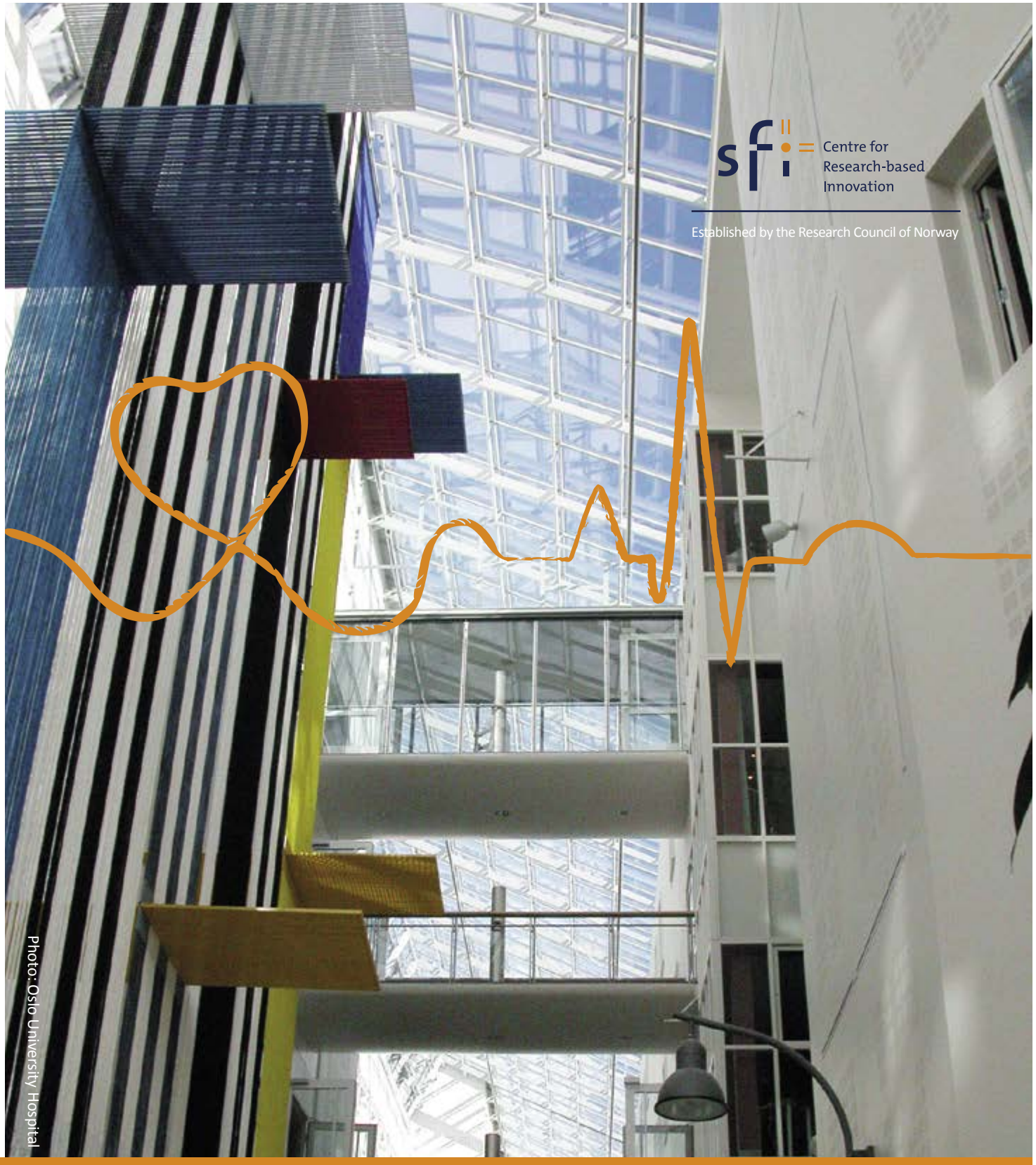

sfi Centre for Research-based Innovation

Established by the Research Council of Norway

Photo: Oslo University Hospital

Annual Report | 2016

CENTER FOR CARDIOLOGICAL INNOVATION

CENTER FOR CARDIOLOGICAL **INNOVATION**

Centre for Research-based Innovation

Established by the Research Council of Norway

Annual Report | 2016

CENTER FOR CARDIOLOGICAL INNOVATION

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Administrative Coordinator

Design: Byråservice as

Cover photo: Oslo University Hospital

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SUMMARY

The Center for Cardiological Innovation (CCI) is hosted by Department of Cardiology, Oslo University Hospital, Rikshospitalet. The scientific idea behind CCI is to develop improved diagnostic methods to detect patients at risk of sudden cardiac death and new treatment principles and diagnostics for patients suffering from heart failure. Advanced imaging techniques, patient specific computer simulation and multimodal visualization will be combined to improve accuracy in these regards. The CCI partners are Oslo University Hospital, Simula Research Laboratory, the University of Oslo, GE Vingmed Ultrasound AS, Kalkulo AS, CardioSolv Inc. and Medtronic Bakken Research Center B.V.

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During the past year Center Director Professor Thor Edvardsen became the new President Elect of the European Association of Cardiovascular Imaging (EACVI). This is the first time that someone from the Nordic countries has been elected to this prestigious position. Prof. Edvardsen also won the Inge Edler Prize in 2016. The award is given for outstanding contribution in the field of echocardiography. Prof. Otto Smiseth was rewarded with the EACVI Honorary Membership in recognition of his outstanding contribution in the field of Cardiovascular Imaging. Prof. Smiseth is one of the world's leading experts on diastolic function and has co-chaired the new official guideline article on diastolic function published by the European Association of Cardiovascular Imaging (EACVI) and American Society of Echocardiography (ASE) in 2016.

Consulting cardiologist and associate professor Kristina Haugaa, one of the foremost experts in Norway in the field of genetic heart diseases, is also the head of the Unit for genetic cardiac diseases, Oslo University Hospital, Rikshospitalet. Ceveral center members are enganged at this clinic, providing crucial follow-up and screening family members of patients with genetic heart diseases. Recent advancements within technology, amongst them the launch of Vivid E95 in 2015 (developed in cooperation between GE Vingmed Ultrasound, Center for Cardiological Innovation and Oslo University Hospital, supported with funding from the Research Council of Norway), has provided cardiologist worldwide with a new set of cardiac imaging tools for better patient diagnosis. The genetic era has provided the ability to test for disease prior to the development of signs and symptoms, and research in the field, contributet to by center members, has increased knowledge of rare genetic heart diseases, assisting in early and correct diagnosis and better treatment for patients and family members disposed to mutations in the encoding genes. Dr. Haugaa recently received a grant from the patient organization the *Association for children with heart disease* for work with national guidelines for patients with genetic cardiac diseases.

The Minister of Education and Research, Torbjørn Røe Isaksen, visited our center in May 2016. Director of the Research Council of Norway Arvid Hallén presented Isaksen a report covering the SFI Research Centres. The centres have strengthened innovation and doctoral degree programs in areas that are important for the development of a competitive business environment. The report showed that the SFI scheme provides an important impetus to collaboration between research institutions and businesses, the centres have helped make Norway more visible in the international arena, said Hallén during the visit. The Minister of Education and Research was shown first-hand how the ultrasound machine Vivid E95 functions, ensuring better patient care by pushing innovations to the bedside.

Throughout 2016, our research has resulted in 72 published scientific articles in peer-reviewed journals. Over 100 presentations, including abstracts, have been held at various national and international conferences within cardiology and biomedicine.
15 new members joined the CCI in 2016. Some work full time at the center whereas others are affiliated members through their research and participation in the center's work packages. All members are equally important when ensuring the best possible innovation in an increasingly competitive international arena. Members receive funding from the center, center partners, or through other public funding. Center PhD fellows Nina Eide Hasselberg, Ida Skrinde Leren, Wasim Zahid and Jørn Bersvendsen successfully defended their PhD thesis last year. The International Scientific Advisory Board was also completed with one more member; Professor Francisco Leyva, MD, PhD, Queen Elizabeth Hospital, Birmingham, United Kingdom.

OBJECTIVES AND RESEARCH PLANS

The center was established to enable the creation of the next generation of ultrasound technology, combining expertise in industrial development, clinical science, and advanced mathematical techniques. The main objectives of the center are focused on developing new tools to help the triage of patients suffering from heart failure (HF) or at risk of sudden cardiac death (SCD).

Sudden cardiac death (SCD) has during the last few years emerged as a topic of immense interest. The limitations of current prediction tools have become evident and the new tool, mechanical dispersion, developed by the CCI has gained international attention. During the last few years, other centers have adapted the technique and published positive studies showing the value of mechanical dispersion and strain echocardiography in predicting malignant arrhythmias and death in a variety of patient populations.

The evolving genetic technology by whole exome sequencing has provided completely new possibilities for detecting genetic diseases. The field is changing rapidly and techniques assessing the risk of arrhythmias and sudden cardiac death are becoming even more important.

To find responders to CRT still remains a challenge in current cardiology. Despite more than 10 years of intense global research on this topic, the responder rate remains at approximately 50-60% of all implanted patients. Further knowledge is therefore needed.
The role of the right ventricle is receiving increasing attention, both regarding impact on CRT response and the role in other diseases. Accurate imaging and assessment of the RV dimensions and functions has been challenging, and requires better techniques. Newer studies have elucidated that patients with diastolic heart failure may also have systolic heart failure, identified by sensitive strain echocardiographic methods. However, the mechanisms and the picture of diastolic heart failure need to be further elaborated.

The CCI stands well posed to create innovation in these challenging clinical areas. Industrial partners GEVU and Medtronic continue to produce better products to image and treat cardiac disease. In the field of cardiac modeling more powerful computing resources, together with improved methods, have made complex simulation based on imaging tractable in clinical time frames. New techniques for methodically linking highly complex simulation data with patient metrics are also emerging.

In contrast to simply adding a new set of measurement indices to an already extensive list of diagnostic guidelines, or prescribing treatment based on those guidelines, the CCI will combine and extend currently isolated technologies into novel, integrated tools and applications. We propose to combine electrical and mechanical information into a new integrated scanning system, which we will then couple advanced techniques to diagnose pathology and prescribe treatment tailored for the *individual* patient. This approach is entirely novel, as integration of these modalities combined with the use of patient-specific simulation has never before been achieved. This innovation has the potential to change the paradigm of diagnostic cardiology and will represent a substantial market edge for the industrial partners.

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ORGANIZATION

The CCI is hosted by Department of Cardiology, Oslo University Hospital, Rikshospitalet. The consortium consists of six partners from both research and industry, in addition to the host institution.

The research partners are Simula Research Laboratory and the University of Oslo.

The user partners are GE Vingmed Ultrasound AS, CardioSolv Inc, Kalkulo AS and Medtronic Bakken Research Center B.V.

The CCI is located at Oslo University Hospital, Rikshospitalet and the University of Oslo, Domus Medica (DM4) at Sognsvannsveien 9 (entrance from Gaustadalléen 34), constitutes as the physical hub for the CCI.

BOARD OF DIRECTORS

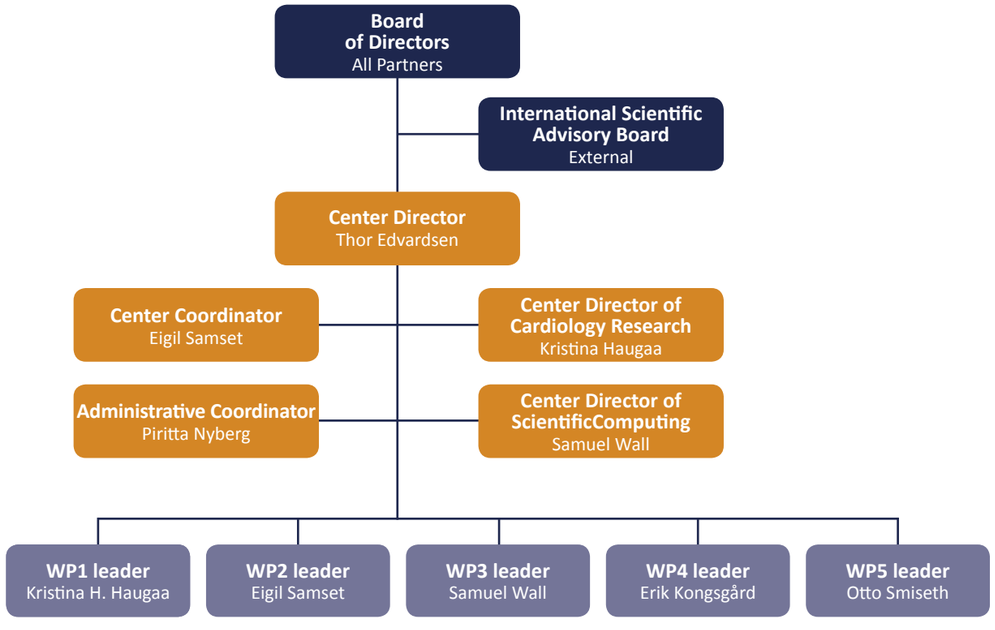
CCI is governed by a Board of Directors, for which representatives have been appointed by each of the partners. The Board comes together twice a year for an overview of the Center's development, financial updates and administrative issues.

Many of the board members participate actively in the Center's research activity and their expertise is of uttermost importance for the development of future technology within the CCI.

The Centers Board of Directors consists of the following members appointed by the consortium participants:

Gunnar Hansen, GE Vingmed Ultrasound, Chair
Mary Maleckar, Simula Research Laboratory
Are Magnus Bruaset, Kalkulo
Theis Tønnessen, Oslo University Hospital
Brock Tice, CardioSolv
Drude Merete Fugelseth, University of Oslo
Lars Ove Gammelsrud, Medtronic

ORGANIZATION STRUCTURE



PARTNERS

Each partner represents an unique and required element in the research and development chain leading to the industrial innovations targeted by the CCI.

Oslo University Hospital

Role: CCI Host institution
Objective: Improve procedures and services related to patient treatments. Obtain new diagnostic and therapeutic approaches to the benefit of patients suffering from cardiac diseases.
Contribution: World class cardiology research group, access to hospital infrastructure and facilities.

UiO : Universitetet i Oslo

Role: Research Partner
Objective: Strengthen quality of research in the field of cardiology and medical imaging. Contribute to research training (completed PhD program) and transfer of knowledge (publication, innovation).
Contribution: Research infrastructure, senior personnel in both clinical research and computer science.

[simula . research laboratory]

Role: Research Partner
Objective: Develop patient-specific simulation models to reveal mechanisms underlying cardiac disease, improve diagnostic techniques, and predict treatment outcome.
Contribution: A research foundation for development of innovative, computationally efficient, and reliable algorithms and software.

GE Vingmed Ultrasound

Role: User Partner
Objective: Develop new and improved products for cardiovascular ultrasound based diagnosis and treatment with high added value for patients and clinicians.
Contribution: Market leading imaging platform and advanced quantitative analysis SW, commercialization pathway, market know-how and access to pre-market hardware and software.

cardiosolv

Role: CCI User Partner
Objective: Become world leader in software development for cardiac electromechanical applications. Bring state-of-the-art cardiac simulation out of academia and to the bed-side.
Contribution: Access to mesh-creation tools, simulators, visualization tools, simulation analysis tools and consultations on cardiac simulation and arrhythmias.

kalkulo

Role: CCI User Partner
Objective: Develop products (as modules or applications) that can be commercialized. Extend current software application framework to strengthen presence in the medical market.
Contribution: Expertise and software tools for advanced computations and visualization.

Medtronic
Further, Together

Role: User Partner
Objective: Contribute to human welfare by application of biomedical engineering in the research, design, manufacture, and sale of instruments or appliances that alleviate pain, restore health and extend life.
Contribution: Extensive expertise in the field of medical technology, research infrastructure and global reach. Risk stratification for sudden cardiac death in the implantable cardioverter defibrillator population and maximized response to cardiac resynchronization therapy. Medtronic will be involved in research tasks directly or indirectly related to patient selection, cardiac device optimization, implant tools, therapy delivery and feedback.

INTERNATIONAL SCIENTIFIC ADVISORY BOARD

The CCI has established an International Scientific Advisory Board (ISAB) to receive feedback by a panel of experts who are not directly involved in the center activities. The ISAB was established in 2012 and consists of: Professor Olaf Dössel, Professor Luigi Paolo Badano, Professor James D. Thomas, Dr. Steven Niederer, Professor Christopher Leclercq, Professor Cecilia Linde and Professor Francisco Leyva.

From left: Professor Otto Smiseth, MD, PhD, Erik Kongsgård, MD, PhD, Associate Professor Kristina H. Haugaa, MD, PhD, Professor Cecilia Linde, MD, PhD, Professor Francisco Leyva, MD, PhD and Samuel Wall, PhD. (Copyright Piritta Nyberg/OUH)

The ISAB was convened in Oslo on October 21th to give advice to the CCI management team and the Board on the progress of the center. The following ISAB members were present: Professor Cecilia Linde and Professor Francisco Leyva. The overall feedback was very positive and enthusiastic although some aspects still need improvement.

The center scored remarkably well in this year's evaluation. The focus was mainly on the electrophysiology aspects of the ongoing studies. The panel noted that the groups are well focused in their areas of research and the friendly atmosphere with emphasis on collaboration and participation by all members of the team contributes to the results produced by the CCI. The collaboration with the industrial partners of the center, as well as with national and international centers, translate the research from bench to bedside and both granted, as well as pending, patents show very promising clinical applicability. Regular meetings with supervisors and other center members, as well as ad hoc meetings are clearly beneficial for all participants. This interaction translates into a number of research articles published in renowed scientific journals, leading the way and affecting international guidelines.

The panel noted that both center members and the international reseach community would benefit from an increased number of visiting international key opinion leaders at the CCI location. The management team of the center has now begun facilitating for more of these meetings and is awaiting a few professors prior to the summer of 2017.

Average: 5.2	1 (weak) - 6 (excellent)
Quality of research	6
Partner collaboration	6
Organization	6
Innovation	6
Total Project score	5.45

Prof. Linde

Prof. Badano

Prof. Thomas

Dr. Niederer

Prof. Dössel

Prof. Leyva

Prof. Leclercq

VISIT FROM THE MINISTRY OF EDUCATION AND RESEARCH

Center for Cardiological Innovation was honoured with a visit from the Minister of Education and Research Torbjørn Røe Isaksen and Director of the Research Council of Norway Arvid Hallén in May 2016. The CEO of Oslo University Hospital Bjørn Erikstein was also present. RCN chose CCI as the SFI Research 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 minister 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 Vivid E95. Two of the analysis tools in Vivid E95 are developed in cooperation between GE Vingmed Ultrasound, Oslo University Hospital and researchers from the CCI. It was launched in 2015 and is an excellent example on how funding through the SFI scheme contributes to industry-oriented innovation. Center leder Thor Edvardsen also pointed out that hosting a center with SFI-status has been very positive for the Department of Cardiology at OUH. 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 several innovation breakthroughs.

The minister was pleased to hear that the cooperation will continue between the current partners also after the completion of financial aid given by the Research Council. The SFI scheme seems to work according to the initial plan and will therefore be an instrument the minister will keep endorsing in the future.

As Gunnar Hansen, Chairman of the CCI Board and research project manager at GEVU, pointed out during the visit, 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. 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.

12 | Finansavisen MANDAG 23. MAI 2016

FORSKNINGSSTØTTE SKRYTER AV BEDRIFTSSAMARBEID

MANDAG 23. MAI 2016 | Finansavisen 13

En hjertesak for kunnskapsministeren

Spleiselag hvor stat, bedrift og forskning dekker 1/3 hver

HELSE: Thomas Abrahamsen endte med hjertestarter, takket være ultralydmaskinen Rikshospitalet og GE Vingmed Ultrasound har utviklet sammen.

ARE HARAM
ARE.HARAM@FINANSAVISEN.NO

I en sykehussenga på Rikshospitalet ligger Thomas Abrahamsen fra Sandefjord. For noen dager siden fikk han skumle symptomer fra hjertet. Torsdag fikk han operert inn en hjertestarter, og fredag småpratet han med kunnskapsminister Torbjørn Røe Isaksen, som har ledet en delegasjon av sykehusledere, leger og forskningsbyråkrater inn på rommet.

– Hvordan har du det nå, spør Røe Isaksen, som et ekko av en lege.

– Jeg føler meg ganske bra. Kanskje får jeg reise hjem allerede i dag.

Lyden av helse

Da Abrahamsen kom til Rikshospitalet ble tilstanden raskt avdekket, blant annet takket være Vivid E-95, en nyutviklet kardiologisk ultralydmaskin.

Den er blitt til ved Rikshospitalets Center for Cardiological Innovation (CCI). Her samarbeider Rikshospitalet med GE Vingmed Ultrasound, en av verdens tre store ultralydprodusenter.

Det offentlige, ved Forskningsrådet, står for en tredjedel av kostnadene. Resten fordeles omtrent likt mellom GE og Rikshospitalet. Det samme mønsteret brukes ved de fleste av Norges for tiden 18 sentre for forskningsdrevet innovasjon (SFI).

– Er du sikker på at dette er noe Norge og norske forskningsmiljøer er tjent med?

– Så sikker som det går an å bli. Som Høyre-mann er det også interessant å se om bedriftene er interessert i dette, og det ser det ut som de er, sier Røe Isaksen til Finansavisen.

– De fleste SFIene får finansiering fra næringslivspartnere. De fleste forteller også etter at den offentlige andelen er borte.

For lite til nå

– Den viktigste ambisjonen bak disse sentrene er å koble forskning og innovasjon tettere sammen, men det har også vært en ambisjon å være med i konkurransen om å være en aktør i internasjonal forskningsaktivitet, sier statsråden.

– Det har vi vært lite opptatt av i Norge, mens andre har det bøyt på agendaen. Det er trolig fordi norsk økonomi har gått så det hjønse.

Røe Isaksen mener spørsmålet om SFIer er en suksess avgjøres av spørsmålene om ordningen får markedsaktører til å sprytte inn penger i forskning og innovasjon, om resultatet er blitt nye produkter og prosesser og om det har ført til utdanning av flere. Selv svarer han klart «ja» på alle disse spørsmålene.

– Vil du være statsråden som bygger ned eller bygger opp denne typen samarbeid?

– Tilbakemeldingene jeg får er at dette er et veldig bra virkemiddel for omstilling og næringsrettet innovasjon, så om noe, vil jeg være en som bygger dette opp, ikke ned.

Deler inntekter

– Vi har flere prosjekter sammen med Rikshospitalet, og har samarbeidet siden lenge før opprettelsen av CCI, sier Gunnar Hansen fra GE Vingmed Ultrasound.

– Er det kamp mellom ulike land om å tiltrekke seg GE som samarbeidspartner i tilsvarende samarbeid?

– Ja, det er mitt inntrykk, sier Hansen, som likevel ikke kan si sikkert om det er andre prosjekter hvor vertslandet og vertsinstitusjonene betaler bruerparten av utviklingskostnadene, slik tilfellet er ved Rikshospitalets CCI, som et «senter for forskningsdrevet innovasjon (SFI).

– Hvem får inntektene når teknologien blir utnyttet kommersielt?

– De blir delt. Rikshospitalet har patentert to deler av dette produktet, og får lisensinntekter fra dette, sier Hansen.

> **Fagmiljøene ser nok først og fremst på de faglige gevinstene, fremfor de økonomiske**
> ARVID HALLÉN, ADM. DIREKTØR I FORSKNINGSRÅDET

Senterleder Thor Edvardsen ved CCI anslår at Rikshospitalet får en tredjedel av lisensinntektene fra teknologien som er utviklet i samarbeid med GE.

Eksport fra Horten

– Denne løsningen produseres ved vår avdeling i Horten, og 95 prosent vil gå til eksport, sier Hansen, som anbyder en pris på rundt 160.000 dollar pr. enhet.

GE Vingmed Ultrasound har 210 ansatte og omsatte i 2014 for 1,5 milliarder kroner.

– Takket være denne enheten alene er vår omsetning opp 16 prosent fra første kvartal i fjor til første kvartal i år. Jeg tipper det vil gå et par tusen enheter årlig.

Forskningsrådets adm. direktør Arvid Hallén understreker at også vertsinstitusjonene har utsikter til kommersielle gevinster av samarbeidet.

– Det er viktig at de sikrer seg nødvendig patentering. Men fagmiljøene ser nok først og fremst på de faglige gevinstene, fremfor de økonomiske, mener han.

– Opplever du at kappløp om å tilby internasjonale bedrifter mest mulig subsidier for å lokke dem til seg?

– Nei, dette er strengt regulert, blant annet i EØS-avtalen.

SPLISELAG: Thomas Abrahamsen undersøkes av Thor Edvardsen. Bak fra venstre Arvid Hallén, Gunnar Hansen og Torbjørn Røe Isaksen, som studerer ultralydutstyret. FOTO: ARE HARAM

Facsimile courtesy of Finansavisen.

COOPERATION BETWEEN PARTNERS

The partners in the CCI bring key competences to the joint projects, enabling everyone in the CCI to effectively pursue the collective goals. A premise behind the CCI research is to provide personalized health and care through analysis, modeling and treatment that is tailored to the individual patient. Ultrasound images of the patient's heart are analyzed to extract anatomical, functional and geometrical information. This information can be used directly in clinical studies or be further analyzed and combined using cardiac modeling and simulation. The intelligent fusion of this information provides decision support that will influence diagnosis, triage and treatment. The CCI also runs clinical studies to validate and investigate the impact of new prognostic parameters.

CCI members during the Workshop in November 2016 at Simula Research Laboratory, Fornebu, Norway. (Copyright Piritta Nyberg/OUH)

The research and innovation work in the CCI is organized in projects with multi-partner involvement, and the Work Packages (WP's) are designed so that they can also benefit from each other.

WP1, headed by Kristina Haugaa, addresses risk assessment for Sudden Cardiac Death (SCD) and myocardial function. Mechanical Dispersion (MD) assessed by myocardial strain from speckle tracking echocardiography together with global longitudinal strain (GLS) have shown promising abilities to improve risk stratification in several cardiac conditions. A tool to measure mechanical dispersion has been incorporated in the Vivid E95 ultrasound scanner released to the market in 2015.

WP2, which is headed by Eigil Samset, is focused on image guidance and fusion and collaborates closely with all the WP's to develop the technical and ultrasound specific solutions for clinical needs. In particular tools for myocardial work calculation will be developed alongside tools for LV lead placement in CRT. This collaboration involves all partners.

A unified goal of the CCI is to improve diagnosis and treatment in two large populations at risk for SCD: both post-MI and ARVC patients. The main goal of WP3, headed by Samuel Wall, is the creation of an index of patient-specific risk that can be incorporated into currently available cU/S scanning technologies for assessment of both post-MI and ARVC patients. Another aim is to provide informative 3D maps of strain and displacement obtained from patient-specific data that could be used to determine population-wide cardiac motion patterns. This task will create patient-specific metrics obtainable from cU/S measurements that will help produce a venerability index for ARVC patients to guide their treatment.

WP4 is mainly focused on Cardiac Resynchronization Therapy and lead placement. Erik Kongsgård is the leader for this work package. The aim is to define acute response parameters that can be used to optimize cardiac resynchronization therapy (CRT). OUH has partnered with Medtronic to address several aspects of device treatment in Heart Failure. New tools are also being developed to create combined visualization of parameters measured intraoperatively, including bioimpedance. This development is done in partnership with Kalkulo and subcontractor Radytek and will now be run in collaboration with Simula/Radytek. Heading this project is Hans Henrik Odland, MD, PhD.

WP5 is headed by Otto Smiseth. This work package focuses on identifying clinical application areas for a new method to estimate the mechanical work performed by the left ventricle; myocardial work. This project in WP5 builds on a background invention of a method to estimate LV pressure non-invasively and thereby enable estimates of cardiac work as a function of time for each segment in the heart. Estimation of constructive and wasted myocardial work may serve as a novel risk marker and will be explored further.

The innovative nature of the center has resulted in a continuous generation of new ideas and projects. In order to foster and fuel idea generation, the CCI has instituted cross-disciplinary meeting places. These meeting places include journal clubs (where research results originating from both within and outside the center are being presented and discussed), work package review meetings (where CCI project achievements and challenges are being discussed) and workshops (where disruptive ideas and out-of-the-box thinking are being encouraged). New project ideas are discussed by the management team to establish feasibility as well as resource allocation.

SCIENTIFIC ACTIVITIES AND RESULTS

AREA OF RESEARCH:
RISK ASSESSMENT FOR SUDDEN CARDIAC DEATH (SCD) AND MYOCARDIAL FUNCTION

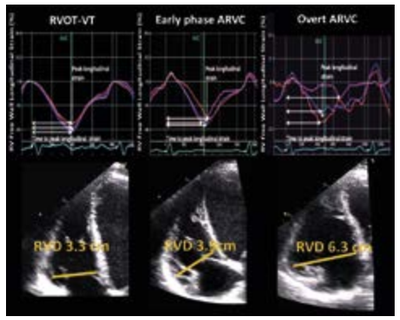
Sudden cardiac death (SCD) is still a challenge in cardiology. Mechanical Dispersion (MD) assessed by myocardial strain from speckle tracking echocardiography can be used to predict risk for SCD in post-MI cases and genetic myocardial diseases. Cardiac genetic diseases predispose to SCD in young individuals. Ongoing research in the CCI is focusing on predicting life threatening ventricular arrhythmias and exploring cardiac function in patients at risk of SCD.

SELECTED PROJECTS:

Comparison of patients with early-phase arrhythmogenic right ventricular cardiomyopathy and right ventricular outflow tract ventricular tachycardia

Saberniak J, Leren IS, Haland TF, Beitnes JO, Hopp E, Borgquist R, Edvardsen T, Haugaa KH

Right ventricular outflow tract ventricular tachycardia (RVOT-VT) is supposed to be a relatively benign condition, while arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inherited cardiomyopathy predisposing to ventricular arrhythmias, heart failure and sudden cardiac death and therefore a far from a benign condition. Both entities may become symptomatic with the same type of arrhythmias from the outflow tract of the RV. Discrimination between overt ARVC and RVOT-VT may be obvious, however, comparison between early phase ARVC and RVOT-VT can be challenging and correct diagnosis is crucial. Totally, we included 165 patients: 44 consecutive RVOT-VT and 121 ARVC patients.
Of the ARVC patients, 77 had overt ARVC and 44 had early phase ARVC disease. We investigated if ECG and cardiac imaging can help to discriminate early phase ARVC from RVOT-VT patients.
We showed that patients with early phase ARVC had structural abnormalities with lower RV ejection fraction, increased RV basal diameter and pronounced RV mechanical dispersion in addition to lower frequency of PVC by Holter compared to RVOT-VT patients. These parameters may help correct diagnosis in patients with unclear phenotypes.

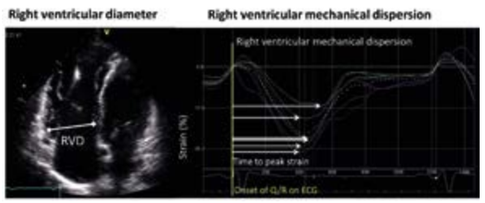


Upper panels: Echocardiographic longitudinal strain curves from RV free wall and contraction inhomogenity, expressed as mechanical dispersion (MD) from a RVOT patient, an early phase ARVC patient and an ARVC patient with overt disease. Early phase ARVC and overt ARVC patients had pronounced MD compared to the RVOT-VT patient. Lower panels: Measures of RV basal diameters in these patients. Patients with early phase ARVC (mid panel) had larger diameters compared to patients with RVOT-VT (left panel). From Saberniak J. et al, Eur Heart J Cardiovasc Imaging 2017 Jan;18(1):62-69.

Combination of ECG and Echocardiography for Identification of Arrhythmic Events in Early ARVC

Leren IS, Saberniak J, Haland TF, Edvardsen T, Haugaa KH

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is a genetic heart muscle disease with an increased risk of life threatening arrhythmias and sudden cardiac death. Arrhythmic events in ARVC are difficult to predict, particularly in the early phase of the disease. The aim of the study was to investigate early markers of arrhythmic events and improve risk stratification. We included 162 ARVC patients of whom 73 had early disease according to 2010 Task Force Criteria. We recorded patient history including previous arrhythmic events, performed resting and signal averaged electrocardiogram (ECG) and a standard 2D echocardiography including novel techniques as strain echocardiography. A combination of electrical and echocardiographic parameters improved identification of subjects with arrhythmic events in early ARVC disease.



Measurement of Right ventricular diameter and right ventricular mechanical dispersion in ARVC patients. From Leren IS et al, JACC Cardiovasc Imaging 2016 Oct 14 [Epub ahead of print].

Soluble ST2 is associated with disease severity in arrhythmogenic right ventricular cardiomyopathy.

Broch K, Leren IS, Saberniak J, Ueland T, Edvardsen T, Gullestad L, Haugaa KH

Diagnostic and prognostic evaluation remains challenging in arrhythmogenic right ventricular cardiomyopathy (ARVC). Soluble ST2 (sST2) is a decoy receptor for interleukin-33 (IL-33). Soluble ST2 reflects hemodynamic stress in non-ischemic heart failure, and plasma sST2 may mirror not only left ventricular function, but also the degree of right ventricular failure. We measured plasma concentration of soluble ST2 (sST2) and assessed its association with myocardial function and ventricular arrhythmias in patients with ARVC.

We included patients with ARVC and genotype positive relatives. Soluble ST2 was determined by ELISA (enzyme-linked immunosorbent assay). We assessed myocardial function by echocardiography including strain by speckle tracking technique. The study concluded that soluble ST2 was associated with both right ventricular and left ventricular function in patients with ARVC. Soluble ST2 may aid in the determination of disease severity in ARVC.

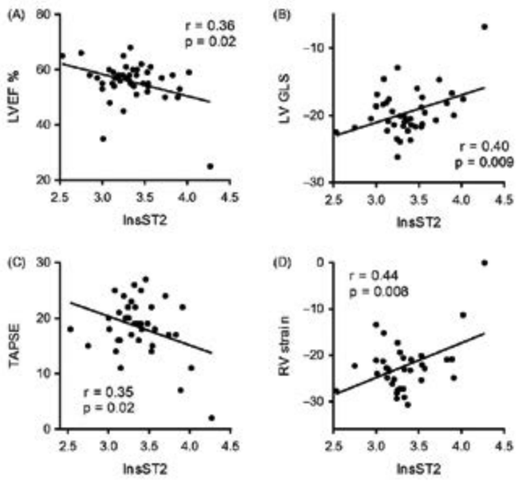


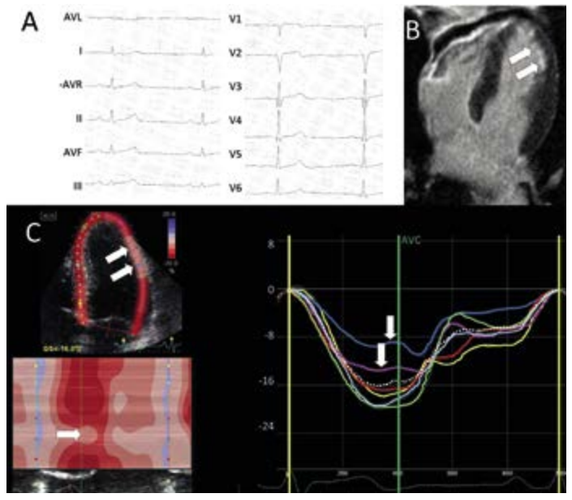
Figure 1. Associations between soluble ST2 and cardiac function. Scatter plots depicting associations between logarithmically transformed soluble ST2 (lnsST2) and indices of left and right ventricular function. Panel A shows the association with left ventricular ejection fraction (LVEF); panel B the association with left ventricular global longitudinal strain (LV GLS); panel C the association with tricuspid annular plane systolic excursion (TAPSE); and panel D the association with right ventricular (RV) strain. From Broch K et al, Biomarkers 2017 Jan 24:1-8 [Epub ahead of print].

Comparison of Electrocardiography Markers and Speckle Tracking Echocardiography for Assessment of Left Ventricular Myocardial Scar Burden in Patients with Previous Myocardial Infarction

Nestaas E, Shih JY, Smedsrud MK, Gjesdal O, Hopp E, Haugaa KH, Edvardsen T

Myocardial scar burden is an important prognostic factor after myocardial infarction. We compared assessment of left ventricle scar burden between pathological Q-waves on electrocardiography (ECG), Selvester multi-parametric ECG scoring system for scar burden and global longitudinal strain (GLS) by speckle tracking echocardiography 6 months after myocardial infarction. The scar burden was defined by late gadolinium enhancement cardiac magnetic resonance as fraction of total left ventricle tissue. ECG measures were presence of pathological Q-waves and Selvester scores. GLS was the average of peak strain from 16 left ventricle segments.

In 34 patients age 58±10 years (mean±SD), the scar burden was 19 (9, 26)% (median (quartiles)) and 79% had scar burden >5%. Patients with scar burden >5% more frequently had pathological Q-waves (63% vs. 14%) and had worse Selvester scores (5 (3, 7) vs. 0 (0, 1)) and worse GLS (-16.6±2.4% vs. -19.9±1.1%).



Electrocardiography (A), late enhancement magnetic resonance 4-chamber image (B) and segmental 4-chamber speckle tracking 2D-strain analysis (C) from a study patient. The white arrows in panel B and C denote findings from a scar in the apical lateral region. The apical (magenta) and mid (dark blue) inferior segmental strain curves in panel C show reduced systolic function compared to the other segments. The dotted white curve is the strain for the entire sample area. X-axis: Time. Y-axis: Longitudinal strain (%). AVC: Aortic valve closure. (American Journal of Cardiology, in press).

Pathological Q-waves, Selvester scores, ejection fraction and GLS related to scar burden in univariable analyses. Sensitivity and specificity for detecting scar burden >5% was 63% and 86% (pathological Q-waves), 89% and 86% (Selvester score), 81% and 86% (ejection fraction), 89% and 86% (GLS) and 96% and 71% (combination of Q-waves, Selvester score and GLS). In conclusion, Selvester score and GLS related to scars 6 months after myocardial infarction, pathological Q-waves were only weakly associated with scar and GLS was associated with scar independently of ECG markers.

Echocardiographic comparison between Left Ventricular Non-Compaction and Hypertrophic Cardiomyopathy

Broch K, Leren IS, Saberniak J, Ueland T, Edvardsen T, Gullestad L, Haugaa KH

Modern imaging technology has improved detection of left ventricle non-compaction cardiomyopathy (LVNC). Hypertrophic cardiomyopathy (HCM) shares genetic and morphological features with LVNC, while prognosis and treatment strategies differ. We aimed to compare echocardiographic parameters in LVNC and HCM.

We studied 25 patients with LVNC according to Jenni criteria, 50 with HCM and 50 healthy individuals. Increased number of trabeculations, thinner maximal wall thickness and lower ejection fraction were echocardiographic characteristics of LVNC disease. These characteristics may help discrimination between these two cardiomyopathies in overlapping phenotypes.

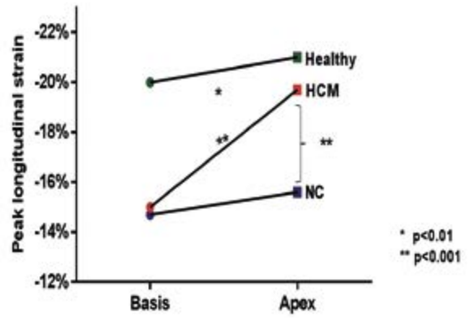


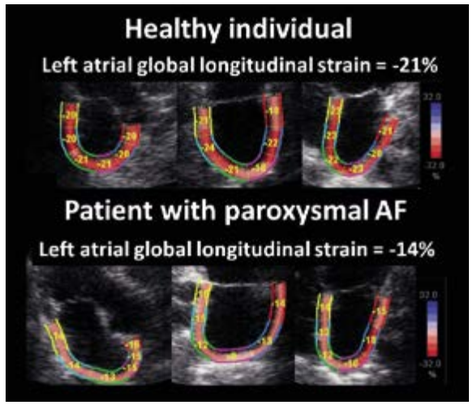
Diagram of LV basal and apical longitudinal strain in patients with LVNC, HCM and healthy controls. Patients with HCM and healthy controls have better strain in apical segments compared to basal segments, while there is no difference in basal and apical function in patients with LVNC. The apical-basal gradient was significantly more pronounced in HCM patients than in healthy controls. From Haland TF et al, Int J Cardiol. 2017 Feb 1;228:900-905.

Strain Echocardiographic Assessment of Left Atrial Function Predicts Recurrence of Atrial Fibrillation

Sarvari SI, Haugaa KH, Stokke TM, Ansari HZ, Leren IS, Hegbom F, Smiseth OA, Edvardsen T

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice, with an estimated prevalence of 0.4% to 1% in the general population, increasing with age to 9% in those above 80 years.
We evaluated if a dispersed left atrial (LA) contraction pattern was related to AF in patients with normal left ventricular (LV) function, and normal or mildly enlarged LA.
We included 61 patients with paroxysmal (PAF). Of these, 30 had not while 31 had recurrence of AF after radiofrequency ablation (RFA). Twenty healthy individuals were included for comparison.

Echocardiography was performed in patients in sinus rhythm the day before RFA. LA function by strain was reduced in both patients with and without recurrent AF after RFA compared to controls. We found a dispersed LA contraction pattern and reduced LA deformation in patients with paroxysmal AF and normal or only mildly enlarged LA, and apparently normal LV structure and function when comparing to healthy individuals. LA dispersion before RFA treatment was most pronounced in AF patients who experienced recurrence of AF after RFA. We propose that LA dispersion by strain echocardiography may be useful as a marker of paroxysmal AF and as a predictor of AF recurrence after RFA

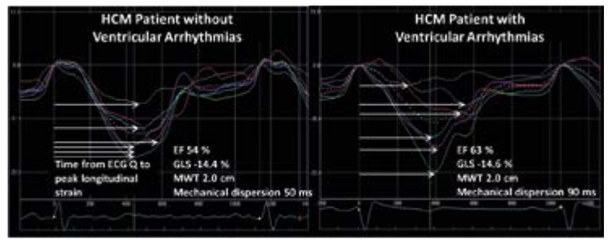


LA strain curves from a healthy individual and a patient with paroxysmal AF. LA function by strain was reduced in AF patients compared to controls. From Sarvari SI et al, Eur Heart J Cardiovasc Imaging 2016 Jun;17(6):660-7.

Strain echocardiography is related to Fibrosis and Ventricular Arrhythmias in Hypertrophic Cardiomyopathy

Haland TF, Almaas VM, Hasselberg NE, Saberniak J, Leren IS, Hopp E, Edvardsen T, Haugaa KH

Hypertrophic cardiomyopathy patients (HCM) are at risk of ventricular arrhythmias. We aimed to explore if systolic function by strain echocardiography is related to ventricular arrhythmias (VAs) and to the extent of fibrosis by cardiac magnetic resonance imaging.
We included 150 HCM patients and 50 healthy individuals. We found that global longitudinal strain, pronounced mechanical dispersion and fibrosis were markers of VAs in HCM patients. Mechanical dispersion was a strong independent predictor of VAs and related to the extent of fibrosis. Strain echocardiography may improve risk stratification of VAs in HCM.



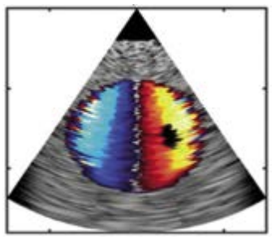
Mechanical dispersion by strain echocardiography in two patients with hypertrophic cardiomyopathy. Left panel displays longitudinal strain curves and mechanical dispersion in an HCM patient without ventricular arrhythmias. Horizontal white arrows indicate time to peak strain defined as the time from onset of Q/R to peak negative strain in each segment. Right panel shows more pronounced mechanical dispersion in a HCM patient with ventricular arrhythmias. From Haland TF. et al, Eur Heart J Cardiovasc Imaging 2016 Jun;17(6):613-21.

AREA OF RESEARCH:
MULTIMODAL IMAGING FOR ISCHEMIA DETECTION

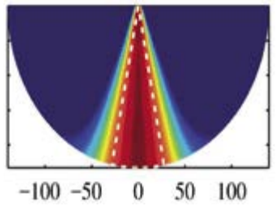
This area of research tackles image acquisition, processing, fusion and presentation as a horizontal activity in the CCI. There is an increasing need for combining multiple information modalities and visualize these in an intuitive manner for both diagnostic use and for intra-procedural guidance. Today's interventional procedures are heavily relying on imaging, acquired both before and during the procedure. Images are important for planning, monitoring, guidance, navigation and evaluation.

SELECTED PROJECTS:

Ultra-fast ultrasound imaging

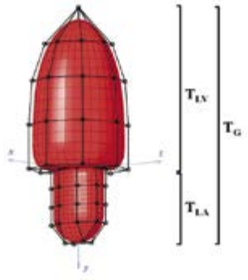


Ultra-fast ultrasound imaging can be performed by transmitting a wide (un-focused) ultrasound beam into tissue instead of many narrow beams. One type of wide beam is a diverging wave. The implementation of this method may be limited by the configuration of clinical 3D ultrasound probes. We tested diverging wave imaging in a commercial ultrasound system and tried to estimate velocities after off-line beam forming of the received signals. We were able to estimate tissue velocities with acceptable accuracy by optimizing the trade-off between image quality and frame rate.

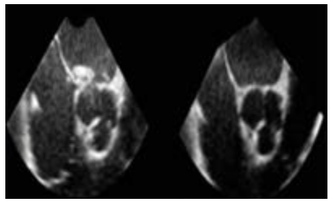


Automatic image interpretation of the left atrium

For diagnosis, treatment planning and intra-operative guidance, it is important to have tools that can automatically interpret image features such as boundaries between blood and tissue. Such features can be used to extract morphological and functional information such as volumes and volume changes over the cardiac cycle.
We have developed image segmentation tools for the left atrium (LA), that can be applied to 3D ultrasound images of the LA acquired throughout the cardiac cycle. Our method is able to reliably detect and track the boundaries of the atrium, allowing not only its easy visualization in 3D, but also to derive relevant LA functional indices. The method is also capable of quantifying the coupling between the left atrium and the left ventricle.

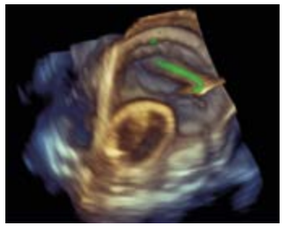


Automatic view stabilization



Cardiac interventions in the catheterization laboratory (cath lab) are often guided by a combination of x-ray and Trans-Esophageal Echocardiography (TEE). The TEE probe is usually controlled by another person than the interventionalist who is manipulating the catheters. Rotation and translation of the TEE probe will alter the displayed ultrasound image and can often be confusing to the interventionalist. We have developed a stabilization method that helps to visualize consistent TEE views without the need to repeatably maneuver the probe to the exact same position and orientation.

Catheter visualization



Real time image guidance during catheter based procedures is mainly done using x-ray fluoroscopy due to its ability to image intra-procedural tools (like catheters and guidewires). The drawbacks are repeated contrast injection (to view anatomic context in real time), radiation exposure and lack of depth information.

We found that real time catheter tracking has the potential to visualize anatomy and the intra-procedural tools simultaneously, during interventional procedures. We have developed a method using raw ultrasound data that can differentiate the tools from tissue and detect both the position and orientation of the tools. The method has been validated in both 2D and 3D.

AREA OF RESEARCH:
CARDIAC MODELING

In recent years, the field of computational cardiac modeling and simulation has matured in both scope and methodology such that it can contribute significantly to the present understanding of heart physiology and disease. The computational cardiac modeling effort involves mathematicians and computer scientists working collaboratively with both experimentalists and clinicians to address current challenges in cardiology through basic research and industrially driven innovation projects.

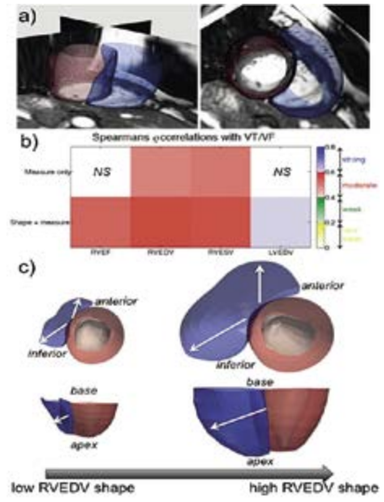
SELECTED PROJECTS:

Relating Structural Features in ARVC Patients to Clinical Outcomes
McLeod SK, Saberniak J, Leren IS, Haugaa KH, Wall S

Analysing structural features common in a population using computational methods can provide quantitative descriptors of structural abnormalities that can help to better understand disease manifestations. These descriptors can be correlated to clinical outcomes to potentially establish predictors of adverse clinical outcome.

We aim to go beyond current measures of ventricular structure abnormalities such as volumes and ejection fraction by coupling these with automatically identified and structural abnormalities in ARVC patients extracted from CMR. Statistical analysis was performed to determine how structural features are related to clinical diagnostic indices. More specifically, we compute the shape modes most descriptive of clinically derived measures in an ARVC cohort of patients and compare the correlation of these with history of arrhythmias to the correlation with the clinical measures alone.

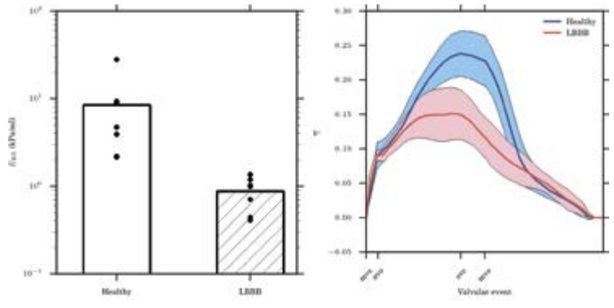
Results are shown on the right for the correlation with history of VT/VF between the clinical measures alone and shapes extracted from CMR (a) combined with the clinical measures (b), and the RVEDV (right ventricular end diastolic volume) shape given as an example at ±1 standard deviation (c).



Using statistical methods, the dominant structural patterns can be extracted in the population with respect to clinical measures, defining improved methods to relate structure to arrhythmic events.

Patient-Specific Simulation to Measure Mechanical Dysfunction
Finsberg HF, Balaban G, Sundnes J, Ross S, Odland HH, Wall S

Image-based patient-specific cardiac modeling has emerged as a potential tool for future medical diagnostic and treatment planning. By relating mechanical information observed in medical images to physical processes, mathematical models can provide us with additional insight into the cardiac function or dysfunction of the individual.
The need for building adequate patient-specific models that captures the geometrical information as well as the underlying biophysical processes is recognized as one of the key challenges in modern bioengineering. Adjoint-based data assimilation offers a new way of fitting high dimensional parameters to clinical measurements, and makes it possible to create a simulation of a patient's heart, that moves in the same way as what is observed in the medical images. Moreover, from these simulations we can extract features that are otherwise impossible to measure without surgical interventions. Such features include indices of myocardial contractility and fiber stress. By combining strain data obtained using 4D echocardiography methods, with left ventricular pressure and volume, we have used these methods to show that patients suffering from left bundle branch block have significant decreases in estimated myocardial contractility.



To the left, end systolic elastance estimated from perturbed model for healthy controls and patients with left bundle branch block. Dots show individuals, while bars show the mean. To the right, Mean and +/- 1 std of time varying relative active fibre shortening for healthy controls (blue) and patients with left bundle branch block (red).

AREA OF RESEARCH:
CARDIAC RESYNCHRONIZATION THERAPY

The aim of this work package is to define acute response parameters that can be used to optimize cardiac resynchronization therapy (CRT). With the current worldwide empiric implantation practice of CRT, a 50-60% responder rate is expected. Through clinical studies and innovative study design novel acute response parameters are investigated in order to pick optimal response parameters that can be used to characterize cardiac electric, mechanic and tissue properties to predict long-term response of CRT. Furthermore, different pacing configurations will be assessed and compared. An important work of this group is the development of the Pacertool and the transition of this tool into clinical practice.

SELECTED PROJECTS:

CCI Impact study

This study was completed in 2015. Results will be published in 2016-2018. In the CCI IMPACT study, OUH and Medtronic try to leverage on all recent advances within the field of CRT research. The PATIENT SELECTION process has shifted from a mere HF treatment focus to a more proactive approach, where CRT is used to prevent HF progression in mildly symptomatic patients or patients in need of cardiac pacing. Appropriate patient selection is essential to achieving CRT therapy success, and OUH has taken a leading role in developing consensus documents which comment, summarize and endorse the most current European and US guidelines for CRT. When the appropriate patient is selected for CRT, we need to streamline the pre-planning phase. The other research partners, GEVU and Simula, have and will continue to work on the collected imaging data (cMR and Echo) to find the optimal way of presenting crucial patient-specific information to the implanting physician before he/she enters the operation room.

The CCI IMPACT study was designed to give insight to the CRT IMPLANT procedure. Enrollments are finished and the data analysis has started. We hope the results will help us to better understand the acute mechanisms at play during device delivered resynchronization therapy. There are several factors that may affect the final LV lead location: varied venous anatomies, LV lead delivery and stability challenges, presence of phrenic nerve stimulation and high LV pacing thresholds. There is an unmet need of a parameter quantifying and/or confirming acceptable therapy delivery at any given lead position, and the CCI Impact study will assess the predictive properties of a set carefully selected parameters.

CCI 2xImpact study

This study is currently recruiting patients. It has the similar design as the impact study but will now explore effects of fusion pacing (pacing with different degrees of intrinsic activation of conduction system) and multisite pacing (pacing from more than one site on the left ventricle) and the interaction of both.

This study will analyze the non-inferiority of LV pacing only towards multisite biventricular pacing with the rational that LV only pacing will save battery and hence lessen the burden on patients with replacement of the device and reduce costs associated with treatment. Furthermore the study is collecting data on underlying pathophysiology and will analyze this as part of a PhD project. Data from this study will also be utilized together with the Pacertool software.

WP4 leader Erik Kongsgård monitoring the screens. (Copyright Oslo University Hospital)

Impel study

This study is currently including patients.
The aim of the study is to optimize bioimpedance measurements through analyses of substudies designed for optimization of analyses. Blocks of 10 patients will be analyzed at a time, allowing for adjustments of current frequencies and impedance configuartions.
The aim of this study is to define candidate bioimpedance markers of volume changes, mechanical activation and scar tissue.

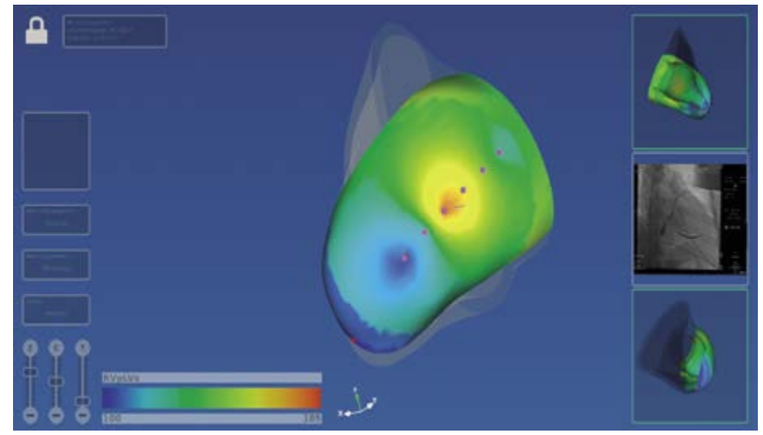
Pacertool-project

The Pacertool-project has received funding through the Biotek2021 program and will continue as a stand-alone project outside the WP4, however with close collaboration into the WP4. The Pacertool-project includes both development of hardware and software in a clinical system for use during implantation of CRT. The system will provide feedback to the operator when implanting a cardiac resynchronization device (CRT) and represents the interface between measured parameters and the operator. The aim of this system is to improve the current 50-60% responder rate of CRT.

The pacertool software will allow the implanter to individualize pacing lead positions to optimize the resynchronization effect of the CRT device. Parameters that are measured during implantation will be collected and displayed to highlight the optimal site of electrode placement. Imaging from pre-implantation studies, as echocardiography and magnetic resonance imaging can be incorporated to display patient-specific cardiac geometry. When coronary sinus angiography is performed during the implantation procedure, the patient-specific anatomy can be segmented and utilized during the procedure. When incorporated in research different positioning can be compared and analyzed.

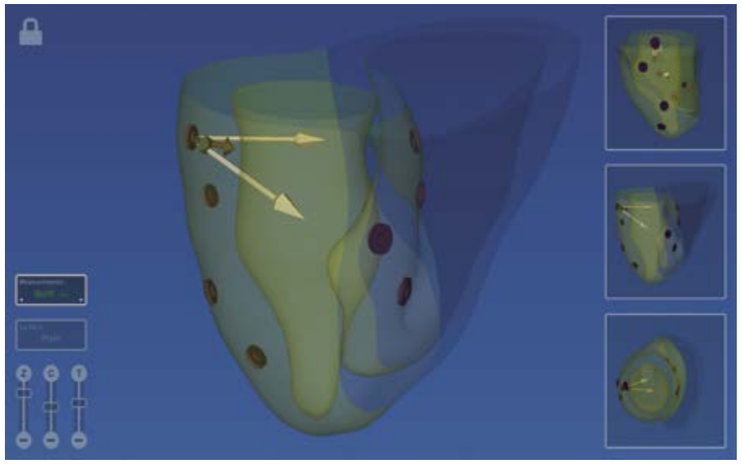
The data from any procedure can be used for predictive patient-specific simulation. Data collected from every patient is stored together with geometry. This will allow for validation of simulation algorithms and for calculating predictive reverse remodeling.

When performed during the implantation procedure, optimal sites for lead placement can be highlighted and compared to acute study hemodynamic parameters. This may provide validity to the simulation protocol and possibly provide insight into patient-specific reverse remodeling processes.



Pacertool software. The software is used to display a heart model during the CRT procedure. The project has now received funding as a standalone project from 2017-2020 NFR – Biotek2021 grant. The project will run as a collaboration between OUH, Inven2, Simula (Kalkulo/Radytek), Medtronic and GE Healthcare.

When used in combination with bioimpedance studies, this system will provide the operator with acute feedback from each electrode position and allow the operator to move the electrodes into different positions until optimal sites of stimulation are found. During this process biofeedback will guide positioning in a closed-loop fashion.
Bioimpedance as measured in collaboration with the medical engineering section at OUH will provide insight into hemodynamic and mechanical characteristics of the heart during each procedure.



A geometrical model of Pacertool.

AREA OF RESEARCH:
WORK EFFICIENCY AND DIASTOLIC FUNCTION

It is well known that the work performed by the heart can be estimated as the area of the pressure-strain loop. This project in WP5 builds on a background invention of a method to estimate LV pressure non-invasively and thereby enable estimates of myocardial work as a function of time for each segment in the heart. A further development of these ideas has resulted in the principles of Wasted Work Ratio (WWR). Left ventricular WWR is a method which quantifies the negative impact of dyssynchrony and discoordination on cardiac function and myocardial energy consumption. WWR may serve as a means to identify patients who will benefit from cardiac resynchronization therapy (CRT) and may also serve as a marker of severity of heart failure.

SELECTED PROJECTS:

Ultrasound based estimation of left ventricular filling pressure
Andersen, OS, Gude E, Skulstad H, Broch, K, Andreassen AK, Smiseth OA, Remme EW

Non-invasive estimation of left ventricular (LV) filling pressure is clinically important. Elevated filling pressure also increases pulmonary capillary pressure, which is a common cause of dyspnea. However, a patient presenting with dyspnea may not necessarily have elevated filling pressure as dyspnea can result from a number of other causes. It is therefore essential to determine if filling pressure is elevated.
For this purpose an easy method to evaluate if the filling pressure is normal or elevated, is highly desired. Echocardiography is often used for this purpose, but its applicability to estimate filling pressure is debated.

PhD fellow Øyvind S.Andersen giving an oral presentation at ESC meeting in Rome, Italy. (Copyright Trygve Berge)

We test the ability of echocardiography to estimate filling pressure and also try novel indices such as left atrial strain, which has been shown to correlate well with filling pressure, to see if these indices can improve the estimation. In this study echocardiography is performed simultaneously with measurement of pulmonary capillary wedge pressure (an estimate of LV filling pressure) in patients referred to right side heart catheterization. In this manner we can investigate if echocardiographic indices may serve as clinical tools to estimate LV filling pressure. Over 100 patients have been included so far and promising preliminary findings have been presented at the ESC and EuroEcho-Imaging Conferences in 2016.

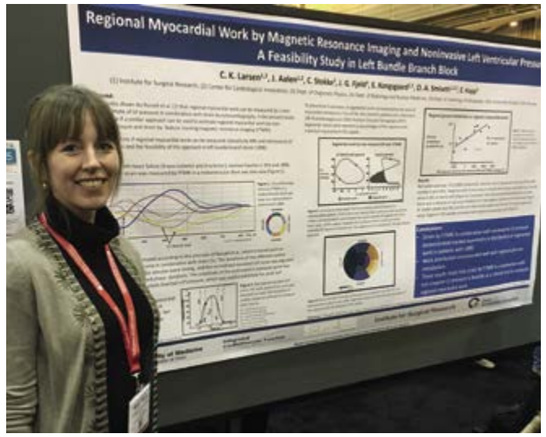
Increased Heart Rate Aggravates Diastolic Dysfunction in Left Bundle Branch Block
Andersen OS, Krogh MR, Boe E, Storsten P, Aalen J, Larsen CK, Skulstad H, Odland HH, Smiseth OA, Remme EW

In left bundle branch block (LBBB), mechanical dyssynchrony causes slowing of left ventricular (LV) relaxation. At low heart rates this may not affect late diastolic pressure, as there is still sufficient time for complete relaxation prior to end diastole. We hypothesize that the combination of LBBB-induced slowing of LV relaxation with tachycardia-induced abbreviation of diastole may lead to incomplete relaxation at end diastole (ED), and therefore cause diastolic stiffening and increase LV filling pressure.

The hypothesis is tested in a canine model where LV volume is measured by sonomicrometry and LV and left atrial (LA) pressures are measured by micromanometer catheters. Before and after ablation of LBBB, pacing is performed at low and high heart rates. PV relations, LV diastolic pressure and LA pressure are measured at each heart rate. Preliminary results have been presented at AHA Scientific Sessions 2016. The results showed that LBBB indeed aggravates diastolic dysfunction.

Regional Myocardial Work by Magnetic Resonance Imaging and Noninvasive Left Ventricular Pressure: A Feasibility Study in Left Bundle Branch Block
Larsen CK, Aalen J, Stokk C, Fjeld JG, Kongsgaard E, Smiseth OA, Hopp E

We aimed to determine if regional myocardial work can be measured clinically by MRI and non-invasive LV pressure, and to test the feasibility of this approach in left bundle branch block (LBBB).
Regional work was estimated according to the principle of Russell et al. (European Heart Journal, 2012), which is based upon an estimated LV pressure curve in combination with strain. The durations of the different cardiac phases were measured by valvular event timing, and the normalized standard LVP curve was adjusted according to the measured phase durations. The amplitude of the estimated LV pressure curve was scaled by the patient's systolic brachial cuff pressure, which was used as a surrogate for peak LVP.



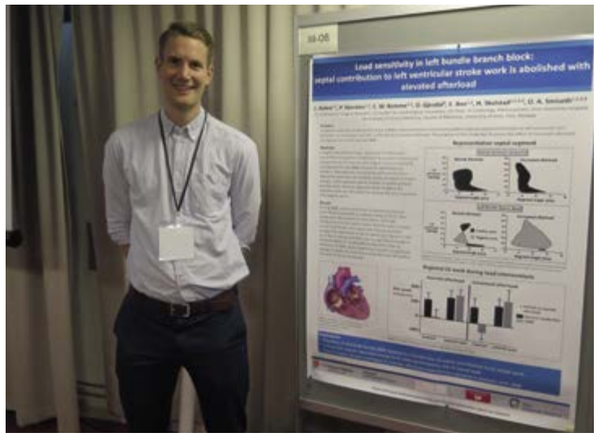
PhD fellow Camilla K. Larsen in front of her poster at AHA Scientific Session in New Orleans, Louisiana, USA. (Copyright Einar Hopp/OUH)

By definition, work during myocardial shortening is positive and work during lengthening is negative. Net work is the sum of positive and negative work. We concluded that strain by FTMRI in combination with noninvasive LV pressure demonstrated marked asymmetry in distribution of segmental work in patients with LBBB.
Work distribution corresponded well with regional glucose metabolism.
These results imply that strain by FTMRI (functional tracking magnetic reconance imaging) in combination with non-invasive LV pressure is feasible as a clinical tool to measure regional myocardial work.

Contractile Reserve In Dyssynchrony – the CRID-study
Cooperation between Oslo University Hospital (Norway), Rennes University Hospital (France), OLV Hospital Aalst (Belgium), Karolinska University Hospital (Sweden) and University Hospitals Leuven (Belgium)

As previously validated in our laboratory, left ventricular pressure (LVP) can be measured non-invasively using peak systolic blood pressure as a surrogate for peak LVP. An index of regional myocardial work can thereby be calculated as the area of the pressure-strain loop, where strain is obtained by speckle-tracking echocardiography.
In the multicenter CRID-study, the distribution of regional myocardial work in the LV is studied as a potential tool to determine CRT-response.

Constructive work when the segment shortens is compared to wasted work when the segment lengthens and the work efficiency (WE) can be calculated as the relationship between these two. A low WE indicates an ineffective contraction and hence a large potential for recovery with CRT. To determine myocardial viability and metabolism CMR and FDG-PET are also performed.



PhD fellow John Aalen in front of his poster at the CHFR Symposium at Holmenkollen, Oslo in September 2016. (Copyright Piritta Nyberg/OUH)

The study has now included 140 patients at five different locations (Oslo, Leuven, Rennes, Aalst and Stockholm). Inclusion is expected to be finished in August 2017 with follow-up for one additional year.

DISSERTATION

Nina Eide Hasselberg

Echocardiographic Assessment of Left Ventricular Function and Clinical Outcome in Heart Failure
April 27th 2016

Nina Hasselberg, MD, PhD (in the middle) together with Professor Thor Edvardsen, Associate professor Kristina Haugaa and two of Hasselberg's opponents Associate professor Ruxandra Oana Jurcut and Professor Jutta-Bergler Klein. (Copyright Piritta Nyberg/OUH)

In her PhD-thesis, researcher Nina Eide Hasselberg, MD, PhD, studied the ability of strain echocardiographic techniques to assess myocardial function, functional capacity and outcomes in patients with heart failure.

Heart failure affects 1-2% of the adult population in developed countries. Effective treatment, including lifesaving implantable device therapy, has improved prognosis, but risk stratification for the individual heart failure patient remains difficult. Left ventricular function is a predictor of outcome in patients with heart failure and traditionally ejection fraction (EF) has been considered the best prognostic left ventricular function marker. However, increasing evidence in recent years suggest that there are more sensitive methods for LV function assessment.

In her PhD-thesis Dr. Hasselberg performed studies with a main focus on echocardiographic strain (i.e. myocardial deformation) as a cardiac imaging method. Echocardiographic strain is considered a sensitive clinical method to assess both myocardial deformation and dyssynchrony. Furthermore, mechanical dispersion, derived from strain, has been shown as a predictor of ventricular arrhythmias.

The general aim of Hasselberg's thesis was to quantify regional and global myocardial function by the use of speckle tracking strain echocardiography and relate this myocardial function to exercise capacity and clinical outcomes in heart failure patients of different etiologies and different levels of myocardial dysfunction.
In conclusion, Dr. Hasselberg and co-workers showed that strain echocardiography was closely related to exercise capacity and could predict clinical outcome in addition to providing insights into regional and global myocardial function and mechanics in patients with heart failure.

In detail, Dr. Hasselberg's thesis consisted of the following three studies:

Risk prediction of ventricular arrhythmias and myocardial function in Lamin A/C mutation positive subjects.
Europace 2014;16(4):563-71
Dr. Hasselberg and co-workers explored electrical, mechanical and structural properties in lamin A/C mutation positive subjects and investigated for risk markers of life threatening ventricular arrhythmias in this patient group. The study concluded that there was a coupling between electrical, mechanical and structural properties in Lamin A/C mutation positive subjects providing mechanic insight into myocardial dysfunction and the pathogenesis of conduction disorders and arrhythmias in these subjects. PR-interval on resting ECG was the strongest predictor of ventricular arrhythmias in this cohort.
For her sub-study of Lamin A/C cardiomyopathy, Dr. Hasselberg won two best poster awards with her abstract Prevalence and cardiac penetrance of Lamin A/C mutation in Norway presented at the ESC Congress and the Center for Heart Failure Research Symposium during 2015, respectively.

Left ventricular global longitudinal strain is associated with exercise capacity in failing hearts with preserved and reduced ejection fraction (Eur Heart J Cardiovascular Imaging 2015 Feb;16(2):217-24)
In this study Dr. Hasselberg and co-workers showed that LV function by GLS was a strong, independent predictor of exercise capacity in heart failure patients, including in patients with heart failure with preserved EF (HFpEF) as a separate group. RV function was also related to exercise capacity (as shown previously). HFpEF patients showed slightly reduced systolic function by GLS and the authors therefore concluded that preserved EF in these patients should not be equalled to preserved systolic function.
This study is also featured on unikard.org

Left ventricular markers of mortality and ventricular arrhythmias in heart failure patients with cardiac resynchronization therapy (Eur Heart J Cardiovasc Imaging 2016 Mar;17(3):343-50)
Dr. Hasselberg and co-workers found that lack of resynchronization by cardiac resynchronization therapy (CRT) at 6 months, assessed by mechanical dispersion, was a predictor of ventricular arrhythmias in heart failure patients with CRT. Longitudinal LV function by GLS before CRT was a strong predictor of death and heart transplantation or left ventricular assist device (LVAD) implantation during the 2-year follow-up, independently of CRT response. Circumferential function improved relatively more compared to longitudinal function by CRT pacing. Nevertheless, volumetric CRT response by reverse remodeling was dependent on the improved longitudinal function in addition to improved circumferential function.

DISSERTATION

Ida Skrinde Leren

Ventricular arrhythmias in cardiac ion channel diseases; occurrence, treatment and risk stratification
June 15th 2016

Ida Skrinde Leren, MD, PhD together with her supervisors Associate professor Kristina Haugaa and Professor Thor Edvardsen. In the background are her opponents (from right to left) Associate Professor Lia Crotti, Associate Professor Håvard Dalen, Professor Ole M. Sejersted and chair of defence Associate Professor Are Martin Holm. (Copyright Piritta Nyberg/OUH)

Ida Skrinde Leren, MD, defended her thesis June 15th 2016.
Her research has been focused on monitoring, treatment and risk assessment of patients and family members with genetic ion channel diseases. Leren and co-workers included subjects with catecholaminergic polymorphic ventricular tachycardia (CPVT) and long QT syndrome (LQTS), which both are inheritable ion channel diseases with high risk of malignant arrhythmias, syncope and sudden cardiac death.
However, risk stratification of arrhythmic events is challenging, and monitoring of disease and optimal treatment choices are not fully explored. Patients were mainly recruited at the Unit for genetic cardiac diseases, Oslo University Hospital, Rikshospitalet. Through repeated exercise testing and 24-hour ECG monitoring Leren and co-workers evaluated the occurrence of ventricular arrhythmias in CPVT, and antiarrhythmic effects of specific beta blockers. They found that the phenotype in CPVT was highly penetrant.

The first study showed a high occurrence of previously undiagnosed cardiac symptoms and exercise-induced arrhythmias in CPVT mutation carriers detected by genetic family screening.

In the follow-up study, Leren and co-workers showed by serial investigations of the same patients untreated, during treatment with beta-1 selective beta blockers and during nadolol treatment, that nadolol seemed to be the most efficient beta blocker to suppress ventricular arrhythmias in CPVT patients.

In the final study included in the thesis, Leren and co-workers investigated LQTS patients by cardiac ultrasound, including strain echocardiography, which is a modern echocardiographic technique able to detect even subtle mechanical alterations. They found that LQTS subjects showed subtle alterations in both systolic and diastolic cardiac function compared to healthy controls. Interestingly, they could also demonstrate genotype specific differences in systolic cardiac function by strain echocardiography. These findings may help elucidate cardiac electro-mechanical interactions in ion channel disease. Dr. Leren won the Oslo University Hospital prize for outstanding research for this publication and the study is also featured on unikard.org. Ida Skrinde Leren has also been interviewed by forskning.no about long QT syndrome and her research. Finally, her abstract "Long QT syndrome - an electro mechanical disease," which was based on the same patient material and presented at the CHFR Symposium in 2014, won the best poster award in its category.

Included papers:

Leren IS, Saberniak J, Majid E, Haland TF, Edvardsen T, Haugaa KH.
Nadolol decreases the incidence and severity of ventricular arrhythmias duringexercise stress testing compared with β1-selective β-blockers in patients with catecholaminergic polymorphic ventricular tachycardia.
Heart Rhythm. 2016;13:433-440

Leren IS, Hasselberg NE, Saberniak J, Haland TF, Kongsgaard E, Smiseth OA, Edvardsen T, Haugaa KH
Cardiac Mechanical Alterations and Genotype Specific Differences in Subjects With Long QT Syndrome.
JACC Cardiovasc Imaging. 2015 May;8(5):501-10

Haugaa KH, Leren IS, Berge KE, Bathen J, Loennechen JP, Anfinsen OG, Früh A, Edvardsen T, Kongsgaard E, Leren TP, Amlie JP
High prevalence of exercise-induced arrhythmias in catecholaminergic polymorphic ventricular tachycardia mutation-positive family members diagnosed by cascade genetic screening.
Europace 2010;12:417-23.
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DISSERTATION

Wasim Zahid

Myocardial function by echocardiography for risk stratification in patients with heart disease
October 6th 2016

Wasim Zahid (in the middle) with his opponents Professor Henrik Schirmer and Professor Leila Elif Sade to the left. His supervisors Professor Thor Edvardsen and Professor Erik Fosse are to the right.(Copyright Piritta Nyberg/OUH)

Doctor and researcher Wasim Zahid has in his PhD-thesis focused on investigating whether myocardial function by tissue Doppler imaging and two-dimensional strain echocardiography can be used in the assessment of diagnosis and prognosis in patients with heart disease. Tissue Doppler imaging and speckle tracking measure systolic function more directly than the most commonly used ejection fraction (EF).
Acute myocardial infarction damages myocardial tissue and leads to impaired systolic function, causing inadequate cardiac output. The hearts failed ability to pump out all the blood from the ventricle may lead to pulmonary edema or cardiac arrest. On the basis of electrocardiographic (ECG) characteristics, patients are divided into two main categories; ST-elevation myocardial infarction (STEMI), and non ST-elevation acute coronary syndrome (NSTE-ACS). The latter is further divided into non ST-elevation myocardial infarction (NSTEMI) and unstable angina pectoris (UAP) on the basis of biochemical changes.

Among specific aims of this thesis were assessments on whether myocardial function by MAD (mitral annular displacement) and GLS (global longitudinal strain) can distinguish between small and large infarcts, coronary occlusions and non-occlusions, and predict mortality in patients with NSTEMI, and whether myocardial function by MAD and GLS can distinguish between patients with NSTEMI from stable CAD (coronary artery disease) patients without acute coronary syndrome. The journal article Mitral annular displacement by Doppler tissue imaging may identify coronary occlusion and predict mortality in patients with non-ST-elevation myocardial infarction (J Am Soc Echocardiogr. 2013;26:875-84) showed that the performance of MAD was comparable with that of the other indices of myocardial function (GLS, LVEF, and WMSI). The study results imply that decreased MAD is associated with decreased myocardial function, larger infarcts, and higher risk for mortality in patients with NSTEMI. To the authors knowledge the study was the first to show such an association between MAD and mortality exclusively for patients with NSTEMIs without previously known acute myocardial infarctions undergoing modern revascularization therapy.

The journal article Early systolic lengthening may indentify minimal myocardial damage in patients with non-ST-elevation acute coronary syndrome (Eur Heart J Cardiovasc Imaging. 2014;15:1152-60) showed that DESL (duration of early systolic lengthening) by two-dimensional speckle tracking echocardiography shows good correlation to final infarct size and a short DESL can accurately identify NSTEMI patients with minimal myocardial damage, as defined by lack of scarring on cardiac MRI.

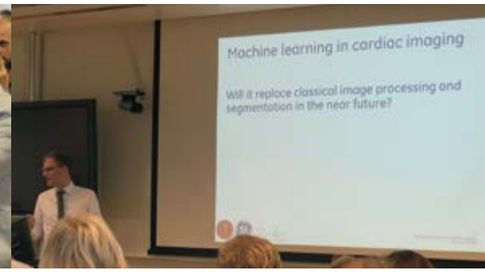
Myocardial function by two-dimensional speckle tracking echocardiography and Activin A may predict mortality in patients with carcinoid intestinal disease, published in Cardiology, 2015 Jun;132:81-90, showed that myocardial function by LV strain and MAD, and the biomarkers Activin A and OPG, are independently associated with mortality in patients with intestinal carcinoid disease. The data also showed that these patients have a biventricular deterioration of myocardial function.

DISSERTATION

Jørn Bersvendsen

Segmentation of cardiac structures in 3-dimensional echocardiography
June 21st 2016

Ultrasound is one of the most important tools doctors use to assess the heart. Normally, cardiologists use 2-dimensional ultrasound, which shows one what the heart looks like if one were to “slice” through it. Although this is a great tool, it doesn’t let one properly appreciate the real and complex shape of the heart, as one cannot see what lies outside of this “slice” through the heart.



Jørn Bersvendsen during his trial lecture in the picture on the left. In the picture on the right are Bersvandsen’s opponents Associate Professor Andreas Austeg, Associate Professor Johan G. Bosch and Professor Bart Bijnes. Bersvandsen’s supervisors were Professor II Eigil Samset, Professor Martin Reimers and Professor Knut Mørken. (Copyright Piritta Nyberg/OUH)

In the past decade or so, 3-dimensional ultrasound has been making its way onto the market. Although this technique allows clinicians to capture the full anatomy, adoption into clinical practice has so far been very limited. This is in large part due to the vast increase in information when going from a 2D image to a 3D image, as well as challenges relating to image quality. Interpreting such 3D images is hard, and without computer guidance, clinicians often fail to perform reliable measurements.

In this thesis, Bersvendsen presented computer algorithms that were designed and developed to extract the shape and function of different parts of the hearts anatomy. With these methods, the clinician can extract the geometry of the anatomy of interest from a 3D ultrasound image within seconds, and use this geometry to quantify the shape and function of the heart. It is demonstrated how these algorithms can be applied in two main clinical cases. Firstly, it’s shown that they can be used to quantify the pumping function of the heart’s main chambers. Here, the focus is spesifically on one of the most challenging – and often overlooked – chambers of the heart. Secondly, it is demonstrated that the methods can be used to select the size of a prosthetic aortic valve before performing a minimally invasive valve replacement procedure.

The study described in Automatic measurement of aortic annulus diameter in 3-dimensional transoesophageal echocardiography (BMC Med Imaging. 2014 Sep 8;14:31) demonstrates the feasibility of an efficient and fully automatic measurement of the aortic annulus in patients with aortic disease. The algorithm robustly measured the aortic annulus diameter, providing measurements indistinguishable from those done by cardiologists. This study is featured on unikard.org.

In the second study Automated Segmentation of the Right Ventricle in 3D Echocardiography: A Kalman Filter State Estimation Approach (IEEE Trans Med Imaging. 2016 Jan;35(1):42-51) an automated method for segmenting the right ventricle in 3D echocardiography has been described and validated against MRI and manual echocardiographic segmentation. The method is robust and computationally efficient, and resulted in good correlation with both MRI and manual 3DTTE reference in 17 clinical cases. This study is also featured on unikard.org.

Registration of multiple 3D ultrasound sectors in order to provide an extended field of view is important for the appreciation of larger anatomical structures at high spatial and temporal resolution. In the study Robust Spatio-Temporal Registration of 4D Cardiac Ultrasound Sequences (Proc SPIE Int Soc Opt Eng. 2016 Feb 27;9790) presented at the SPIE Medical Imaging Conference, a method was proposed for fully automatic spatio-temporal registration between two partially overlapping 3D ultrasound sequences. The temporal alignment is solved by aligning the normalized cross correlation-over-time curves of the sequences. For the spatial alignment, corresponding 3D Scale Invariant Feature Transform (SIFT) features are extracted from all frames of both sequences independently of the temporal alignment. A rigid transform is then calculated by least squares minimization in combination with random sample consensus. The method is applied to 16 echocardiographic sequences of the left and right ventricles and evaluated against manually annotated temporal events and spatial anatomical landmarks.

INTERNATIONAL COOPERATION

CCI has established collaborations with several world leading medical centres and the CCI host, Oslo University Hospital (OUH) is the leading center in several international multicenter studies. One of these studies is a prospective study on arrhythmias after myocardial infarction (IMPROVE). The study has been acknowledged as a study supported by the European Association of Cardivascular Imaging. Many European universities and hospitals collaborate in IMPROVE; Sykehuset Sørlandet, Université Rennes-1, Rennes, France, University Hospital Liege, University Hospital Brussels and Silecian Heart Center, Zabrze, Poland. Other important collaborators are Mayo Clinic, Rochester, MN, University of Pittsburgh, PA and Johns Hopkins University, Baltimore, MD, USA.

OUH is also participating in the DOPPLER-CIP study, funded under EU's 7th framework program. This project has included almost 700 patients with suspected coronary artery disease in collaboration with hospitals in Leuven, Madrid, Pisa, London, Linköping and Turku. OUH is also collaborating in ongoing studies on diseases prone to cause severe arrhythmias with several University Hospitals in Denmark and Sweden. Important collaborations have also been established to Maastricht University Hospital, the Netherlands, with ongoing publications. A large multicenter study including patients with heart failure is performed at the CCI in collaboration with Leuven in Belgium and Rennes in France.

Simula has close ties with several academic groups in the USA and Europe including the University of California, San Diego (UCSD), the University of California, Berkeley (UCB), King's College London, the University of Utah, INRIA Sophia Antipolis, and the University of Lugano, and the Helmholz Institute.

In particular, UCSD remains a strong research and educational partner, with researchers at Simula Research Laboratory engaging in active collaboration with researchers across numerous fields of study. This is made possible by a joint educational venture between UiO, Simula Research Laboratory, and UCSD, which began in 2015 and educates PhD students while performing cutting edge research in scientific computing and biomedical challenges.

GEVU has an extensive global network and engages actively in research collaborations with luminaries globally including KU Leuven (Belgium), University of Padova (Italy), UCSF (California) and University of Tasmania (Australia). Many of these research collaborations are related directly to research at the CCI within topics such as functional ultrasound imaging for assessment of heart failure and risk of sudden cardiac death.
GEVU has also coordinated an EU-funded Marie Curie project where OUH was an associated partner. The project was an industrial doctorate project that trained 5 PhD students and focused on improved ultrasound imaging for guidance of treatment for patients with cardiac arrhythmia. This project was finalized in 2016.

Medtronic 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".

NEW MEMBERS

Mathis Korseberg Stokke
Postdoctoral fellow, MD, PhD
Affiliation: Oslo University Hospital
Focus: Mechanisms for triggered arrhythmias.

Tove-Elizabeth Frances Hunt
MD, PhD fellow
Affiliation: Oslo University Hospital
Focus: Atrial fibrillation and advanced treatment planning.

Caroline Stokke
PhD Head of Nuclear Medicine / PET physics
Affiliation: Oslo University Hospital
Focus: PET and CRT.

Ole Jakob Elle
PhD, Associate Professor
Affiliation: Oslo University Hospital
Focus: Image guided surgery, image navigation, sensor control and haptic feedback in robotic surgery, biosensor development and monitoring.

Magnus Krogh
M. Sc., PhD fellow
Affiliation: Oslo University Hospital
Focus: Monitoring heart function by a miniaturized motion sensor.

Liubov Nikitushkina
PhD fellow
Affiliation: University of Oslo
Focus: Development of improved methods for myocardial stress estimation and investigation of the relation between myocardial stress and remodeling.

Brede Kvisvik
MD, PhD fellow
Affiliation: University of Oslo
Focus: Advances in both high-sensitivity Troponins and echocardiography in the assessment of myocardial function.

Sigmund Rolfsjord
M.Sc., PhD fellow
Affiliation: University of Oslo
Focus: Image fusion from ultrasound and computed tomography (CT) data.

Kaja Kvåle
M.Sc., PhD fellow
Affiliation: GE Vingmed Ultrasound
Focus: Visualization and quantification of ischemia in the myocardium.

Kristian Valen-Sendstad
PhD, Postdoctoral fellow
Affiliation: Simula Research Laboratory
Focus: Investigating the extent and role of turbulent-like flows in the cardiovascular system.

Hermenegild Arevalo
PhD, Postdoctoral fellow
Affiliation: Simula Research Laboratory
Focus: Development of a virtual electrophysiology lab that can predict arrhythmia susceptibility in patients with myocardial infarction.

Aslak Wigdahl Bergersen
M.Sc., PhD fellow
Affiliation: Simula Research Laboratory
Focus: Development of computational fluid structure interaction tools that allows for realistic simulations of heart flows.

Anna Isotta Castrini
MD, visiting researcher
Focus: Echocardiographic study of cardiomyopathies, with emphasis on ARVC/D patients.

Esther Scheirlynck
MD, visiting researcher
Focus: Sudden cardiac death and imaging in structural and non-structural heart disease.

Hava Izci
Visiting Master student
Focus: Basic and translational biomedical research

AWARDS

Center Director Prof. Thor Edvardsen was honoured with the Inge Edler Prize in October 2016. The award is given to people who have contributed outstandingly to the development of echocardiography. Prof. Edvardsen was also announced the new President Elect of the European Association of Cardiovascular Imaging (EACVI) during the EuroEcho-Imaging Conference in December. This is the first time that someone from the Nordic countries has been elected to this prestigious position. EACVI is the world leading organization for cardiovascular imaging, promoting excellence in clinical diagnosis, research, technical development and education in cardiovascular imaging in Europe.
(Copyright Oslo University Hospital)

During the EuroEcho-Imaging Conference Prof Otto A. Smiseth was rewarded with the EACVI Honorary Membership in recognition of his outstanding contribution in the field of Cardiovascular Imaging.
(Copyright European Society of Cardiology)

Associate prof. Kristina H. Haugaa was elected best teacher for the spring of 2016 by the 12th semester medical students. Dr. Haugaa also received a grant of 500 000 nok from the patient organization the *Association for children with heart disease* for work with national guidelines for patients with genetic cardiac diseases. *(Copyright Oslo University Hospital)*

Center PhD fellow Øyvind H. Lie won the prize for the best poster in his category during the CHFR Symposium. His poster was titled “QRS-duration of premature ventricular contractions relates to ventricular tachycardia in patients with outflow tract arrhythmia”
(Copyright Piritta Nyberg/OUH)

PhD fellow Ravinea Manotheepan won the prize for best abstract presentation at the annual autumn meeting for the Norwegian Society of Cardiology. Her supervisors are center postdoc Mathis K. Stokke and Prof. Ivar Sjaastad at Institute for experimental medical research at OUH.
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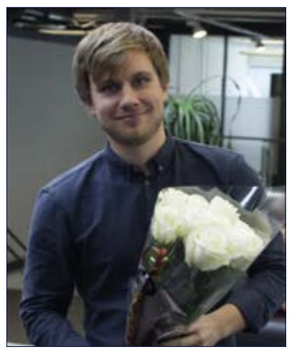

PhD fellow at Simula Research Laboratory Aslak Bergersen won the award for best Master’s thesis in Mathematics and Computer science at the University of Oslo.
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HIGHLIGHTS

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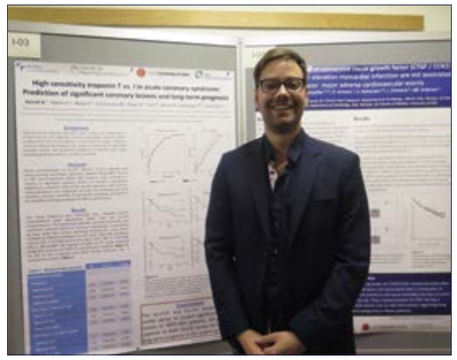

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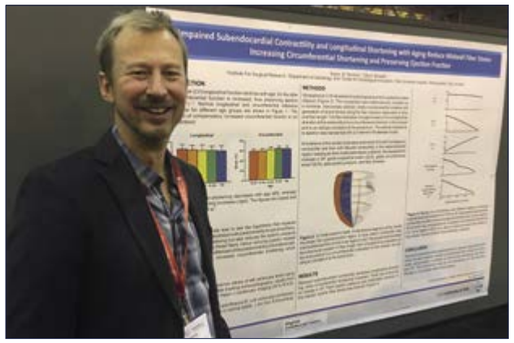

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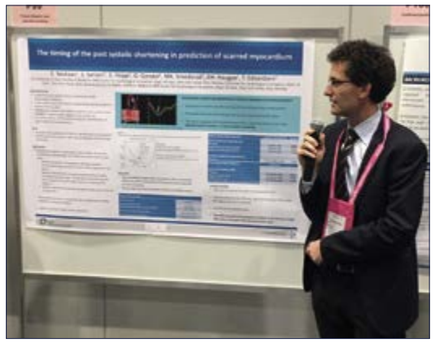

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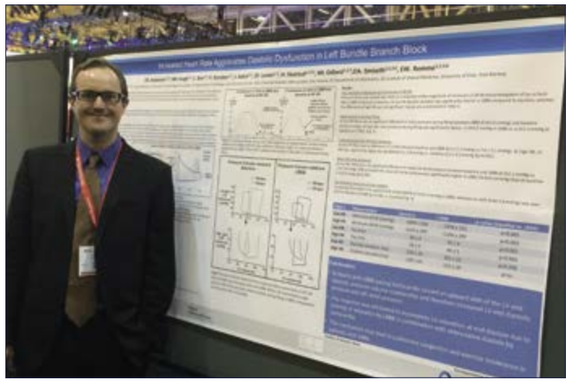

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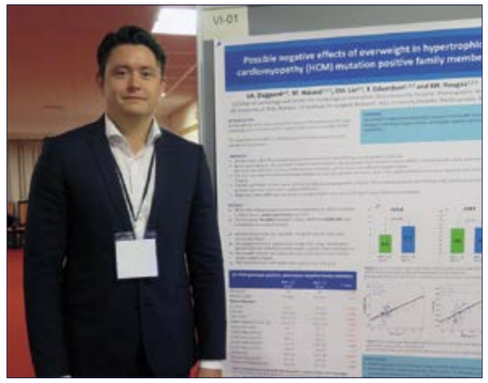

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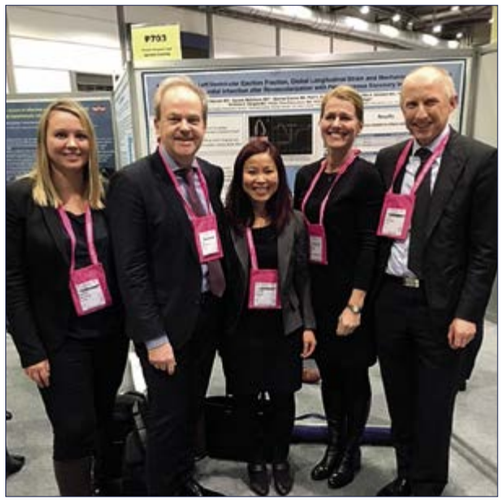

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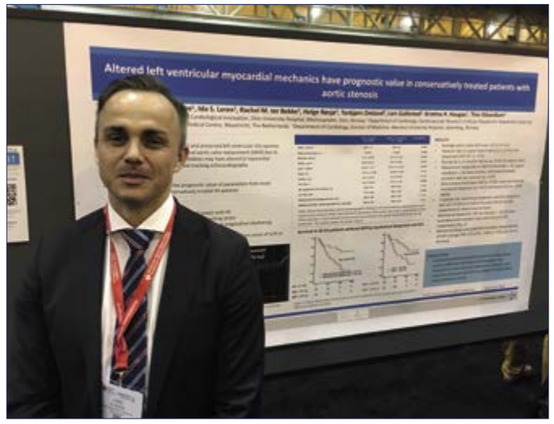

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APPENDIX

Annual accounts

Funding	Amount*
The Research Council	10 000
The Host Institution (Oslo University Hospital)	4 897
Research Partners	
University of Oslo	251
Simula Research Laboratory	5 303
Enterprise partners	
GE Vingmed Ultrasound	4 171
Medtronic	1 908
Kalkulo	287
Cardiosolv	523
Other Public Funding	5 335
Total	**32 675**

Costs	Amount*
The Host Institution (Oslo University Hospital)	12 382
Research Partners	
University of Oslo	868
Simula Research Laboratory	8 731
Enterprise partners	
GE Vingmed Ultrasound	7 642
Medtronic	1 207
Kalkulo	254
Cardiosolv	22
Equipment	1 569
Total	**32 675**

**All figures in 1000 NOK*

Personnel

Researchers

Name	Institution	Main Research area
Thor Edvardsen	OUH / UiO	Myocardial function and cardiac imaging
Kristina Haugaa	OUH / UiO	Myocardial function and cardiac imaging
Ole-Gunnar Anfinsen	OUH	Myocardial function and cardiac imaging
Mette-Elisa Estensen	OUH	Myocardial function and cardiac imaging
Thomas Helle-Valle	OUH	Myocardial function and cardiac imaging
Einar Hopp	OUH	Myocardial function and cardiac imaging
Per Kristian Hol	OUH	Myocardial function and cardiac imaging
Alessia Quattrone	OUH	Myocardial function and cardiac imaging
Margareth Ribe	OUH	Myocardial function and cardiac imaging
Kari Melberg	OUH	Myocardial function and cardiac imaging
Elin Bjurstrøm	OUH	Myocardial function and cardiac imaging

Personnel

Researchers

Name	Institution	Main Research area
Erik Kongsgård	OUH	Electrophysiology and cardiovascular function
Hans Henrik Odland	OUH	Electrophysiology and cardiovascular function
Torbjørn Holm	OUH	Electrophysiology and cardiovascular function
Erik Lyseggen	OUH	Electrophysiology and cardiovascular function
Finn Hegbom	OUH	Electrophysiology and cardiovascular function
Svend Aakhus	OUH	Echocardiography and heart failure
Richard Massey	OUH	Echocardiography and heart failure
Jan Otto Beitnes	OUH	Echocardiography and heart failure
Marit Kristine Smedsrud	OUH	Echocardiography and heart failure
Vibeke Marie Almaas	OUH	Echocardiography and heart failure
Kristoffer Russell	OUH	Echocardiography and heart failure
Sebastian Sarvari	OUH	Echocardiography and heart failure
Lars Aaberge	OUH	Invasive cardiology and intensive coronary care
Einar Gude	OUH	Heart failure, heart transplant, LVAD
Otto Smiseth	OUH / UiO	Cardiovascular function, imaging and biomechanics
Espen Remme	OUH	Cardiovascular function, imaging and biomechanics
Morten Eriksen	OUH	Cardiovascular function, imaging and biomechanics
Caroline Stokke	OUH	PET and imaging
Jan Gunnar Fjeld	OUH	PET and imaging
Jan Olav Høgetveit	OUH	Medical technology and bioimpedance
Håvard Kalvøy	OUH / UiO	Medical technology and bioimpedance
Morten Flattum	OUH	Medical technology and bioimpedance
Ole M. Sejersted	OUH / UiO	Calcium homeostasis and the failing heart

Personnel

Researchers

Name	Institution	Main Research area
William Louch	OUH / UiO	Calcium homeostasis and the failing heart
Ole Jakob Elle	OUH / UiO	Image guided surgery
Helge Skulstad	UiO	Myocardial function and cardiac imaging
Martin Reimers	UiO	Geometric modeling
Gunnar Hansen	GEVU	Ultrasound acquisition, processing and visualization
Eigil Samset	GEVU/ UiO	Ultrasound acquisition, processing and visualization
Andreas Heimdal	GEVU	Ultrasound acquisition, processing and visualization
Fredrik Orderud	GEVU	Ultrasound acquisition, processing and visualization
Olivier Gerard	GEVU	Ultrasound acquisition, processing and visualization
Line Rørstad Jensen	GEVU	Ultrasound acquisition, processing and visualization
Fredrico Veronesi	GEVU	Ultrasound acquisition, processing and visualization
Jakub Czana	GEVU	Ultrasound acquisition, processing and visualization
Christian Tarrou	Kalkulo	Geometric modeling and computer visualization
Joakim Berdal Haga	Kalkulo	Geometric modeling and computer visualization
Lukas Paszkowski	Kalkulo	Geometric modeling and computer visualization
Lars Ove Gammelsrud	Medtronic	Biomedical engineering
Alfonso Aranda Hernandez	Medtronic	Biomedical engineering
Richard Cornelussen	Medtronic	Biomedical engineering
Brock Tice	CardioSolv	Computational cardiac simulation methods and tools
Robert Blake	CardioSolv	Computational cardiac simulation methods and tools
Aslak Tveito	SRL	Computational cardiac electrophysiology
Mary Maleckar	SRL	Computational cardiac electrophysiology
Samuel Wall	SRL	Computational cardiac electrophysiology

Personnel

Researchers

Name	Institution	Main Research area
Glenn Lines	SRL	Computational cardiac electrophysiology
Joakim Sundnes	SRL / UiO	Computational cardiac electrophysiology
Bjørn Fredrik Nielsen	SRL	Computational cardiac electrophysiology
Hermenegild Arevalo	SRL	Computational cardiac electrophysiology
Kristian Valen-Sendstad	SRL	Computational cardiac electrophysiology
Andrew Edwards	SRL	Cellular and subcellular electrophysiology
Associated members		
Eirik Gjertsen	Vestre Viken	Heart Failure and cardiac arrhythmias

Postdoctoral researchers with financial support from the Centre budget

Name	Nationality	Period	Gender	Topic
Eirik Nestaas	Norwegian	01.01.2015-31.12.2015	M	Use of deformation analysis by echocardiography in cardiac resynchronization therapy (CRT).
Kristin McLeod	New Zealand	01.10.2013-30.09.2017	F	Development of clinically useful cardiac models and indices from patient specific data that will bridge the gap between highly detailed biophysical simulations of the heart and empirical clinical relationships.
Eirik Nestaas	Norwegian	01.01.2015-31.12.2017	M	Use of deformation analysis by echocardiography in cardiac resynchronization therapy (CRT)
Nina Eide Hasselberg	Norwegian	17.10.2016-29.01.2017	F	Peak Strain Dispersion and Clinical Outcomes in the EchoCRT trial
Mathis. K Stokke	Norwegian	01.05.2016-30.04.2018	M	Arrhythmias and cardiac electrophysiology, with a focus on mechanisms for triggered arrhythmias
Kristin McLeod	New Zealander	01.10.2013-30.09.2017	F	Development of clinically useful cardiac models and indices from patient specific data that will bridge the gap between highly detailed biophysical simulations of the heart and empirical clinical relationships

Postdoctoral researchers working on projects in the centre with financial support from other sources

Name	Nationality	Period	Gender	Topic
Hermenegild Arevalo	Philippines	01.01.2016-31.12.2018	M	SCD after MI

Personnel

Visiting Researchers

Name	Nationality	Period	Gender	Topic
Anna Isotta Castrini, MD	Italian	11.01.2016-30.06.2016 01.11.2016-31.01.2017	F	ARVC in pregnancy
Esther Scheirlynck, MD	Belgian	01.09.2016-30.11.2016	F	Sudden cardiac death and imaging in structural and non-structural heart disease
Hava Izci, Master student	Belgian	12.09.2016-21.12.2016	F	Basic and translational biomedical research

PhD students with financial support from the Centre budget

Name	Nationality	Period	Gender	Topic
Wasim Zahid*	Norwegian	01.10.2010-06.10.2016	F	Left ventricular function and risk of arrhythmia in patients with cardiomyopathies. Echocardiographic studies
Nina Eide Hasselberg*	Norwegian	06.06.2011-27.04.2016	M	Myocardial function and prediction of ventricular arrhythmias in patients with arrhythmic right ventricular cardiomyopathy
Jørg Saberniak*	Norwegian	19.09.2011-31.01.2016	M	CRT LV lead placement optimization
Trine S. Fink Håland	Norwegian	01.09.2013-29.02.2016	M	Patient Specific Simulation for Improved Cardiac Resynchronization Therapy (CRT)
Petter Storsten	Norwegian	01.10.2013-30.04.2019	F	European multicenter validation of the accuracy of E/è ratio in the estimation of invasive left ventricular filling pressure in patients undergoing coronary angiography
Ida Skrinde Leren	Norwegian	04.03.2013-18.06.2016	F	Myocardial function and prediction of ventricular arrhythmias in patients with genetic cardiac diseases
Stian Ross	Norwegian	10.02.2014-31.01.2018	M	Cardiac resynchronization therapy Evaluation of acute response parameters
Lars Dejgaard	Norwegian	02.02.2015 -31.01.2018	M	The use of different echocardiographic techniques for assessment of risk of sudden cardiac death in cardiomyopathies
Aleksandar Babic	Serbian	01.10.2012-31.12.2016	M	CRT LV lead placement optimization
Kaja Kvåle	Norwegian	02.05.2016-30.04.2019	F	Visualization and quantification of ischemia in the myocardium
Siri Kallhovd	Norwegian	27.10.2012-30.06.2016	F	Electrophysiology modeling in ARVC and modeling of cardiac electromechanics
Henrik Finsberg	Norwegian	01.10.2014-30.09.2017	M	Patient Specific Simulation for Improved Cardiac Resynchronization Therapy (CRT)

Personnel

PhD students working on projects in the centre with financial support from other sources

Name	Funding	Nationality	Period	Sex M/F	Topic
Fred-Johan Pettersen*	OUH	Norwegian	28.04.2009-31.12.2016	M	Bioimpedance methods for cardiology
Ingvild Billehaug Norum	VHT	Norwegian	01.10.2012-30.09.2018	F	3D echocardiography in severity grading of aortic stenosis and coronary heart disease
Daniela Melichova	SENRHA	Norwegian	01.04.2014-31.03.2017	F	Improved prediction of clinical outcome with the use of global strain and mechanical dispersion in patients with myocardial infarction, heart failure, and patients who receive primary prophylactic internal cardioverter defibrillator
Thuy Mi Nguyen	SENRHA	Norwegian	01.04.2014-31.03.2018	F	Improved prediction of clinical outcome with the use of global strain and mechanical dispersion in patients with myocardial infarction, heart failure, and patients who receive primary prophylactic internal cardioverter defibrillator
Øyvind Senstad Andersen	SENRHA	Norwegian	01.09.2014-31.08.2017	M	Left ventricular filling mechanics and left bundle branch block
Lars Gunnar Klæboe	RCN	Norwegian	15.09.2014-14.09.2017	M	Medical radar and imaging in patients with moderate heart failure
John Aalen	NHA	Norwegian	01.04.2015-31.03.2018	M	Contractile Reserve in Dyssynchrony (CRID): A novel principle to identify candidates for cardiac resynchronization therapy
Øyvind Haugen Lie	SENRHA	Norwegian	01.05.2015-03.05.2018	M	Myocardial function and prediction of ventricular arrhythmias in patients with arrhythmic right ventricular cardiomyopathy
Camilla Kjellstad Larsen	SENRHA	Norwegian	14.09.2015-13.09.2018	F	Contractile Reserve in Dyssynchrony (CRID): Role of cardiac magnetic resonance imaging
Magnus Krogh	SENRHA	Norwegian	01.07.2014-30.01.2018	M	Monitoring Heart Function by a Miniaturized Motion Sensor
Tove-Elizabeth Frances Hunt	RCN	Norwegian	01.09.2016-31.08.2019	F	Atrial fibrillation and advanced treatment planning
Brede Kvisvik	SENRHA	Norwegian	01.01.2014-31.12.2016	M	Advances in both high-sensitivity Troponins and echocardiography in the assessment of myocardial function

Personnel

PhD students working on projects in the centre with financial support from other sources

Name	Funding	Nationality	Period	Sex M/F	Topic
Jørn Bersvendsen	Industrial PhD	Norwegian	01.06.2012-21.06.2016	M	Cardiac modeling
Pawel Kozlowski	BiA	Polish	01.01.2013-31.12.2016	M	Real-time 3D rendering of ultrasound on holographic display
Raja Sekhar Bandaru	EU	Indian	01.08.2013-31.07.2016	M	Detection of catheters in ultrasound.
Nuno Almeida	EU	Portuguese	01.04.2013-31.03.2016	M	Left atrium modeling
Pedro Santos	EU	Portuguese	01.08.2013-31.07.2016	M	Fast 3D ultrasound imaging
Margot Pasternak	EU	French	01.06.2013-30.05.2016	F	Temperature monitoring of EP ablation with U/S
Adriyana Danidubroto	EU	Indonesian	01.08.2013-31.07.2016	F	Medical imaging
Sigmund Rolfsjord	UiO	Norwegian	01.09.2015-30.08.2019	M	Image fusion, from ultrasound and computed tomography (CT) data
Gabriel Balaban	RCN	Czech- Canadian	01.02.2013-30.06.2016	M	Optimization of computational cardiac models
Viviane Timmermann	SUURPH	German	15.01.2015-14.01.2018	F	Electromechanical coupling in cardiac cells and arrhythmic risk prediction
Liubov Nikitushkina	SUURPH	Russian	01.12.2015-30.11.2018	F	Myocardial stress estimation using biomechanical models in order to predict the need for aortic valve surgery

Students

Name	Nationality	Period	Gender	Topic
Iselin Dahl	Norwegian	01.08.2012-30.06.2016	F	Long QT Syndrome and epilepsy
Marit Aas	Norwegian	15.08.2014-30.06.2018	F	Genetic counseling
Thomas Muri Stokke	Norwegian	05.01.2012-05.01.2016	M	Pocketsize cardiac ultrasound
Aslak Wigdahl Bergersen	Norwegian	01.10.2016-31.09.2017	M	Computational fluid structure interaction tools

* 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

Scientific articles

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Almeida N, Papachristidis A, Pearson P, Sarvari SI, Engvall J, Edvardsen T, Monaghan M, Gérard O, Samset E, D'hooge J
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Computational rabbit models to investigate the initiation, perpetuation, and termination of ventricular arrhythmia.
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Scand Cardiovasc J. 2016 Apr;50(2):65-77
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Edvardsen T: Strain imaging in valvular heart disease: when and how to use it?
Annual meeting, the working groups on Echocardiogr, Valvular Heart Disease and Cardiac Surgery, Monte Real, Portugal. Feb 2016

Edvardsen T: Is it heart failure? 63 Year Old Woman 3 Months After Chemotherapy Treatment for Breast Cancer.
ACC meeting, Chicago, IL, USA. Apr 2016

Edvardsen T: Strain echocardiography in the prediction of Malignant Arrhythmias.
6th Congress of the Brazilian Department of Cardiovascular Imaging SBC, Belo Horizonte, Brazil. Apr 2016

Edvardsen T: LV function in Aortic Stenosis beyond Ejection Fraction – Prognostic implication.
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Edvardsen T: Up-to-date assessment of left ventricular function.
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Edvardsen T: Heart failure with preserved EF - Clinical case.
ESC Congress, Rome, Italy. Aug 2016

Edvardsen T: Imaging in Acute Cardiovascular Care.
55th annual meeting, Rumanian Society of Cardiology, Sinaia City, Rumania. Sep 2016

Edvardsen T: Tips and tricks for imaging deformation acquisition and analysis.
55th annual meeting, Rumanian Society of Cardiology, Sinaia City, Rumania. Sep 2016

Edvardsen T: Global longitudinal strain and aortic stenosis.
EACVI Course: Echo and valves (advanced level), Naples, Italy. Oct 2016

Edvardsen T: EACVI/ASE Recommendations: Evaluation during and after cancer diseases for assessment of cardiotoxicity.
15th annual National Congress of Cardiology, Bulgarian Soc Cardiology, Sofia, Bulgaria. Oct 2016

Edvardsen T: Clinical cardiac ultrasound in research
Medical imaging in cardiac research, OUH, Norway. Oct 2016

Edvardsen T: Inge Edler Lecture: Up-to-Date Assessment of Left Ventricular Systolic Function
EkokardiografiNS Dag, Skånes universitetssjukhus, Lund, Sweden. Oct 2016
Professor Edvardsen was rewarded the Inge Edler Prize for his outstanding contribution in the field of echocardiography

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Geilo Winter School, Geilo, Norway. Jan 2016

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Haugaa KH: Imaging in ARVC
ESC Congress, Rome, Italy. Aug 2016

Haugaa KH: Characterstics of Regional Myocardial Function and Patient Outcome
German echocardiographic conference Cologne, Germany. Nov 2016

Haugaa KH: ARVC diagnosis: do we need a new diagnostic Task Force?
1st athletes heart and cardiomyopathy meeting, Lisboa, Portugal. Oct 2016

Haugaa KH: Risk stratification and preventive treatment for SCD in patients with inherited heart disease
Nordic Baltic EP meeting, Oslo, Norway. Nov 2016

Haugaa KH: How should we image to diagnose ARVC?
Nordic imaging meeting, Fornebu, Norway. Oct 2016

Haugaa KH: Risk stratification and management in inherited heart disease.
Autumn meeting, Norwegian Society of Cardiology, Fornebu, Norway. Oct 2016

Hopp E: Aortitt og arteritt
Dagskurs, Norsk Forening for Thoraxradiologi, Oslo Lufthavn. Mar 2016

Hopp E: Cardiac MRI
PhD-kurs FYS-MED 9750 Medisinsk avbildning, Oslo. Sep 2016

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Bildediagnostikk i Revmatologi, Oslo. Sep 2016

Hopp E: Måling av taggingopptak i hjertet
Magnetomforum, Oslo. Sep 2016

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Louch WE: Structure:Function Relationships in Cardiomyocytes: Implications for Development and Disease
Department of Cardiology, Charité Hospital, Berlin, Germany. Jan 2016

Louch WE: Disease Mechanisms of Heart Failure
Inauguration Symposium, Bioimaging Core Unit, Ludwig Maximilians University, Munich, Germany. Feb 2016

Louch WE: Dyadic Structure and Function in Cardiomyocytes: Implications for Heart Failure
Department of Pharmacology, University of Davis, California, USA. Apr 2016

Louch WE: Cardiomyocyte Ca2+ Handling During Heart Failure
International Conference of Physiological Sciences, Beijing, China. Sept 2016

Louch WE: Structure:Function Relationships in Cardiomyocytes
Department of Cell and Molecular Biology, Karolinska Institute, Stockholm, Sweden. Oct 2016

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Using pacemaker leads for bioimpedance and electromyography
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Remme EW: What can modelling contribute to our understanding of cardiac dysfunction based on ultrasound and MRI?
Medical imaging in cardiac research, OUH, Oslo, Norway. Oct 2016

Remme EW: Anatomy and mechanics of myocardial contraction
Heart Failure and Pacing, OUH, Oslo, Norway. Nov 2016

Remme EW, Smiseth OA
Impaired Subendocardial Contractility and Longitudinal Shortening with Aging, Reduce Midwall Fiber Stress, Increasing Circumferential Shortening and Preserving Ejection Fraction
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European Working Group on Cardiac Cellular Electrophysiology, Glasgow, United Kingdom. Aug 2016

Samset E: Bringing Myocardial Velocity and Deformationg Imaging into the cath lab
Velocity and Deformation Imaging Symposium, Leuven. Feb 2017

Samset E: CCI experiences on how to make innovation work in an SFI
SFI CIUS board meeting. Aug 2016

Samset E: Collaboration between GE Vingmed and Oslo University Hospital - Center for Cardiological Innovation.
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Strain echocardiography demonstrates alterations in left ventricular deformation in preadolescents with fetal growth restriction.
ESC Congress, Roma, Italy. Aug 2016

Skulstad H: Shunts and shunt calculation
NSC, Fornebu, Norway. Oct 2016

Smiseth OA: New recommendations for evaluation of LV diastolic function: is there a role for strain imaging?
Myocardial Velocity and Deformation Imaging, Leuven, Belgium. Feb 2016

Smiseth OA: Diastolic left ventricular dysfunction: from pathophysiology to clinic.
XIV National Congress on Cardiac and Coronary Multi-Imaging, Naples, Italy. Feb 2016

Smiseth OA: Putting it all together: What do the guidelines say.
American Society of Echocardiography 27th Annual Scientific Sessions, Seattle, USA. Jun 2016

Smiseth OA: Cardiac and non-cardiac causes of suspected HFpEF
ESC Congress, Roma, Italy. Aug 2016

Smiseth OA: How should key data be measured and integrated: E/e', left atrial volume, PA pressure
ESC Congress, Roma, Italy. Aug 2016

Smiseth OA: Nye retningslinjer for diastolisk funksjon
Regionsmøte i kardiologi, OUS, Norge. Sep 2016

Smiseth OA: The Heart in Color and Loops.
50 years anniversary Institute for Surgical Research, Oslo, Norway. Oct 2016

Smiseth OA: Collaboration between GE Vingmed and Oslo University Hospital – Center for Cardiological Innovation.
Corporate Innovation Day, Oslo, Norway. Oct 2016

Stokke MK: Translational research on arrhythmias
Meeting of the Special Interest Group for Cardiac Physiology, Oslo, Norway. Aug 2016

Stokke MK: Cardiac arrhythmias: from basic science to bedside treatment.
Cardiovascular Pathophysiology, NORHEART PhD course. Oct 2016

Stokke MK: Trening for pasienter med arvelige kardiomyopatier.
Norsk hjertesviktforum. Nov 2016

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Impact of material parameter uncertainty on stress in patient specific models of the heart
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UNIKARD

Kan pacemaker redde liv for småbarn med lang QT-tid syndrom
www.unikard.org, 17.10.2016

Ny ultralydmetode kan avdekke hvilke hjertesvikt-pasienter som har nytte av resynkroniseringsterapi
www.unikard.org, 20.04.2016

Skiller farlig og ufarlig hjertesykdom ved hjelp av ultralyd
www.unikard.org, 14.04.2016

Simuleringer viser betydningen av fettvev i hjertet for farlige rytmeforstyrrelser ved ARVC
www.unikard.org, 04.04.2016

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www.unikard.org, 14.04.2016

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Hvorfor beveger skilleveggen mellom hjertekam-rene seg unormalt ved venstre grenblokk?
www.unikard.org, 04.02.2016

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Dagens Næringsliv, 04.07.2016, side 13

Fant større pacemakerrisiko for proffsyklister
www.dn.no, 01.07.2016

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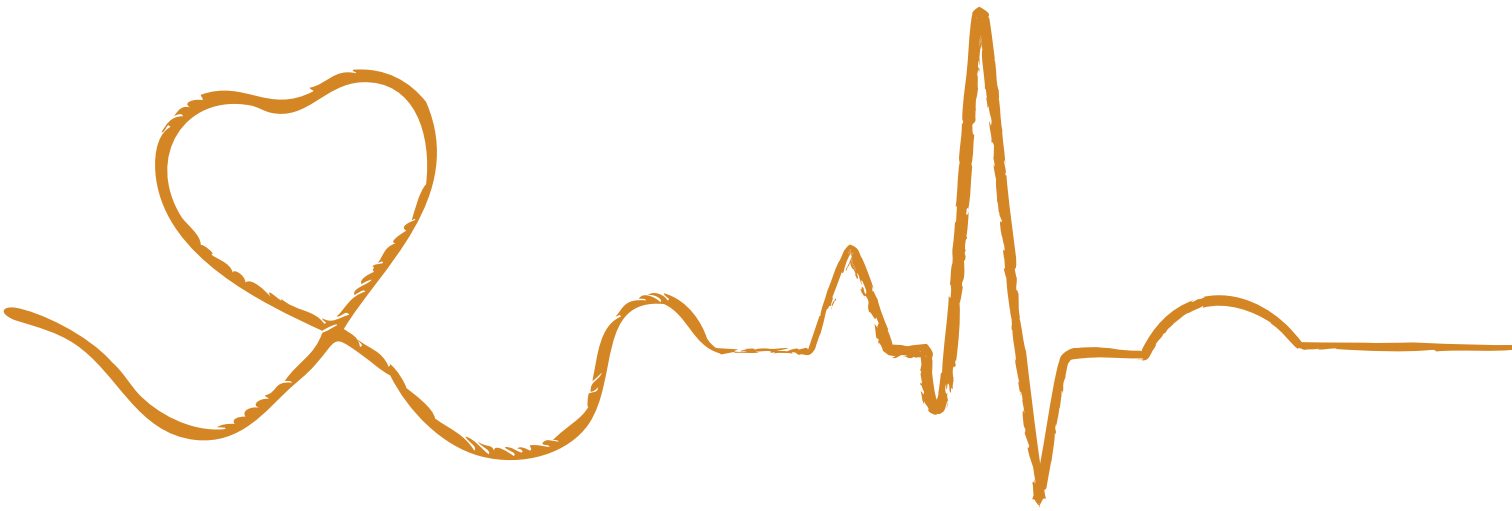

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