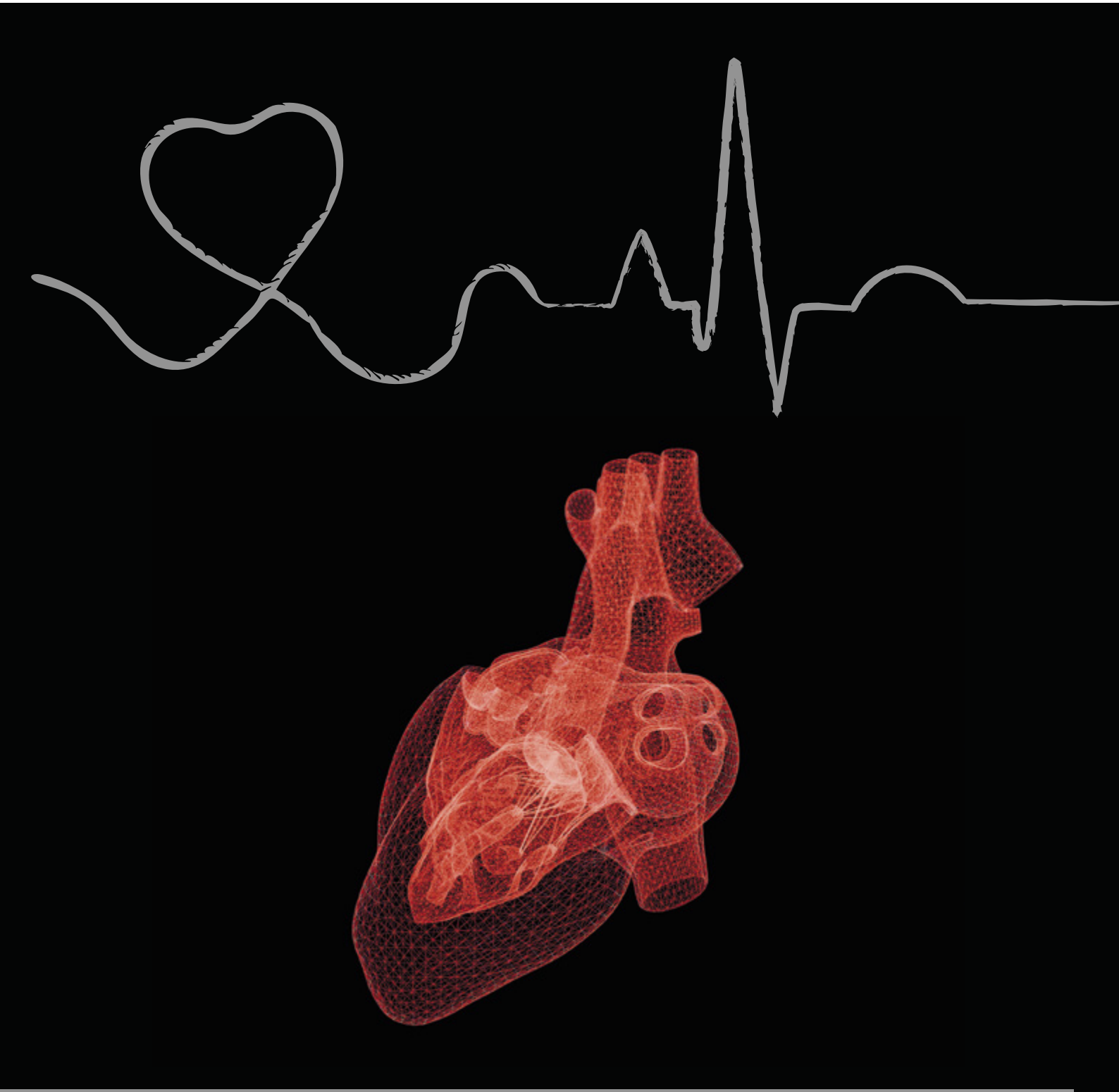
Centre for Research-based Innovation

Established by the Research Council of Norway



Final Report | 2019

CENTER FOR CARDIOLOGICAL INNOVATION

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CENTER FOR CARDIOLOGICAL INNOVATION

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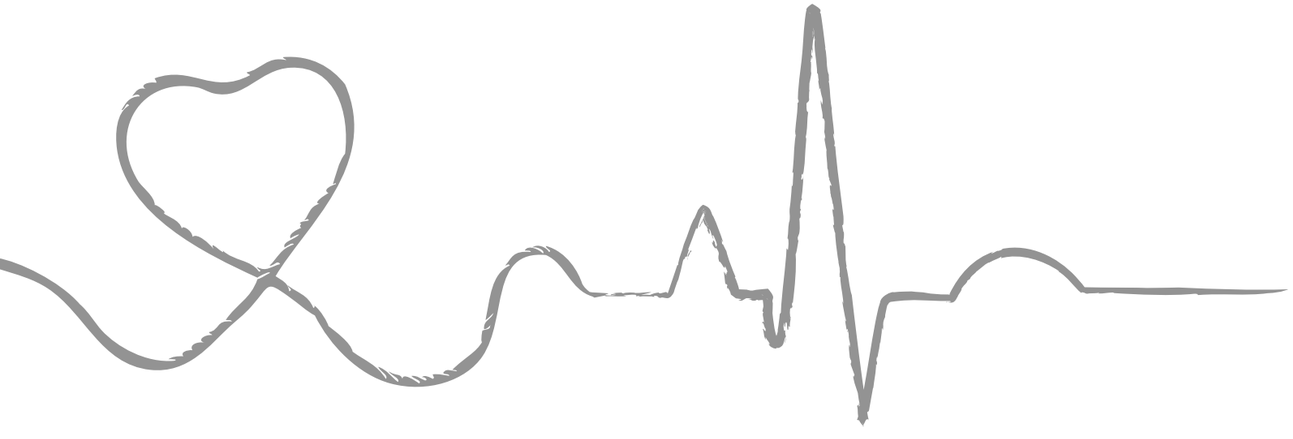

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Photo: Katrine Lunke, Apeland

Foreword by center director

The Center for Cardiological Innovation (CCI) was established with the aim of identifying patients at risk of sudden cardiac death and improve care for patients suffering from heart failure. Our research results and innovation during the last eight years have added value for our industry partners and for the society at large. Most important of all: Our results will be beneficial for patients and improve outcome.

Photo: Katrine Lunke, Apeland

Developing new clinical tools and technology based on novel research takes a lot of time, often longer than the SFI timeframe of eight years. Nevertheless, we have succeeded in creating several innovations that are already in clinical use across the globe. And we believe there is a lot more to come as a result of our work.

SFI has forced cardiologists like myself to innovate, not just to perform research and investigate clinical problems. It has forced all of us to communicate across different scientific disciplines and fields of study, cooperating to come up with the very best and most innovative answers to pressing clinical challenges. Some of the most exciting results are described in this report.

Along the way, we have educated a great number of PhD students and postdocs that will prove their value and contribution to society in the coming years. In this report, you can read about what the CCI experience have meant for their career.

The Department of Cardiology at Oslo University Hospital, Rikshospitalet (OUS), have had the honour of hosting the centre from 2011 until 2019, in partnership with the University of Oslo (UiO), Simula Research Laboratory, GE Vingmed Ultrasound, Cardiosolv, Kalkulo (until 2017) and Medtronic (from 2013). More than 200 scientists and professionals from hospitals, universities, research institutes and industry partners have participated.

The cooperation between industry and clinical researchers has fostered a relationship that will continue to grow and develop in the coming years, hopefully leading to innovations and breakthroughs beyond the period funded by the Norwegian Research Council. We are proud of our eight CCI years, and we hope this report will give the reader a good overview of our activities and achievements.

Å avsløre hjertets hemmeligheter

Gjennom åtte år har vi lyktes med å avsløre noen av hjertets hemmeligheter. Vi har skapt innovasjon som bidrar til å redusere dødeligheten – både blant dem som får hjertesvikt og blant unge mennesker som lider av arvelige genetiske hjertelidelser.

Det viktigste for oss har vært målet om å redde liv. Hjertet er en av de mest kompliserte organismene i menneskekroppen, og hvert år rammes tusenvis av mennesker av hjerteinfarkt eller plutselig hjertestans. Mer kunnskap om hvordan hjertet arbeider, og hvorfor det noen ganger ikke arbeider som det skal, kan spare samfunnet for store behandlingsutgifter, og pasienter og pårørende for mye menneskelig lidelse. Et kjerneoppdrag for CCI har vært å forbedre ultralydbaserte diagnostiske parametere for å kunne gi optimalisert behandling til *den enkelte pasient*.

- Det er viktig å få overført kunnskapen som leger innehar til kliniske verktøy som kommer pasienter til gode, vi kan ikke bare ha fokus på publikasjoner, sa senterleder Thor Edvardsen under markeringen av skanneren og metoden Myocardial Work før selve lanseringen på ESC kongressen i 2017.
Fra venstre; Professor Otto Smiseth, Eigil Samset og Gunnar Hansen fra GE Vingmed Ultrasound, Øyvind Lie, MD, PhD, Professor Thor Edvardsen, MD, PhD.
Foto: OUS

Et dedikert konsortium

Oslo universitetssykehus produserer halvparten av all medisinsk vitenskap i Norge, men det er viktig å få mer ut av denne kunnskapen enn vitenskapelige artikler og innlegg på kongresser. I CCI har sykehusets ledende kardiologer fått muligheten til å samarbeide med industri- og forskningspartnere som er ledende på sine felt: GE Vingmed Ultrasound som er verdensledende i utviklingen av avanserte hjerteultralydmaskiner, Simula Research Laboratory som kan simulere hjertefunksjoner med ekstremt høy grad av nøyaktighet, CardioSolv med internasjonal ekspertise i utvikling av software-verktøy, Medtronic med sin omfattende medisinske teknologikunnskap og Universitetet i Oslo som har bidratt bredt til aktiviteten i senteret.

Vi har ikke vært det største konsortiet målt i antall partnere. Til gjengjeld har deltakerne vært svært dedikerte til forskningen og til det vi kan lære av hverandre. Og totalt har over 200 mennesker vært tilknyttet senteret på en eller annen måte i løpet av disse åtte årene.
Våre felles lokaler ved OUS, med formelle og uformelle møteplasser for de vitenskapelige og kommersielle partnerne, har vært en suksessfaktor. Her har industripartnerne kunnet snakke med kardiologer for å lære hvordan produktløsninger bør utformes til det beste for pasientene. Samtidig har det vært viktig for kardiologer å treffe høyteknologisk medisinsk industri, som har erfaring med kommersialisering og marked.

Skreddersydd hjertebehandling

Åtte år er ikke lang tid i et hjerteforskningsperspektiv. Likevel har vi på denne tiden klart å bringe innovasjoner frem til markedet, hvor de allerede redder liv. CCI-samarbeidet har bidratt til at gode forskningsidéer som «Mechanical dispersion» og «Myocardial work». Disse har blitt utviklet, testet og integrert som nye verktøy i ultralydprodukter raskere enn de ellers ville gjort. Dermed kan flere pasienter få skreddersydd hjertebehandling tilpasset akkurat dem.

Norge er et lite land i utkanten av verden, og vårt samarbeid med anerkjente internasjonale kardiologimiljøer – som Leuven i Belgia, Rennes i Frankrike, Rigshospitalet i Danmark, samt Johns Hopkins University, University of Maryland og Mayo Clinics i USA – har gitt oss tilgang på fremragende ekspertise og bidratt til å bringe innovasjonene raskere ut til markedet. Det har også gitt oss større pasientpopulasjoner å teste innovasjonene på, noe som er uvurderlig innen hjerteforskningen.

Stipendiatene sammen med sine hovedveiledere under mottakelsen av utmerkelsene på EuroEcho-Imaging konferansen 2017.
Professor Smiseth fikk tildelt EACVI æresmedlemskap i 2016 for sitt enestående bidrag innen kardiovaskulær avbilding.
Fra venstre; Øyvind Lie, MD, PhD, Professor Kristina Haugaa, MD, PhD, Professor Otto Smiseth, MD, PhD og John Aalen, MD.
Foto med tillatelse fra EACVI

Har satt vitenskapelige spor

Selvsagt er også de vitenskapelige resultatene viktige for et SFI. Til sammen har CCI produsert 29 doktorgrader, nærmere 500 publikasjoner i fagfellevurderte tidsskrifter og opp mot 700 konferansebidrag. Dette er tall som er langt høyere enn våre opprinnelige mål og 18 stipendiater er fortsatt i ferd med å fullføre sin doktorgrad.

Samtidig har CCI-forskningen bidratt til at våre forskere og doktorgradsstipendiater har vunnet prestisjetunge priser både nasjonalt og internasjonalt, som H.M. Kongens gullmedalje for beste medisinske doktorgrad i 2016, Young Investigator Award i begge klassene under EuroEcho-Imaging konferansen i Lisboa i 2017 og Early Career Award under Oslo University Hospital Research Awards i 2018. Senterleder Thor Edvardsen ble i tillegg valgt som første nordiske president i European Association of Cardiovascular Imaging (EACVI).

Veien videre

Etter åtte år er CCI historie, men vi har fremdeles mye ugjort. Hjertet bærer fortsatt på utfordringer, og potensialet for ytterligere innovasjon på feltet er enormt. Derfor ønsker alle partnerne å fortsette samarbeidet, og å knytte til oss enda flere samarbeidspartnere for å kunne utnytte mulighetene som for eksempel ligger i kunstig intelligens og Big Data. Sammen har vi søkt om et nytt SFI, ProCardio, og venter spent på tildelingen i 2020.

Men uansett hvordan utfallet av søknaden blir, er det alle partnernes klare intensjon å fortsette vårt gode samarbeid i årene som kommer. Vi har mer å lære av hverandre og mer å innovere sammen. Vi er ikke ferdige med å redde liv.

Revealing the secrets of the heart

The vision when CCI was established in 2011 was developing the next generation heart ultrasound products, combining expertise in industrial development, clinical science, and advanced mathematical techniques. During these eight years, we have succeeded in revealing some of the heart's secrets. We have created innovations that helps reduce mortality – both among those who suffer from heart failure and among young people suffering from hereditary genetic heart diseases.

Our most important mission has been saving lives. The heart is one of the most complicated organs in the human body, and every year, thousands of people suffer from heart attack or sudden cardiac arrest. More knowledge about how the heart works, and why it sometimes does not work properly, can save society huge treatment costs, while saving patients and their relatives a lot of pain. A core mission of CCI has always been to improve ultrasound-based diagnostic parameters for optimized treatment of the *individual patient.*

Analysis tools developed at the center is an excellent example on how funding through the SFI-scheme contributes to industry-oriented innovation. The development of these diagnostic tools was also covered by NRK Dagsrevyen in August 2015. On the left is Professor Kristina Haugaa with the new scanner. On the picture to the right are cameraman Tom Arne Søyland, Managing Director at GEVU Dagfinn Sætre, Helge Skulstad, PhD, MD, Eigil Samset, reporter Martin Roalsø and Prof. Thor Edvardsen. Photos: OUS

A dedicated consortium

Oslo University Hospital produces half of all medical science in Norway, but it is important to utilize this knowledge for more than scientific papers and congress speeches. At CCI, the hospital's leading cardiologists have been given the opportunity to collaborate with industry and research partners who are leaders in their fields: GE Vingmed Ultrasound, a world leader in the development of advanced cardiac ultrasound machines; Simula Research Laboratory, who can simulate cardiac functions with an extremely high degree of accuracy; CardioSolv with their international expertise in the development of software tools; Medtronic with their extensive medical technology knowledge, and the University of Oslo who have contributed extensively to the activity in the center.

In terms of number of partners, we have not been the largest consortium. However, all our participants have been very dedicated to the research and to what we can learn from each other. A total of over 200 people have been associated with the center in one way or another during these eight years.

Our common office space at OUS, offering formal and informal meeting places for the scientific and commercial partners, has been a success factor. Here, industry partners have been able to learn from cardiologists how product solutions should be designed to best serve the patients. At the same time, it has been important for cardiologists to meet the high-tech medical industry partners, with their experience in commercialization and the market.

Tailor-made heart treatment

Eight years is not a long time in a cardiac research perspective. Nevertheless, during this time we have managed to bring innovations to the market, where they are already saving lives. The CCI collaboration has helped good research ideas such as "Mechanical dispersion" and "Myocardial work" to be developed, tested and integrated as new tools in ultrasound products faster than they otherwise would have. Thus, more patients may receive tailor-made heart treatment.
Norway is a small country on the outskirts of the world, and our collaboration with renowned international cardiology communities – such as Leuven in Belgium, Rennes in France, Rigshospitalet in Denmark, as well as Johns Hopkins University, University of Maryland and Mayo Clinics in the US – has given us access to outstanding expertise and helped bring innovations faster to market. It has also given us larger patient populations on which to test the innovations, which is invaluable in cardiac research.

Leaving scientific marks

Of course, the purely scientific results are also important for an SFI. In total, CCI has produced 29 doctorates, close to 500 publications in peer-reviewed journals and up to 700 conference contributions. These numbers are far higher than our original goals and 18 fellows are still in the process of completing their PhD.

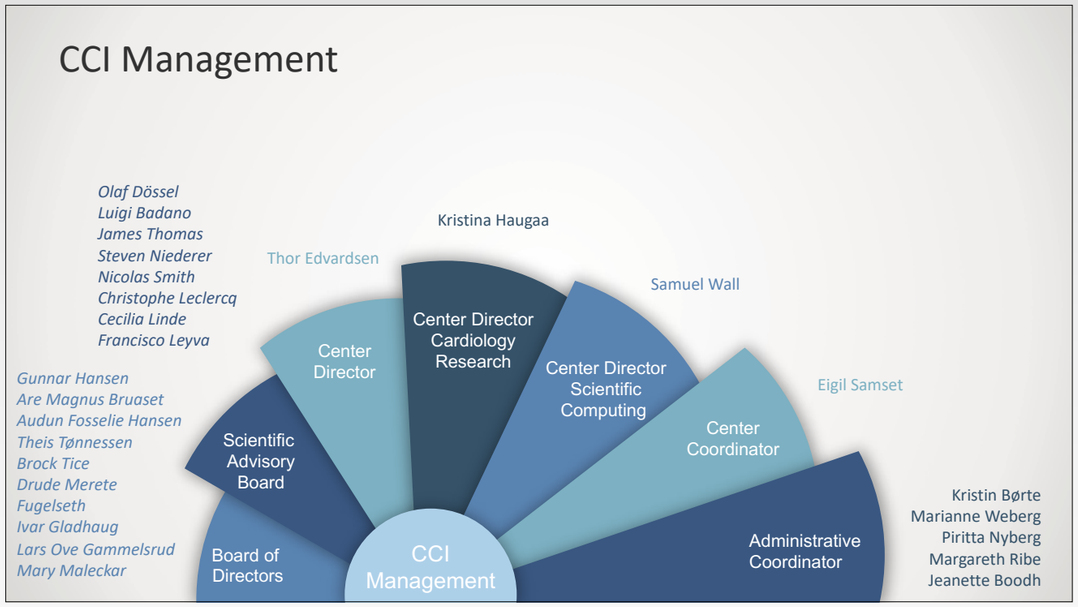
Simultaneously, CCI has helped our researchers and doctoral fellows win prestigious awards both nationally and internationally, such as H.M. The King's Gold Medal for Best Medical Doctorate in 2016, the Young Investigator Award in both classes at the 2017 EuroEcho-Imaging Congress in Lisbon and the 2018 Early Career Award at the Oslo University Hospital Research Awards. In addition, Center Director Thor Edvardsen was elected as the first Nordic President of the European Association of Cardiovascular Imaging (EACVI).

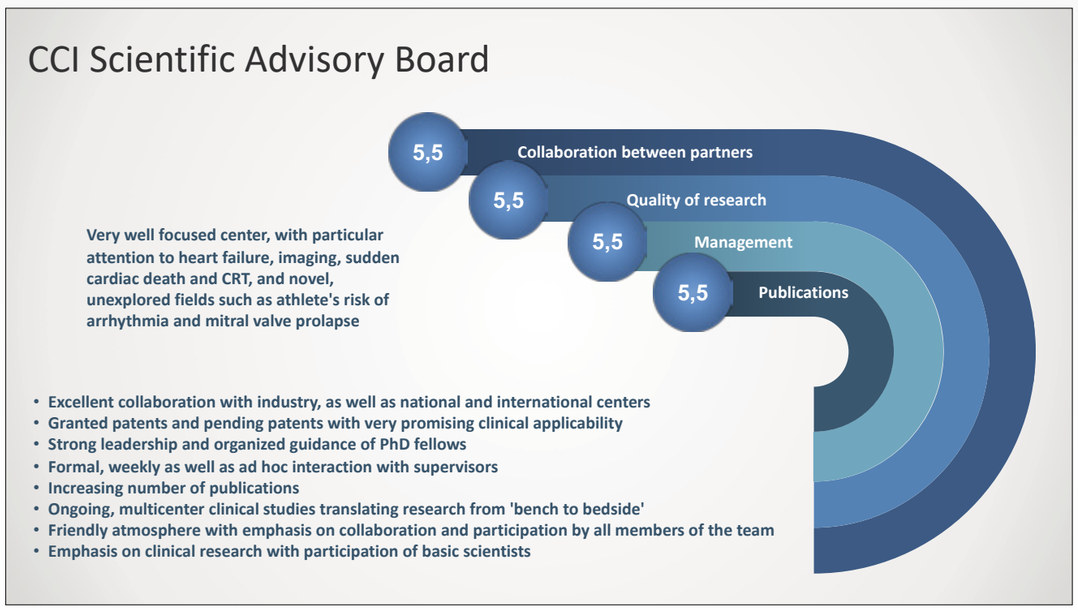
His Majesty the King's Gold Medal for Best Doctoral Thesis within Medicin anno 2016 was awarded Ida Skrinde Leren, MD, PhD, for her thesis "Ventricular arrhythmias in cardiac ion channel diseases; occurrence, treatment and risk stratification". The findings in the thesis gained wide international attention and helped change clinical practice and guidelines for the treatment of CPVT (catecholaminergic polymorphic ventricular tachycardia). The recommendations now state that asymptomatic family members receive pre-treatment with beta-blockers as preventative care. Photo: Rune Enger, UiO

Future prospects

After eight years, CCI is now history. But we have a lot of work left to do. The heart still carries challenges, and the potential for further innovation within the field is enormous. This is why all the partners want to continue our collaboration – and connect with even more partners in order to take advantage of the opportunities that lie in Artificial intelligence and Big Data, to name just two examples. Together, we have applied for a new SFI center, PROCardio, and we are eagerly awaiting the results from the selection process in 2020.

But no matter what the outcome of the application is, it is the clear intention of all partners to continue our good cooperation in the years to come. We have more to learn from each other, more to innovate together. We haven't finished saving lives.





«CCI has made me a better researcher»

"It would be the easiest thing in the world to just conduct research within our own hospital walls. The CCI experience, where I had to work closely with the industry and other partners, has expanded my horizon and made me a better researcher" says Center Director of Cardiology Research Kristina H. Haugaa. She believes active partners and commitment to PhD education has been two of the center's success factors.

Kristina has been a key part of the leadership team since day one. For her, this way of working has been a real eye-opener.

"As researchers, we are driven by the idea of making scientific discoveries. But being part of CCI has forced us to think differently when we do our research. We can no longer just ask: ´Why do patients die? How can we pick out those at high risk? Now, we also have to consider how these discoveries can be developed into commercial products to be used by others and benefit patients directly."
"This is not something we are taught in medical school. It takes practice to add this perspective to your thinking. For me, it has been very exciting and something completely new."

Award-winning research
In 2018, Kristina received Oslo University Hospital's prestigious «Early Career Award» for her outstanding research work.
"I have no doubt that my 'CCI education' and the research opportunities the center has given me was instrumental in making this possible."
"The PhD fellows have been another success story. One of my fellows at the CCI was awarded the King's Gold Medal for best PhD thesis, we have received the award for best research paper at OUS five times, as well as prestigious international awards," she notes. Haugaa herself was elected best teacher for the spring of 2016 by the 12th semester medical students, in addition to receiving research funds from the local branch of LHL in Oslo West and the Association for children with heart disease (Forening for hjertesyke barn).

Professor Otto Smiseth and Professor Kristina Haugaa after receiving her «Early Career Award». Photo: Margareth Ribe, OUS

Common commitment to innovation
OUS has had extensive research activity within cardiology for many years before CCI was established. Kristina believes it has been a big advantage to be able to include existing knowledge and competency in the center activities, building on and refining an ongoing activity instead of having to start from scratch.
"It's been a lot of fun and a real privilege to work in a team with so many brilliant people dedicated to their subject. Together we have created a completely new constellation of people and several exciting innovations, all for the benefit of the patients."

Compared to some other SFIs, CCI has consisted of relatively few partners. Kristina believes this has been to the center's advantage. "We may not have the largest partner group. In return, our cooperation has been very close, with every single team member extremely committed. Active collaboration with regular workshops and not least our shared office locations with bi-weekly management meetings has been important. Now I just hope we can continue our good work, creating even more exciting innovations in the future."

Mechanical dispersion: The Arrhythmia Detector

Convincing the medical community to start using a new method in clinical practice takes a long time. Not so for mechanical dispersion, an ultrasound technique that detects uneven, and potentially fatal, heart contractions at an early stage. Fully developed within CCI, the method is already in use all over the world.

What is an ICD?

ICD monitors heart rhythms and detects any life-threatening, rapid heartbeat. If it senses dangerous rhythms, it delivers shocks. This treatment is called defibrillation. An ICD can help treatment of life-threatening arrhythmias, especially those that can cause sudden cardiac arrest (SCA). All ICDs can act as both a pacemaker and a defibrillator, while also recording the heart rhythm. This can help the doctor plan future treatment.
Receiving an ICD requires minor surgery and the patient will normally be back to normal activities within a few days.

Normally, the heart's left and right ventricle has symmetric contractions. When they are not timed, it indicates some form of rhythm disruptor within the heart. This arrhythmia is a clear marker that you have a higher risk of potentially fatal heart rhythm disorders. Often, this can occur from scarring after an infarct. However, you cannot see these scars on ordinary ultrasound images. Instead, we had to find a way to detect the contraction disorders themselves. Traditionally, you only monitor heart function, for instance poor pumping power. The mechanical dispersion method looks at the timing of how the heart pumps, and makes it possible to detect arrhythmia at a much earlier stage than previous methods. This helps you select people at high risk for life-threatening arrhythmias who should receive life-saving treatment by an implantable cardioverter defibrillator (ICD).

CCIs first studies were within this target group, looking for uneven heart contraction in over 600 myocardial infarction patients. The ultrasounds using mechanical dispersion showed that those with uneven contraction were at a higher risk of sudden cardiac arrest. In several patients where we would not see an increased risk with traditional methods, we managed to detect it now.

Wide area of use
We have also used this technique to detect high risk individuals with other heart diseases, such as cardiomyopathies – hereditary heart diseases that often affects young people and can cause them to die suddenly at a young age. These diseases also develop scars that cause uneven contractions. There have been several high-profile cases of top athletes who die suddenly from sudden cardiac arrest because of this. CCI have shown that the mechanical dispersion ultrasound technique can also be used to detect individuals at risk for cardiomyopathies, as well as other cardiac diseases.

To further convince the medical community, the IMPROVE study is now under way, including more than 1,000 patients in Norway, to demonstrate that the concept works. The aim of the study is to investigate if global strain and mechanical dispersion may predict death and ventricular arrhythmias better than ejection fraction (EF) in patients with myocardial infarction and heart failure regardless of cause.

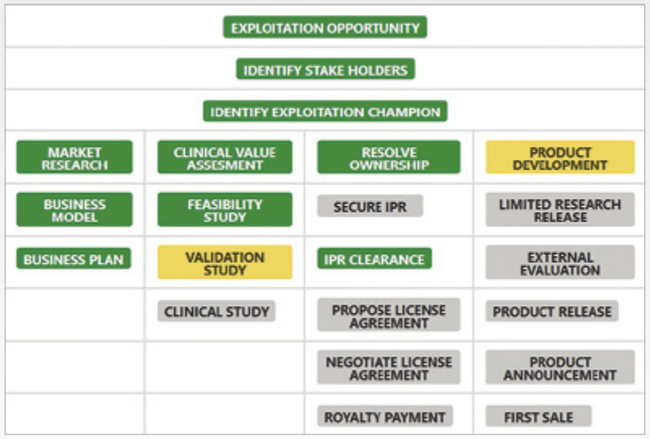
A Center success
Mechanical dispersion was largely developed in CCI, under the leadership of Center Director of Cardiology Research, Dr. Kristina H. Haugaa and Center Director Thor Edvardsen. OUS patented the method during the study, developing the software in close cooperation with center partner GE Vingmed Ultrasound – who then bought the license, developed the interface and implemented it in its ultrasound machines.
In this way, the close innovation collaboration in SFI CCI has made sure that the method is already widely used to save lives both in Europe, the United States, South America, Asia and Australia.

PhD fellows Marianne Forså, MD and Thuy Mi Nguyen, MD will utilize the Vivid E95 scanner in the IMPROVE study, the largest of its kind. The study was also mentioned in Federlandsvennen in 2015. Photo courtesy of Marianne Forså, OUS

From local ideas to global impact

Turning cutting-edge scientific innovation ideas into commercially viable ultrasound products is at the core of CCIs objectives. To achieve innovation that helps patients and has a global impact, it is vitally important that our research results are easily exploitable for the industry partners. Developing the CCI roadmap for innovation has been especially valuable in bringing scientific and commercial aspects together.

If you ask a researcher what it would take for their idea to become a commercial product, many of them won't be able to come up with a good answer. Conversely, the same will happen if you ask someone from the industry how to make sure an idea for a product will work in medical practice. This is why CCI has developed our own dedicated roadmap for the innovation management process, highlighting the activities required to transform a good idea into a finished product that is commercially viable.



Answering the important questions
The roadmap serves several purposes. It ensures that important clarifications are made in relation to the market, asking questions such as: "Who are the possible buyers? How big is the market? What could a sensible business model look like?"
It also makes sure we ask the important clinical questions: "Does this idea work? Which clinical trials are required to prove that the product works?"
Then it helps us clarify necessary steps regarding patents and intellectual property rights, as well as mapping out the actual product development that needs to be done by the industry partners.
For each of these activities, the roadmap highlights where we stand right now, what is required to move the innovation process forward and what is missing at any moment. This rigorous process has a proven track record, is easy to implement/adopt, and is familiar to key partners. It has proved a very helpful tool for managing our resources and knowing when to step up our efforts in developing the most promising innovation projects. Each step in this innovation process is a stage gate, where a decision to pivot, preserve or terminate is made.

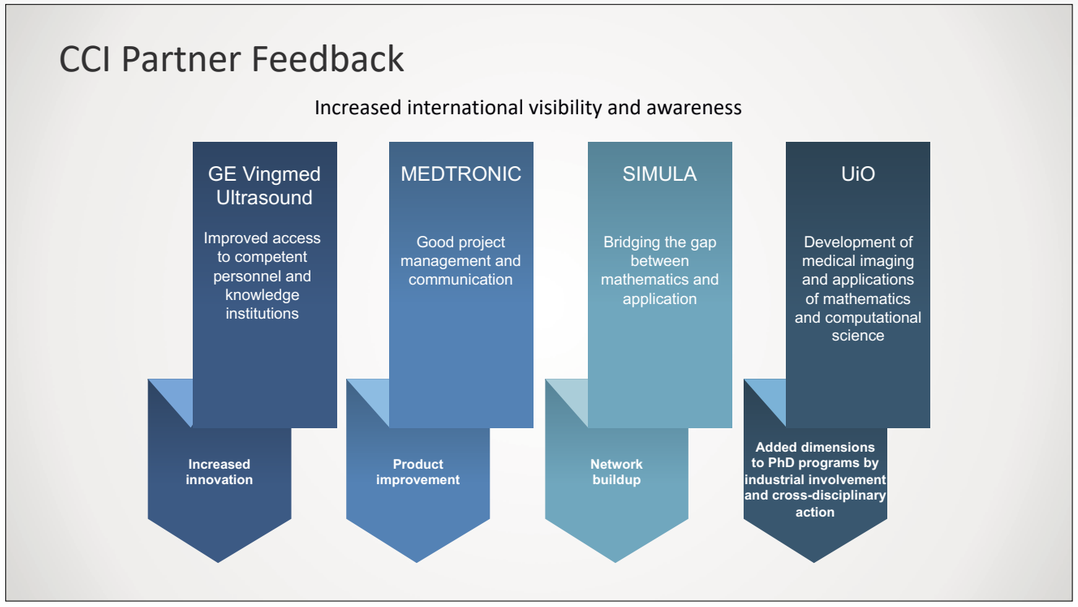
From local ideas to global impact

A new innovation dimension
The objective of CCI is not for a research project to end up with an article which is read by a few dozen people in the cardiological community. We are looking for a completely different impact than you do when working purely academically. Our goal is creating new products or improving existing products, to be used in patient care by thousands of people all over the world every single day.

However, researchers are still measured by their publications and articles, not on innovation results. For many, saying that we are going to create innovation is a new dimension. At the same time, the industry is very focused on their next release to market in a few months. In a high-speed business world, it can be difficult to prioritise and see the potential value of innovation projects with eight-year time horizons. It requires a level of clinical and medical understanding that not every industry partner has.

Added value for all parties
We have found that working together in a true interdisciplinary innovation environment provides added value for both research and industry partners – and ultimately for the patients. Active participation from both the internationally recognised research environment at the hospital and from companies at a similar high level has built mutual competency and led to the development of high-level ultrasound equipment. Our management of the innovation processes has helped streamline this work.

Targeted product launches have been an important part of this. Both research and industry partners have been present at international heart ultrasound conferences, creating a complementary effect which has boosted our global impact. Innovations such as “mechanical dispersion” and “myocardial work” were developed by center researchers at OUS. The CCI partnership with GE made it possible for these ideas to become much more than scientific articles from a research group. Instead, they are now commercialised and used globally, daily impacting medical practice and patient care.

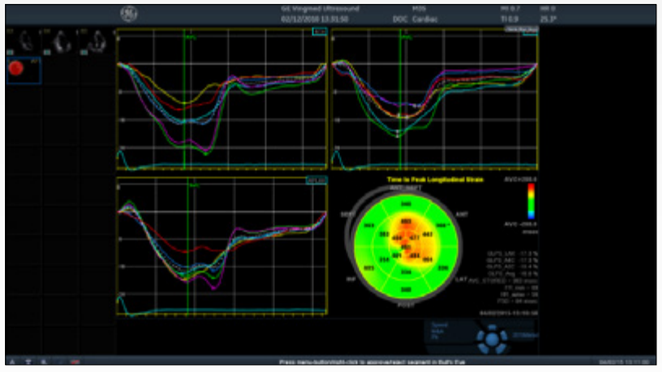


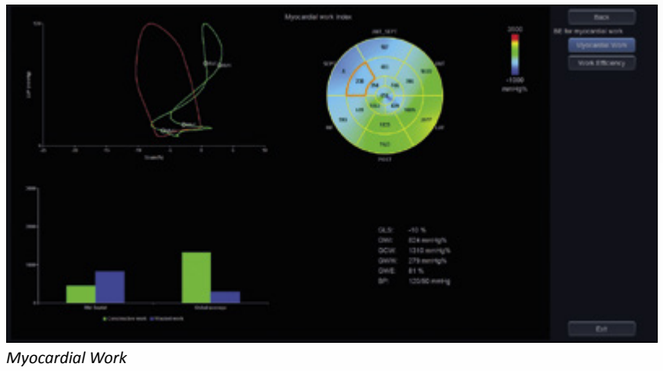
International recognition

The innovations coming out of CCI are making waves in the international cardiovascular society.
Prof. Dr. Erwan Donal, one of the world’s foremost cardiac imaging experts, has already started putting them to good use at Centre Hospitalier Universitaire de Rennes, France. We asked him to tell us why.

“*Mechanical dispersion* is a simple tool that is automatically calculated based on the segmental longitudinal strain assessment. The global longitudinal strain is the, or one of the, most robust measurements that we can get from transthoracic echocardiography if the images are acquired appropriately. Thus, the dispersion is simple, robust and the evidences are consistent for demonstrating that it is a prognostic marker, associated with the amount of myocardial fibrosis. It is especially valuable for its predictive value in regard to the risk of ventricular arrhythmias.”

“*Myocardial work* is also based on the semi-automated calculation of the global longitudinal strain. This is an extremely promising tool combining the estimation of the intra left ventricular pressure and the calculation of longitudinal strain. Pressure/strain loops are computed for the left ventricle and for each of its segments. From these pressure-strain loops, myocardial work indices that are less load dependant than the single strain data can be calculated. Very promising results have been published in the field of the ischemic heart diseases, in the field of heart failure for the function assessment, and for quantifying mechanical dyssynchrony.”


Peak Strain dispersion / Mechanical dispersion


Myocardial Work

Myocardial Work: Understanding the Cause of Heart Failure

Myocardial work has potential to become the new leading method to measure cardiac function, helping to customize therapy and thereby save patients from fatal heart failure. Thanks to CCI, the novel clinical idea has reached a worldwide market in record time.

Heart failure is a major health problem worldwide, and there is a need for better therapies to save lives and improve life quality. Currently, cardiac function is evaluated either by measuring how much blood is ejected from the left ventricle with each beat (ejection fraction) or how much the heart muscle shortens (strain).

However, the problem in heart failure is not only reduced heart muscle shortening, but also low efficiency. Until now there has been no clinical method to measure efficiency. With the introduction of the myocardial work method, it is feasible to measure cardiac efficiency.

The first clinical test of the work method is in patients with heart failure due to none-coordinated ventricular contractions. In this condition, which is named dyssynchrony, different parts of the heart muscle work against each other; some are contracting, while other parts are stretched. The result is wasted energy and aggravation of heart failure.

- So far, heart function has been measured as a percentage contraction, while the new method also measures how much work is done in the different parts of the heart. With the new method we hope to be able to detect heart disease at an early stage so that the treatment can be started before the disease has come too far, Professor Otto Smiseth tells Dagbladet in 2017.

An ideal measurement method
Some of these patients may benefit from implantation of an advanced pacemaker system named cardiac resynchronization therapy (CRT). Still, up to 50 percent of patients have no benefit from CRT. The problem is that currently we have no good method for identifying which patients will benefit from CRT.
The myocardial work method could be a breakthrough in the search for patients who will respond to CRT, which is a life-saving therapy. It is currently being tested in an international multicentre study under the leadership of Professor Otto A. Smiseth.

What makes myocardial work such an ideal measure for cardiac function is its ability to incorporate blood pressure into measurements of myocardial shortening. The current dominant methods for measuring ventricular function are blood pressure dependent, a built-in weakness that can cause you to misinterpret measurements as cardiac illness when in fact it is a normal response to increased blood pressure.
By taking blood pressure changes into account in a refined way, myocardial work is, in principle, a more robust and reliable measure of cardiac function, helping the doctors avoid false diagnoses.

Members of the research group "Integrated cardiovascular function", headed by Professor Otto Smiseth. Photo; Øyestein Horgmo, UiO.

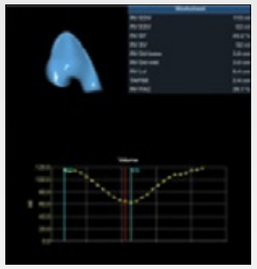
From patent to product
The idea was conceived in 2010 by Professor Otto A. Smiseth, Head of Division of Cardiovascular and Pulmonary Diseases at Oslo University Hospital. Working with a dedicated team of PhD fellows, research partners and industry partners in CCI, they were able to develop the patent into the first worldwide product launch in 2017. For a novel clinical idea, this is an extremely quick time-to-market.

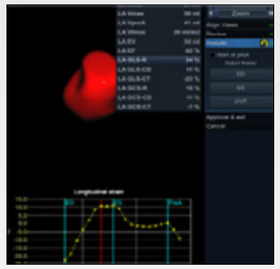
A test of the concept was carried out at The Heart Centre of OLV Hospital in Aalst, Belgium, with financial support from CCI. The benefit of having others test a concept is avoiding conscious or unconscious biases. This small study of 20-30 patients showed that the principle worked.

Following this, a larger international study is currently going on at hospitals in Belgium, France, Norway and Sweden.
So far, the results look very promising, but it remains to be seen if the concept is robust enough to be the new leading measurement method.
Even so, myocardial work is already in global use, attracting huge interest at medical conventions all over the world.
According to Professor Smiseth, this shows one of the big advantages of being part of CCI. The researchers have been given access to a great deal of expertise at industry partner GE, making sure that what otherwise might just have been a good idea and a patent may now be saving lives.

Innovations that have been commercialized

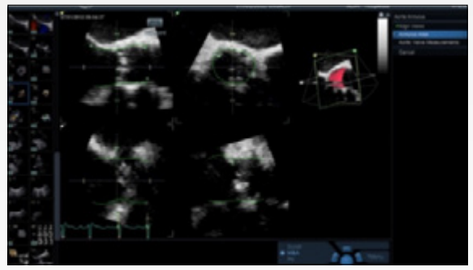
The cross-disciplinary nature of the CCI allows new ideas to form in the intersection between the clinical problems we try to solve and the different scientific methods and approaches employed. The breadth of the research within the CCI has been widened substantially by the addition of Medtronic as a user partner, and the research program has been structured across our broad core competencies by defining a set of work packages as a combination of clinical application areas and scientific methods.

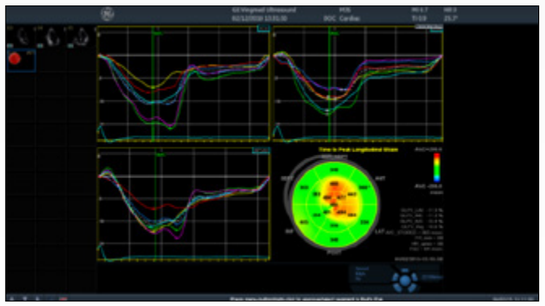




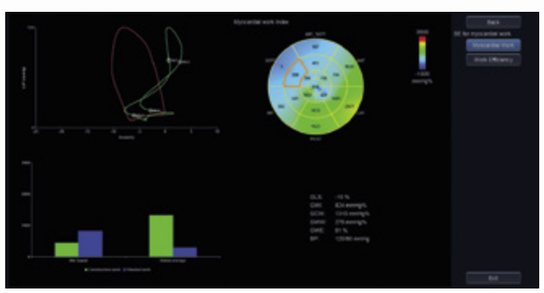
4D Auto AVQ is a tool to measure the size of the aortic valve in 3D. The tool can be helpful in analysing patients with aortic stenosis to determine how rapidly the disease progresses and to prepare for treatments, such as implanting an artificial aortic valve. The feature is available in ultrasound products from GE.

4D Auto RVQ and LAQ are two different features that allows for volume measurements of the right ventricle and the left atrium. These heart chambers are often considered secondary to the main pump of the heart – the left ventricle – but are seen as increasingly important to detect disease early and to predict outcome. These tools are providing automated contouring and and functional assessment of these heart chambers.



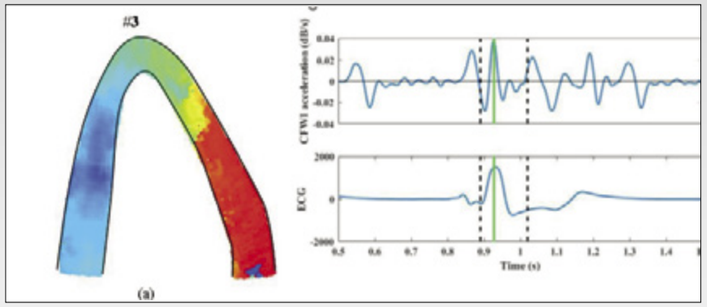


Peak Strain Dispersion is the GE marketing name for Mechanical Dispersion. This is a risk marker for sudden cardiac death and is computed automatically from a speckle tracking analysis. The feature is available in GE ultrasound scanners and the EchoPAC analysis station.

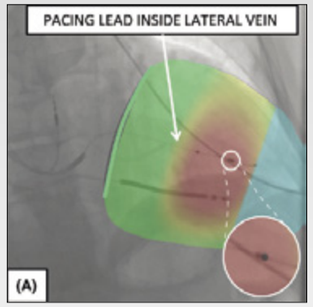


Myocardial Work is a new way to analyse how work is distributed within the heart. It can differentiate between constructive work, that means work that contributes to pumping blood, and wasted work. The method takes into account blood pressure and provides new insights into energy consumption and energy balance in the heart.

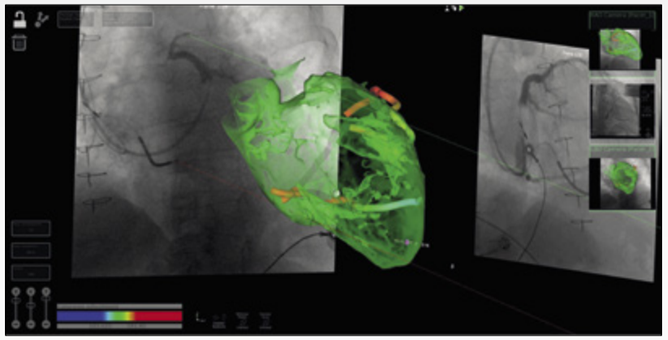
Innovation with future commercial potential



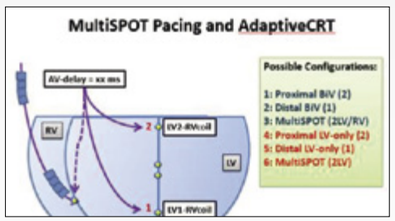
Electromechanical wave imaging is applying ultrafast imaging (more than 1000 frames per second) to uncover movement patterns in the heart that cannot be seen in regular imaging. This has the potential to remove the need for tedious invasive mapping procedures to determine the precise treatment targets in arrhythmic patients.



CRTFusion is a novel software for combining functional information from ultrasound with x-ray. It was designed and tested to help the cardiologist implanting a CRT to ensure optimal placement of the leads that go into the coronary veins of the patient.



Pacer tool is an advanced research tool that can bring together all relevant date for a patient treated for heart failure with cardiac resynchronization therapy. The project was awarded Biotek funding and was spun out from the CCI as a separate project with large innovation potential.



Advanved pacemakers that provides cardiac resynchronization therapy are small computers with the ability to sense and stimulate the heart using advanced patterns. Initial results using adaptive pacing in multiple locations are promising to futher improve the effect of such implantable devices.

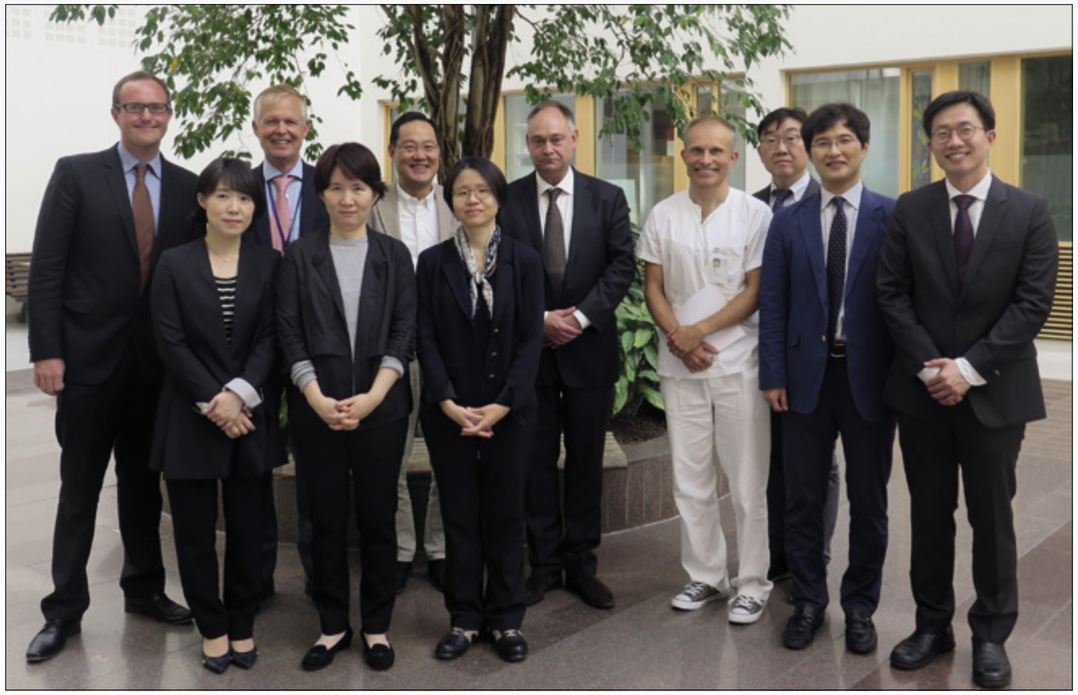
Patent/Application number	Title	Assignee
US20150182187A1	System and method for tracking an invasive device using ultrasound position signals	General Electric Co
US10143442B2	Ultrasonic diagnosis apparatus	General Electric Co
US9622724B2	Ultrasound imaging system and method for tracking a specular reflector	General Electric Co
US20170100091A1	Ultrasound system and method for use with a heat-affected region	General Electric Co
US8626279B2	Methods for estimating the risk for ventricular arrhythmias in a subject	Oslo universitetssykehus HF
WO2012055498A1	Method for myocardial segment work analysis	Oslo universitetssykehus HF

Collaboration

Over the lifetime of the center, CCI has utilized and extented its wide-reaching international network to foster collaborative science and innovation. These collaborations encompass a broad scope of activities, distributed across the partners, including multi-center clinical studies, academic collaborations, education, EU-funded projects and global exchange of researchers. All of these activities have been critical to raise the awareness of the center and work done, as well as to fuse new ideas into the center by tapping into international expertise.

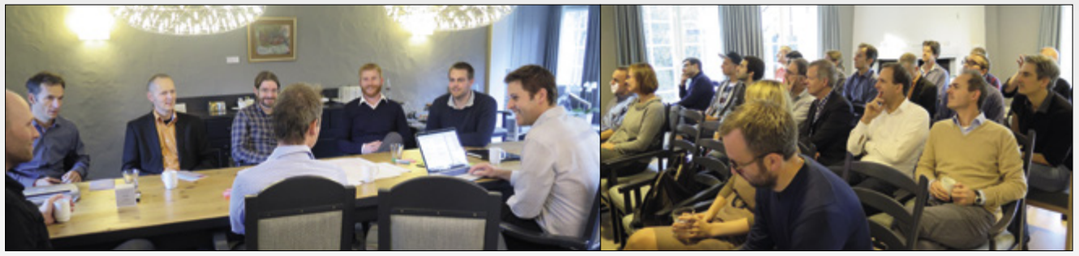
In terms of clinical science and development, the CCI host, Oslo University Hospital (OUS) has been the leading center in several international multi-center studies. Of note was a prospective study on arrhythmias after myocardial infarction (IMPROVE), a study acknowledged and supported by the European Association of Cardivascular Imaging, and performed in collaboration with many European universities and hospitals , including Sykehuset Sørlandet, Universitе́ Rennes-1, Rennes, France, University Hospital Liege, University Hospital Brussels and Silecian heart center Zabrze, Poland. OUS also participated in the DOPPLER-CIP study, funded under EU's 7th framework program. This project has included 676 patients with suspected coronary artery disease and is performed in collaboration with hospitals across Europe, specifically in Leuven, Madrid, Pisa, London, Linköping and Turku.
In addition, a multicentre study including patients with heart failure was performed in the CCI in collaboration with Rennes, France, and CCI has been instrumental in initiating several European multi-center studies, including the CRID study (for studying left-wing block patients and their treatment), which has partners in France, Belgium, Sweden and Norway. Meanwhile, OUS has also continued to develop clinical collaborations within the Scandinavian countries, and is currently working on an emerging prospective study on ventricular arrhythmias in athletes in collaboration with Lund University Hospital, and several University Hospitals in Denmark.

OUS continues to maintain a strong set of research collaborations. Important research collaborations have been established with Maastrich University Hospital, the Netherlands, Mayo Clinic, Rochester, MN, University of Pittsburgh, PA, University Clinic in Brussels, Belgium and Johns Hopkins University, Baltimore, MD, USA. The center has also received visiting researchers from Italy, Belgium, South-Korea and Japan.



Copyright OUH
In the picture you see the delegation from South-Korea, including following prominent cardiologists; Jong Won-Ha, Geu-Ru Hong, Chi Young Shim, Sung-Ai Kim, Stig Se-Jung Yoon, In-Cheol Kim. Present from Oslo Univeristy Hospital were Otto Smiseth, Kaspar Broch and Øyvind Senstad Andersen. Stig Urheim from the University Hospital at Bergen chaired the second session together with Sung Kee Ryu

Research partner Simula has worked closely over the lifetime of the CCI with a wide network of research groups in the United States and Europe. Its largest collaboration has been with the University of California, San Diego (UCSD), with a program called SUURPh that focuses on research education and exchange of PhD candidates in scientific computing and biomedical applications. A number of PhD fellows in the CCI have been a part of this program, and Simula has yearly exchange of researchers with UCSD to work on projects related to cardiovascular disease and innovation.
Simula also has a wide range of international partners who have contributed to their research in the center including University of California, San Francisco (UCSF), Stanford University, the University of Utah, Emory University, University of Massachusetts Amherst, University of Toronto, Ontario, Canada and Michigan State University, all in the US and Canada, as well as INRIA Sophia Antipolis, INRIA Epione, University Heart Center Hamburg, Karlsruhe Institute of Technology, Università di Parma and Bergamo in Italy, and Ghent University in Belgium.



Center members during the 2014 work package review meeting at Lysebu. Photo: OUS

In addition to research partners, the CCI industrial partners have also been a key factor to the internationalization of the project. GE Vingmed Ultrasound, for example, has an extensive global network and actively engages in international research collaboration. Several of these projects have been linked directly to CCI research on subjects such as functional ultrasound imaging for the assessment of heart failure and the risk of sudden cardiac death.
In particular, GE Vingmed Ultrasound has been a strong participant in the international EU Marie Curie framework, having successfully received funding using the European Industrial Doctorate scheme together with KU Leuven in Belgium. The project trained 5 PhD students and focused on improved ultrasound imaging for guidance of treatment for patient with cardiac arrhythmia. Further, GE Vingmed Ultrasound and Oslo University Hospital have also participated in the Marie Curie Project Personalized In-Silico Cardiology (PIC), coordinated by King's College, London, United Kingdom, and a new Marie Curie project with KU Leuven began in 2019.

Related to CCI research, GE has started a range of clinical studies in collaboration with renowned international centers within the area of functional ultrasound imaging for assessment of heart failure and risk of sudden cardiac death, these include KU Leuven (Belgium), University of Padova (Italy), UCSF (California) and University of Tasmania (Australia). GE Vingmed Ultrasound has intensified its work through the later years of the center to develop a solution for artificial intelligence in ultrasound, and has collaborated with some of the world's leading environments; UCSF, Brigham and Women's Hospital, Massachusetts General Hospital.

Industrial partner Medtronic has also brought an international vision to the CCI. Medtronic is highly international, is found in 155 countries around the world, hosts 26 research centers and has direct presence in most European countries. With an industry leading research portfolio, Medtronic has partnered with a large number of hospitals to drive innovation in the field of medical technology. The clinical research range from small exploratory studies with one physician-investigator and just a few patients to multinational, randomized trials intended to demonstrate superior clinical and economical outcomes with new device therapies in hundreds, sometimes thousands of patients. Major European Research facilities include: Bakken Research Center (BRC) in Maastricht (The Netherlands), Therapy and Procedure Training Center in Tolochenaz (Switzerland), and Vascular Manufacturing and Customer Innovation Center in Galway (Ireland).

BRC has more than 20 large international multicenter studies running within the field of Cardiac Rhythm and Heart Failure in Europe. Around 60 projects are ongoing in the Nordic area. Support for the CCI initiated CRT research is mainly provided by the R&T department at BRC, but with a strong link to the research dept. at Medtronic HQ in Minneapolis US. At the BRC R&T department about 30 scientists, engineers and technicians are working closely with medical innovators in hospitals and universities to develop, build and study new devices or methods to "alleviate pain, restore health, and extend life".

A Golden Opportunity

Electrical heart diseases are responsible for sudden, unexpected deaths every year. Ida Skrinde Leren focused on this in her PhD work, with invaluable help from fellow CCI members. The findings in her doctoral thesis has gained wide international recognition and helped changed clinical practice. It also earned her a gold medal from the King of Norway.

“The experience of doing my doctoral work at an SFI, working closely with a large group of scientists, industry experts and PhD fellows with different areas of expertise, was invaluable to me. The CCI group mentality has been a recipe for success,” says Ida.

Predicting the rhythm of the heart

When the heart’s electrical system malfunctions, the normal rhythm of the heart can be disrupted. Cardiac arrhythmias occur when the electrical impulses that coordinate your heartbeats don’t work properly, causing the heart to beat too fast, too slowly, or irregularly.

Arrhythmic heart diseases can be hereditary or acquired. Ida has focused on hereditary cardiac diseases, where patients may have a genetic defect leaving them susceptible to serious cardiac arrhythmias without causing any prior, detectable symptoms. Genetic testing makes it possible to find these patients before they experience severe cardiac symptoms or even cardiac death, and offer them prophylactic medications.

“My PhD work focused on evaluating the severity of cardiac arrhythmias and how to most effectively prevent them in patients with the genetic heart diseases Long QT syndrome and cateholaminergic polymorphic ventricular tachycardia, using both echocardiography, ECGs and exercise stress testing,“ Ida explains.

Two of the studies in Ida´s theses focused on CPVT *(Catecholaminergic polymorphic ventricular tachycardia)*, an inherited and highly malignant arrythmic heart disease.

“Importantly, we studied the effect of two different beta blockers, and found that one was superior to the standard treatment in protecting patients from malignant arrhythmias. This work produced results that are clinically applicable and has already helped patients getting the best treatment to prevent cardiac arrest,” she points out.

The King and Ida

She successfully defended her thesis *”Ventricular arrhythmias in cardiac ion channel diseases; occurrence, treatment and risk stratification”* in June 2016. And the following year, Dr. Leren received the prestigious award **His Majesty the King’s Gold Medal for Best Doctoral Thesis within Medicine anno 2016**.

“This was a real honour. I spoke with H.M King Harald for about ten minutes, explaining the basics of my thesis. It was a very nice experience.”

“But I have to stress that this was a collaboration. I would never have been able to win this award on my own. My fantastic supervisors, Kristina and Thor, have been invaluable, as has the input from other PhD fellows and the rest of the CCI group.”

The King’s Gold Medal is not the only award Leren has been awarded during her years as a PhD fellow at the center. She was also recognized for her work on “Cardiac Mechanical Alterations and Genotype Specific Differences in Subjects With Long QT Syndrome“ when she won the OUS prize for best research article in 2015.

PhD fellow Ida Leren together with Erlend Smeland, head of division for research, innovation and education, after receiving her award for “Cardiac Mechanical Alterations and Genotype Specific Differences in Subjects With Long QT Syndrome“ published in JACC Cardiovascular Imaging. Photo: Børge Einrem, OUS

Cross-disciplinary team spirit

Having joined CCI in 2013, straight after medical school and an internship, Ida jumped at the chance to cooperate with leading cardiologists and other experts within the field.

“I was a real rookie and felt very lucky to be given this opportunity. We were just three clinical PhD students at the time, so I have been able to follow the development of the center almost from the beginning,” Ida says.

Today, she is a resident focusing on cardiology at Diakonhjemmet Hospital in Oslo, and has followed the developments at CCI closely since leaving. Ida believes the interdisciplinary collaborations an SFI facilitates, offer fantastic opportunities.

“Working in a big, but still close-knit, group of PhD fellows, scientists and industry partners, creates a great cross-disciplinary environment for innovation and spin-off effects. It has taught me a lot about how to communicate my work and see things from different perspectives. And I will certainly always cherish the CCI team spirit.”

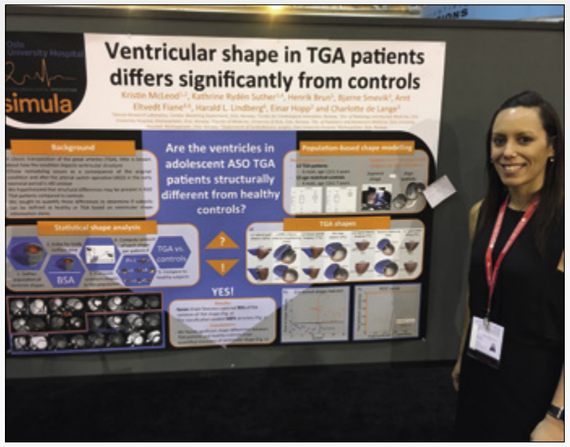
More than the sum of its parts

The interface between technology industry needs and clinical application is where a lot of CCI innovations have been developed. Working as a postdoc at CCI partner Simula Research Laboratory for four years gave Kristin McLeod a first-hand experience of the value these synergies can add. It also opened up new job opportunities.

“I certainly believe this kind of collaboration adds up to more than the sum of its parts. It’s a win-win situation,” Kristin states. Having completed her Engineering PhD in France, she had always been very interested in clinical work.

“Being able to interact with cardiologists and radiologists on a regular basis was exactly what I was looking for. The kind of close interaction CCI could offer is very unique. A big part of this was learning how to communicate and collaborate, using the different languages of medicine and technology,” says Kristin.

The heart in 3D



Center Post doc. Kristin McLeod presented two posters at AHA Scientific Sessions in 2016. The first poster showed that ventricular shape, when quantified in 3D and used in conjunction with volumes and ejection fraction, could be potential predictors of ventricular arrhythmias in patients with Arrhythmogenic Right Ventricular Cardiomyopathy. The second study was an investigation into ventricular shape in adolescent patients with arterial switch operated Transposition of the Great Arteries, for which the authors found that despite being asymptomatic and have seemingly normal anatomy via visual analysis of CMR images, these patients undergo ventricular remodelling which could suggest the need for further intervention later in life. Photo: Einar Hopp, OUS

Born and raised in Taranaki, New Zealand, Kristin had visited Norway before and knew it was a place she would like to live when Simula and CCI recruited her in 2013. Her PhD work on finding new ways to describe structural abnormalities was perfectly suited for the center.

“The current clinical measurements are limited. Describing body shape by height only, or even using parameters such as fainting, shortness of breath or ECG abnormalities, doesn’t give you the full complexity. We wanted to add more measurements that doctors can use when making diagnosis and predicting risk in patients. Using advanced 3D imaging techniques to describe the heart shape can give more information about which particular shapes make cardiological abnormalities more likely,” Kristin explains.

During her research fellowship Kristin focused on the evolution of arrhythmic right ventricular cardiomyopathy (ARVC). “In terms of therapy planning for ARVC patients, the main challenge is to determine which patients are at risk of sudden cardiac death and heart failure to determine who will benefit most from a given method of treatment”, Kristin explains.

The decision making is based on the severity of the symptoms. A key difficulty though is in the moderate group that is taken on a case-by-case basis. Knowing which patients are likely to develop to the high risk group is not so clear. To address this point, it’s important to understand the evolution of the disease.

Breaking down the barriers

Sharing office space – and lunches – with cardiologists and getting to know them, made it easy to ask whenever she had any questions. “We got to know each other really well, and the social interaction made it much easier to break down the barriers between the scientific societies. I would come in with my results, and together we would see what useful information they could give us. The CCI was extremely innovation-driven and has been very useful for me and my work.”

For Kristin, it also led to a new job offer at center partner GE Vingmed Ultrasound, where she has been working since 2017, currently as AI / Data Science team leader in the cardiac ultrasound division.

«My CCI work at Simula was mainly about creating insight for making new tools in the future. At GE, I am more focussed on hands-on tools to be applied in the short term, based on clinical guidelines. In both cases, seeing how my research can have impact on clinical practice is very rewarding,” Kristin concludes.

Athletic treatment

We all know that working out is good for you. But for some athletes, it can lead to fatal cardiac arrest. As part of his PhD research at CCI, Øyvind Lie analysed how to predict this – and prevent it from happening. His life-saving findings earned him international recognition.

“There is no evidence that light jogging and hiking in the woods is dangerous. But in our studies we were able to show why high intensity exercise is dangerous for a particular patient group suffering from a genetic disease called arrhythmogenic cardiomyopathy. This is the most common cause of cardiac arrest for athletes under 35 years,” Øyvind explains.

PhD fellow Øyvind Lie, MD with his poster prize. Photo courtesy of Øyvind Lie

Saving athletes with mechanical dispersion
After some years working and specializing within cardiology and internal medicine, he decided to seek his PhD degree, successfully applying for a fellowship at CCI in 2015. In his PhD research, Øyvind also assessed the clinical utility of the mechanical dispersion method, which was being developed at CCI, particularly related to his discoveries regarding physical activity.

“Integrating analyses of exercise exposure with mechanical dispersion and ECG studies, we were able to create a very precise prediction model for who runs the risk of sudden cardiac arrest in the future. This makes it easier to offer these athletes individualized treatment. For some, it’s providing lifestyle intervention or modifying the exercise exposure, while others need to have an implantable defibrillator.”

Top of the world
His scientific work in CCI certainly didn’t go unnoticed. In 2017, Øyvind won the prestigious Young Investigator Award for Clinical Research at the EuroEcho congress in Lisbon, ahead of participants from all over the world. “That was very surprising and a great experience. There were well over 1,000 submitted research studies, and traditionally Norwegians very rarely get nominated. But this time both me and my CCI colleague John Aalen were nominated in the two separate award categories. And after presenting our research in front of prominent judges, who are the foremost experts in their field, we both won!” Øyvind smiles.

Lie also won the best poster prize in the session for “Diagnostic and therapeutical strategies for cardiac disease” at the annual Center for Heart Failure Research Symposium two years in a row.

Using each other’s strengths
During his research, he found that being co-located with other PhD fellows, both within his own field and from center partners GE Vingmed Ultrasound and Simula, was very helpful. This close collaboration allowed me to access tools faster and use them for research before they were in clinical use. Most important of all were the interdisciplinary colloquia and brainstorming, where we all took part in the technological evolution, providing clinical insights into the development of new analysis tools. This way, we get to know people’s strengths and can utilise each other’s clinical expertise and statistical capabilities. When we come together, it turns out we have more in common than we think. For me, being able to incorporate my clinical understanding of diseases into the concepts developed by industry partners felt both meaningful and important. Together, we could identify needs for further innovation and non-existing products, Øyvind says, finishing up by offering some advice for future PhD fellows within his field.

“If you want a research career, you should definitely apply for a fellowship within a consortium in a large and established environment like CCI. The eldorado of tools and access to compelling research environments facilitate an effective and thorough research education, ultimately making you a better scientist and physician,” Øyvind concludes.

Communication

We consider it important to share our work and explain the CCI innovations and objectives to the public.

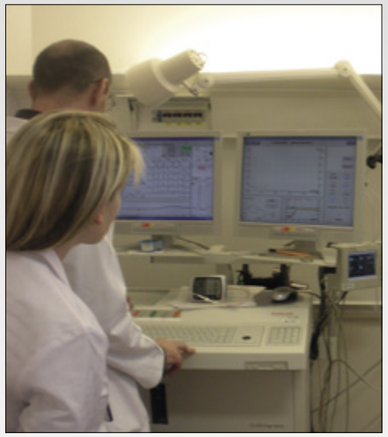
CCI was launched to the public in 2011, when Center Director Thor Edvardsen performed a cardiac ultrasound on the host of NRK PULS Helene Sandvig in the opening segment of the show «Jakten på hjertets hemmelighet», which aired in August.

“We wish to identify those at risk of sudden cardiac death and provide these patients protective care in the best way possible,” Edvardsen stated in the following interview.

NRK, Dagbladet and Aftenposten are among the biggest nationwide contributors for public information regarding CCI research and innovations, an interest welcomed by the center.

Professor Thor Edvardsen demonstrating a cardiac ultrasound on PULS host Helene Sandvig. Photo courtesy of NRK

Communication



Study authors Nina Hasselberg, MD, PhD and Sebastian Sarvari, MD, PhD looking at data for the study in 2015. Photo: Margareth Ribe, OUS

Dissemination activities at conferences and workshops have always been of importance and many members have taken home awards and prizes for excellent research over the years. Unikard, a national commitment for research communication in the field of heart disease, showed particular interest for center members and their achivements writing about the studies an astonishing 40 times.

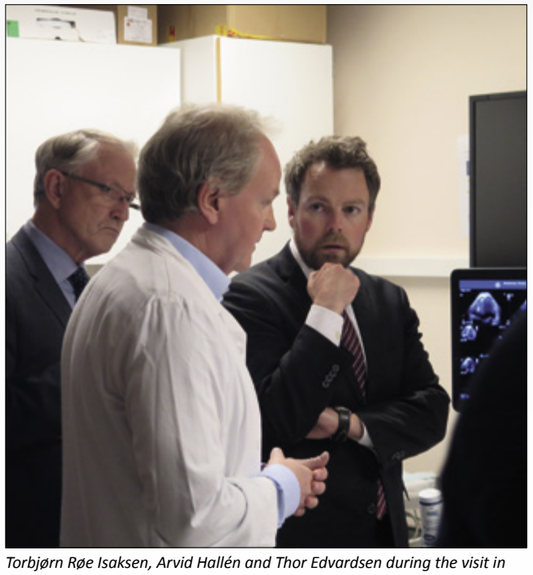
"Both the physical work capacity and the pump function of the left ventricle (the systolic function) are crucial for the prognosis of patients with heart failure. However, previous studies have not been able to demonstrate any association between heart pump function and physical work capacity in this patient group. Using new ultrasound methods, researchers at Oslo University Hospital have now shown that such a relationship exists, which may be important for early identification of high-risk heart failure patients." – Unikard wrote in 2015 about the study "Left ventricular global longitudinal strain is associated with exercise capacity in failing hearts with preserved and reduced ejection fraction" published in European Heart Journal-Cardiovascular Imaging.

Center for Cardiological Innovation was honoured with a visit from the Minister of Education and Research Torbjørn Røe Isaksen and former Director of the Research Council of Norway Arvid Hallén in May 2016. The former CEO of Oslo University Hospital Bjørn Erikstein was also present. RCN chose CCI as the SFI-center to present the published report on the success of the first SFI-centres in the scheme. The report showed that the SFI-scheme has been instrumental in laying a foundation for cooperation between the industry and research sector, paving way for creation of jobs and increased innvoation, thus playing a role in the development of a competitive business environment, ensuring Norway's visibility on the international arena.

During the visit the minster met with a patient who was diagnosed to be at risk for a sudden cardiac arrest after being submitted to the hospital following a silent heart attack. The patient was examined with the ultrasound equipment developed in cooperation with GE Vingmed Ultrasound, Oslo University Hospital and researchers from the CCI.

"I have no doubt that this will save many lives all over the world. The ultrasound device is the most important tool for a cardiologist. It is of great importance to provide the right diagnosis and treatment, and when we get clear images like this, it makes it easier." said Thor Edvardsen to the Research Council of Norway during the visit. He also pointed out that hosting a center with SFI-status has been very positive for the Department of Cardiology at OUS.

"This cooperation has been crucial for speeding up the process from getting a product from the research and development phase to the market. This gives the company a competetive edge while simultaniously providing better patient care and potentially saving lives on a global scale." Gunnar Hansen, Chairman of the CCI Board and research project manager at GE Vingmed Ultrasound pointed out.



Torbjørn Røe Isaksen, Arvid Hallén and Thor Edvardsen during the visit in 2016, which was also covered by Khrono and Finansavisen. Photo: OUS

Bjørn Erikstein said the cooperation in CCI has showed how benefitial interdiciplinary collaboration is. Erikstein believes that interdiciplinary collaboration within the Faculty of Mathematics and Natural Sciences and between the Faculty of Medicine will only increase in the years to come.

Facsimile courtesy of Dagens Næringsliv, photo: Sigurd Fandango, DN

Sensitive parameters are of importance in identification of different cardiomyopathies and channelopathies, due to treatment strategies. Central research areas have included identification and risk stratification of arrhythmic cardiomyopathies. Many of these are considered inherited cardiomyopathies predisposing to ventricular arrhythmias, sudden cardiac death (SCD), and more rarely ventricular dysfunction and heart failure. Cardiomyopathies are not, however, always inherited and in some cases the cause is yet unknown. As a result of this center members have been active in following the development of the athlet's heart, since it could be that an underlying cause is in fact an undiagnosed and possibly not yet know cardiomyopathy. As world's first researchers at CCI and Rikshospitalet showed the link between ARVC and exercise, indicating that exercise for four hours or more a week for a consecutive period of minimum six years may result in a weakened musculature in the right ventricle. Central to this is scarring in the heart, caused by possible cell death in the heart muscle as a result of hard training. A unique MRI method for detecting micro scars as well as sensitive ultrasound machines is used in the search for answers.

Discovering the CCI spirit

Achieving mutual understanding and a good collaborative relationship between research partners and end users can be a challenge within the SFI model. At CCI, we had an advantage: The main research partners are the users.

The world class cardiologists at our host institution Oslo University Hospital are the center's main sources of basic medical knowledge, as well as novel research ideas and patents for future diagnostics and treatments. They are also among the clinicians who will ultimately utilise our innovations for the benefit of patients suffering from cardiac diseases. This circularity has been a key factor in the CCI workflow, and an important reason why we have succeeded in creating several exciting innovations during the last eight years.

But of course, this factor alone would never have been sufficient to build a truly successful SFI center. Being able to utilise the competencies of our other research and user partners, and making the collaboration useful for their daily and long-term operations, has been equally important in order to secure active cross-disciplinary participation from everyone involved.

Our own dedicated roadmap for the innovation management process has been an important success factor in securing progression and cross-center involvement in our innovation activities. An important part of the roadmap is that for each project, we have defined a champion – one person responsible for driving it forward towards an innovation result.

Creating our own spaces

To achieve a true CCI spirit, creating physical spaces for meetings, active cooperation and discussions has been very important. Our shared office space at Oslo University Hospital has been a natural hub, and we noticed a marked progression in our innovation efficiency after moving in. Many partners located elsewhere visit regularly, both for professional and social reasons, and it has given our PhD fellows invaluable opportunities for working together across interdisciplinary fields.

The Research Council of Norway visited CCI together with the Midterm Evaluation Panel in 2015. Photo: OUS

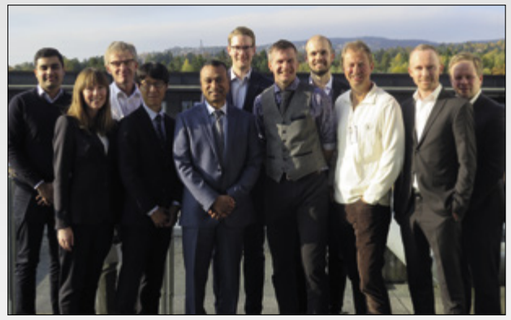
Every year, CCI has held two major workshops for all our center partners. This has been a very important arena for creating unity and developing new ideas. At these workshops we have presented our projects for each others and discussed current and future projects freely in groups of people representing different partners and work packages to improve the outcome. Monthly journal clubs, where PhD fellows have presented their work – or scientific articles relevant to the center – have been an important meeting place for cross-disciplinary discussions. Correspondingly, center management and work package leaders have met regularly to discuss research progress and recommendations from the scientific advisory board.

Our end symposium at Holmen Fjordhotell was held in April 2019. CCI innovations and achievements were presented followed by group sessions where members across the board discussed what lessons we have learned. We also took this opportunity to look ahead, discussing how center partners can continue our fruitful collaboration, either in the new SFI ProCardio or with other means of funding. Because we all agree on one thing: There is still work left to do.

Future prospects

Our most important plan for continuing to develop what the CCI has achieved is the proposal for a new SFI, the Precision Health Center for Cardiology (ProCardio).

If approved by the Research Council, ProCardio will develop, test and validate new tools that can reliably predict an individual patient's disease progression, and provide a longitudinal view of past and future care pathway options, enabling optimal disease treatment and prevention of disease progression.



Faraz Kahn Hameed, MD, Camilla K. Larsen, MD, Associate professor Helge Skulstad, MD, PhD, Associate professor Katsuji Inoue, MD, PhD, Professor Theodore P. Abraham, MD, PhD, John Aalen, MD, Professor Eigil Samset, PhD, Ole Jakob Sletten, MD, Espen Remme, M.Sc.Eng, PhD, Petter Storsten, MD and Espen Bøe, MD, PhD. Photo: OUS

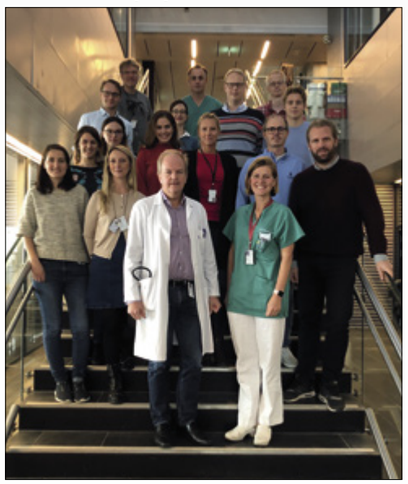
Creating new digital solutions, which are necessary to more effectively exploit the wealth of data produced in modern cardiology, will require integrating rich patient data across all levels of healthcare, while harnessing clinical expertise combined with cutting edge ICT solutions.

ProCardio will build on the achieved world-leading research and previous cooperation by developing novel machine learning methods to overcome the «black-box» nature of artificial intelligence. Linking these to physiological cardiac computer models will pave the way to reaching ProCardio's ambitious goals.

We are continuing the successful collaboration between the partners Oslo University Hospital, GE Vingmed Ultrasound, SIMULA and Medtronic, but we have also performed important regrouping to include partners that can contribute knowledge and insight regarding data registries and databases, eHealth and data management, data science and AI infrastructure, while bringing several of the largest players in the cardiac medtech arena together with leading Norwegian and international research centres.

During his time as Center Director, professor Thor Edvardsen was elected the President of European Association of Cardiovascular Imaging for 2018-2020, mapping out his ambition to help all member countries receive as much education as they require in different areas of cardiovascular imaging. The aim is to better unify the whole thinking around how to make diagnoses and improve patient care, pushing forward technical development in close collaborations with the industry.

The MARCIUS project



Members from the research groups "Myocardial function and cardiac imaging" and "Cardiogenetics and sudden cardiac death" in 2019. Photo: OUS

In light of this, GE Vingmed Ultrasound and researchers from CCI initiated the MSCA-ITN (MARIE SKŁODOWSKA-CURIE ACTIONS, Innovative Training Networks) funded MARCIUS project, that will offer a scientifically cutting-edge training program for Early Stage Researchers (ESR), providing them with the ideal combination of scientific, technological, entrepreneurial, innovation and management skills.

A training network will enable young scientists to develop tools to tackle the central research questions, to be validated and implemented within the industry and in hospitals. In addition, fellows will learn how to identify challenges in the industry and at hospitals, and bring these to academia for solutions.

The objective is creating an active, long-term network of young researchers whose personal contacts, support and expertise will help Europe shape the future of research in medical imaging and intelligent software tools, enabling the future of medical imaging industry in Europe in the coming years. MARCIUS will cascade expertise and spread good practice throughout Europe by personnel exchange, delivering European researchers able to become leaders in the fields of medical imaging in the near and mid-term future.

Financing through the life of the centre

Contributor	*Cash*	*In-kind*	*Total*
Host		35 106	35 105
Research partners		42 253	42 253
Companies		51 864	51 864
Public partners		6 795	6 795
Other public funding		22 906	22 906
RCN	80 000	0	80 000
Sum			238 923

Type of activity	*NOK million*
Research projects	225
Common centre activities	1
Administration	13
Total	239

Statement of accounts for the complete period of centre financing

Funding

Activity/ Item	RCN	Host institution	UiO	Simula	Kalkulo	GE	Medtronic	CardioSolv	Other public	Total
WP 1	27 909	18 140	4 584	2 024		9 068	252		14 497	76 474
WP 2	6 559	568	944	1 970		13 929			1 975	25 944
WP 3	26 318	1 703	1 268	35 735	540	2 529		3 543	1 063	72 699
WP 4	3 951	7 708		1 070	1 833	717	6 215		2 959	24 453
WP 5	3 790	3 198				3 043			2 412	12 443
Equipment	165	2 276		1 140	46	3 859	2 432	3 338		13 256
Management	11 308	1 514		315		518				13 622
Sum	80 000	35 106	6 795	42 253	2 419	33 664	8 900	6 881	22 906	238 923

Cost

Activity/ Item	Host institution	UiO	Simula	Kalkulo	GE	Medtronic	CardioSolv	Total
WP 1	51 813	8 015	2 024		14 370	252		76 474
WP 2	1 335	1 107	1 970		21 533			25 944
WP 3	1 703	1 696	60 519	540	4 697		3 543	72 699
WP 4	12 993	391	1 070	1 833	1 951	6 215		24 453
WP 5	6 436	156			5 851			12 443
Equipment	2 431		1 140	46	3 869	2 432	3 338	13 256
Management	10 342		742		2 571			13 655
Sum	87 051	11 365	67 465	2 419	54 842	8 900	6 881	238 923

Results - Key figures

	2011	2012	2013	2014	2015	2016	2017	2018	2019	Total
Scientific publications (peer reviewed)	24	29	34	55	71	71	77	75	53	489
Dissemination measures for users	38	43	42	67	136	105	115	118	31	695
Dissemination measures for the general public	2			6	2	2			2	14
PhD degrees completed			2		2	4	8	5	8	29
PhD degrees in the process of completion										18
Master degrees				2			1		1	4
Number of new/improved methods/models/ prototypes finalised						7	5	2	1	14
Number of new/improved products/processes/ services finalised		1		1	3	1	3	3	2	14
Patents registered	1			5	2					8
New business activity										0

List of Post-docs, Candidates for PhD and MSc degrees during the full period of the centre

Postdoctoral researchers with financial support from the centre budget

Name	M/F	Nationality	Scientific area	Years/period in the centre	Scientific topic	Main contact
Jussi Koivumäki	M	Finnish	Computational cardiology	2011 - 2014	Electrophysiological Modeling	Samuel Wall
Kristin McLeod	F	New Zealand	Computational cardiology	2013 - 2017	Clinical cardiac models	Samuel Wall
Eirik Nestaas	M	Norwegian	Myocardial function and cardiac imaging	2015 - 2017	Deformation analysis by echocardiography	Drude Fugelseth
Nina Eide Hasselberg	F	Norwegian	Myocardial function and cardiac imaging	2016 - 2017	EchoCRT trial	Thor Edvardsen
Mathis K. Stokke	M	Norwegian	Myocardial function and cardiac imaging	2016 - 2018	Arrhythmias and cardiac electrophysiology	Kristina Haugaa
Jørn Bersvendsen	M	Norwegian	Ultrasound acquisition, processing and visualization	2017 - 2019	Machine learning models	Eigil Samset
Pål Brekke	M	Norwegian	Myocardial function and cardiac imaging	2017 - 2019	New ultrasound technologies and methods	Kristina Haugaa

Post-doctoral researchers working on projects in the centre with financial support from other sources

Name	M/F	Nationality	Source of funding	Scientific area	Years/period in the centre	Scientific topic	Main contact
Hermenegild Arevalo	M	Philippines	RCN	Computational cardiology	2016 - 2018	SCD after MI	Samuel Wall
Sebastian Sarvari	M	Swedish	SENRHA	Myocardial function and cardiac imaging	2017 - 2018	SCD after MI	Thor Edvardsen

PhD candidates who have completed with financial support from the centre budget

Name	M/F	Nationality	Scientific area	Years/period in the centre	Thesis title	Main thesis Advisor
Nina Eide Hasselberg	F	Norwegian	Myocardial function and cardiac imaging	2011 – 2016	Echocardiographic Assessment of Left Ventricular Function and Clinical Outcome in Heart Failure	Kristina Haugaa
Trine Håland	F	Norwegian	Myocardial function and cardiac imaging	2013 – 2018	Hypertrophic cardiomyopathy – Systolic function, differential diagnosis and risk stratification	Thor Edvardsen
Siri Kallhovd	F	Norwegian	Scientific computing	2012 – 2017	Computational tools for clinically driven models of cardiac electro-mechanics	Joakim Sundnes
Henrik Finsberg	M	Norwegian	Scientific computing	2014 – 2017	Patient-Specific Computational Modeling of Cardiac Mechanics	Joakim Sundnes
Aleksandar Babic	M	Serbian	Ultrasound acquisition, processing and visualization	2012 – 2019	Echocardiographic fusion imaging in cardiac resynchronization therapy and coronary computed tomography angiography	Eigil Samset
Jørg Saberniak	M	German	Myocardial function and cardiac imaging	2011 - 2017	Arrhythmogenic right ventricular cardiomyopathy (ARVC) – Impact of exercise on cardiac outcome, differential diagnoses and risk stratification of arrhythmic events	Kristina Haugaa

PhD candidates who have completed with other financial support, but associated with the centre

Name	M/F	Nationality	Source of funding	Scientific area	Years in the centre	Thesis title	Main thesis Advisor
Adriyana Danudibroto	F	Indonesian	EU	Ultrasound acquisition, processing and visualization	2013 – 2017	Data Fusion for Enhanced Visualization of Echocardiography	Jan D'hooge
Nuno Almeida	M	Portuguese	EU	Ultrasound acquisition, processing and visualization	2013 – 2017	Automated echocardiographic assessment of the left atrium	Jan D'hooge
Pedro Santos	M	Portuguese	EU	Ultrasound acquisition, processing and visualization	2013 - 2017	New beamforming methodologies for fast transoesophageal volumetric cardiac imaging using ultrasound	Jan D'hooge
Raja Sekhar Bandaru	M	Indian	EU	Detection of catheters in ultrasound.	2013 – 2018	Novel methods for real-time catheter tracking in volumetric cardiac ultrasound	Jan D'hooge
Jørn Bersvendsen	M	Norwegian	RCN (BiA)	Ultrasound acquisition, processing and visualization	2012 - 2016	Segmentation of cardiac structures in 3-dimensional echocardiography	Eigil Samset
Fred-Johan Pettersen	M	Norwegian	OUS	Electrophysiology and cardiovascular function	2009 - 2017	Bioimpedance as a tool in cardiac resyncronisation therapy	Ørjan Grøttem Martinsen
Vibeke Marie Almaas	F	Norwegian	UiO	Myocardial function and cardiac imaging	2010-2015	Obstructive hypertrophic cardiomyopathy. Pathophysiology and clinical management	Jan Peder Amlie
Marit Kristine Smedsrud	F	Norwegian	UiO	Myocardial function and cardiac imaging	2007-2012	Assessment of incipient global myocardial dysfunction by speckle tracking echocardiography. Clinical studies with emphasis on patients with stable coronary artery disease and patients with chronic aortic regurgitation.	Thor Edvardsen
Kristoffer Russel	M	Norwegian	UiO	Work efficiency and diastolic function	2008-2012	Novel methods for assessing left ventricular dyssynchrony and myocardial function.	Otto Smiseth
Vidar Ruddox	M	Norwegian	VHT	Myocardial function and cardiac imaging	2011 - 2015	Implementation of new echocardiographic modalities in routine practice in a general hospital – Pocket-size cardiac ultrasound and 3 dimensional echocardiography. Studies on feasibility and diagnostic accuracy	Jan Erik Otterstad
Wasim Zahid*	M	Norwegian	SENRHA	Myocardial function and cardiac imaging	2010 – 2016	Myocardial function by echocardiography for risk stratification in patients with heart disease	Erik Fosse
Øyvind Haugen Lie	M	Norwegian	SENRHA	Myocardial function and cardiac imaging	2015 – 2019	Risk stratification and management of patients with right ventricular arrhythmias	Kristina Haugaa
Ida Skrinde Leren*	F	Norwegian	NHA	Myocardial function and cardiac imaging	2013-2016	Ventricular arrhythmias in cardiac ion channel diseases; occurrence, treatment and risk stratification	Kristina Haugaa

Name	M/F	Nationality	Source of funding	Scientific area	Years in the centre	Thesis title	Main thesis Advisor
Sebastian Sarvari*	M	Swedish	SENRHA	Myocardial function and cardiac imaging	2011-2017	Detection of subtle myocardial alterations by echocardiographic techniques for improved prognostic information in patients with heart disease	Thor Edvardsen
Jørg Saberniak*	M	German	SENRHA	Myocardial function and cardiac imaging	2011 – 2017	Arrhythmogenic right ventricular cardiomyopathy (ARVC) – Impact of exercise on cardiac outcome, differential diagnoses and risk stratification of arrhythmic events	Kristina Haugaa
Espen Bøe*	M	Norwegian	SENRHA	Work efficiency and diastolic function	2014 - 2018	Evaluation of left ventricular function by pressure-volume and pressure-dimension analyses: Studies in myocardial ischemia and ventricular dyssynchrony	Helge Skulstad
Arild Hetland	M	Norwegian	ØHT	Myocardial function and cardiac imaging	2012 - 2018	Adaptive servo-ventilation as supplemental treatment in patients with chronic heart failure and Cheyne- Stokes respiration	Thor Edvardsen
Anne Günther	F	Norwegian	SENRHA	Cardiac imaging	2015 - 2017	Imaging in the diagnosis and prediction of allograft vasculopathy after heart transplantation	Jarl Åsbjørn Jakobsen
Lars Gunnar Klæboe*	M	Norwegian	RCN	Myocardial function and cardiac imaging	2014 - 2019	Cardiac imaging in patients with moderate heart failure	Thor Edvardsen
Stian Ross*	M	Norwegian	SENRHA	Cardiac Resynchronization Therapy	2014 - 2019	Cardiac resynchronization therapy Evaluation of acute response parameters	Erik Kongsgård
Lars Dejgaard*	M	Norwegian	UiO	Myocardial function and cardiac imaging	2015 - 2019	The use of different echocardiographic techniques for assessment of risk of sudden cardiac death in cardiomyopathies	Kristina Haugaa
Gabriel Balaban	M	Czech-Canadian	RCN	Computational cardiology	2013 – 2016	Adjoint Data Assimilation Methods for Cardiac Mechanics	Marie E. Rognes
Viviane Timmermann	F	German	SUURPh	Computational cardiology	2015 - 2019	A Computational Study of Mechano-Electric Feedback Mechanisms	Joakim Sundnes

- *Note: Several of these PhD fellows have received financial support through the center budget either in operational costs or periodical salary costs*

* SENRHA = South-Eastern Norway Regional Health Authority (HSØ)
* SSHF = Sørlandet Sykehus Helseforetak
* VHT = Vestfold Hospital Trust (Sykehuset i Vestfold Helseforetak)
* NHA = Norwegian Health Association (Nasjonalforeningen for folkehelsen)
* EHR = Extrastiftelsen Helse og Rehabilitering
* ØHT = Østfold Hospital Trust

PhD students with financial support from the centre budget who still are in the process of finishing studies

Name	M/F	Nationality	Scientific area	Years in the centre	Thesis topic	Main thesis Advisor
Thomas Muri Stokke	M	Norwegian	Myocardial function and cardiac imaging	2017 - 2019	Left ventricular systolic function by different echocardiographic methods	Sebastian Sarvari
Kaja Kvåle	F	Norwegian	Ultrasound acquisition, processing and visualization	2016 - 2019	Visualization and quantification of ischemia in the myocardium	Eigil Samset

PhD students who are still in the process of finishing studies with other financial support, but associated with the centre

Name	M/F	Nationality	Source of funding	Scientific area	Years in the centre	Thesis title	Main thesis Advisor
Petter Storsten	M	Norwegian	SENRHA	Work efficiency and diastolic function	2013 - 2019	Dyssynchrony in the systemic and non-systemic right ventricle	Helge Skulstad
Lars Dejgaard	M	Norwegian	UiO	Myocardial function and cardiac imaging	2015 - 2019	Use of different echocardiographic techniques for the assessment of the risk for sudden cardiac death in cardiomyopathies	Kristina Haugaa
John Aalen	M	Norwegian	NHA	Work efficiency and diastolic function	2015 - 2019	Contractile Reserve in Dyssynchrony (CRID): A novel principle to identify candidates for cardiac resynchronization therapy	Otto Smiseth
Camilla K. Larsen	F	Norwegian	SENRHA	Work efficiency and diastolic function	2015 - 2019	Contractile Reserve in Dyssynchrony (CRID): Role of cardiac magnetic resonance imaging	Einar Hopp
Øyvind Senstad Andersen	M	Norwegian	SENRHA	Work efficiency and diastolic function	2014 - 2019	Left ventricular filling mechanics and left bundle branch block.	Otto Smiseth
Tove-Elizabeth Hunt	F	Norwegian	RCN	Myocardial function and cardiac imaging	2016 – 2019	Atrial fibrillation and advanced treatment planning	Kristina Haugaa
Alessia Quattrone	F	Italian	SENRHA	Myocardial function and cardiac imaging	2015 - 2019	Outcome and influence of pregnancy in women with tetralogy of Fallot.	Mette-Elise Estensen
Daniela Melichova	F	Norwegian	SENRHA	Myocardial function and cardiac imaging	2014 – 2019	Improved prediction of clinical outcome with the use of global strain and mechanical dispesrion in patients with myocardial infarction, heart failure, and patients who receive primary prophylactic internal cardioverter defibrillator.	Thor Edvardsen
Thuy Mi Nguyen	F	Norwegian	SENRHA	Myocardial function and cardiac imaging	2014 – 2019	Improved prediction of clinical outcome with the use of global strain and mechanical dispesrion in patients with myocardial infarction, heart failure, and patients who receive primary prophylactic internal cardioverter defibrillator.”	Thor Edvardsen

Appendix

Name	M/F	Nationality	Source of funding	Scientific area	Years in the centre	Thesis title	Main thesis Advisor
Marianne Forså	F	Norwegian	SENRHA	Myocardial function and cardiac imaging	2018 – 2019	Improved prediction of clinical outcome with the use of global strain and mechanical dispesrion in patients with myocardial infarction, heart failure, and patients who receive primary prophylactic internal cardioverter defibrillator.”	Thor Edvardsen
Anders Wold Bjerring	M	Norwegian	SENRHA	Myocardial function and cardiac imaging	2017 – 2019	use of different echocardiographic techniques for the assessment of late cardiotoxic effects of cancer treatments and the impact of exercise on the hearts of preadolescent and adolescent athletes	Sebastian Sarvari
Eystein Skjølsvik	M	Norwegian	RCN	Myocardial function and cardiac imaging	2017 – 2019	Impact of exercise on myocardial function and ventricular arrhythmias in patients with cardiomyopathies and risk markers for sudden cardiac death in patients with valvular heart disease	Kristina Haugaa
Brede Kvisvik	M	Norwegian	UiO	Myocardial function and cardiac imaging	2014 - 2019	Advances in both high-sensitivity Troponins and echocardiography in the assessment of myocardial function	Jørgen Gravning
Pawel Kozlowski	M	Polish	RCN (BiA)	Ultrasound acquisition, processing and visualization	2013 - 2019	Real-time 3D rendering of ultrasound on holographic display.	Eigil Samset
Liubov Nikitushkina	F	French / Russian	SUURPh	Scientific computing	2015 – 2019	Improved methods for myocardial stress estimation	Ole Jakob Elle
Magnus Krogh	M	Norwegian	SENRHA	Biosensor development and monitoring	2014 - 2019	Monitoring Heart Function by a Miniaturized Motion Sensor	Ole Jakob Elle

Appendix

MSc candidates with thesis related to the centre research agenda and an advisor from the centre staff.
This list also includes medical students that enrolledl for research studies with an advisor from the centre

Name	M/F	Nationality	Scientific area	Year(s) in the centre	Topic	Main Advisor
Iselin Dahl	F	Norwegian	Myocardial function and cardiac imaging	2012 – 2016	Long QT Syndrome and epilepsy	Kristina Haugaa
Marit Aas	F	Norwegian	Myocardial function and cardiac imaging	2014 – 2018	Genetic counseling	Kristina Haugaa
Christine Rootwelt	F	Norwegian	Myocardial function and cardiac imaging	2017	Risk stratification of VA in ARVC	Kristina Haugaa
Thomas Muri Stokke	M	Norwegian	Myocardial function and cardiac imaging	2012 – 2016	Pocketsized cardiac ultrasound	Thor Edvardsen
Kjell Wilhelmsen	M	Norwegian	Ultrasound acquisition, processing and visualization	2017	Optical Flow based classification of periodical heart events on ultrasound image sets	Eigil Samset
Maria Roald	F	Norwegian	Ultrasound acquisition, processing and visualization	2019	Detecting valvular event times from echocardiograms using deep neural networks	Eigil Samset
Jacob Norenberg	M	Norwegian	Ultrasound acquisition, processing and visualization	2013	Analysis of time variations of cardiac ultrasound image sequences	Eigil Samset
Ievgeniia Zhovtobriukh	M	Russian	Ultrasound acquisition, processing and visualization	2013	Automatic landmark detection in 3D cardiac ultrasound images	Eigil Samset
Aslak Wigdahl Bergersen	M	Norwegian	Scientific computing	2016 - 2017	Investigating the Link Between Patient-specific Morphology and Hemodynamics: Implications for Aneurism Initiation?	Kristian Valen-Sendstad
Guttorm Magnus Leiel Kvaal	M	Norwegian	Scientific computing	2016 - 2017	Numerical Simulations of Pharmaceutical Particles Depositing in the Human Respiratory System	Kristian Valen-Sendstad
Sebastian Gjertsen	M	Norwegian	Scientific computing	2016 - 2017	Development of a Verified and Validated Computational Framework for Fluid-Structure Interaction: Investigating Lifting Operators and Numerical Stability	Kristian Valen-Sendstad
Andreas Slyngstad	M	Norwegian	Scientific computing	2016 - 2017	Verification and Validation of a Monolithic Fluid-Structure Interaction Solver in FEniCS. A comparison of mesh lifting operators	Kristian Valen-Sendstad

Employment of PhD candidates (number)							
By centre company	By other companies	By public organisations	By university	By research institute	Outside Norway	Other	Total
4	4	22	1	0	0	1	32

List of Publications

2011

Aarones M, Gullestad L, Aakhus S, Ueland T, Skaardal R, Aass H, Wergeland R, Smith HJ, Aukrust P, Kongsgaard E
Prognostic value of cardiac troponin T in patients with moderate to severe heart failure scheduled for cardiac resynchronization therapy
Am Heart J. 2011, 161(6): 1031-7

Aase SA, Snare SR, Dalen H, Støylen A, Orderud F, Torp H
Echocardiography without electrocardiogram
Eur J Echocardiography 2011, 12(1): 3-10

Cannataro M, Weber dos Santos R, Sundnes J Biomedical and Bioinformatics Challenges to Computer Science
Bioinformatics, Modeling of Biomedical Systems and Clinical Applications
Procedia Computer Science 2011,1(4): 1058-1061

Edvardsen T
Can modern echocardiographic techniques predict drug induced cardiotoxicity?
J Am Coll Cardiol 2011, 57(22): 2271-2272

Edvardsen T, Haugaa KH
Imaging assessment of ventricular mechanics
Heart 2011, 97(16): 1349-56

Eek C, Grenne B, Brunvand H, Aakhus S, Endresen K, Smiseth OA, Edvardsen T, Skulstad H
Post systolic shortening is a strong predictor of viability in patients with non ST-elevation myocardial infarction
Eur J Echocardiography 2011, 2(7): 483-91

Gjesdal O, Remme EW, Opdahl A, Skulstad H, Russell K, Kongsgaard E, Edvardsen T, Smiseth OA Mechanisms of Abnormal Systolic Motion of the Interventricular Septum during Left Bundle-Branch Block Circulation Cardiovasc Imaging 2011(3): 264-734

Goebel B, Gjesdal O, Kottke D, Otto S, Jung C, Lauten A, Figulla, HR, Edvardsen T, Poerner TC Myocardial function in patients with isolated hypertensive heart disease: a two dimensional ultrasound speckle tracking study
J Hypertension 2011, 29(11): 2255-64

Gjesdal O, Edvardsen T
Tissue Doppler in Ischemic Heart Disease
Doppler Echocardiography. In Establishing Better Standards of Care in Doppler Echocardiography, Computed Tomography and Nuclear Cardiology, Edited by: Richard M. Fleming, In-Tech 2011,
ISBN 978-953-307-366-8

Grenne B, Eek C, Sjøli B, Dahlslett T, Hol PK, Ørn S, Skulstad H, Smiseth OA, Edvardsen T, Brunvand H Mean Strain Throughout the Heart Cycle by Longitudinal Two-Dimensional Speckle-Tracking Echocardiography Enables Early Prediction of Infarct Size
J Am Soc Echocardiogr 2011, 24(10): 1118-25

Hanslien M, Artebrant R, Tveito A, Lines GT, Cai X
Stability of two time-integrators for the Aliev-Panfilov system
International Journal of Numerical Analysis and Modeling 2011 8(3): 427-442

Haugaa KH, Edvardsen T, Amlie JP
Prediction of Life-Threatening Arrhythmias - Still an Unresolved Problem
Cardiology 2011, 118(2): 129-137

Haugaa KH, Bergestuen DS, Sahakyan L, Skulstad H, Aakhus S, Thiis-Evensen E, Edvardsen T
Evaluation of Right Ventricular Dysfunction by Myocardial Strain Echocardiography in Patients with Intestinal Carcinoid Disease
J Am Soc Echocardiogr 2011, 24(6): 644-50

Haugaa KH, Amlie JP, Edvardsen T
Prediction of Ventricular Arrhythmias in Patients at Risk of Sudden Cardiac Death In Cardiac defibrillation – prediction, prevention and management of cardiocascular arrhythmic events, Edited by: Joyelle J. Harris, In-Tech 2011, ISBN 978-953-307-692-8

Hopp E, Lunde K, Solheim S, Aakhus S, Edvardsen T, Smith HJ
Regional myocardial function after intracoronary bone marrow cell injection in reperfused anterior wall infarction – a tagging MR study
J Cardiovasc Magnetic Res 2011: 13:22

McDowell K, Arevalo H, Maleckar MM, Trayanova N
Susceptibility to reentry in the infarcted heart depends on the active fibroblast density
Biophysical Journal 2011, 110(6):1307-15

Nagueh SF, Bhatt R, Vivo RP, Krim SR, Sarvari SI, Russell K, Edvardsen T, Smiseth OA, Estep JD Echocardiographic Evaluation of Hemodynamics in Patients with Decompensated Systolic Heart Failure
Circulation Cardiovasc Imaging 2011(3): 220-74

Niederer SA, Kerfoot E, Benson A, Bernabeu MO, Bernus O, Bradley C, Cherry EM, Clayton R, Fenton FH, Garny A, Heidenreich E, Land S, Maleckar M, Pathmanathan P, Plank G, Rodríguez JF, Roy I, Sachse FB, Seemann G, Skavhaug O, Smith NP
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Appendix 3

Appendix 3

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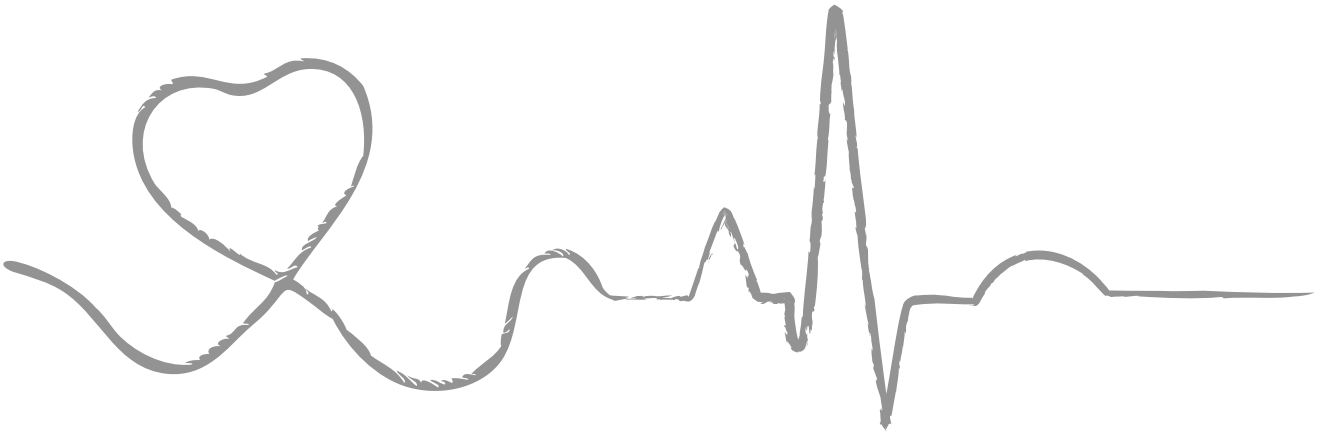

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