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SUMMARY

2017 has been a good year for the center. Several of its members have brought home prestigious prizes for their research. Center partners ensure that the research and innovation reach the patients and the bedside.

In August, CCI invited to a symposium in celebration of the release of a new ultrasound scanner. National media was invited and among those who wrote about this innovation was Dagbladet. The scanner is a result of a cooperation between researchers at Oslo University Hospital and GE Vingmed Ultrasound. It was launched globally at the American Society of Echocardiography (ASE) in June in Baltimore, where Professor Otto Smiseth presented the novel method to measure heart function which was invented at the CCI and is an important feature of the new scanner. Until now, heart function has been measured as percent contraction, while the new method also measures how much work is done in the different parts of the heart. Using the new method, we hope to be able to detect early heart disease so that treatment can start before the disease has progressed too far.

During the EuroEcho-Imaging Congress in Lisbon, Portugal, PhD fellows from CCI won both Young Investigator Awards. “Negative crosstalk between the septum and left ventricular lateral wall in left bundle branch block: the lateral wall paradox“ was selected for presentation in the Young Investigators Award – Basic Science session, where John Aalen, MD, PhD fellow, was named the winner. Prof. J. Roelandt’s Young Investigator Award is awarded to the best original work in clinical science. This year’s award was given to CCI PhD fellow Øyvind H. Lie, MD, in recognition of the work “Harmful effects of exercise intensity and exercise duration in patients with arrhythmogenic cardiomyopathy”.

Center PhD fellows Jørg Saberniak MD, Gabriel Balaban M.Sc, Siri Kallhovd M.Sc, Nuno Almeida M.Sc, Fred Johan Pettersen M.Sc, Anne Günther MD, Adriana Darudibrotolo M.Sc and Pedro Santos M.Sc successfully defended their PhD thesis in 2017. Center Director Thor Edvardsen will take over as President of the European Association of Cardiovascular Imaging (EACVI) during 2018 after being voted in as President Eletct in 2016.

Center for Heart Failure Research organizes their annual symposium in September at the height of Oslo, Holmenkollen.

Each year CCI members present the latest results from their research. During this year’s symposium Øyvind H.Lie won the prize in the session “Diagnostic and therapeutical strategies for cardiac disease” and John Aalen won the prize in the session “Cardiac function during heart failure and exercise training”.

Also in September, Center member Ida Skrine Leren, MD, PhD was awarded with H.M. the King’s gold medal for best medical PhD during 2016. The medal is awarded to an outstanding young researcher for a scientific work assessed at the University of Oslo. The work must be recognized as an effective contribution to the field of research’s literature. Center PhD fellow Øyvind Senstad Andersen, MD won the prestigious prize given by Oslo University Hospital for outstanding research for his article “Estimating Left Ventricular Filling Pressure by Echocardiography” published in the renowned Journal of The American College of Cardiology. PhD fellow John Aalen, MD, was awarded bronze winner in the moderated poster session at the Cardiology Update Conference in Davos, Switzerland for his presentation of the study “Left Ventricular Dysynchrony in Left Bundle Branch Block is Markedly Load- and Contractility Dependent”.

Kalkulo announced its withdrawal from the CCI in June. Kalkulo has over the last years focused entirely on the energy sector, and the activity in the CCI has become less relevant for their core business. The activity that was originally performed by Kalkulo in the CCI (development of a pacertool for cardiac resynchronization research and therapy) has been taken over by Simula and its subsidiary Radyre. This activity has received additional funding and continues as a separate project under the CCI.

The year reached its end with close to 80 published scientific articles in peer-reviewed journals, contributed to by center members. The research resulted in over 100 presentations, including abstracts, at various national and international conferences within cardiology and biomedicine.

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) is the cause of over 7 million deaths per year worldwide. The limitations of current tools to predict SCD have become evident. The CCI has proposed and validated a new tool, mechanical dispersion, which has gained international attention. During the last few years, other centers have adapted the technique and published studies showing the value of mechanical dispersion and strain echocardiography in predicting malignant arrhythmias and cardiac 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. Cardiac Resynchronization Therapy (CRT) can be an effective treatment for patients suffering from heart failure, but to find responders to CRT remains a challenge. 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 is in the front of knowledge development and innovation in these challenging clinical areas. Industrial partners Medtronic and GEVU 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 mathematically analyzing 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 are developing new decision support tools to provide insight into both electrical and mechanical factors of cardiovascular disease and couple this with 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. Innovations in this space have the potential to change the paradigm of diagnostic cardiology and will represent a substantial market edge for the industrial partners.
The CCI is hosted by Department of Cardiology, Oslo University Hospital, Rikshospitalet. The consortium consists 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 partners are GE Vingmed Ultrasound AS, CardioSolv Inc and Medtronic Bakken Research Center B.V. Kalkulo AS withdrew from the consortium in June 2017.

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

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
- Are Magnus Brusset, Kalkulo until June 2017 and Simula Research Laboratory from June 2017
- Theis Tønnessen, Oslo University Hospital
- Brock Tice, CardioSolv
- Drude Merete Fugelseth, University of Oslo
- Lars Ove Gammelstrøm, Medtronic
- Mary Maleckar, Simula Research Laboratory until June 2017

Each partner represents a 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.

**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.

**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.

**Medtronic**

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.

**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.
DISSECTIONS

Jørg Saberniak; Arrhythmogenic right ventricular cardiomyopathy (ARVC) - Impact of exercise on cardiac outcome, differential diagnoses and risk stratification of arrhythmic events, October 20th 2017

Doctor and researcher Jørg Saberniak has in his PhD thesis focused on investigating arrhythmogenic right ventricular cardiomyopathy (ARVC) and right ventricular outflow tract ventricular tachycardia (RVOT-VT), together with his fellow researchers with main results:
1. Too much exercise may accelerate and aggravate cardiac dysfunction in patients and mutation-positive family members with ARVC.
2. Electric parameters, echocardiography and cardiac MR are useful tools to improve the diagnosis of early ARVC, distinguishing ARVC from the benign condition RVOT-VT.
3. Identification of early ARVC patients with severe arrhythmias can be improved by combining electrical and echocardiographic parameters.

Dr. Saberniak won the Oslo University Hospital prize for an outstanding research article in 2014 for the publication of his first study which was also featured on unikard.org. Dr. Saberniak has also been interviewed by Unikard in regards ARVC and RVOT-VT and the research around these diseases. He won two prizes for high quality poster presentations at EuroEcho-Imaging congress in Istanbul in 2013 and in Wien in 2014. Furthermore he had oral presentations at the Heart Rhythm congress in Denver, USA in 2013, at the ACC congress in Washington, USA in 2014 and at the EuroEcho-Imaging congress in Sevilla, Spain in 2015.

Papers:
Vigorous physical activity impairs myocardial function in patients with arrhythmogenic right ventricular cardiomyopathy and in mutation positive family members, Eur J Heart Fail 2014 Dec; 16(12):1337-44
Comparison of patients with early phase arrhythmogenic right ventricular cardiomyopathy and right ventricular outflow tract ventricular tachycardia, Eur Heart J Cardiovasc Imaging. 2017 Jan;18(1):62-69
Combination of ECG and Echocardiography for Identification of Arrhythmic Events in Early ARVC, JACC Cardiovasc Imaging. 2017 May;10(5):503-513

Fred-Johan Pettersen; Bioimpedance as a tool in cardiac resynchronisation therapy, December 11th 2017

Of the patients who receive Cardiac Resynchronisation Therapy (CRT) today, about 30% are non-responders. Among the reasons for the high number of non-responders are the underlying heart failure severity, suboptimal device programming, inadequate viable myocardium, lack of baseline dysynchrony, and LV lead position. Positioning of the LV lead is not based on individual patient data, but on data from retrospective studies. This means that there is a potential for improving positioning of the LV lead if it is possible to assess quality of placement acutely when the leads are implanted. Among the candidates for assessing quality of LV contraction is electrical bioimpedance measurements. Electrical bioimpedance (EB) is a measure of how different tissues are impeding an electric current in a volume conductor — in this case the heart and thorax region. The measured impedance is a function of the electrical properties of tissues and blood as well as a function of the geometry of tissues and electrode placements. This work has been aimed at enabling EB research in cardiology on human subjects, and in particular by using the CRT lead electrodes after the leads are placed, but before the CRT device is connected to the leads. Work has been done to develop and build necessary equipment, and to understand the influences on measured impedance. Furthermore, a number of measurements have been done to gain experience of what we can expect. We have also presented a method of capture detection for CRT devices based on morphology changes in EB signals.

Papers:
Comparison of four different FIM configurations—a simulation study, Pettersen FJ, Ferdous H, Kalvøy H, Martinss ØG, Høgetveit JO, Physiological Measurement. 35 (6) (2014) 1067-1082
Optically isolated current source, Pettersen FJ, Høgetveit JO, Journal of Electrical Bioimpedance. 6 (2015) 18-21
Bioimpedance measurements of temporal changes in beating heart, Pettersen FJ, Martinss ØG, Høgetveit JO, Kalvøy H, Odland HH, Biomedical Physics & Engineering Express. 2 (2016) 065015
Use of bioimpedance measurements to verify capture with biventricular pacing, Pettersen FJ, Martinss ØG, Gammelsrød LO, Kangsgård E, Odland HH. Submitted to Europeace in August 2017.

Adriyana Danudibroto; Data Fusion for Enhanced Visualization of Echocardiography, June 8th 2017

The development of 3D echocardiography has brought added value in clinical examinations due to the ability to show the complex spatial relationship between structures. Despite the advantages, the modality is still confronted with limitation: the dependency of the appearance of structures on the insonification angle, the spatially limited acquisition window, the reciprocity between the field of view (FOV), the resolution, and the possibility of artifacts from signal dropouts.

In this thesis work, a solution was proposed to alleviate some of these limitations through image post processing. The aim was to enhance the visualization of echo images and the field of view so that the workflow in the examination can be improved. The proposed solution to achieve the aforementioned aim was data compounding which is a method that combines images from several 3D echocardiograms to form one enhanced FOV image. The data compounding solution consisted of registration and fusion wherein the images were brought to alignment through registration and the overlapping voxels were effectively combined through the rules of fusion. The study looked at the existing state-of-the-art methods for 3D echo registration defined for fusion. From the study it was noted that the registration for echo images requires alignment in both spatial and temporal dimension. Building upon the existing methods, both spatial and temporal registration methods were developed.

Papers:
3D Farnebäck optic flow for extended field of view of echocardiography (Proc. FIMH, 2015 June 25)
Image-based temporal alignment of echocardiographic sequences (Proc. SPIE, 2016 Feb 27)
Spatial-temporal registration of multiple three-dimensional echocardiographic recordings for enhanced field of view imaging (SPIE JMI, 2016 July 1)
Anatomical view stabilization of multiple 3D transesophageal echocardiograms (Proc. IEEE IUS, 2016 September 18)

Nuno Almeida; Automated echocardiographic assessment of the left atrium, July 10th, 2017

This thesis presents a thorough review and new contributions to the state-of-the-art of echocardiographic assessment of the left atrium. The problem is approached from both the clinical and technical perspectives, to identify and overcome some of the limitations associated with the current tools and measurement practices. A systematic comparison between two-dimensional and three-dimensional echocardiography (2D, 3D) shows the superiority of the latter in accuracy, reproducibility, and prognostic ability. However, 2D is most commonly used in clinical practice, in part due to the lack of validation and good tools for 3D analysis. We present algorithms (using B-splines, Subdivision Surfaces, and Kalman Filter methods) that allow a completely automatic delineation of the left atrial endocardial surface in 3D recordings over the complete cardiac cycle. An automatic tool is proposed and validated with clinical data, demonstrating its ability to measure LA volumetric indices (e.g. volume, emptying fraction) and functional indices (e.g. global longitudinal strain and global circumferential strain), at all LA phases: reservoir, conduit, and contractile. The potential added value of the proposed methods is also demonstrated in clinical studies where we report LA size and its determinants in a general population, as well as changes in LA size and function after acute myocardial infarction.

Papers:
**DISSERTATIONS**

**Pedro Santos;** New beamforming methodologies for fast transoesophageal volumetric cardiac imaging using ultrasound, July 4th 2017

As cardiovascular diseases remain the leading cause of death worldwide, the scientific community strives to develop advanced diagnostic tools to detect early cardiac dysfunction. Echocardiography has established itself as a major tool in this quest. Novel treatments have also emerged, offering new hope in combating these pathologies. With them, came the need for new monitoring tools and there again, ultrasound - and especially, transoesophageal echocardiography - appears as an appealing choice. There is, therefore, a clear urge for new echocardiographic methodologies that combine additional clinical value with a reduction of the examination burden, for both the clinician and the patient.

Notably, recent technological breakthroughs have improved echocardiography in the last decade. However, the use of 3D ultrasound imaging in the clinical environment remains very limited, mainly due to the insufficient spatio-temporal resolution. Therefore, the full understanding of the cardiac condition requires the clinician to acquire multiple 2D views, which can be obtained at much higher frame rates. However, this significantly prolongs the examination time and increases the complexity of the acquisition and analysis. Creating a tool for the detailed analysis of the heart directly in 3D would therefore improve the prognostic and diagnostic value of medical ultrasound and, ultimately, contribute to a better clinical outcome for patients.

Papers:

**Gabriel Balaban;** Adjoint Data Assimilation Methods for Cardiac Mechanics January 10th 2017

Medical images provide detailed information which doctors can use to diagnose heart disease and plan treatment. Conditions such as myocardial infarctions and dysynchrony can be recognized by their distinct motion patterns in images. The progression of these diseases however, is influenced by elastastic forces and the ability of the muscles to contract. This cannot be viewed in images by themselves, but can instead be determined with the help of a mathematical model which is personalized to a patient.

In this thesis I, together with my fellow researchers, have developed methods for the creation of personalized models of heart motion using data from medical images. The result is a computer model of a patient’s heart which moves the same way as in the images. The personalized model can then be used to provide elastic force and contraction information. Such models have been constructed before, but with the methods developed in this thesis, much greater resolution and accuracy is possible.

Papers:

**Siri Kallhovd;** Computational tools for clinically driven models of cardiac electro-mechanics, June 8th 2017

Cardiac mathematical modeling is becoming an important facet of modern cardiological research. Encompassing both electrophysiology and mechanics, this topic spans phenomena from the molecular scale to the level of the whole heart. Challenges include determining the validity of models and capturing the inherent physiological variability of the problem. This thesis explores such topics in both healthy and diseased hearts, through investigation of the sensitivity of computational results to model parameters.

For cardiac mechanics, this work investigates the problem that when using cardiac imaging, the geometry of the heart can be determined during the cardiac cycle. However, to determine the mechanical state, a stress free reference geometry is needed, which is unavailable from imaging due to intrinsic in vivo loadings. We explored how key assumptions may alter the mechanical calculations in this framework, and test general sensitivity of unknowns.

Meanwhile, in electrophysiology, we investigated Arrhythmogenic Right Ventricle Cardiomyopathy (ARVC), a disease that affects the connections between myocytes, and eventually causes myocyte cell death so that fibrotic and fatty tissue infiltrates or replaces functional myocardium. This thesis includes an exploratory study of the influence of several factors related to fatty tissue infiltration that cannot easily be determined from clinical measurements, such as the role of placement of diseased tissue, and fraction of fatty infiltration, with the ultimate goal of arrhythmia risk evaluation.

The last topic involved applying PDE-constrained gradient-based optimisation with the adjoint method to investigate its applicability to estimating timings and dynamics of the initial electrical activation of cardiac tissue. We consider several sources of model observations, and test the system with severe degrees of noise.

Papers:
- **Localization and not Extent of Fibrofatty Infiltration is the Primary Factor Determining Conduction Disturbance in a Computational Model of Arrhythmogenic Cardiomyopathy.** Kallhovd S, Gjerald SU, Wall ST, Saberniak J, Haugaa KH, Maleckar MM, the 5th IEEE International conference on E-Health and Bioengineering, EHB 2015, pages 1-6
- **Inverse estimation of cardiac activation times via gradient-based optimization.** Kallhovd S, Maleckar MM, Rognes ME Int J Numer Method Biomed Eng 2018 Feb;34(2)
- **Sensitivity of stress calculation to passive material parameters in cardiac mechanical models.** Kallhovd S, Sundnes J, Wall ST Submitted for publication to CMBBE
RISK ASSESSMENT FOR SUDDEN CARDIAC DEATH (SCD) AND MYOCARDIAL FUNCTION

Sudden cardiac death (SCD) is still a challenge in cardiology. Cardiac genetic diseases predispose to SCD in young individuals. Ongoing research in the CCI is focusing on predicting life threatening ventricular arrhythmias, the role of exercise and exploring cardiac function in patients at risk of SCD.

SELECTED PROJECTS:

Lower than expected burden of premature ventricular contractions impairs myocardial function

Lie OH, Saberniak J, Dejgaard LA, Stokke MK, Hegbom F, Anfinsen O-G, Edvardsen T, Haugaa KH

Frequent premature ventricular contractions (PVCs) can induce myocardial dysfunction. Patients with outflow tract arrhythmia (OTA) commonly have frequent PVCs without structural heart disease. In this study we aimed to explore the burden of PVCs associated with myocardial dysfunction in patients with OTA. We hypothesized that this threshold is lower than the previously suggested threshold of 24 000 PVCs/24 h (24%PVC) when systolic function is assessed by strain echocardiography. Furthermore, we aimed to characterize OTA patients with malignant arrhythmic events.

We included 52 patients referred for OTA ablation. Left ventricular global longitudinal strain (GLS) and mechanical dispersion were assessed by speckle tracking echocardiography. A subset underwent cardiac magnetic resonance imaging. PVC burden (%PVC) was assessed by Holter recordings and reported as the percentage of total heart beats. Sinus rhythm QRS durations and PVC QRS durations were recorded from 12-lead electrocardiogram, and the QRS ratio was calculated (PVC QRS duration / sinus rhythm QRS duration). %PVC correlated with GLS with mechanical dispersion, but not with ejection fraction. %PVC was higher in patients with impaired systolic function by GLS (worst than -18%) compared with patients with normal function. Greater than 8%PVC optimally identified patients with abnormal GLS. Serious arrhythmic events occurred in 21 (21%) patients. These were characterized by high QRS.

Figure: Outflow tract arrhythmia on the electrocardiogram. Twelve-lead electrocardiogram of patient X with outflow tract arrhythmia and history of sustained ventricular tachycardia and syncope. There is dominating left bundle branch block morphology, and inferior electrical axis of the premature ventricular contraction (PVC), and the QRS ratio, calculated by dividing the PVC QRS duration (AL) by the sinus rhythm QRS duration (AQ). This is suggestive of a right ventricular outflow tract free wall PVC origin. In Holter recording, this patient had 33% PVCs. From Lie OH, Saberniak J, Dejgaard LA, et al. Lower than expected burden of premature ventricular contractions impairs myocardial function. ESC Heart Fail 2017;4(4):585-94.

Vigorous exercise in patients with hypertrophic cardiomyopathy

Dejgaard LA, Håland TF, Lie BH, Ribe M, Rynne T, Leren IS, Benge KE, Edvardsen T, Haugaa KH

Cardiac adaptations to regular vigorous exercise include left ventricular hypertrophy, increased left ventricle volume and improved left ventricular diastolic function. Hypertrophic cardiomyopathy (HCM) is a cardiac genetic disease characterized by left ventricular hypertrophy, but contrary to athletes, HCM patients have smaller left ventricle volume and reduced diastolic function. How vigorous exercise impacts left ventricular morphology in HCM patients is unknown.

In 121 patients with HCM and 66 healthy HCM mutation carriers (HCM G+P), we explored the relationship between lifetime vigorous exercise and cardiac morphology and function and occurrence of ventricular arrhythmias (VA).

Lifetime vigorous exercise was correlated with larger left ventricle volume in both HCM and HCM G+P, but was only associated with increased left ventricular mass within physiologic limits. Vigorous exercise was associated with improved left ventricular diastolic function in HCM G+P and occurrence of VA was equal across tertiles of lifetime vigorous exercise compared to sedate HCM G+P (Figure). We did not find harmful cardiac effects of exercise in HCM or HCM G+P, and our results indicate beneficial effects of exercise, worth exploring further in larger studies. Current guidelines discouraging all competitive sports in HCM may be too restrictive.

Figure: 121 HCM patients divided according to lifetime vigorous exercise tertiles and sedate group. Range of lifetime vigorous exercise (hours) is parenthesis on X-axis. Red color in the bars indicate proportion of patients with ventricular arrhythmia. Occurrence of ventricular arrhythmias were similar across groups. Int J Cardiol 2018 Jun 1;250:157-163.
Preserved left ventricular (LV) ejection fraction (EF) and reduced myocardial strain are reported in patients with hypertrophic cardiomyopathy, ischemic heart disease, and more. We performed a combined mathematical and echocardiographic study to understand the inconsistencies between EF and strain.

An equation showing the relationship between EF and the 4 parameters global longitudinal strain (GLS), global circumferential strain (GCS), wall thickness and short-axis diameter was derived from an elliptical LV model. The equation was validated by echocardiography in 100 subjects, comparing model-predicted EF with measured EF. The effect of the different parameters on EF was explored and compared with patient findings.

Calculated EF had very good agreement with measured EF. The model showed that GCS contributes more than twice as much to EF than GLS. A significant reduction of GLS could be compensated by a small increase of GCS or wall thickness or reduced diameter. The model further demonstrated how EF can be maintained in ventricles with increased wall thickness or reduced diameter, despite reductions in both GLS and GCS. This was consistent with patient findings. Reduced strain despite preserved EF can be explained through geometric factors. Due to geometric confounders, strain better reflects systolic function in patients with preserved EF.

Lamin A/C cardiomyopathy: Young onset, high penetrance, and frequent need for heart transplantation

Hassellberg NE, Håland TF, Servén S, Haugea KH, Smedsrud MK, Sarvari SI, Haugaa KH, Edvardsen T, Remme EW

Lamin A/C mutation causes dilated cardiomyopathy associated with life-threatening ventricular arrhythmias and development of severe heart failure. Sudden cardiac death can occur at a young age, but risk factors for serious events have so far been poorly defined. Furthermore, the natural course of disease in family members diagnosed by genetic screening and testing has not previously been systematically studied. This study was conducted to give a better overview of the prevalence and penetrance of disease as well as risk factors of serious events in Lamin A/C genotype positive probands and family members. The prevalence of Lamin A/C gene mutations was 6.2% among those referred to genetic testing with positive probands and family members. Furthermore, the natural course of disease in family members diagnosed by genetic screening and testing has not previously been systematically studied.

The study was conducted to give a better overview of the prevalence and penetrance of disease as well as risk factors of serious events in Lamin A/C genotype positive probands and family members. The prevalence of Lamin A/C gene mutations was 6.2% among those referred to genetic testing with positive probands and family members.

In aortic stenosis, subtle alterations in myocardial mechanics can be detected by speckle-tracking echocardiography prior to reduction of left ventricular ejection fraction (LVEF). In this prospective study, 162 patients with severe aortic stenosis and preserved LVEF (60 ± 13%) were included. Surgical aortic valve replacement was performed in 120 patients, whereas 42 were deemed ineligible for surgery. During follow-up (37 ± 13 months), thirty-seven patients died. Mechanical dispersion was pronounced (64 ± 20 msec) in the total patient population. Pronounced mechanical dispersion at baseline was a predictor of mortality in patients with severe aortic stenosis independently of LVEF, flow status, or treatment (AVR vs medical treatment), providing incremental prognostic information in addition to LVEF, GLS, and correlates of flow and gradient.

Figure: Speckle-tracking echocardiography showing longitudinal strain curves in the four-chamber view from patients with aortic stenosis demonstrating a more homogeneous contraction pattern (lower mechanical dispersion) in a survivor than in a nonsurvivor (pronounced mechanical dispersion).


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From: Klaeboe et al. A Pilot Study of the Usefulness of Strain Echocardiography

Klaeboe K, Niland TF, Leren TF, Brekke PH, Brekke PM, Rygje H, Omland T, Gullestad L, Aakhus S, Haugaa KH, Edvardsen T

Title: Prognostic Value of Left Ventricular Deformation Parameters in Patients with Severe Aortic Stenosis: A Pilot Study of the Usefulness of Strain Echocardiography

Klaeboe K, Niland TF, Leren TF, Brekke PH, Brekke PM, Rygje H, Omland T, Gullestad L, Aakhus S, Haugaa KH, Edvardsen T

In aortic stenosis, subtle alterations in myocardial mechanics can be detected by speckle-tracking echocardiography prior to reduction of left ventricular ejection fraction (LVEF). In this prospective study, 162 patients with severe aortic stenosis and preserved LVEF (60 ± 13%) were included. Surgical aortic valve replacement was performed in 120 patients, whereas 42 were deemed ineligible for surgery. During follow-up (37 ± 13 months), thirty-seven patients died. Mechanical dispersion was pronounced (64 ± 20 msec) in the total patient population.

Pronounced mechanical dispersion at baseline was a predictor of mortality in patients with severe aortic stenosis independently of LVEF, flow status, or treatment (AVR vs medical treatment), providing incremental prognostic information in addition to LVEF, GLS, and correlates of flow and gradient.

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Integrated mechanisms of mechano-electric feedback in ischemic arrhythmogenesis

Mechanical heterogeneity during ischemia is thought to contribute to arrhythmogenic alterations in cardiac electrophysiology. Several forms of mechano-electric feedback (MEF) have been proposed to underlie these changes, and two major mechanisms are: (1) myofilament-dependent calcium surges, and (2) opening of stretch-activated channels (SAC). In this study, we tested the individual and combined contribution of these mechanisms to generating calcium waves and arrhythmogenic substrate in the ischemic border zone. In particular, we investigated how changes in calcium dynamics depend upon regional alterations in mechanics similar to those observed during an acute ischemic challenge.

To assess the potential role of MEF in arrhythmias we began by constructing a coupled model of ventricular myocyte electrophysiology and sarcoplasmic reticulum contraction dynamics. We connected fifty of these coupled sarcomeric models in series, thus creating a 1D myocyte in which contracile mechanics and electrophysiology are bidirectionally coupled in time (via calcium), and in space via calcium diffusion, strain, and stress. Multiple myocytes were coupled via gap junctions to create a 1D tissue strand. These models capture the effects of mechanical feedback at the sarcoplasmic level, and the combined effects of mechanical and calcium heterogeneities at the multi-cellular level. When perturbed by pathologically realistic variations in stretch, we observe that both SAC and myofilament-dependent alterations in calcium sensitivity contribute to changes in action potential (AP) morphology. Additionally, in this 1D tissue strand we noticed that MEF is capable of modulating the velocity of calcium waves through accompanying regional crossbridge attachment dependent on internal stretch heterogeneity and calcium distribution.

Our study investigates the impact of heterogeneous regional stretch/strain on cellular and tissue electrophysiology via myofilament calcium release and SAC opening. The combined effects of these mechanisms may be sufficient to create arrhythmogenic spatial variation in action potential duration in (APD) during ischemia, particularly in the border region.

Patient-Specific biventricular simulation pipeline

Patient specific computational models of heart mechanics can be used to estimate clinically relevant biomarkers that are difficult or even impossible to measure in vivo. One example is myoelber stress, that is the average force per unit area in the direction normal to the cardiac muscle fibers, which is believed to be a dominant driver in remodeling processes related to heart failure. In this study we have developed an efficient framework for creating personalized biventricular simulations of heart mechanics, using data from MRI and non-invasive measurements of ventricular pressures. The sensitivity to different modeling choices, such as the choice of fiber architecture, is assessed and system performance is evaluated. A typical simulation can be performed on a regular laptop within less than 2 hours, yielding an excellent fit between model and data. Therefore, this framework has the potential to be integrated as a part of a clinical diagnostic toolbox, and could potentially provide a way to assess important physiological biomarkers.

Predicting Thrombosis Formation in the Left Atrial Appendage Using Computational Fluid Dynamics

Patients with atrial fibrillation (AF) have a six-fold increased risk of cerebral stroke caused by thrombus formation, therefore patients classified with a high risk are prescribed anticoagulants. However, the risk classification is only informed by retrospective population-statistics and causes an under- and over-medication. We hypothesize that the underlying mechanisms ultimately are shear rate driven and can be rivalled by patient-specific image-based computational fluid mechanics (CFD). To investigate thrombus formation we have extended our previously well-validated open-source finite element CFD solver, Oasis, with additional functionality such that we can solve for deforming domains. We are now in the process of re-validating our solver for the purpose of left heart blood flow modeling. Current efforts include validating against high-resolution in-vitro data. In future efforts, we will use dynamic 4D CT images to extract the motion of the left atrium and left atrial appendage and use that as an input for our CFD simulations. We can then investigate how contraction and morphology of the pulmonary veins, left atrium, and appendage affects the thrombus formation in the left atrial appendage, and ultimately improve the stroke risk stratification for AF patients and reduce the under- and over-medication.

Increased Heart Rate Aggravates Diastolic Dysfunction in Left Bundle Branch Block

In Left Bundle Branch Block (LBBB), LV diastolic dysfunction causes a slowing of LV pressure decay, potentially causing a stiffening of the left ventricle (LV). In an animal experiment we demonstrated how this effect is aggravated with increased heart rate (HR) when diastole is shortened.

We increased HR by atrial pacing, and demonstrated how this resulted in increased LV stiffness, and elevated LV pressures during diastole in LBBB when compared to baseline (Fig). This mechanism might cause dyspnea during exercise in patients with LBBB.
Increased diffuse fibrosis in septum compared to the left ventricular lateral wall in heart failure patients with left bundle branch block

Larsen CK, Aalen J, Kongsgård E, Fjeld JG, Smiseth OA, Hopp E

Left bundle branch block (LBBB) causes the left ventricle (LV) to contract dys synchronously, with an early inefficient septal contraction and a more powerful contraction of the LV lateral wall later in systole. This dys synchronous contraction pattern is reflected in a heterogenic distribution of myocardial workload. We aimed to investigate if heart failure patients with LBBB display regional differences in diffuse fibrosis, and if such a difference could be reflected in heterogeneity in regional myocardial work. Extracellular volume fraction (ECV), assessed by T1 mapping cardiac magnetic resonance (CMR), was used as an estimate of diffuse fibrosis.

Myocardial work was calculated from strain by feature tracking (FT) CMR and a non-invasive estimate of the LV pressure curve. We concluded that septum had a higher level of diffuse fibrosis than the LV lateral wall in non-ischemic patients with reduced systolic function and LBBB. Interindividual ECV in septum and the lateral wall correlated strongly, but neither septal nor lateral wall ECV correlated to age, heart rate, blood pressure, QRS-width, ventricular volumes, ejection fraction, septal or lateral wall work. These results must be considered with caution given the low number of patients. We plan larger scale studies to explore these issues.

Systemic right ventricular function


In patients with transposition of the great arteries (TGA) and atrial switch, the right ventricle (RV) becomes the systemic ventricle. These patients have increased risk of heart failure. We have previously demonstrated reduced septal function by regional strain and work analyses. Our purpose was to determine whether reduced septal function in TGA-patients is reflected in reduced metabolism.

This clinical study utilizes a non-invasive method by echocardiography to assess regional work in adults with a systemic RV. This method demonstrates that interventricular septal function is reduced and was recently confirmed by PET imaging, revealing reduced metabolism. The change in septal function and metabolism may be early markers of decompensation of the systemic ventricle.

Patients with left bundle branch block are hypersensitive to afterload: Moderate elevation of systolic pressure caused marked depression of left ventricular function.


In epidemiological studies left bundle branch block (LBBB) in otherwise healthy individuals carries a good prognosis, whereas LBBB in patients with arterial hypertension is associated with increased morbidity and mortality.

We hypothesized that elevated blood pressure has a direct depressive effect on left ventricular (LV) function in individuals with LBBB.

To test the hypothesis, we compared 11 otherwise healthy LBBB-patients with 11 age-matched controls with similar LV ejection fraction (EF). Arterial pressure was increased by simultaneous cuff inflation and handgrip exercise.

We concluded that moderate elevation of afterload in patients with LBBB caused marked depression of LV systolic function in terms of LV EF and global longitudinal strain. This was attributed to aggravation of septal function.
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, mechanical 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. Cardiac resynchronization therapy (CRT) is an effective treatment in severe heart failure patients, and leads to decreased mortality, less hospitalizations and relief of symptoms. But not all CRT patients benefit from therapy. Different novel echocardiographic indices by tissue Doppler imaging (TDI) and speckle tracking strain have been proposed to improve selection, but have failed to increase responder rates in randomized trials. Therefore, wide QRS duration, impaired LV function and symptoms of heart failure remain the only guideline criteria for selection of patients for CRT. Following these criteria, however, approximately 30% of implanted patients will not respond to therapy. OUH has partnered with Medtronic to address several aspects of device treatment in Heart Failure. By maximizing the benefit of CRT across the continuum of care, we believe even more patients will respond to this therapy.

**SELECTED PROJECTS:**

**CCI IMPACT I STUDY**

The patient enrollment was completed in 2015. In the ongoing study CCI IMPACT, 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 enters the operation room.

The CCI IMPACT study was designed to give insight to the CRT implant procedure. We hope the results will help us 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. Center PhD fellow Stan Ross, MD, is coordinating the analysis efforts in the study. Medtronic has utilized staff from both Bakken Research Center in Maastricht NL and the HQ Research Center in Minneapolis, MN US to support the research tasks in this study. On local level, Lars Ove Gammelsrud has been the Medtronic representative in Work Package 4 and provided the day-to-day support needed. In parallel to the clinical study, Medtronic and OUH have also partnered in projects addressing other aspect of the implant procedure.

The first publication from CCI IMPACT was accepted in June 2017. “Cardiac resynchronization therapy when no lateral leads 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. From this project, Fred-Johan Pettersen defended his PhD thesis “Bioimpedance as a tool in cardiac resynchronization therapy” in December 2017.

CCI IMPACT II STUDY

CRT has been one of the most important advancements in the past decade for patients with systolic heart failure (HF) and a wide QRS. An analysis of various definitions of response showed response rates ranging from 32% to 91%. Multiple reasons for such a substantial non-responder rate have been proposed, such as underlying HF severity and etiology, suboptimal device programming, inadequate viable myocardium, lack of baseline dysynchrony, and LV lead position. Therefore, efforts to increase the responder rate is to pace from multiple LV sites, achieved either by the introduction of a second LV lead or by pacing on two electrodes on one lead. The use of one-lead with multiple electrodes stimulated (i.e. Multipo) to improve CRT response has recently been investigated in more detail in CRT patients. The overall outcome of these studies is difficult to interpret scientifically. Some studies have failed to prove additional benefit while others show acute benefit but are difficult to interpret because of their used methodology, like using non-optimal AV-delays. Other studies show only marginal but significant hemodynamic response benefit of multipoint pacing over standard biventricular (BiV) pacing. Recently, both mid- (3 months)- and long-term (12 months) single center data indicated positive results of multipoint pacing over conventional CRT as evidenced by greater LV reverse remodeling and function. In contrast, the down-side of multipoint pacing is the higher energy consumption. The 2xImpact study will within each patient simultaneously assess and compare different lead configurations, use multiple repetitions to reduce inherent measurement variability and may assess different AV-delay on cardiac dynamics. Patient enrollment is expected to be completed within Q1 2018.

**PACERTOOL**

Pacertool is a spin off study from WP 4. Financial support has been granted for this project in 2017 (NRC Bioteik 2021). The software is a part of a system that 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. With different electrode positions, data 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.

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. From this project, Fred-Johan Pettersen defended his PhD thesis “Bioimpedance as a tool in cardiac resynchronization therapy” in December 2017.
INNOVATION

A part of the research at CCI has been focused on a highly promising concept called myocardial work, for measuring work done by the heart non-invasively. The method has been implemented in GE’s ultrasound scanner and was launched at ASE in Baltimore in 2017.

In the past, invasive measurement of pressure in the left ventricle has been required, but the newly developed method does this by means of ultrasound in combination with normal blood pressure measurement.

Research findings have been published showing that myocardial work has utility in diagnosing infarction and in the treatment of patients with disturbances in the heart’s electrical management system. This innovation has been patented through Inven2.

Accurate assessment of the mitral valve is important before treatment of patients with a diseased valve.

Due to the complex anatomy and physiology of the mitral valve, 3D visualization and quantification are becoming increasingly important.

Use of 3D imaging before, during and after mitral valve repair, is mandatory for certain procedures.

In 2017, GE launched a new automatic mitral valve quantization tool that was developed and evaluated as part of the CCI.

Right ventricular quantification has become increasingly important, especially in patients with pulmonary hypertension or left ventricular dysfunction, where the functional and anatomical performance in this chamber is the key.

In current clinical practice, manual measurements in magnetic resonance imaging (MRI) are considered the gold standard for quantitative assessment of RV volumes and ejection fraction. However, MRI isn’t always available, and it is also time consuming to perform. Echo-based 4D quantum tool for right ventricle has existed for some time, and is available from multiple vendors.

These tools provide more objective and accurate measurements relative to those derived from 2D, where access to desired views can be more difficult. The 3D Right Ventricle Quantification tools are usually (semi-) automated to achieve quick access to the measurements of interest.

In 2017, GE launched a new automatic right ventricular quantification tool that was developed and evaluated as part of the CCI. Within CCI this has particular interest in studies of athlete’s hearts and of patients with arrhythmic cardiomyopathy.

SELECTED PROJECTS:

Ultrasound temperature monitoring of cardiac RF-ablation

Treatment of atrial fibrillation by radio-frequency ablation relies on adequate heating, and can thus benefit from perioperative temperature monitoring to increase its efficiency and safety. We have evaluated the feasibility of an ultrasound thermometry monitoring method using channel data from the ultrasound probe.

The feasibility was tested in an in-silico setup to determine expected changes to the ultrasound channel data. It was found that the delays would be too small to be detectable with an intra-cardial ultrasound probe, while a transesophageal probe might allow for detection of speed of sound changes in the relevant range.

Bi-ventricular segmentation

With the advancement of three-dimensional (3D) real-time echocardiography in recent years, automatic creation of patient specific geometric models is becoming feasible and important in clinical decision making.

However, the vast majority of echocardiographic segmentation methods presented in the literature focus on the left ventricle (LV) endocardial border, leaving segmentation of the right ventricle (RV) a largely unexplored problem, despite the increasing recognition of the RV’s role in cardiovascular disease.

We have developed a method for coupled segmentation of the endo- and epicardial borders of both the LV and RV in 3D ultrasound images.

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 injections (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 and published 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:
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.

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The third article illustrated the connection between the electrical and mechanical function of the heart utilizing sensitive image surveys developed at OUH. This finding has been important for the selection of drugs for these young patients and is the largest study of its kind. The fourth article illustrated the connection between the electrical and mechanical function of the heart utilizing sensitive image surveys developed at OUH. This finding has been important for the selection of drugs for these young patients and is the largest study of its kind. The fifth article illustrated the connection between the electrical and mechanical function of the heart utilizing sensitive image surveys developed at OUH. This finding has been important for the selection of drugs for these young patients and is the largest study of its kind. The sixth article illustrated the connection between the electrical and mechanical function of the heart utilizing sensitive image surveys developed at OUH. 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HIGHLIGHTS

INTERNATIONAL COOPERATION

CCI has close collaboration with several world-leading medical centers and Oslo University Hospital is a leading center in several international multi-center 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 Cardiovascular 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.

CCI has initiated several European multi-center studies, including the CRID study (for studying left bundle branch block patients and their treatment), which has partners in France, Belgium, Sweden and Norway.

During 2017 the Center received visiting researchers from Italy, Belgium, South-Korea and Japan. Isotta Castrini from the Brescia University Clinic, Italy is investigating heart function in women diagnosed with ARVC (AC) and the implications of pregnancy. Esther Scheirlynnck from the University Clinic in Brussels, Belgium has participated in the research on mitral valve disease together with center PhD fellow Lars Deiggaard. This winter Associate Professor Kasumi Masuda from Osaka, Japan, spent two months at the Institute for Surgical Research as a guest researcher. She participated in animal experiments and learned how to acquire and analyze sonomicrometry data. Furthermore, she has been working on a joint Oslo-Osaka project on diastolic function during left bundle branch block (LBBB). This project is headed by Professor Otto Smieeth in close cooperation with Professor Satoshi Nakatani and Dr. Marie Stugaard in Osaka. An abstract on this topic was submitted for the ESC 2018 congress. Nina Eide Hasselberg, who has previously completed her PhD at CCI, traveled to USA as a postdoctoral fellow visiting the University of Pittsburgh Medical Center to analyze data from the EchoCRT study using mechanical dispersion to see how this affects the risk of arrhythmic events.

GEVU has an extensive global network and actively engages in international research collaboration. Several of these projects are linked directly to CCI research on subjects such as functional ultrasound imaging for the assessment of heart failure and the risk of sudden cardiac death.

GEVU has intensified its work in 2017 to develop a solution for artificial intelligence in ultrasound, collaborating with some of the world’s leading environments; UCSF, Brigham and Women’s Hospital, Massachusetts General Hospital. Collaboration with several European environments has been launched. GEVU and Oslo University Hospital have also participated in the Marie Curie Project Personalized In-Silico Cardiology (PIC), coordinated by King’s College, London, United Kingdom.

Simula works closely with research groups in the United States and Europe, including the University of California, San Diego (UCSD), University of California, San Francisco (UCSF), King’s College London, University of Utah, INRIA Sophia Antipolis, and Karlsruhe Institute of Technology, Germany. An extensive collaboration with UCSF (called SUURPh) focuses on research education and exchange of PhD candidates in scientific computing and biomedical applications, primarily related to cardiovascular disease and neurophysiology. A related project, NeuroComp, is funded by the INTPART program at the Norwegian Research Council and was established in 2016. NeuroComp focuses on mobility, research and education in the calculation and modeling of neurophysiology. This field has many methods and challenges common to cardiophysiology, and the project has contributed to more travel and research stays for researchers in the CCI.

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”.

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OSLO - SEOUL COLLABORATION

During the fall of 2017 OUH received a visit from several renowned international cardiologists for a symposium on diastolic function. The symposium was organized under the auspices of Yonsei University College of Medicine, University of Oslo and Oslo University Hospital, Rikshospitalet. The symposium addressed important new insights into diastolic function, including biomarkers, the clinical application of LV vortex flow analysis and diastolic dysfunction in organ rejection. Chairing the symposium was Professor Jong-Won Ha from Seoul, South-Korea and Professor Otto A. Smiseth, Oslo University Hospital.

The symposium was a success, inspiring future collaboration between the two institutions. Of special interest will be research areas including the diastolic stress test and evaluation of diastolic function in heart transplants.

Professor Ha is also among the co-authors of the article “Estimating Left Ventricular Filling Pressure by Echocardiography”, published in Journal of The American College of Cardiology with center PhD fellow Øyvind Senstad Andersen as first author. Professor Ha has a wide experience with the diastolic stress test, being one of his most important fields of interest. Even though the current guidelines recommend the diastolic stress test for evaluation of diastolic function, this test is seldom used clinically. To Professor Ha’s knowledge this test is currently performed at Mayo Clinic, USA, a University Hospital in Queensland, Australia, and in hospitals in Japan, in addition to about six to seven hospitals in Korea. In the beginning of his PhD, Øyvind Senstad Andersen traveled to Seoul to learn more about the diastolic stress test from professor Ha.

Cardiologists at Yonsei Hospital have so far evaluated 2 200 patients using the diastolic stress test, and this test has become part of the routine practice for the evaluation of patients with dyspnea on exertion. Supine bicycling is used as exercise, simultaneous to echocardiograph. The echocardiographic examination assesses regional wall motion abnormality, MR, mitral inflow and annular velocity and TR velocity during exercise and recovery phase. O2 uptake using cardiopulmonary gas analysis system and ECG during exercise is also measured. In this way, the diastolic stress test not only tests patients for diastolic dysfunction, it also estimates pulmonary function and evaluates whether coronary disease is present or not.

According to Ha the current recommendation on the use of diastolic stress test in the guidelines is well written and reasonable, and he hopes that further experience and accumulated data will lead to implementation of current recommendations into clinical practice.

NEW MEMBERS

Ana Monica Chivulescu MD, visiting researcher
Affiliation: Oslo University Hospital and Institute for cardiovascular diseases “Prof Dr C C Iliescu” Bucharest.
Focus: The use of advanced cardiovascular imaging techniques in improving the knowledge of inherited and acquired cardiomyopathies

Christine Rootwelt MD, visiting researcher
Affiliation: University of Oslo
Focus: Risk stratification of VA in patients with arrhythmogenic right ventricular cardiomyopathy

Pål Brekke MD, PhD
Affiliation: Oslo University Hospital
Focus: Development of new ultrasound technologies and methods

Anders Wold Bjerring MD, PhD fellow
Affiliation: Oslo University Hospital
Focus: Long term cardiovascular adverse effects after cancer treatment

Thomas Muri Stokke MD, PhD fellow
Affiliation: Oslo University Hospital
Focus: Novel echocardiographic methods for bedside assessment of cardiac function

Ana Monica Chivulescu

Kasumi Masuda

Eystein Skjølsvik MD, PhD fellow
Affiliation: Oslo University Hospital
Focus: Impact of exercise on myocardial function and ventricular arrhythmias in patients with cardiomyopathies and risk markers for sudden cardiac death in patients with valvular heart disease

Kasumi Masuda

Jong-Won Ha

Professor, visiting researcher
Affiliation: Yonsei University College of Medicine, Seoul, South Korea
Focus: Diastolic function, valvular heart disease, arterial function using ultrasound

Jørn Bersvendsen

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

**APPENDIX**

#### Annual accounts

<table>
<thead>
<tr>
<th>Funding</th>
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*All figures in 1000 NOK

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#### Personnel

**Key Researchers**

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<thead>
<tr>
<th>Name</th>
<th>Institution</th>
<th>Main Research area</th>
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<tbody>
<tr>
<td>Thor Edvardsen</td>
<td>OUH / UiO</td>
<td>Myocardial function and cardiac imaging</td>
</tr>
<tr>
<td>Kristina Haugaa</td>
<td>OUH / UiO</td>
<td>Myocardial function and cardiac imaging</td>
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<tr>
<td>Ole-Gunnar Anfinnsen</td>
<td>OUH</td>
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<tr>
<td>Mette-Elisa Estensen</td>
<td>OUH</td>
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<tr>
<td>Thomas Helle-Valle</td>
<td>OUH</td>
<td>Myocardial function and cardiac imaging</td>
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<tr>
<td>Einar Hopp</td>
<td>OUH</td>
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<tr>
<td>Per Kristian Hol</td>
<td>OUH</td>
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<td>Pål Brekke</td>
<td>OUH</td>
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<td>Trine Håland</td>
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<tr>
<td>Margareth Ribe</td>
<td>OUH</td>
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<tr>
<td>Kari Melberg</td>
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### Key Researchers

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<th>Main Research area</th>
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<tr>
<td>Elin Bjurstrøm</td>
<td>OUH</td>
<td>Myocardial function and cardiac imaging</td>
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<tr>
<td>Kristin Nordvoll</td>
<td>OUH</td>
<td>Myocardial function and cardiac imaging</td>
</tr>
<tr>
<td>Erik Kongsgård</td>
<td>OUH</td>
<td>Electrophysiology and cardiovascular function</td>
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<tr>
<td>Hans Henrik Odland</td>
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<td>Electrophysiology and cardiovascular function</td>
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<td>Torbjørn Holm</td>
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<td>Erik Lyseggen</td>
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<td>Finn Hegbom</td>
<td>OUH</td>
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<tr>
<td>Svend Aakhus</td>
<td>OUH</td>
<td>Echocardiography and heart failure</td>
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<td>Jan Otto Beinnes</td>
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<td>Echocardiography and heart failure</td>
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<td>Marit Kristine</td>
<td>OUH</td>
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<td>Smedsrud</td>
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<td>Vibeke Marie</td>
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<td>Kristoffer Russell</td>
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<td>Lars Aaberge</td>
<td>OUH</td>
<td>Invasive cardiology and intensive coronary care</td>
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<tr>
<td>Einar Gude</td>
<td>OUH</td>
<td>Heart failure, heart transplant, LVAD</td>
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<tr>
<td>Otto Smiseth</td>
<td>OUH / UiO</td>
<td>Cardiovascular function, imaging and biomechanics</td>
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<tr>
<td>Espen Remme</td>
<td>OUH</td>
<td>Cardiovascular function, imaging and biomechanics</td>
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<tr>
<td>Morten Eriksen</td>
<td>OUH</td>
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<td>Caroline Stokke</td>
<td>OUH</td>
<td>PET and imaging</td>
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<td>Jan Gunnar Fjeld</td>
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<td>Jan Olav Høgetveit</td>
<td>OUH / UiO</td>
<td>Medical technology and bioimpedance</td>
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<tr>
<td>Håvard Kalvøy</td>
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<td>Medical technology and bioimpedance</td>
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<tr>
<td>Morten Flattum</td>
<td>OUH</td>
<td>Medical technology and bioimpedance</td>
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<tr>
<td>William Louch</td>
<td>OUH / UiO</td>
<td>Calcium homeostasis and the failing heart</td>
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### Personnel

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<tr>
<th>Name</th>
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<tbody>
<tr>
<td>Ole Jakob Elle</td>
<td>OUH / UiO</td>
<td>Image guided surgery</td>
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<tr>
<td>Helge Skulstad</td>
<td>OUH</td>
<td>Myocardial function and cardiac imaging</td>
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<tr>
<td>Martin Reimers</td>
<td>UiO</td>
<td>Geometric modeling</td>
</tr>
<tr>
<td>Gunnar Hansen</td>
<td>GEVU</td>
<td>Ultrasound acquisition, processing and visualization</td>
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<tr>
<td>Egil Samset</td>
<td>GEVU / UiO</td>
<td>Ultrasound acquisition, processing and visualization</td>
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<tr>
<td>Andreas Heimdal</td>
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<td>Fredrik Orderud</td>
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<td>Lars Ove Gammelsrud</td>
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<td>Brock Tice</td>
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<td>Robert Blake</td>
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<td>Joakim Sundnes</td>
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<tr>
<td>Kristian Valen-Sendstad</td>
<td>SRL</td>
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<tr>
<td>Andrew Edwards</td>
<td>SRL</td>
<td>Cellular and subcellular electrophysiology</td>
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### Personnel

#### Postdoctoral researchers with financial support from the Centre budget

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<tr>
<td>Eirik Nestaas</td>
<td>Norwegian</td>
<td>01.01.2015-31.12.2017</td>
<td>M</td>
<td>Use of deformation analysis by echocardiography in cardiac resynchronization therapy (CRT)</td>
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<tr>
<td>Nina Eide Hasselberg</td>
<td>Norwegian</td>
<td>17.10.2016-13.08.2017</td>
<td>F</td>
<td>Peak Strain Dispersion and Clinical Outcomes in the EchoCRT trial</td>
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<tr>
<td>Mathis, K. Stokke</td>
<td>Norwegian</td>
<td>01.05.2016-30.04.2018</td>
<td>M</td>
<td>Arrhythmias and cardiac electrophysiology, with a focus on mechanisms for triggered arrhythmias</td>
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<tr>
<td>Kristin McLeod</td>
<td>New Zealander</td>
<td>01.10.2013-31.07.2017</td>
<td>F</td>
<td>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</td>
</tr>
<tr>
<td>Jørn Bersvendsen</td>
<td>Norwegian</td>
<td>01.07.2017-30.09.2019</td>
<td>M</td>
<td>Development of tools for diastolic dysfunction integrated into GE products as well as new machine learning basted models for automatic measurements in echocardiography</td>
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#### Postdoctoral researchers working on projects in the centre with financial support from other sources

<table>
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<tr>
<td>Hermenegild Arevalo</td>
<td>Philippines</td>
<td>01.01.2016-31.12.2018</td>
<td>M</td>
<td>SCD after MI</td>
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<td>Sebastian Sarvari</td>
<td>Swedish</td>
<td>01.09.2017-01.01.2018</td>
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#### Visiting Researchers

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<tr>
<td>Anna Isotta Castrini, MD</td>
<td>Italian</td>
<td>01.11.2016-31.01.2017</td>
<td>F</td>
<td>ARVC in pregnancy</td>
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<td>Esther Scheirlynck, MD</td>
<td>Belgian</td>
<td>01.11.2017-19.11.2017</td>
<td>F</td>
<td>Sudden cardiac death and imaging in structural and non-structural heart disease</td>
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<td>Monica Chivulescu</td>
<td>Romanian</td>
<td>20.11.2017-20.05.2018</td>
<td>F</td>
<td>Myocardial function and prediction of ventricular arrhythmias in patients with arrhythmic right ventricular cardiomyopathy</td>
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<td>Kasumi Masuda</td>
<td>Japanese</td>
<td>28.11.2017-31.01.2018</td>
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<td>Estimation of left ventricular filling pressure in LBBB</td>
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<td>Christine Rootwelt</td>
<td>Norwegian</td>
<td>23.01.2017-14.08.2017</td>
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<td>Risk stratification of VA in ARVC</td>
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<td>Professor Jong Won-Ha</td>
<td>Korean</td>
<td>15.08.2017-30.09.2017</td>
<td>M</td>
<td>Diastolic function</td>
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### PhD students with financial support from the Centre budget

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<tr>
<td>Lars Dejgaard</td>
<td>Norwegian</td>
<td>02.02.2015-31.01.2018</td>
<td>M</td>
<td>The use of different echocardiographic techniques for assessment of risk of sudden cardiac death in cardiomyopathies</td>
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<td>Kaja Kvalø</td>
<td>Norwegian</td>
<td>02.05.2016-30.04.2019</td>
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<td>Visualization and quantification of ischemia in the myocardium</td>
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<td>Henrik Finsberg</td>
<td>Norwegian</td>
<td>01.10.2014-30.09.2017</td>
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<td>Patient Specific Simulation for Improved Cardiac Resynchronization Therapy (CRT)</td>
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<tr>
<td>Thomas Muri Stokke</td>
<td>Norwegian</td>
<td>01.09.2017-31.08.2018</td>
<td>M</td>
<td>Novel echocardiographic methods for bedside assessment of cardiac function</td>
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### PhD students working on projects in the centre with financial support from other sources

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<tr>
<td>Alessia Quattrone</td>
<td>SENRHA</td>
<td>Italian</td>
<td>06.02.2017-31.01.2020</td>
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<td>Outcome and the influence of pregnancy in women with tetralogy of Fallot</td>
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<td>Petter Storsten</td>
<td>SENRHA</td>
<td>Norwegian</td>
<td>01.10.2013-30.04.2019</td>
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<td>Dysynchrony in the systemic and non-systemic right ventricle</td>
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<tr>
<td>Jørg Saberniak</td>
<td>SENRHA / RCN</td>
<td>Norwegian</td>
<td>19.09.2011-30.01.2017</td>
<td>M</td>
<td>Myocardial function and prediction of ventricular arrhythmias in patients with arrhythmic right ventricular cardiomyopathy</td>
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<tr>
<td>Sian Ross</td>
<td>SENRHA</td>
<td>Norwegian</td>
<td>10.02.2014-31.01.2018</td>
<td>M</td>
<td>Cardiac resynchronization therapy Evaluation of acute response parameters</td>
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<tr>
<td>Richard John Massey</td>
<td>HER</td>
<td>Australian</td>
<td>01.04.2017-31.03.2018</td>
<td>M</td>
<td>Cardiac function in young survivors after allogeneic haematopoetic stem cell transplantation</td>
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<tr>
<td>Daniela Melichova</td>
<td>VHT</td>
<td>Norwegian</td>
<td>01.04.2014-30.11.2018</td>
<td>F</td>
<td>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</td>
</tr>
<tr>
<td>Thuy Mi Nguyen</td>
<td>SENRHA</td>
<td>Norwegian</td>
<td>01.04.2014-04.08.2018</td>
<td>F</td>
<td>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</td>
</tr>
</tbody>
</table>
Personnel


John Aalen NHA Norwegian 01.04.2015-31.03.2018 M Contractile Reserve in Dysynchrony (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 arrhythmogenic right ventricular cardiomyopathy

Camilla Kjellstad Larsen SENRHA Norwegian 14.09.2015-13.09.2018 F Contractile Reserve in Dysynchrony (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

Eystein Skjøtvik RCN Norwegian 01.03.2017-28.02.2020 M Impact of exercise on myocardial function and ventricular arrhythmias in patients with cardiomyopathies

Anders Wold Bjerring SENRHA Norwegian 01.03.2017-28.02.2020 M Long-term cardiovascular adverse effects after cancer treatment

Brede Kvisvik UiO Norwegian 01.01.2014-31.12.2018 M Advances in both high-sensitivity Troponins and echocardiography in the assessment of myocardial function

Sigmund Rolfsjord UiO Norwegian 01.09.2015-30.08.2019 M Image fusion, from ultrasound and computed tomography (CT) data

Viviane Tommymann SUURPH German 15.01.2015-14.01.2018 F Electromechanical coupling in cardiac cells and arrhythmic risk prediction

Liubov Nikitushkina SUURPH Russian 01.09.2015-30.11.2018 F Myocardial stress estimation using biomechanical models in order to predict the need for aortic valve surgery

Aslak Wigdahl Bergersen Simula Norwegian 01.10.2016-30.09.2018 M Computational Fluid Structure Interaction in the Left Heart

Scientific articles

A


B


Edvardsen T: The Mechanics of Synchronous RV and LV Contraction
28th Annual meeting. American Society of Echocardiography. Baltimore, MD, USA.

Edvardsen T: Invasive Assessment of Left Ventricular Diastolic Function
28th Annual meeting. American Society of Echocardiography. Baltimore, MD, USA.


Edvardsen T: Strain Imaging in Heart Failure

Edvardsen T: Up-to-date multimodality assessment of left ventricular systolic function
18th Congresso Nazionale, Echocardiography. Naples, Italy.

Edvardsen T: Ventricular arrhythmia prediction: value of imaging techniques
27th annual meeting. Paris, France.

Edvardsen T: Cardiac imaging in Hypertrophic Cardiomyopathy Spring meeting. Norwegian Society of Cardiology. Trondheim, Norway.

Edvardsen T: Future cardiac Imaging
Spring meeting. Norwegian Society of Cardiology. Trondheim, Norway.

Edwards A: Dissecting complex cardiac dynamics: the need for multiple disciplines.University of Copenhagen, Denmark.


Estensen ME: Timing and mode of re-intervention in Tetralogy of Fallot ESC Congress, Barcelona, Spain.

F

Finsberg H, Xi, Tan JL, Zhong L, Lee LC, Wall ST: Mechanical analysis of pulmonary hypertension via adjoint based data assimilation of a finite element model SB3C Conference, Tucson Arizona, USA.

H
Haugaa KH: Risk of ventricular arrhythmias Palermo, Italy.

Haugaa KH: The right ventricle in AC Padua, Italy.

Haugaa KH: Echo findings in cardiomyopathies. European Working group on Cardiomyopathies, Nyborg, Denmark.

Haugaa KH: Imaging in early phase arrhythmogenic cardiomyopathy and risk stratification for ventricular arrhythmias AHa Scientific Sessions, Anaheim, California, USA.

Hunt TEF: Sleep apnea in patients with paroxysmal atrial fibrillation - the A3 study Lysíbu, Oslo, Norway.

Hunt TEF: Predictors of successful pulmonary vein isolation? Workshop, Lugano, Switzerland.

K
Klaaboe IG: Strain imaging in aortic stenosis Myocardial Velocity and Deformation Imaging, Leuven, Belgium

Klaaboe IG: Aortic stenosis CCI Workshop (with prof Vannan and prof Friedberg). Oslo, Norway.

Lie ØH: Høyere hjerktakmer: 3D avslører "den glemte ventrikkel" Lansering av revolutionerende ny ultralydsmaskin for bedre hjertesykdom. Oslo, Norway.

Lie ØH: Echocardiography of right ventricle cardiomyopathies current possibilities and challenges Workshop, echocardiography, Oslo, Norway.


L
Larsen CK, Aalen J, Stokke J, Fjeld JG, Kongsåg E, Smiseth DA, Hopp E: Regional myocardial work by magnetic resonance imaging and non-invasive left ventricular pressure: a feasibility study in left bundle branch block CCI Workshop, Heart Failure, Oslo, Norway.

Larsen CK, Aalen J, Kongsåg E, Fjeld JG, Smiseth DA, Hopp E: Increased diffuse interstitial fibrosis in the septum compared to the left ventricular wall in patients with heart failure and left bundle branch block EURO-Echo imaging congress, Lisbon, Portugal.


Lie ØH, Saberniak J, Deigdaug LA, Anfinsen OG, Hagbom F, Edvardsen T, Haugaa KH: How many are too many – Frequent premature ventricular contractions and left ventricular hypertrophy CCMH Symposium, Heart Failure, Oslo, Norway.


Lie ØH: Cardiac arrest in the well trained SSFI-CTVA, Oslo, Norway.

M

N
Nestaas E, Gjedal O, Sarvari S, Hopp E, Smith HI, Haugaa KH, Edvardsen T: Late occuring post systolic shortening is a marker of myocardial scar EuroEcho Imaging congress, Lisbon, Portugal.


Nestaas E: Functional echocardiography in the neonatal ward 18th World Congress of Perinatal Medicine, Belgrade, Serbia.


Nestaas E: Advanced echocardiographic technologies Masterclass Neeratolgoriet Performed Echocardiography (NPE) JENS Congress, Venice, Italy.


Nyberg P: Kommunikasjon i sfi SF-forum. NFR, Oslo, Norway.

O
Odland HH: Precision clearly matters, ablation of complex arrhythmias Nordic Cardiac AF meeting, St.Jude Medical, Norway.

Odland HH: Ventricular extrasystoles in genetic channelopathies AEPC 2017 Lyon, France.

Odland HH: Indications for ablation in children, Nordic Pediatric Cardiology meeting, Turku, Finland.

Odland HH: Resynkroniseringsbehandling, Pace-makers, Engø Gård, Norges, Norway.

Odland HH: Tak og brabelytter i GIH populasjonen Artimkius, Legeforeningen, Oslo universitetssykehus, Norway.

Odland HH: Resynkroniseringsbehandling Artimkius, Legeforeningen, Oslo universitetssykehus, Norway.


P


Q
Quadrature A: Fallet tetralogy CCI Workshop (with prof Vannan and prof Friedberg). Oslo, Norway.

R
Remme EW, Stokke TM, Haugaa KH, Smiseth OA, Edvardsen T: Subendocardial speckle tracking overestimates myocardial shortening and may falsely indicate preserved systolic function in hypertrophic cardiomyopathy patients EuroEcho Imaging congress, Lisbon, Portugal.

Remme EW: The relations between left ventricular geometry, strains, region of interest, and ejection fraction Myocardial Velocity and Deformation Imaging in Leuven, Belgium.

S
Smiseth OA: Left atrial function by velocity- and strain imaging Myocardial Velocity and Deformation Imaging in Leuven, Belgium.

Smiseth OA: Echo: From M-mode to strain imaging Cardiology Update. Davos, Switzerland.


Smiseth OA: I like the new Diastolic Guidelines, but I still Need More Data. ACC’17. Washington DC, USA.

Smiseth OA: Mechanisms for HFpEF in arterial hypertension From Arterial Hypertension to Heart Disease: an upgrade. Naples, Italy.

Smiseth OA: Myocardial strain imaging: How to apply it in clinical decision making 28th annual meeting of Japanese Society of Echocardiography Nagoya, Japan.

Smiseth OA: Myocardial strain imaging: How to apply imaging of diastolic function in routine clinical practice 28th annual meeting of Japanese Society of Echocardiography Nagoya, Japan.

Smiseth OA: Diastology and Pulmonary Hypertension American Society of Echocardiography 28th Annual Scientific Sessions. Baltimore, USA.

Smiseth OA: Advances in deformation imaging "D" Diobrtna Cardiology Highlights Dubrovnik, Croatia.


Smiseth OA: I like the new Diastolic Guidelines, but I still Need More Data ACC’17. Washington DC, USA.

Smiseth OA: Mechanisms for HFpEF in arterial hypertension From Arterial Hypertension to Heart Disease: an upgrade. Naples, Italy.

Smiseth OA: Myocardial strain imaging: How to apply imaging of diastolic function in routine clinical practice 28th annual meeting of Japanese Society of Echocardiography Nagoya, Japan.

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