead, the technology measures what was received overall.

— So, the electronic noise is baked in, as it is usually too small to make much of a difference. However, if you try to significantly reduce the dose, the electronic noise suddenly becomes important, he says.

Being able to obtain detailed images with a reduced dose of radiation has been important in the development of the new technology.

— The detectors work well, even when we go down to very low flows. Because they count individual photons, they are not drowned in noise when there are only a few photons, says Persson.

Worldwide, there are only three CT machines that use photon-counting technology based on silicon detectors. As mentioned previously, one is at MedTechLabs at Karolinska University Hospital, the other two are at Stanford University (where Mats Persson did his postdoc) and at the University of Wisconsin-Madison. Persson is now looking at what new technology could make the next version of the machine even better — how combining photon-counting computed tomography with enhanced image processing, data processing and physics models could improve imaging.

One element is the use of deep learning, AI, to remove artefacts.

— These can always be removed by calibrating the machine, but if you want the system to be more robust and

During my PhD, I was involved in hardware development and building a new detector. Now I've moved more towards thinking about what to do with the information that's produced — how do we obtain a good image?

Mats Persson

This shows the interface between muscle and fat. Compared with the original image, you can see how fat has infiltrated the muscles.

→ don't want to occupy the hospital staff unnecessarily, you could use this technology instead, he says.

He shows images where the noise in the CT images has been reduced with impressive results **(images 2a and 2b).**

— This shows the interface between muscle and fat. Compared with the original image, you can see how fat has infiltrated the muscles. My doctoral student Dennis Hein has worked on this, he says.

The image was presented in a scientific article that has been available via ArXiv since September 2023.

AI can also improve the differentiation between three materials, as it is possible to distinguish between iodine and calcium.

— Research is ongoing, but I believe that combining these two technologies could be beneficial, so they can work together, says Persson.

Rounding off, he mentions a multi-university collaboration that is being led from Umeå University and funded by the Swedish Cancer Society. The aim is better planning of proton beam therapy for cancer.

— I am involved because my doctoral student, Karin Larsson, is working on this. Photon-counting computed tomography will help us to improve our calculations of how different tissues stop the protons fired into the body during therapy. This project also combines physics measurements with computer tomography and AI, says Persson.

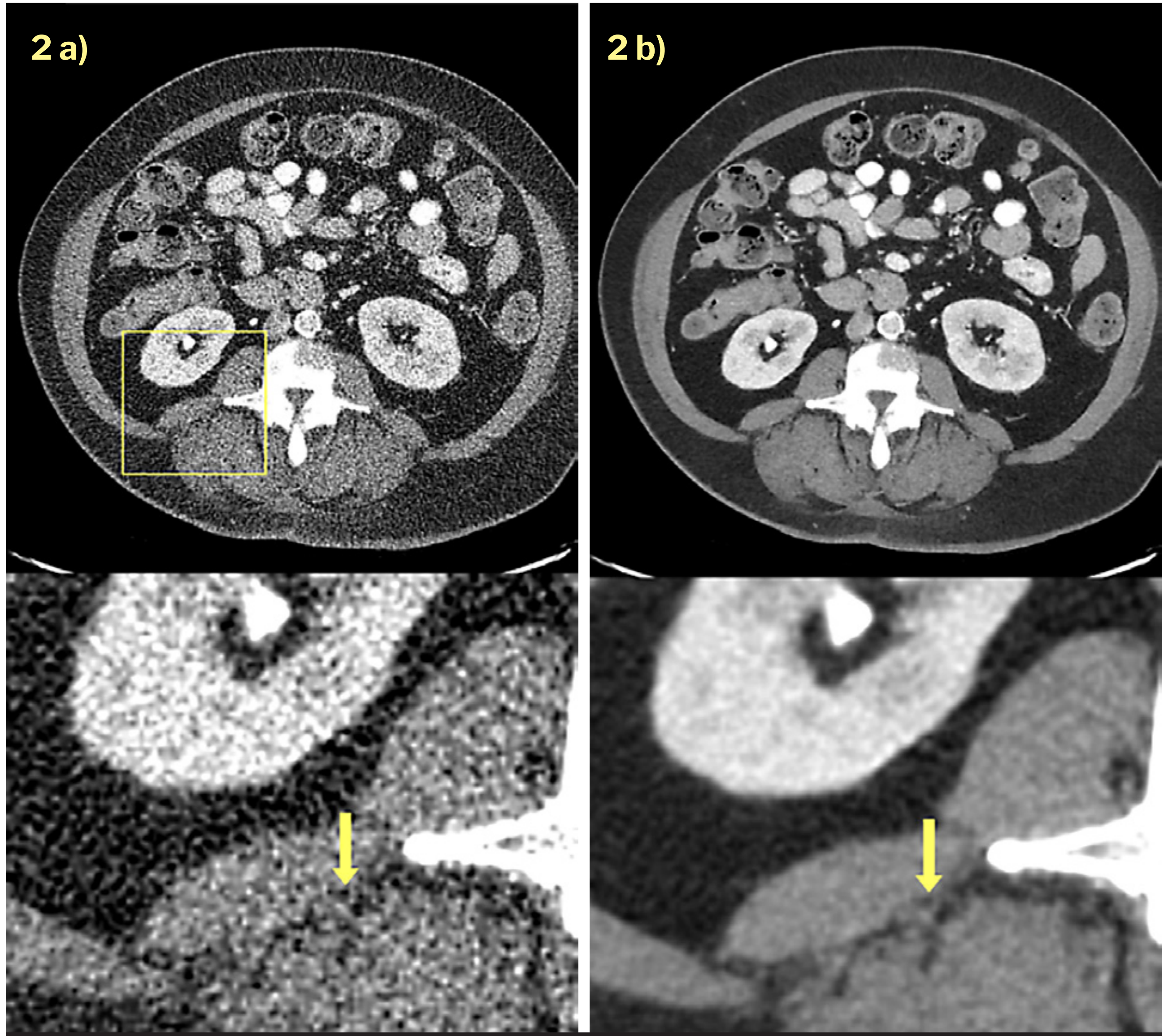
Like Mats Danielsson, he highlights the importance of MedTechLabs in the computed tomography project.

— One advantage is that we can show the outside world, perhaps companies or financiers, that there is collaboration between KTH, the healthcare region and Karolinska Institutet, which we use to gather expertise. To develop new medical technology, you need both engineers and natural scientists who know the technology, as well as doctors, says Persson.

ACCORDING TO MATS DANIELSSON, collaboration with doctors who have clinical expertise in the area in which an engineer wants to develop innovative medical technology is essential in a project's early stages (read more in Twelve Tips on pages 22–23). The HealthMedicineTechnology (HMT) collaboration involves KTH and Region Stockholm, and offers joint project funding for the development of activities at the intersection of health, medicine and technology, with funding available for one to three years — up to SEK 1 million per project per year.

— The idea is that a doctor and an engineer will join forces and see whether a given idea is worth developing, says Danielsson.

He found the doctors' feedback valuable, and using HMT funding to produce a more structured foundation was a way to "convince ourselves that the idea was 50 per cent feasible', as he puts it. If you then want to move the project to a clinic, you can move forward and apply for funding from other sources, such as the EU, which provides substantial grants."



Noise in the image can be reduced using AI. Compared with the original image (a), the AI-processed image (b) shows how some fat has infiltrated the muscles (yellow arrow).

DANIELSSON SOON BEGAN DISCUSSING HIS IDEA for a better CT scanner with *Staffan Holmin*, professor of neuroimaging at Karolinska Institutet and senior consultant at the Department of Neuroradiology at Karolinska University Hospital. Today, Holmin is an important partner in the clinical evaluation of the now full-scale CT scanner.

He says that he and Danielsson, along with Jan Andersson, then director of research for Region Stockholm, developed MedTechLabs, which opened in 2017.

— We started it with funding from Region Stockholm, KI and KTH. Our idea was to further the development of medical and technological research, because it has such an incredible and rapid impact on patients, he says.

Sweden has a strong tradition of innovation in medical technology, thanks to innovations such as the Gamma Knife, artificial heart valves and pacemakers.

—At the same time, much of the recent financial muscle has gone into molecular biology research and drug development. That's not a bad thing, but the fact is that many of the really rapid and dramatic improvements for patients in areas such as cardiovascular research and oncology have occurred in medical technology, he says, and continues.

— We want to help and to support the development of medical technology. MedTechLabs also offers the opportunity to test new technical equipment in a hospital environment, something we are very proud to have been able to achieve.

To develop new medical-technological devices, engineers and technicians also need access to the labs to make any necessary adjustments and customisations, because the equipment does not work optimally at the beginning.

— They need to be able to come in and must have a 'dirty lab' that they can use. This should also be in a hospital environment, so you can access medical resources when scanning patients, such as intensive care doctors if there's an adverse reaction to a contrast agent.

Staffan Holmin

Mats Danielsson with GE HealthCare's leadership, who visited MedTechLabs in August 2023.

On 29 October 2021, the world's first silicon-based CT scanner for clinical use was inaugurated at MedTechLabs. Holmin and his colleagues are working on evaluating it and now, just over two years later, the second prototype has been installed. This is the one that will serve as the basis for FDA authorisation.

— As yet, the technology has not received clinical approval. It is still in the validation phase, where we're evaluating it in the role of healthcare researchers, he says.

To this end, researchers have scanned 27 patients to collect data that will help them to create better images. The patients have a range of diseases, which is important for obtaining images from multiple organ systems. The images are of the head and neck, chest and abdomen, and muscles.

— We need information from all the different organ systems so we can develop algorithms that produce good images. This is the foundation for the new prototype that we are about to start evaluating, says Holmin.

What motivates him to work in frontline research?

— Trying to test the ideas that arise from clinical work is exciting. I started out as a neurosurgeon before becoming an interventional neuroradiologist, which entails treating diseases of the central nervous system via the vessels, he says.

The principle is the same as treating coronary artery disease using balloon catheters. The same thing can now be done in a similar manner in the brain and spinal cord, such as for aneurysms and vascular malformations. In recent years, in strokes where patients have large blood clots blocking vessels in the brain, tools have begun to be used to remove the clots.

— This has brought about a total revolution in stroke care. Here, you use imaging techniques to make a diagnosis. You also see how these techniques need further development to achieve even better patient outcomes, he says.

Holmin appreciates cooperation across professional boundaries.

— Working with both engineers and technicians is very enjoyable. More specifically, in my work, one thing this silicon-based technology means is higher image resolution and better diagnostics for vascular diseases of the nervous system, he says.

Another hundred patients will now be evaluated through scanning using the new prototype. Data collection began in April 2024 and, as with the first 27 patients, researchers are examining different organs, and now also the heart.

— The reason we didn't do this before was that the first prototype lacked "gated technology", where scanning is guided by an ECG, he says.

Because the heart beats, an ECG is used to ensure that the images are taken when the heart muscle is as still as possible.

— This technology was not available in the previous version, but we can now add cardiac scanning and include this important organ system, Holmin says.

He started working on the computer tomography project with Mats Danielsson about ten years ago, as part of the HMT programme.

This technology is not yet clinically approved but is in the validation phase.

— We began working together on requirements. GE HealthCare's senior management and CEO were present when we advocated for these. We also applied for joint research grants and had research group meetings at KTH and KI. It has been a fantastic collaboration,' he says, and continues.

— One personal reflection is just how rewarding it has been to be involved in this project from the early stages, when we used tabletop prototypes from Mats Danielsson's group, all the way to actually having a machine where we scan patients.

DANIELSSON IS meagerly anticipating the implementation of this new CT technology and it becoming part of hospitals' clinical arsenal. He does not want to speculate about when exactly photon-counting silicon-based computerised tomography will come into use, but does believe that the FDA will give its approval. Then, in the first phase, the technology will be available in university hospitals and larger hospitals.

— But computed tomography is a standard technology. If the project goes as far as we want and hope, these devices will be everywhere — even in Eksjö in Småland. That would be great, he says.

From a **Nobel Prize** to photon–counting **computed tomography**

This timeline shows progression, from the 1979 Nobel Prize honouring the development of computed tomography to a new type of photon–counting computed tomography that is based on silicon.

1979. *Allan M Cormack* and *Godfrey Newbold Hounsfield* were awarded the Nobel Prize in Physiology or Medicine for the development of "computer assisted tomography."

1990. *Mats Danielsson* graduated with a degree in engineering physics from the KTH Royal Institute of Technology, Stockholm.

From 1990 to 1996, he worked at CERN, the European Organisation for Nuclear Research, in Geneva, Switzerland, on the CPLEAR experiment, measuring time symmetry, i.e. what happens if you put a minus sign in front of time.

1996. *Mats Danielsson* defended his thesis: *First Direct Measurement of T–violation, Based on the First Measurement of Violation of the Time Symmetry.*

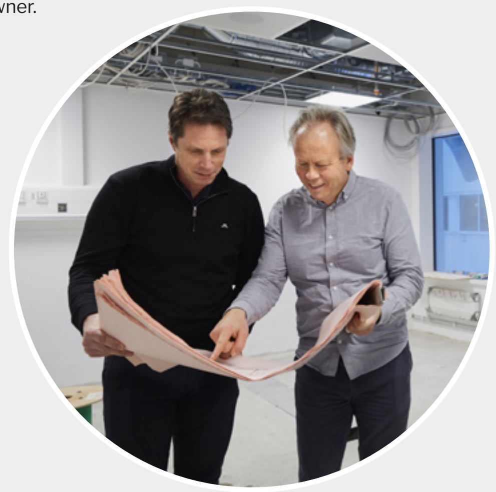
He worked as a postdoc at Lawrence Berkeley National Laboratory, Berkeley, USA, from 1996 to 1998, researching detectors and integrated electronics in X-ray imaging.

1999. *Mats Danielsson* returned to KTH. He is now a professor and leads research on medical imaging.

2000. *Mats Danielsson* founded Mamea Imaging AB, which became Sectra Mamea AB, and launched a new mammography device that produced high—quality images at lower doses of radiation. The company was bought by Philips in 2011.

2008. *Mats Danielsson* received SEK 23.7 million from the Erling–Persson Foundation to develop a type of detector that, when used in computed tomography, provides better images at lower radiation doses.

2012. *Mats Danielsson* founded Prismatic Sensors AB, with *Mats Persson* as part–owner.



2015. *Mats Danielsson* and *Staffan Holmin*, from Karolinska Institutet (KI), were awarded funding from the HealthMedicineTechnology programme, (HMT). This allowed research pairs from KTH and KI to apply for funding for joint projects in medical technology.

2016. *Mats Persson* received his doctorate from KTH and starts a three-year postdoc in the US: two years at Stanford University and one year at General Electric's research facility.

2017. Stockholm County Council approved the establishment of MedTechLabs, which was initiated by *Mats Danielsson* and *Staffan Holmin*, as well as *Jan Andersson* from Region Stockholm. Its activities are funded by KI, KTH and Region Stockholm. Doctors and engineers cooperate within MedTechLabs.

The picture shows Danielsson and Holmin looking at the plans for the CT lab.

2018. MedTechLabs launched the first programme for refining and implementing new CT and endovascular technologies. It was led by *Mats Danielsson* and *Staffan Holmin* and received SEK 35 million in funding for the period 2019–2023.

2020. *Staffan Holmin* is awarded the Hans Wigzell Research Prize of SEK 600,000 for pioneering research work with endovascular instruments that can be guided to specific areas in organs via the blood vessels, to take tissue samples or place pharmaceuticals or materials in the body.

Mats Persson is recruited to KTH. Along with 24 young researchers, he was selected to speak at the Online Science Days organised by the Lindau Nobel Laureate Meeting.

At the end of the year, the US company GE HealthCare bought Prismatic Sensors AB.

2021. *Mats Persson* received the Göran Gustafsson Foundation's prize for promoting scientific research at KTH/Uppsala University. It included a research grant of SEK 2.75 million over three years. He also received the Swedish Research Council's establishment grant for a project focusing on highly accurate photon-counting computed tomography for improved cancer diagnostics.

Version 1 of the CT prototype was unveiled at MedTechLabs on 29 October. To fine-tune the imaging and create a library of different tissues and organ systems, 27 patients were scanned. This concluded in 2023.

2022. *Mats Danielsson* received the Hans Wigzell Research Prize of SEK 925,000 for innovations in the field of medical technology. By bringing together basic physics research and medical science, it is now possible to image details of the human body that were previously too small.

Staffan Holmin freceived the Karolinska Institutet Innovation Prize of SEK 100,000 for his *"ability to build links between Karolinska Institutet, clinics, start–ups and industry"*.

Mats Persson and *Mats Danielsson* joined a consortium granted SEK 8 million from the Swedish Cancer Society in 2023—2026. The project, Emerging CT Technology for Advancing Proton Therapy, is led by Umeå University and will provide better dose planning in proton beam therapy for cancer.

2023. Based on version 1 of the CT prototype, version 2 was developed and installed at MedTechLabs in late autumn.

2024/2025. On 11 April 2024, it was announced that *Mats Danielsson* had been awarded the EU's ERC Advanced Grant, worth SEK 40 million. The five—year project could revolutionise medical PET and SPECT technologies, known as molecular imaging, which detect early-stage cancer and cardiovascular disease. The new technology will dramatically reduce examination times and provide unrivalled image resolution

He is pictured with *Jan Andersson,* co–founder of MedTechLabs (see 2017).

In the process of obtaining regulatory approval from the US Food and Drug Administration (FDA), in 2024/2025, 100 patients will be scanned under the leadership of principal investigator Staffan Holmin.

Twelve Tips from Mats Danielsson

Mats Danielsson's work is a successful example of how scientists can use basic research to develop new and important medical technologies. Below, he provides his top twelve tips for anyone who wants to do something similar – and the most important of all is staying focused.

1

"**Focus** is the most important element of success, so try to avoid doing a little of everything. Even if you think you are hedging your bets, the original 50 per cent chance of success is less than halved – it becomes zero. The most common reason for things going wrong is a lack of focus. If we are developing a good CT scanner for hospital use, as we are, we should not be X-raying fish fillets for bones, even if it sounds like a fun side project."

"In the search for good ideas, you can cast a wide net and see what comes up, but once you've decided on a project, then focus is key."

2

"The product or idea **must solve a problem.** This is the next way you can miss out, and is not at all unusual. You develop what you believe is a great device, but nobody wants it when it's finished, although nobody actually says so. Instead, they blame the 'conservative doctors' who didn't understand the solution's greatness, or that the market is too diffuse. There must be at least one real advantage over current technology."

3

"I like **thought experiments,** ideally with a few people involved. One thing you can ask is if we succeed — what happens then?"

"For example, if our innovation is too expensive, are the components made of 24-carat gold? If they are, then it doesn't matter how good we are or what we do, it will never work."

"Another thing I like to ask is Whose fault is it if we fail? If there are three of us in the room and the correct answer is that it would be our own fault, then we should go for it. As soon as you have to wait for outside expertise, or for someone else to develop something amazing first — then you don't have a chance."

4

"I usually say that there should be at least a **50 per cent chance of success.** The exact percentage is up to you — you might be happy with a two per cent chance, while someone else wants 95 per cent."

5

"In terms of timeframes, I think it should be possible to arrive at some kind of goal **in five years,** rather than aiming for a 20-year perspective, as then everyone dozes off before you've even started telling them what you want to do. Five years, on the other hand, is manageable and worth investing in — getting to a prototype in five years, one that you can prove works on people in hospitals."

6

"As soon as possible, **start talking to doctors,** the ones who understand exactly what you want to develop. This also makes it easier to conduct your thought experiments. It is important to liaise with hospitals very early on. Even if you don't do a great deal to start with, you can still discuss issues and show some prototype images. The earlier you get feedback, the easier it is to manage the project and properly direct your work."

7

"It is also important to **find a clinical principal investigator** for validation. That person has to be able to say — this wasn't very good, yet also be able to point to what is fundamentally positive, otherwise you lose steam."

8

"Financiers who provide **sufficiently large grants** are important when investing in hardware. In academia, we're good at doing things cheaply at the first prototype level. But if you're going to revolutionise something like computed tomography, where a mass-produced unit costs 30 million, and you're going to make a much–improved prototype — then it has to cost at least as much. Otherwise it looks ridiculous, like trying to walk across the Sahara with half a litre of water — it's just not possible."

9

"**Research must be allowed to be research.** You can't start commercialising before you know whether your idea works. You need to do the research before trying anything commercially. Partly because commercial actors do not like the uncertainties of research, partly for your own sake. If you are going to invest your time and energy, you must at least obtain interesting research results."

"That said, I don't think that reasoning holds for applied research. If it is applied research in medicine, the goal must be for it to go out and create a revolution in the healthcare system. It can't be just a little bit better, as some industry will do that instead."

10

"You need to protect your research results with **patents,** but I don't think this should go to extremes. At an early stage, before you are sure things are working, take one or just a few patents, otherwise it will be too expensive and too much work. For many of my patents, we thought they were great ideas, only to realise two years later that they were actually no good at all."

11

"**Working with others is a good idea** when building a prototype. I recommend seeking local support and cooperating with local industry. We have used numerous small businesses, which are also flexible and have a great sense of responsibility. Sweden is an entrepreneurial country, with many family businesses. And they do make an effort if you ask them to – for example if you have a short deadline. They really try to do it a bit faster and are keen to do a good job."

12

"In general, it is important that you **enjoy working together,** otherwise you won't be able to get through those five years. Work has to be fun. Even if there are many problems, looking back should still be fun. You have to try to create that by celebrating the small successes — the worse things go, the more you should celebrate."

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