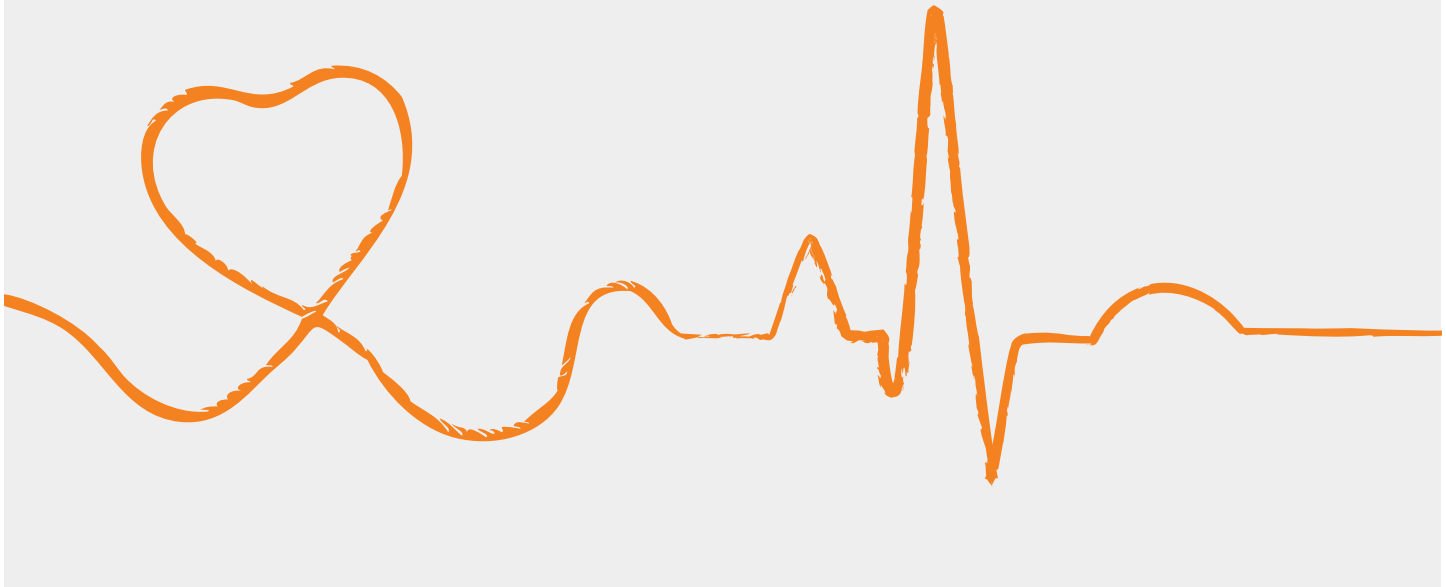
ANNUAL REPORT | 2011

CENTER FOR CARDIOLOGICAL **INNOVATION**



Centre for Research-based Innovation

Established by the Research Council of Norway

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CENTER FOR CARDIOLOGICAL **INNOVATION**

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SUMMARY

The Center for Cardiological Innovation (CCI) was officially established on October 31st 2011. It is hosted by Oslo University Hospital, which constitutes the physical hub for CCI activities. Research partners in the Center are Simula Research Laboratory AS and the University of Oslo. GE Vingmed Ultrasound AS, Kalkulo AS and CardioSolv LLC are the Center's industrial partners.

The main objective of the Center is to develop the next generation of ultrasound systems for cardiology. To achieve this goal, the CCI will conduct translation research integrating ultrasound imaging, mathematical modeling of the heart and clinical research focusing on patients at risk of heart failure and sudden cardiac death.

In 2011, research has resulted in 30 articles published in peer-reviewed journals by researchers affiliated with CCI. In addition 44 presentations and abstracts have been held at various prestigious conferences within cardiology and biomedicine. Three PhD-students within medicine have been recruited and started their work at Oslo University Hospital; in addition one post doctoral fellow has been recruited and started work at Simula Research Laboratory and one scientific programmer has started working 50% at GE Vingmed Ultrasound.

The overall management structure of the Center consists of a board comprised by members from the consortium. A Center director is in charge of the operation of the Center, assisted by a management team.

CENTER FOR CARDIOLOGICAL **INNOVATION**

ESTABLISHING THE CCI

WORDS FROM THE DIRECTOR

In 2010, Oslo University Hospital, together with Simula Research Laboratory, submitted a proposal in response to the Research Council of Norway's call for eight-year projects, the Centers for Research-Based Innovation. The main idea behind the proposal envisioned the next generation of ultrasound systems for cardiology. GE Vingmed, located in Horten, Norway, was therefore a natural business partner in our consortium. We teamed up with other strong research and business partners in the application: University of Oslo, Kalkulo and Cardiosolv.

The competition was tough. In total, the Research Council received 84 proposals from companies and research institutions for the pre-qualification round. In the final round of the competition, the Research Council received 44 proposals. After the final evaluation, the Center for Cardiological Innovation was one out of seven new Centers appointed as Centers for Research-Based Innovation by the Research Council Board on the 16th December 2010.

On October 31st 2011, the Center for Cardiological Innovation was formally established, and the agreement between the Research Council of Norway and Oslo University Hospital was signed. The agreement will ensure an annual funding of 10 MNOK over a period of five years and up to a maximal eight years.

The Center for Cardiological Innovation provides a unique opportunity for researchers, as they can engage in long-term research projects, since the Center provides both predictability and long-term funding. The first, short year of CCI has ended. The kick-off meeting was successful and resulted in a lot of new ideas and plans for research activities. CCI has established a temporary office location in the Institute for Surgical Research, with the excellent assistance of its director, Professor Ansgar Aasen. Research in the first three work packages has started, and plans for work package 4 are soon to be finalized. We have already managed to publish several scientific publications during the first few months since startup. The CCI will bring us a lot of opportunities, so we look forward to continuing this great collaboration and making CCI a success.

Professor Thor Edvardsen MD, Center Director
Photo: Andreas B. Johansen RCN

OBJECTIVE

The Center for Cardiological Innovation (CCI) aims to develop the next generation of ultrasound systems for cardiology.

The proposed tools and technologies will be created through linking currently isolated diagnostic systems with advanced biomedical research, advanced patient-specific computer simulation, and multi-modality visualization techniques. The targeted clinical uses of the proposed innovations are for better triage and treatment of patients at risk of sudden cardiac death or suffering from heart failure, two major challenges in cardiology today.

Every 30 seconds, a person in the Western world suffers sudden cardiac death and/or death from heart failure. These two conditions remain the major challenges in modern cardiology. However, new treatments now emerging offer hope in combating these events: triggers for rhythm disturbances in the heart can be destroyed by heat via ablation therapy, and pacemakers and defibrillators can be implanted to break up deadly fibrillation or ameliorate heart dysfunction. As current diagnostic tools for risk stratification of fatal events are clinically insufficient, the problem facing clinicians is to know when to apply these advanced treatments. The goal of the Centre for Cardiological Innovation (CCI) is to produce commercially and clinically driven advances in cardiac diagnostics and applications.

RESEARCH AREAS

The CCI aims to combine and extend currently isolated technologies into integrated tools and applications. The ultimate goal is the integration of electrocardiogram (ECG) and cardiac ultrasound (cU/S) measurements into a novel scanning system coupled with advanced simulation techniques to prescribe treatment tailored for the individual patient. These innovations have the potential to improve diagnostic cardiology and represent a substantial market edge for industrial partners.

Innovative products and technologies with short, medium, and long-term value may be produced from the research and development areas detailed below.

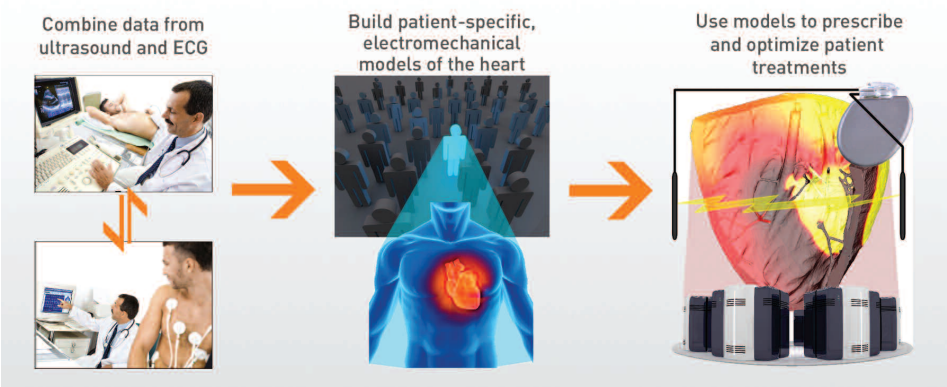


Figure 1. The CCI aims to combine modalities to offer physicians novel tools for diagnosis and treatment planning.

Novel prognostic indices for Heart Failure and risk for Sudden Cardiac Death.
Addition of new metrics into GE Vingmed Ulstrasound (GEVU) scanners and diagnostic workstations will enable clinical end-users to make more accurate decisions about treatment options for heart failure (HF) patients and patients at risk for sudden cardiac death (SCD). The initial work of the CCI has included research working towards incorporation of these emerging diagnostic measurements into proprietary cU/S equipment.

A new concept for diagnosing a subset of those suffering with heart failure (ventricular dyssynchrony) and identification of potential patients who will respond well to cardiac resynchonization therapy (CRT) was identified at Oslo University Hospital (OUH) via animal experiments. The new index is called the onset of active force generation (AFG), and is based on plotting length of a myocardial segment, assessed by speckle tracking using GEVU technology, against the intraventricular pressure, which currently must be measured with an invasive catheter. An elevated AFG variability indicates that a patient may be a candidate for CRT. 2011 saw the launch of a pilot clinical trial of the AFG index, progress towards modification of the ultrasound scanner for unfiltered pressure measurements, and an initial design for a prototype software application that would compute the AFG (within a larger GEVU scanner software package).

Mechanical dispersion (MD) is a way of checking whether different parts of the heart muscle are beating together as they should via non-invasive, speckle-tracking cU/S measurements. In terms of assessing risk for sudden cardiac death, MD can be used in patient cases following a heart attack (post myocardial infarction, MI). However, MD needed to be further evaluated a large, multicentre clinical study of post-MI patients.

In 2011 such an expanded pilot clinical trial began. In addition, the past year saw the simplification of processing data from cU/S scanner systems, in order to help analysis of the data from these clinical patient cases.

Building patient-specific models from data and simulating treatment effects.
The current clinical paradigm for diagnosis and treatment planning in cardiology involves obtaining measurements from patients, and then using simple statistics-based rules. The CCI aims to supplement this via construction of patient-specific models that aid diagnosis and predict the outcome of therapies on an individual level. The combination of clinical data with software systems for modeling and visualization of multimodal data will enable the addition of such diagnostic tools directly into cU/S scanning systems and/or a data review suite. This will provide exciting and completely novel clinical tools to the marketplace. In 2011, focus remained on construction of an image-based modeling pipeline, which would allow usage of patient-specific geometries and mechanical information of the beating heart in computational models. This included defining what can be extracted from currently existing software and outlining workflows such that computer models of each individual patient's physiology may be constructed with relative ease.

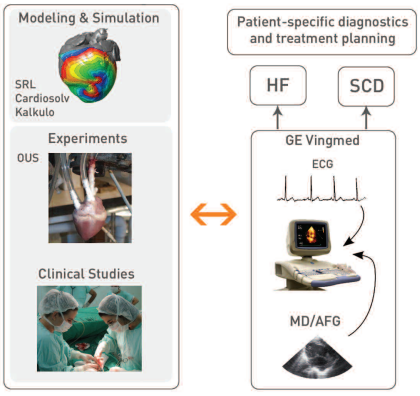
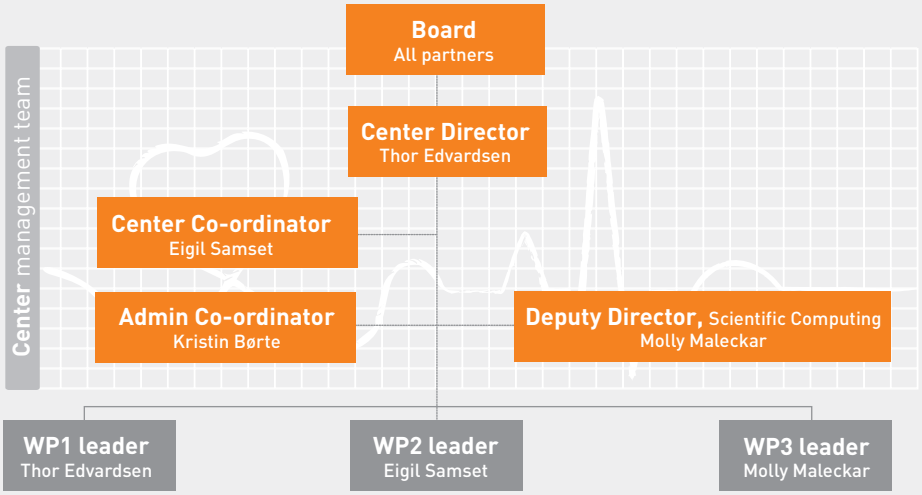


Figure 2. Research that combines modelling and simulation with experimental and clinical studies will drive the development of novel, multimodality ultrasound and ECG-based tools for diagnostics and treatment planning.

ORGANIZATION AND PARTNERS

The Center for Cardiological Innovation (CCI) is hosted by Oslo University Hospital and consists of a consortium of five 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 (industrial) partners are GE Vingmed Ultrasound AS, CardioSolv LLC and Kalkulo AS. The CCI is located in Oslo, thus Oslo University Hospital constitutes the physical hub for CCI research activities.



CCI is governed by a Board of Directors, for which representatives have been appointed by each of the partners. The first Board meeting was held on November 4th 2011 and the following Board members were appointed by the consortium participants:

- Gunnar Hansen, GE Vingmed Ultrasound, Chairman
- Audun Fosselie Hansen, Kalkulo
- Are Magnus Bruaset, Simula Research Laboratory
- Ivar Gladhaug, University of Oslo
- Theis Tønnesen, Oslo University Hospital
- Brock Tice, CardioSolv

Oslo University Hospital

UiO : University of Oslo

[simula . research laboratory]

GE Vingmed Ultrasound

kalkulo

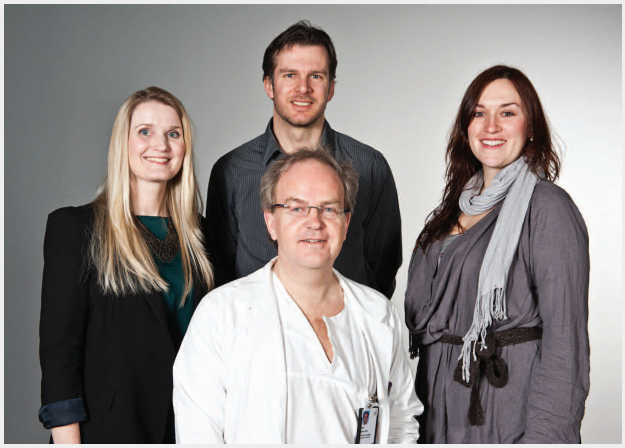
cardiosolv

MANAGEMENT TEAM

The Center's Director is **Professor Thor Edvardsen**. Professor Edvardsen earned his Medical Degree (MD) at Haukeland University Hospital, University of Bergen and his PhD / Dr.Med. at the University of Oslo. He is a board-certified specialist in Internal Medicine and Cardiology and has been a senior staff member in the Department of Cardiology at Rikshospitalet since 2002 and worked at John Hopkins Hospital, Baltimore, USA from 2003-2004. He has more than 100 international scientific publications and 8 book chapters. He is active in clinical and experimental research in the area of myocardial function and has extensive knowledge of cardiac ultrasound, MRI, CT and hemodynamics.

The Center Director is assisted by a management team for daily operations. **Eigil Samset** is the Center Coordinator, representing the largest user partner, GE Vingmed Ultrasound. He helps drive the Center to ensure that the innovation objectives are met. Eigil Samset has his Master's Degree from NTNU in engineering cybernetics with a focus on medical applications. His PhD was conducted at the Medical Faculty of the University of Oslo where he developed new methods for utilizing MRI as an intra-operative imaging modality. He was invited to Harvard (Brigham and Women's Hospital) to complete a postdoctoral fellowship on MRI-guided cardiac ablation. He has also been a visiting researcher at Stanford University Hospital, where he worked on intra-vascular ultrasound. Eigil Samset has worked academically with medical image processing, visualization, navigation and robotics for 11 years, managing research teams in Norway and across Europe. He has also 3 years experience as a product and technology manager in the oil & gas business, where he managed a software development team focused on cutting edge applications for simulation and visualization.

Mary (Molly) Maleckar is the Deputy Director of Scientific Computing in the CCI, representing the research partner Simula Research Laboratory. She assists with technical coordination within scientific computing work packages. Dr. Maleckar received her PhD from the Department of Biomedical Engineering/Institute for Computational Medicine at Johns Hopkins University in 2008 and began work at Simula in the Scientific Computing Department in January 2009. She is now the Head of Department for Computational Cardiac Modeling (CaMo) at Simula Research Laboratory. Her research is strongly focused on applications in cardiac electrophysiology and electromechanics. Her specific research interests include electrophysiological modeling of human atrial cells and tissues, utilization of simulation as a tool for prognostic personalized cardiology, and computation as an avenue for drug discovery and testing.



From left: Kristin Børte, Eigil Samset, Molly Maleckar and Thor Edvardsen in front. Photo: Øystein H. Horgmo, UiO

Kristin Børte is the Administrative Coordinator of the CCI. She provides administrative support and manages responsibilities of the CCI with respect to the Research Council of Norway. Kristin Børte has an Advanced Master's degree in education with specialization in the field of leadership, organizational theory and learning from the University of Oslo. She obtained her PhD degree in Education within the field of workplace learning at the Faculty of Educational Sciences at the University of Oslo in 2011. Her PhD was conducted at Simula Research Laboratory, where she investigated teamwork in software effort estimation. Prior to her PhD, Kristin Børte had worked as an advisor at Simula Research Laboratory and as a researcher at NIFU. She has several years of experience with research administration and reporting.

Management is headed by the Center Director and consists of all scientific (work package) leaders in addition to the administrative coordinator. Research in the center is organized into work packages such that a designated project leader is responsible for a particular work package/research stream.

OSLO UNIVERSITY HOSPITAL

Oslo University Hospital (OUH) is owned by the South-Eastern Regional Health Authority and consists of the former health trusts of Aker University Hospital, Rikshospitalet University Hospital and Ullevål University Hospital.

The hospital is, with its 18,000 employees and 1.2 million patient treatments per year, Scandinavia's largest hospital and also one of the largest hospitals in Europe. OUH is responsible for approximately 50 percent of all medical and healthcare research conducted at Norwegian hospitals. This results in about 1,500 peer-reviewed publications and 100 PhD graduates annually. The driving force for all research investments at OUH is to improve patient care, in both the short and long term. The continuous need to improve patient care is also based on development and implementation of new procedures, targeting diseases that still represent a major burden to the health system as well as to the patients themselves.

One of the major challenges today is related to the treatment of cardiological diseases and the prediction of optimal therapy. Today, many unexpected events could probably have been avoided if better diagnostic tools were available. One such tool is predicted to be the combination of cardiac ultrasound and electrocardiographic methodologies combined into a joint diagnostic modality. It is predicted that such methodology could provide a powerful tool to tailor individual patient therapy.

The Heart and Lung Clinic at the Oslo University Hospital is the largest cardiac center in Scandinavia and the only center in Norway to achieve a rating of excellence in clinical research. This major clinical and research activity within the field of cardiology links the Center for Cardiological Innovation (CCI) to a major strategic operation within Oslo University Hospital. CCI will use defined clinics and departments at OUH as a basis for further progression in the cardiological area, and Oslo University Hospital will collaborate closely with the University of Oslo to constitute the center's hub. Our main objective in hosting the CCI is to improve procedures and services related to patient treatments, i.e. by developing and utilizing current and new competence and results to obtain new diagnostic and therapeutic approaches to the benefit of patients suffering from cardiac diseases.

Oslo University Hospital

UNIVERSITY OF OSLO

UiO : University of Oslo

University of Oslo (UiO) is ranked as the best university in Norway. It has 7,000 employees and 27,000 students and is therefore also the largest university in Norway.

The Faculty of Medicine has approximately 3,300 students (including PhD candidates) attending their study program. The Faculy consists of five institutes: the Institute for Forensic Medicine, the Regional Committees for Research Ethics in Medicine and Health Care, the Institute of Health and Society, the Institute of Basic Medical Sciences and the Institute of Clinical Medicine. The research and education carried out at the Faculty of Medicine are based on a close partnership with the South-Eastern Norway Regional Health Authority and two hospitals: Akershus University Hospital and Oslo University Hospital. Approximately 50 percent of the academic staff at the Faculty is also employed at one of the University Hospitals. This ensures a close connection between medical theory and clinical practice for students and researchers. The Faculty also collaborates with local hospitals and general practitioners in teaching medical students.

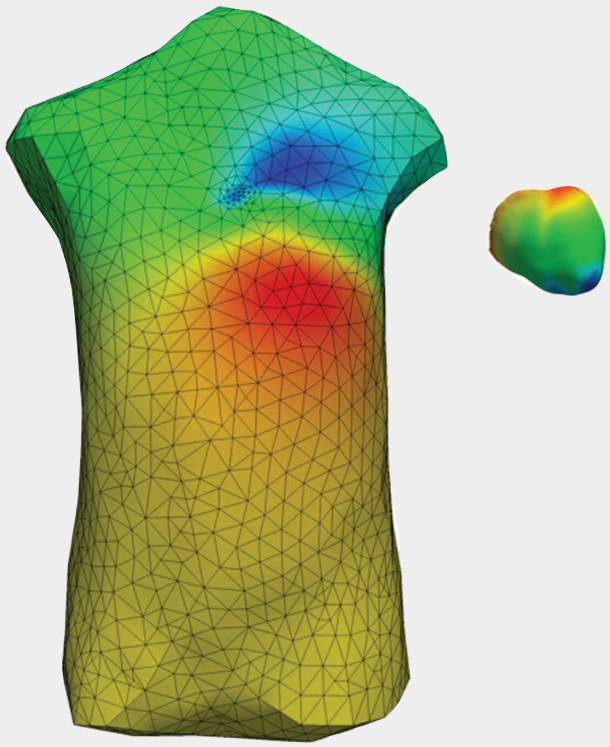
The Faculty of Medicine in collaboration with the Department of Cardiology, Oslo University Hospital has two key research areas: myocardial function/cardiac imaging and heart failure. This collaboration has been a strong scientific contributor in order to establish modern cardiac imaging principles for assessment of regional and global left ventricular function. Moreover, research in cardiology has been defined as one of the main medical research areas at the University of Oslo.

The University of Oslo, together with Oslo University Hospital, constitutes the hub of the Center for Cardiological Innovation (CCI). University of Oslo acts as a research partner in the CCI and hosts PhD students in the PhD program at either the Faculty of Medicine or the Faculty of Mathematics and Natural Sciences.

SIMULA RESEARCH LABORATORY

Simula Research Laboratory was established in 2001, and has been headed by Professor Aslak Tveito since 2002. Dedicated to tackling scientific challenges with long-term impact and of genuine importance to real life, Simula offers an environment that emphasises and promotes basic research at a top international level, while still covering the broader landscape from postgraduate education to application-driven innovation and commercialisation.

Simula is a non-profit, public utility enterprise, organised as a limited company owned by the Ministry of Education and Research. Focus remains on industry cooperation in order to provide solutions and increase relevance of research results. Simula`s largest stand-alone industry collaboration is with Statoil, and the current contract portfolio is worth over 150 million NOK. Simula counts diversity as an additional strength, and is proud of its international environment that employs 126 exceptional minds from 25 different countries.



Basic research at Simula is focused in the fields of communication systems, scientific computing, and software engineering. The endeavours in all three areas have been quite successful: Simula is ranked by the Journal of Systems and Software as the world`s most productive institution in systems and software research, serves as the host for the Center of Biomedical Computing, a Centre of Excellence (SFF), as well as the Certus center for software verification and validation, a center for research-based innovation (SFI) (both awarded by the Research Council of Norway). Simula is also a main research partner in the Centre for Cardiological Innovation (SFI), with primary participation through its Department of Cardiac Modeling (CaMo).

CaMo features a range of competencies in cardiac modeling. These include the development of methods to study electrophysiology and mechanics in heart tissue, and the use of these tools to study selected questions related to cardiac dysfunction and arrhythmia. Complex mathematical models are required to accurately simulate heart physiology, which creates a series of research challenges. First, it is necessary to approach problems via mathematical theory, which can lead to advanced understanding but may require novel analytical approaches. Solving models of cardiac electrophysiology and mechanics on a computer also requires stable, rapid numerical methods. There are additional challenges related to how such complex systems can be implemented in software in efficient, yet flexible ways. CaMo research has and will continue to focus on developing and applying these sophisticated numerical models and software tools, as well as creating quantitative, human-specific models of the heart. Targeted models can then be applied to elucidate responsible mechanisms and potential medical consequences of cardiac pathologies. Key application areas for the CCI within our research group focus on the electrophysiological modeling in cardiac muscle cells and, at the organ level, cardiac electromechanics aimed at understanding dysfunction in the post-infarct and failing ventricles. CaMo`s partnership will contribute concretely to the CCI by providing a basic research foundation for the development of patient-specific modeling techniques and software development for their implementation in commercial systems.

GE VINGMED ULTRASOUND

GE Vingmed Ultrasound (GEVU) is a world-leading provider of ultrasound systems for cardiovascular applications. GEVU is recognized as Center of Excellence for cardiac ultrasound within GE Healthcare – a $17B revenue business area within General Electric Coorporation.

GE Vingmed Ultrasound has 190 employees, with headquarter in Horten, Norway and offices in Oslo and Trondheim. GEVU collaborates closely with medical and technological research institutes in Norway and abroad, and more than 60 PhD theses have been published based on work related to development or use of equipment produced by GEVU. GEVU won the Norwegian Engineering Achievement Award for 2009 for one of its latest new product, the Vscan handheld ultrasound scanner.

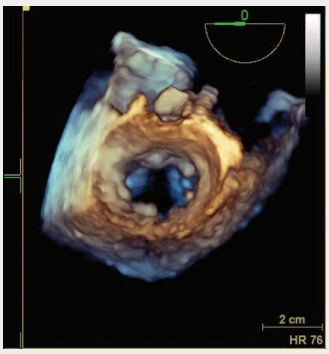
Business areas
GEVU supplies a range of products for cardiac ultrasound imaging. The high-end scanner, Vivid E9, is used in hospitals for diagnostic examinations of patients suffering from different heart problems. Vivid E9 is GE Healthcare's first cardiovascular ultrasound system built specifically for 4D imaging – from ergonomics to image acquisition to data management with quantification tools, 4D Stress and advanced ergonomics. One-touch ease of use puts 4D effortlessly at the doctor's fingertips and provides innovative features designed to improve image quality, quantification and workflow. In addition to regular examinations done in the echocardiography lab, it is also used during stress exams (exercise) and to guide interventions in the operating room.

VScan, a pocket size ultrasound scanner

The VScan is "the new stethoscope" that addresses primary care in the local doctor's office as well as a handy tool to bring ultrasound to the patient's bedside in hospitals.

The VScan is a powerful visualization tool despite its size. Small and lightweight, Vscan slips easily into the doctor's lab coat pocket. Its ample battery capacity provides over one hour of scanning on a single charge – plenty of power for a full day's worth of patient exams.

Type of expertise brought to the CCI
GEVU brings a substantial body of expertise in development, manufacturing and applications of cardiovascular ultrasound systems. The R&D team at GEVU is highly skilled with competence spanning electronics, ultrasound acoustics, software engineering, image processing, visualization, quantitative analysis of cardiac function and clinical applications.



3D ultrasound image of the mitral valve, taken with the new 3D TEE probe

Type of activities within the CCI
GEVU will support the CCI with prototype ultrasound scanners, implementing new research results from the CCI. GEVU is particularly interested in methods that can help predict sudden cardiac death as well as predicting if a patient will benefit from cardiac resynchronization therapy (a new generation of pacemakers). GEVU will also perform research on methods for advanced cardiac analysis and new imaging techniques, including new imaging probes.

GE Vingmed Ultrasound

KALKULO

Kalkulo is a Norwegian software company providing software solutions for technical applications. The company was founded in 2006 and currently has 10 employees. Kalkulo is owned by Simula Research Laboratory. One of the objectives of Kalkulo is to provide an outlet for Simula's research activities, into applications.

Business areas
Kalkulo develops services and products within three markets: computational biomedicine, oil and gas exploration and renewable energy. The business idea is to provide tailored solutions based on expert competence.

Type of expertise brought to the CCI
Geometric modeling. This type of expertise deals with how to represent, construct and manipulate geometries (shapes) on a computer. Types of relevant geometries involve curves, surfaces, volumetric grids and scalar/vector fields. One important way of constructing geometries is by interpolation. That is, by turning sparse measurements into continuous representations (for instance turning point clouds into surfaces).

Computer visualization. Important aspects of this expertise are: 1) transformation of data into information, 2) choosing the right level of detail, 3) highlighting important features of the data, and 4) handling large and inhomogeneous data sets efficiently.

Software application development. Realizing many of the commercial ambitions of the CCI rely on this type of expertise. This includes the development of user friendly, efficient, robust and re-usable software. Relevant skills are software and user interface design, handling of large data sets, data communication, software integration and data conversion.

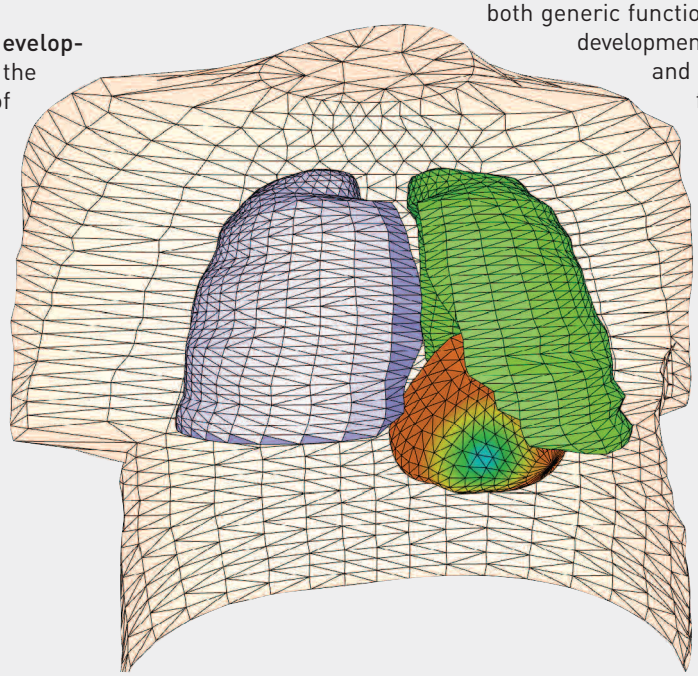
Type of activities Kalkulo will perform as part of the CCI
Kalkulo's main activities are focused on software development. We will collaborate with the other partners in order to develop software for:

Generation of tailored geometric models. One of the main goals of the CCI is to simulate patient specific effects of the treatment of cardiac diseases. Kalkulo will develop software that generates patient-specific 3D models, suitable for simulation, in terms of surfaces, volumes and vector fields.

Data visualization and integration. Kalkulo will develop software representing an interface for both clinicians and researchers. The software shall provide access to different simulation models, as well as all relevant data types, such as surface geometries, vector fields (fiber directions), 3D imagery and simulation results.

Kalkulo plan to realize the above software by further development of its own technology platform called KAF (Kalkulo Application Framework). KAF is a software library containing both generic functionality for software application development (user interfacing, input/output and so on) as well as specialized functionality for visualization and geometric modeling.

In the end, Kalkulo aims at developing products, either as modules or stand-alone applications that can be commercialized.



A patient-specific geometric model of the human torso, showing the heart (in red) in between the lungs. This patient is suffering from ischemia and a computer model of the ischemic part of the heart is shown in blue/green.

kalkulo

© Oslo University Hospital

CARDIOSOLV

CardioSolv LLC (http://cardiosolv.com) is a private scientific services and consulting company founded in 2008 specializing in predictive cardiac modeling and simulation.

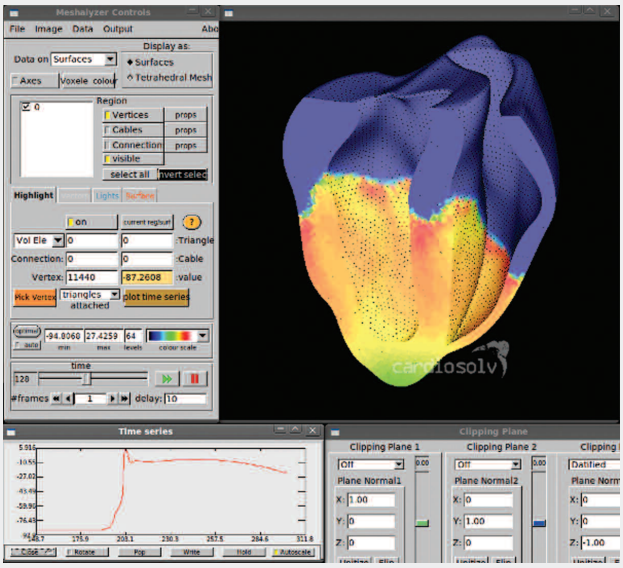
CardioSolv's goal is to be the world leader in software development for cardiac electromechanical applications and to provide computational biomedicine engineering analysis to the academic research community, biomedical technology companies, and the cardiology profession. Our services include medical device design and optimization, virtual cardiac electrophysiology and electromechanics solutions, and personalized-medicine planning tools for anti- arrhythmia therapy. The mission of CardioSolv, LLC is to bring the state of the art in cardiac simulation out of academia and to the bedside.

The founders of CardioSolv, LLC come from leading labs in their fields, and have extensive background in cardiac electrophysiology and mechanics, cardiac modeling, image processing, image-based model reconstruction, numerical analysis, computer science, and high-performance computing. We generate personalized heart models from medical imaging data, simulate electrical and mechanical activity, and interpret the results of such simulations. We are using our expertise to develop intuitive solutions for those who could benefit from our services, while continually striving to increase model detail, reduce turnaround time, and increase model accuracy.

Within the CCI, CardioSolv is providing access to our mesh creation tools, simulators, visualization tools, and simulation analysis tools. We are also providing consultation to other members of the CCI regarding cardiac simulation and arrhythmias. In particular:

CardioSolv has developed a fast, simple, and unique algorithm for assigning anatomically-accurate fiber orientations in arbitrary heart geometries, accurate to within 95% of histological measurements. This capability is needed for several of the simulation projects within the CCI. CardioSolv will provide and support the use of this algorithm and associated software.

CardioSolv also owns and develops the fastest, most sophisticated known cardiac simulator available, CARP. The CARP simulator is capable of running human-heart meshes at appropriate mesh resolutions, and scales well on thousands of CPU cores. CCI partners will be able to use CARP secure in the knowledge that it has been thoroughly tested and compared against numerous experimental and clinical studies, and used to publish hundreds of peer-reviewed publications in the cardiac electrophysiology field over the last six years. The CARP simulator interoperates with our other tools including the Meshalyzer visualization package, the CepMods parallel post-processing suite (open source - https://github.com/cardiosolv/Cardiac-Electrophysiology-Modules), and our revolutionary graphical electrode and region definition tool.
(http://www.youtube.com/watch?v=P-ccLr9MKvs)



Analyzing simulation results with the Meshalyzer visualization and analysis package. Shown is a trace of transmembrane potential from a transmural cutaway view of a rabbit ventricular mesh.

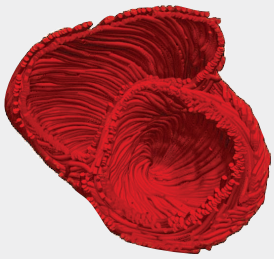
cardiosolv

SCIENTIFIC ACTIVITIES AND RESULTS

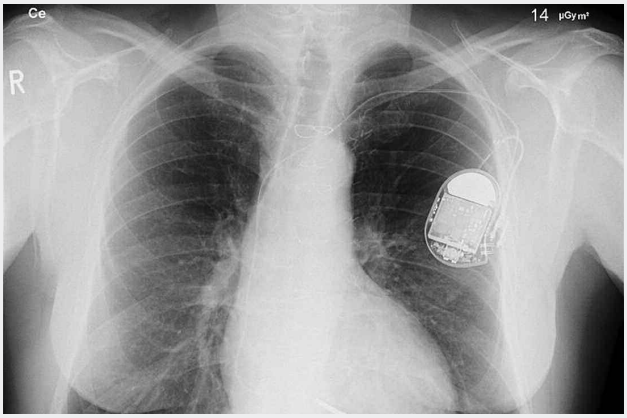
Heart failure
Heart disease is the most common cause of death in the West. Heart failure, in particular, is a rapidly growing health problem in the industrialized world. Cardiologists have powerful treatments to combat heart failure, but these can only postpone the progression the disease. Cardiac resynchronization therapy (CRT) is a powerful treatment for severe heart failure patients, and leads to decreased mortality and relief of symptoms. The treatment involves the implantation of an artificial pacemaker device. However, approximately 30% of patients will experience a lack of response to this treatment. Different echocardiographic indices have been proposed to improve patient selection criteria for CRT, but have failed. A new concept for identifying potential CRT responders has been identified by CCI. These methods have, so far, been carried out in experimental studies and in small-scale patient studies. The next step will be to integrate these metrics into ultrasound scanners and to employ these novel principles in larger clinical trials.

Malignant arrhythmias
Approximately 500,000 people in the U.S. will suffer annually from sudden cardiac arrest; a correspondingly smaller, but no less significant, number in Norway is 5,500 deaths. Effective treatments currently exist; the most effective is implantation of an internal cardioverter defibrillator (ICD). However, current guidelines for implantation of ICD fail to include all patient groups who would benefit from this treatment. CCI has therefore developed a new strategy for the prediction of severe arrhythmias in patients with preserved pump function after cardiac infarction. Measurement of mechanical dispersion in the heart by ultrasound has been promising in small studies of patients who have suffered infarction and other cardiac diseases which result in scar tissue. Mechanical dispersion is essentially a measure of how synchronously the heart is able to contract.

Model-based cardiac simulation
The shape of an individual patient's heart and its ability to deform can be imaged and measured with ultrasound. ECG can be used to measure information about the electrical activity in the heart. By combining this information, which can be measured, with advanced mathematical models of the heart's inner workings at micro-level, we hope to be able to unveil important information that cannot otherwise be measured. This requires development of a signal and image-based modelling pipeline in order to connect the imaging technology with the mathematical simulation technology.



Estimation of the muscle fibre structure of the heart. Courtesy of CardioSolv LLC (a CCI partner).



X-ray photography of thorax demonstrating an implanted ICD.

The CCI has made the first steps in developing data models that can connect the ultrasound images with the mathematical equations used in computer simulation of the heart. The heart muscle is constructed of muscle fibers organized into sheets. This structure is not possible to image with ultrasound. However the CCI has developed a reliable method to estimate fiber directions based on information from the ultrasound images. This is an important element of being able to simulate the complex function of an individual patient's heart.

3D TEE probe
Ultrasound imaging of the heart is limited by the narrow imaging windows between the ribs, as ultrasound cannot penetrate bone. However, more up-close imaging can be achieved by using a trans esophageal echocardiogram (TEE) probe. Such a probe is inserted down the esophagus while the patient is intubated. It can give a non-obstructed, high-resolution view of the heart.

Sebastian Sarvari, MD, and Margareth Ribe doing stress echo on a patient. Photo: Øystein H. Horgmo, UiO

2D TEE has been available for a long time, but to make a 3D TEE probe (with many hundreds more transducer elements) is an engineering challenge. 3D imaging can acquire volumes in real-time, which can be rendered semi-transparently in 3D, or as multiple 2D slices. GEVU has put an extensive effort into developing the market's best 3D TEE probe, and will start selling this as a product shortly.

RECRUITMENT

The CCI has recruited three PhD students within medicine that have begun work on tasks related to the Center's workplan.

- Nina Eide Hasselberg, MD, will work on the project "Left ventricular function and risk of arrhythmia in patients with cardiomyopathies. Echocardiographic studies".
- Jørg Saberniak, MD, will work on the project "Myocardial function a prediction of ventricular arrhythmias in patients with arrhythmic right ventricular cardiomyopathy".
- Jan Vecera, MD, will work on the project "The onset of active myocardial force generation as a novel method for the assessment of the left ventricle dyssynchrony and its clinical value for the detection of responders in resynchronisation therapy".

Nina and Jørg will both work at OUH, while the third recruited PhD student, Jan Vecera, will work onsite in a collaborating hospital in Belgium.

The CCI has also recruited one post doctoral fellow:

- Jussi Koivumäki, PhD, who will work on the project "Developing an image-based modeling pipeline; comparison of multi-modality image based models and simulation results; Electrophysiological Modelling".

Jussi has begun working at the CCI partner Simula Research Laboratory.

A scientific programmer has been recruited by the CCI.

- Pawel Kozlowski will work 50% (next to computer science studies at UiO) with developing software prototypes for novel concepts for assessment of cardiac functions.

Pawel has begun working at the CCI partner GE Vingmed Ulstrasound.

COMMUNICATION AND DISSEMINATION ACTIVITIES

CCI has published 30 scientific papers and held 44 presentations at international conferences as part of dissemination of results to users. In addition, the CCI has already appeared extensively in the media, resulting in interviews with core researchers and participation in a TV-show about the heart.

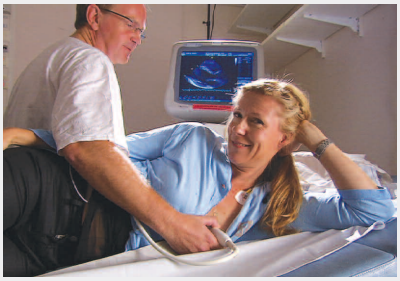
Researcher with a good heart

Thor Edvardsen – Researcher of the month in April – interview in South-Eastern Norway Regional Health Authority, 28.04. 2011
Photo: Oslo University Hospital

This is where the hottest IT-research take place

Interview with Molly Maleckar at Simula Research Laboratory in Computerworld 13.05.2011
Photo: Leif Martin Kirknes

Puls: Pursuing the secrets of the heart NRK Aug 2011



Center Director Thor Edvardsen doing an ultrasound examination on the reporter from NRK Helene Sandvig for the program PULS.
Photo: NRK

New center for research-based innovation
Oslo University Hospital 02.11. 2011

Division director Anne Kjersti Fahlvik from the RCN and acting director Jan Erik Thoresen, OUH ready to sign the agreement formally opening the CCI.
Photo: Andreas B. Johansen RCN

KEY PERSONNEL

Key Researchers

Name	Institution	Main Research area
Ole-Gunnar Anfinsen	OUH	Cardiovascular function
Thor Edvardsen	OUH/UiO	Myocardial function and cardiac imaging.
Christian Eek	OUH	Echocardiographic stratification of patients with acute coronary syndrome
Morten Eriksen	OUH	Development and validation of methods for analysis of myocardial strain recordings, with emphasis on assessment of mechanical work.
Kristina Hermann Haugaa	OUH	Ventricular arrhythmias and prediction of SCD. Mechanisms of arrhythmias, impact of imaging in risk assessment of SCD and cardiogenetics.
Torbjørn Holm	OUH	Inflammatory mediators and endothelial function as markers of prognosis in heart failure and after heart transplantation.
Erik Kongsgård	OUH	Electro Physiology-treatment
Espen Remme	OUH	Cardiac mechanics, cardiovascular function, diastolic function/ dysfunction/ heart failure, dyssynchrony, myocardial deformation in the ischemic heart, mathematical heart modeling, cardiac miniaturized motion sensors.
Helge Skulstad	OUH	Mechanisms of myocardial function, Cardiac Imaging and Adult Congenital Heart disease.
Otto Smiseth	OUH	Cardiovascular function, imaging and biomechanics
Lars Aaberge	OUH	Invasive cardiology and intensive coronary care
Thomas Dahlslett	UIO	Echocardiography/Cardiology
Per Grøttum	SRL	Inverse solutions and identification of ischemic regions from ECG recordings; extension of this solution for other applications
Glenn Lines	SRL	Computational cardiac electrophysiology (multiscale)
Ola Marius Lysaker	SRL	Inverse solutions and identification of ischemic regions from ECG recordings; extension of this solution for other applications
Bjørn Fredrik Nielsen	SRL	Inverse solutions and identification of ischemic regions from ECG recordings; extension of this solution for other applications
Molly Maleckar	SRL	Computational cardiac electrophysiology (multiscale)
Joakim Sundnes	SRL	Computational cardiac electromechanics
Aslak Tveito	SRL	Computational cardiac electrophysiology (multiscale)
Sam Wall	SRL	Computational cardiac electromechanics; development of geometric models from echocardiographic data
Olivier Gerard	GEVU	Ultrasound acquisition, processing and visualization
Gunnar Hansen	GEVU	Ultrasound acquisition, processing and visualization
Andreas Heimdal	GEVU	Ultrasound acquisition, processing and visualization
Stian Langeland	GEVU	Ultrasound acquisition, processing and visualization
Fredrik Orderud	GEVU	Ultrasound acquisition, processing and visualization
Stein Inge Rabben	GEVU	Ultrasound acquisition, processing and visualization

KEY PERSONNEL

Key Researchers

Name	Institution	Main Research area
Eigil Samset	GEVU	Ultrasound acquisition, processing and visualization
Tangui Morvan	Kalkulo	Geometric modeling and computer visualization
Ola Skavhaug	Kalkulo	Computational electrophysiology
Christian Tarrou	Kalkulo	Geometric modeling
Robert Blake	CardioSolv	Computational cardiac simulation methods and tools
Brock Tice	CardioSolv	Computational cardiac simulation methods and tools

Postdoctoral researchers with financial support from the centre budget

Name	Nationality	Period	Sex	Topic
Jussi Koivumäki	Finnish	2011-2013	M	Developing an image-based modeling pipeline; Clinical pilot study for comparison of multi-modality image based models and simulation results; Electrophysiological Modeling

PhD students with financial support from the centre budget

Name	Nationality	Period	Sex	Topic
Nina Eide Hasselberg	Norwegian	2011–2014	F	Left ventricular function and risk of arrhythmia in patients with cardiomyopathies. Echocardiographic studies.
Jørg Saberniak	German	2011–2014	M	Myocardioal function a prediction of ventricular arrhythmias in patients with arrhythmic right ventricular cardiomyopathy.
Jan Vecera	Czech	2011–2014	M	The onset of active myocardial force generation as a novel method for the aseessment of the left ventricle dyssynchrony and its clinical value for the detection of responders in resynchronisation therapy.

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

Name	Funding	Nationality	Period	Sex	Topic
Vibeke Marie Almaas	UiO	Norwegian	2010-2013	F	Echocardiographic changes in patients with hypertrophic cardiomyopathy and arrhythmias.
Marit Kristine Smedsrud	UiO	Norwegian	2007-2012	F	Myocardial viability assessment by echocardiography in patients with coronary artery disease.
Kristoffer Russell	OUH/ UiO	Norwegian	2008-2011	M	Dyssynchrony in the heart and novel methods for assessing global and regional myocardial function.

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ANNUAL ACCOUNTS

Funding	
	Amount*
The Research Council	3 199
The Host Institution (Oslo University Hospital)	1 237
Research Partners	2 427
Enterprise partners	1 643
Total	**8 506**

Costs	
The Host Institution (Oslo University Hospital)	2 809
Research Partners	3 405
Enterprise partners	2 217
Equipment	75
Total	**8 506**

* (All figures in 1000 NOK)

PUBLICATIONS 2011

Articles in International Journals

1. Cannataro M, dos Santos RW, Sundnes J: Biomedical and Bioinformatics Challenges to Computer Science: Bioinformatics, Modeling of Biomedical Systems and Clinical Applications, Procedia Computer Science, pp. 1058-106,1(4), 2011.

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

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

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

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

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

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

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

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

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

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

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

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15. Odland HH, Brun H, Sejersted Y, Dalen M, Edvardsen T, Saugstad OD, Thaulow E: Longitudinal Myocardial Contribution to Peak Systolic Flow and Stroke Volume in the Neonatal Piglet Heart Pediatric Research Pediatr Res. pp. 345-570, (4), 2011.

16. Remme EW, Opdahl A, Smiseth OA. Mechanics of left ventricular relaxation, early diastolic lengthening and suction investigated in a mathematical model. American Journal of Physiology, 300:H1678-87, 2011.

17. Røsjø H, Andreassen J, Edvardsen T, Omland T: Prognostic Usefulness of Circulating High Sensitivity Troponin T in Aortic Stenosis and Relation to Echocardiographic Indices of Cardiac Function and Anatomy. Am J Cardiol pp. 88-91, 108(1), 2011.

18. Sarvari SI, Haugaa KH, Anfinsen OG, Smiseth OA, Amlie JP, Edvardsen T: Right Ventricular Mechanical Dispersion Predicts Malignant Arrhythmias in Patients With Arrhythmogenic Right Ventricular Cardiomyopathy. Eur Heart J, pp. 1089-1096, 32(9), 2011.

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20. Smedsrud MK, Pettersen E, Gjesdal O, Svennevig JL, Andersen K, Ihlen H, Edvardsen T: Detection of Left Ventricular Dysfunction by Global Longitudinal Systolic Strain in Patients with Chronic Aortic Regurgitation J Am Soc Echocardiogr, pp. 1253-9, 24(11), 2011.

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25. Tveito A, Lines GT, Skavhaug O, and Maleckar MM: Unstable eigenmodes as possible drivers for cardiac arrhythmias, Journal of the Royal Society Interface, pp. 1212-6, 8(61): 2011.

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Books/ Chapters in Books

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

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

Dissemination of results to users: Presentations and abstracts

1. Boe E, Russell K, Remme EW, Gjesdal O, Smiseth OA, Skulstad H. Poster: Detrimental effect of biventricular and left ventricular pacing in acute heart failure with narrow QRS and mechanical dyssynchrony. ESC Congress Paris, August 27-31st, 2011

2. Broch K, Eek C, Wergeland R, Ueland T, Skårdal R, Aukrust P, Skulstad H, Gullestad L: N-terminal pro-B-type natriuretic peptide is a marker of reversible myocardial dysfunction after non-ST-elevation acute coronary syndrom. Heart failure 2011. P1314.

3. Cannataro M, dos Santos RW and Sundnes J. Biomedical and Bioinformatics Challenges to Computer Science: Bioinformatics, Modeling of Biomedical Systems and Clinical Applications, Workshop at International Conference on Computational Science, June 2011.

4. Dahlslett T, Grenne B, Eek C, Sjøli B, Skulstad H, Smiseth OA, Edvardsen T, Brunvand H: Early Strain Echocardiography May Exclude Significant Coronary Artery Stenosis in Suspected Non-ST-Elevation Acute Coronary Syndrome. Circulation, Nov 2011; 124: A11678.

5. Edvardsen, T. Mechanical consequences of ion channel dysfunction. AHA Scientific sessions 11. Orlando, US. November 15th, 2011.

6. Edvardsen T. How to predict malignant arrhythmias by strain echocardiography. XV1th World Congress of Cardiology & Echo: Sept 30th-Oct 2nd, 2011, Delhi NCR. India.

7. Edvardsen T. Are All Measurements Created Equal? How Do We Compare Various Methods and Platforms? 22nd Annual meeting. American Society of Echocardiography. June 11-14th 2011, Montreal, Canada.

8. Edvardsen T. Informative use of echocardiography in patients with non-ST-elevation myocardial infarction. Pre session meeting, ACC 60th Annual Scientific sessions. April 2011, Chicago, US.

9. Edvardsen, T. The future for echocardiography. The 25th national meeting in echocardiography. Oct 2011. Org: Norwegian Society of Cardiology.

10. Edvardsen, T. Research at Dept of Cardiology, OUS, Rikshospitalet. Nov 22nd, 2011. Norwegian PhD conference in Medical Imaging.

11. Goebel B, Haugaa KH, Meyer K, Lauten A, Jung C, Otto S, Figulla HR, Edvardsen T, Poerner TC: Remodelling of left ventricular mechanic in dilated cardiomyopathy: a two-dimensional speckle tracking echocardiography study. European Heart Journal (2011) 32 (Abstract Supplement), 779.

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13. Haugaa KH, Goebel B, Dahlslett T, Meyer K, Jung C, Lauten A, Figulla HR, Poerner T, Edvardsen T. Risk of ventricular arrhythmias in patients with idiopathic dilated cardiomyopathy can be identified by left ventricular global strain. European Heart Journal (2011) 32 (Abstract Supplement), 11-12.

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27. Russell K, Work shop in arrhythmia. Electrical Dyssynchrony and Regional Myocardial Work, Oslo University Hospital, Ullevål June 9th, 2011.

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PUBLICATIONS 2011

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41. Aaberge L. Kardiogent sjokk og mekaniske komplikasjoner etter hjerteinfarkt, 11.10.2011

42. Aaberge L. Kirurgisk behandling ved hjertesvikt? 12.10. 2011

43. Aaberge L. Akutt koronarsyndrom - klinikk og akuttbehandling. CardioVascular Update 14.10.11

44. Aaberge, L., Helsedirektoratet 04.06.2011: Hvilke endringer kan vi forvente oss innen kardiologien de neste 10 år.

Dissemination of results to the general public: Popular science publications

1. Maleckar M. "The heart of the matter: Simula and the Center for Cardiological Innovation." Presented at a general meeting with representatives from the Norwegian Ministry of Trade and Industry, 14.04.2011.

2. Sundnes J. "Kan vi regne ut hvordan hjertet virker? Og hva kan vi i så fall bruke det til?". Presented at Idéfestivalen 2011, University of Oslo, September 17th, 2011.

Media

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2. "Nytt senter for kardiologisk innovasjon". Dagens Medisin, 31.10. 2011.

3. "Forsker med godt hjerte". South-Eastern Norway Regional Health Authority, 28.04. 2011.

4. "Puls, Jakten på hjertets hemmelighet", Norwegian state television (NRK) Aug 2011.

5. "Nytt senter for forskningsdrevet innovasjon". Oslo University Hospital 02.11. 2011.

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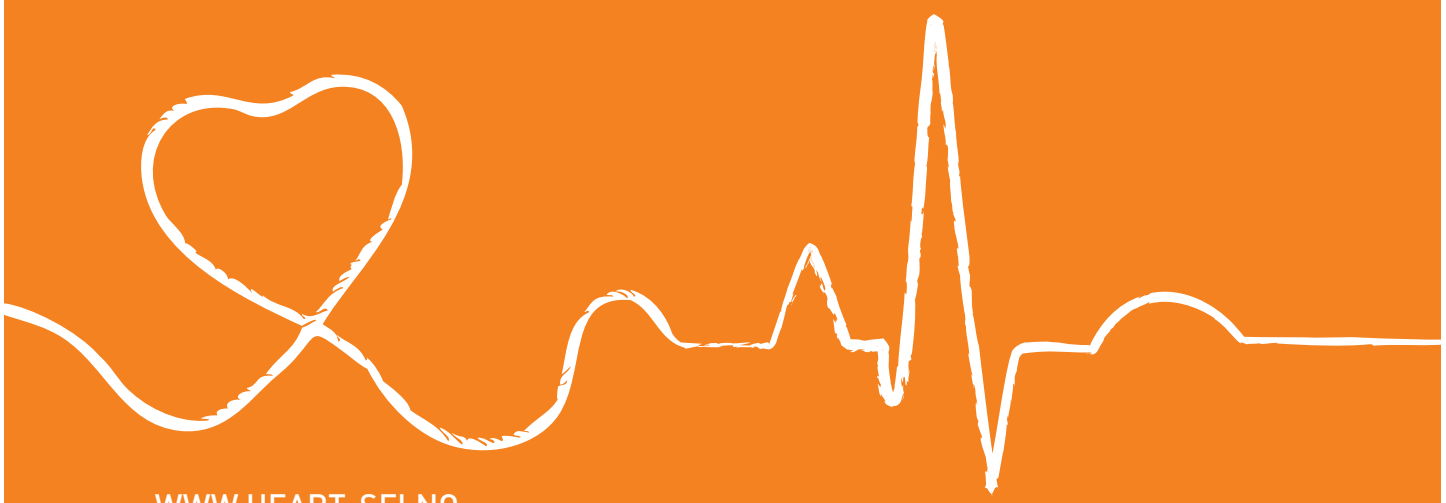

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