

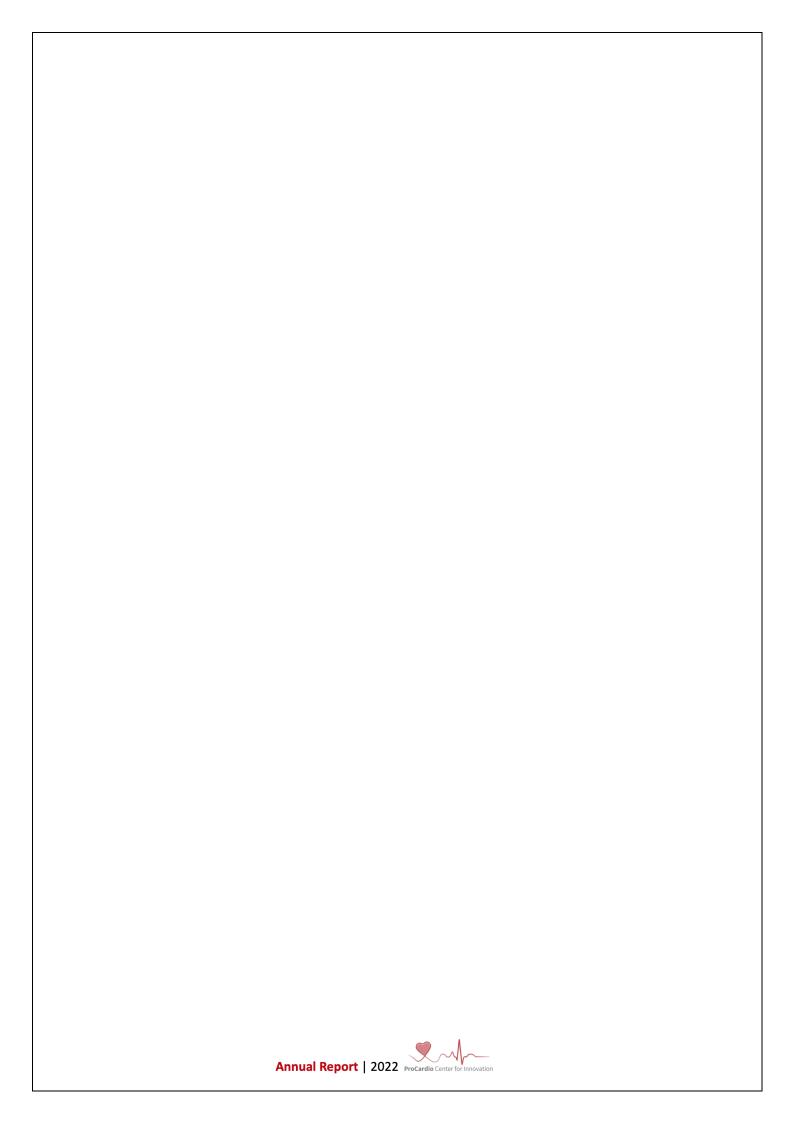


The Research Council of Norway



# PRECISION HEALTH CENTER FOR OPTIMIZED CARDIAC CARE

**Annual Report 2022** 







ProCardio Center for Innovation

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**SUMMARY** 

Dear colleagues, partners and friends,



Our second year as ProCardio was successful. We have worked on our projects with engagement and skills, and we achieved considerable results in 2022. Thank you to every single one of you.

Eight new talented members joined ProCardio in 2022. Jannike Ausland started as our new center coordinator, we welcomed six new PhD fellows, and Bård Moseng joined us from GE Vingmed Ultrasound. Warmest welcome to Jannike, Bård, Sverre Høie, Katarina Vlaisaljevic, Henrik Agerup Kildahl, Christiana Tiago, Müjde Akdeniz and Giulia Monopoli.

In 2022, ProCardio published 53 scientific papers and had 77 scientific communications/abstracts. These are impressive numbers.

Center PhD fellows Alessia Quattrone and Christine Rootwelt-Norberg successfully defended their PhD theses during 2022, and they were celebrated accordingly. Congratulations and thanks for your great work for ProCardio.

We had two meetings for all ProCardio center members, the spring workshop in April, and the "traditional" meeting at Holmen Fjordhotell in September. Both events were well attended and we again concluded that this is the way to bring collaboration to the next level. Also, we attended international conferences with EHRA in Copenhagen and ESC in Barcelona as important examples. ProCardio members were active with abstracts, presentations, networking and learning.

Our funders, the Research Council of Norway, visited ProCardio in September. The feedback was encouraging with terms as "great start", "well organized" "finances under control" "satisfying recruitment" as examples from the report. We are happy that our guests liked our center.

Thank you all, together we are ProCardio. I look forward to a continued productive, exciting, and joyful collaboration.

Center Director Kristina Hangaa



#### **OBJECTIVES AND RESEARCH PLANS**

The center was established to create a clinically driven, validated ICT platform for cardiology that will enable a major change in individualized healthcare, providing the best possible treatment and risk prevention by using big data and artificial intelligence. Based on leading edge research, this platform will facilitate fusion and analysis of rich and diverse data, integrating a wealth of available information into the workflow of clinical cardiology, and tailor individual care to prevent over- and undertreatment.

The most substantial impact of the ProCardio on Norwegian and European societies will be its impact on healthcare. In spite of recent advances leading to decreased mortality rates, cardiovascular disease remains the most common cause of death in Norway accounting for more than one in four deaths.

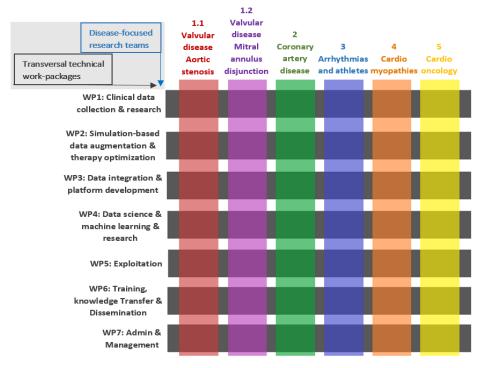
The envisioned uptake of ProCardio tools will have substantial impact for individual patients with metrics such as cost per Quality Adjusted Life Year (QALY) gained. Even more important, these improvements will benefit patients by;

- 1) improved selection criteria
- 2) individually optimized treatment
- 3) more accurate follow-ups
- 4) reduced hospitalization stays and procedures
- 5) personalized advise on health bringing activities e.g. exercise

ProCardio will have governing structures and an operating mechanism that will guarantee a targeted effort to produce results that can be exploited by the partners and lead to value creation in Norway, through the engaged industrial endusers. The center is also strongly in line with the strategies of research partners (NTNU, SRL, UiO, OUS) who are all members of the NHT cluster. Head of Innovation at OUS is invited

as part of the management team to ensure continuous focus on innovations. Lastly, clinical partners participating in ProCardio will benefit from sizeable value pools from more effective cardiac care.

In order to foster an application-driven mindset and to uncap technical synergies across ongoing projects, ProCardio methodology was designed to focus on a bidimensional approach concept of having "vertical" research teams focusing on a target cardiac disease, while the technical work will be coordinated "horizontally" to enable crosspollination of breakthroughs and integration of knowledge in a single platform. Lastly, common management, coordination and knowledge transfer mechanisms will work across the entire center.



#### **ORGANIZATION**

ProCardio is hosted by Oslo University Hospital. The consortium consists of ten partners from both research and industry, in addition to the host institution. ProCardio is located at Oslo University Hospital, Rikshospitalet.

The University of Oslo, Domus Medica (DM4) at Sognsvannsveien 9 (entrance from Gaustadalléen 34), constitutes as the physical hub.

The center director, Kristina Haugaa is responsible for heading the center management. The center director will be assisted by the Scientific and Technical Manager who will be responsible for coordinating work of the teams.

Each clinical task group (T) is led by clinical research and innovation deputies, liaising with WP leaders which ensure transversal synchronization of technical work among the different teams. In parallel, exploitation, dissemination and innovation activities will be supervised by designated managers, Bård Moseng (GEVU), Thor Edvardsen (UiO) and a representative from OUS Dept. of Innovation, Christian Skattum. Mary Maleckar from SRL

will act as a Scientific & Technical Manager and Jannike Ausland replaced Maria Rud as the Administrative Coordinator in 2022.

#### **BOARD OF DIRECTORS**

ProCardio 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 to discuss the Center's development, financial aspects 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 ProCardio. The Center's Board of Directors consists of the following members appointed by the consortium participants:

Eigil Samset, GE HealthCare, Chair

Bjørn Bendz, OUS

Axel Borge, Sesam

Liv Bollvåg, DIPS

Mirco de Melis, Medtronic

Rune Wiseth, NTNU

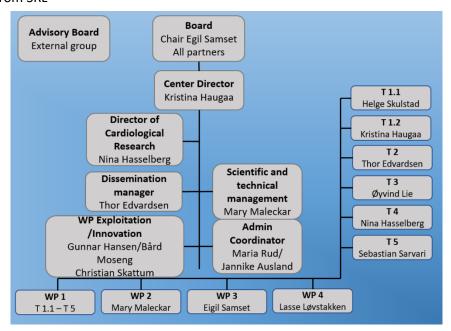
Hilde Nebb, UiO

Samuel Wall, Simula

Gunnar Hansen/Bård Moseng, GE Vingmed Ultrasound

Harald Brunvand, Sørlandet Sykehus HF

Tom Marwick, The Baker Heart and Diabetes Institute



The organizational map of ProCardio

#### **PARTNERS**

The ProCardio Center for Innovation is comprised of 11 partners with OUS being the host partner. Each partner represents a unique and required element in the research and development chain leading to the industrial innovations targeted by ProCardio.



Partner name: Oslo University Hospital

#### Knowledge:

- Department of Cardiology at OUS is the largest interventional department in the Nordic countries with more than 4100 PCIs and 1600 ablations every year
- Front line in cardiac research and with world-class clinical expertise
- Hosted the SFI Center of Cardiological Innovation, which was a highly successful SFI

#### Resources:

- Infrastructures to host the ProCardio center
- Administrative support towards the daily run of the center
- Image and EMR data (>1000 patients)

## simula

Partner name: Simula Research Laboratory AS

#### Knowledge:

- Host of several SFF, SFI, and EU networks focused on excellence in biomedical computing and computing in cardiology
- Mathematical growth models for cardiac physiology, growth, and remodeling
- Data-driven models and analysis for risk prediction
- Computational Cardiology Models for biophysical simulation

#### Resources:

- Access to large computational cluster facilities for training and deployment of resource-intensive algorithms and models



Partner name: Norwegian University of Science and Technology

#### Knowledge:

- Acknowledged as a SFI center for Innovative Ultrasound Solutions (CIUS)
- Extensive know-how on medical imaging technology, in particular ultrasound
- Expertise in artificial intelligence and machine learning algorithms
- Centre of Excellence for translational medical research at the interface of epidemiology, genetics, statistics, bioinformatics and systems biology

#### Resources:

- Extensive databases with follow-up echocardiographic studies and outcome data
- Computational infrastructure to train and run resource-intensive AI algorithms
- Databases on genetic markers to be coupled with cardiac imaging in the HUNT database and its digital infrastructure
- A substantial number of other omics data, such as NMR-based metabolomics, CVD related protein arrays, transcriptomics and other targeted protein biomarkers



## • SØRLANDET SYKEHUS

Partner name: Sørlandet Hospital HF

#### Knowledge:

- Leading clinical and experimental research expertise in the area of myocardial function
- Extensive hands-on experience on clinical trials to assess new diagnostic technologies and therapies (e.g. established the IMPROVE-study)

#### Resources:

- Image data and EMR data (>2000 patients) -
- Inclusion of cardiac patients with heart failure and myocardial infarction in ongoing and future research projects



Partner name: GE HealthCare

#### Knowledge:

- World class design and manufacturing of diagnostic imaging and monitoring systems
- Extensive expertise in cardiology diagnostics, artificial intelligence development for imaging and waveforms
- Deep market understanding

#### Resources:

- Direct access to Edison Al Workbench
- Fast-track integration of innovations into commercial products and implementation to other imaging modalities beyond ultrasound



UiO University of Oslo

Partner name: University of Oslo

#### Knowledge:

- Oldest and largest research and educational institution in medicine in Norway
- K.G. Jebsen Centre for Cardiac Research is a global reference in the field of cardiology, combining outstanding PIs with an extensive international network of research partners

#### Resources:

- PhD training for OUS-hosted researchers



**GE Vingmed Ultrasound** 

Partner name: GE Vingmed Ultrasound

#### Knowledge:

- Center of excellence on ultrasound engineering at GE HealthCare (GEHC)
- World-class know-how in cardiovascular ultrasound acquisition, processing and analysis, speckle-tracking and strain imaging, artificial intelligence in ultrasound, 3D visualization and quantification
- Extensive insight on regulatory requirements and ultrasound market intelligence

#### Resources:

- Provide ultrasound equipment and software to the center to ensure successful execution of clinical projects and data acquisition
- Through the Developer Partnership Program industrial partners can benefit from a "fast-track to innovation", which allows 3rd party solutions to be distributed to the GEHC installed based through the GEHC Marketplace





Partner name: Medtronic Plc

#### Knowledge:

- World's largest medical technology company, offering a large breadth and depth of innovative therapies, including forefront treatments for cardiac and vascular diseases -
- Extensive expertise in clinical trial protocol development and implementation
- VBHC approaches for therapy optimization and chronic care programs
- Manufacturing of devices; both for delivering therapies, as well as for diagnostic purposes (sensors)

#### **Resources:**

- Access to state-of-the-art medical devices
- Capable of designing and building custommade devices addressing the needs of individual patients, or groups of patients, according to the specifications provided by a physician or in accordance with a project description

## sesam

Partner name: Sesam AS

#### Knowledge:

- Development of GDPR compliant data management solutions
- Data privacy expertise
- Creation of interfaces and standards for sharing of data in of Health analytics

#### Resources:

- Access to the Sesam Data Integration Hub Platform-as-a-service
- Consulting services around architecture, along with assistance to connect data sources, transforming data and delivering data where it is needed



Partner name: The Baker Heart and Diabetes Institute

#### Knowledge:

- Outstanding diabetes & cardiac research center, with global visibility, contributing to ProCardio with strong complementary expertise in the field of cardio-oncology

#### Resources:

- Extensive clinical database of multi-modal data



Partner name: DIPS AS

#### Knowledge:

- Leading supplier of electronical patient medical records software solutions to Norwegian hospitals
- Expertize in eHealth, data integration activities and IT platform development

#### Resources:

- Access to DIPS Arena - a fully integrated patient record system including closed loop medication, charting, booking and planning, electronic document workflow, CPOE, multimedia and reporting



#### **COOPERATION BETWEEN PARTNERS**

The partners at ProCardio bring key competences to the joint projects, enabling everyone in ProCardio to effectively pursue the collective goals. In order to ensure effective dissemination of management goals and coordination of efforts among the partners, an integrated meeting schedule has been established. This includes weekly meetings within individual project teams, biweekly meetings among management and PhD-students as well as monthly meetings with center leaders and all members of ProCardio. The supervisory board meet bi-annually, in sync with the planned training and dissemination workshops.

#### Specific international project collaboration with ProCardio partners

- Host partner Oslo University Hospital (OUS) is a leading center in several international multicentre studies.
- From 2022, ProCardio has become part of an international multicentre drug study where a new and ground-breaking drug will be tested for patients with hypertrophic cardiomyopathy a disease which is a main area of research in ProCardio. From ProCardio, both OUS and GE HealthCare are involved and center manager Kristina Haugaa is the study's project manager in Norway.
- In 2022, ProCardio has started an international research collaboration, in collaboration with Chaim Sheba Medical Center, Israel, by Dr. Sabbag, regarding research on patients with arrhythmogenic mitral valve prolapse, one of ProCardio's main focus areas in terms of disease category.
- ProCardio has an ongoing study on ischemic heart disease in collaboration with the University of Copenhagen, Rigshospitalet and Nationalt Genom Center, Denmark, NTNU and deCODE, Iceland.
- ProCardio participates in an international collaboration for arrhythmogenic cardiomyopathies led by Johns Hopkins University, Baltimore, MD, USA.
- Simula has close collaborations with world-class research groups in the US and Europe, including University of California, San Diego (UCSD), University of California, San Francisco (UCSF), University of California, Berkeley, University of Washington, Seattle, King's College London, Imperial College London, University of Utah, INRIA Sophia Antipolis, Karlsruhe Institute of Technology, Germany, and Copenhagen University, Denmark. Among other internationally-funded projects, Simula is a work-package leader for the large European project <a href="SimCardioTest">SimCardioTest</a> focused on demonstration of a standardised and rigorous approach for in-silico clinical trials for cardiac therapies, creating an integrated and secure platform standardising & bridging model simulations, in-silico trials, and certification support.
- Simula has a particularly extensive collaboration with UCSD (called SUURPh) which focuses on research training and the exchange of PhD candidates within scientific data processing and biomedical applications, primarily related to cardiac physiology, running an annual summer school which has quickly become a premier venue for education within computational cardiology. In addition, Simula has a close collaboration with UC Berkeley through the project SIMBER (The Simula Berkeley Education and Research Collaboration), funded through the INTPART programme.

- GEVU has an extensive global network and is actively involved in international research collaboration. Several of these projects are directly linked to research in ProCardio in subjects such as functional ultrasound imaging for the assessment of heart failure and the risk of sudden cardiac death.
- GEVU collaborates with some of the world's leading environments; UCSF, Brigham and Women's Hospital and Massachusetts General Hospital.
- In 2022, the collaboration between ProCardio and the European Union's Horizon 2020 MARCIUS project has been strengthened. The two MARCIUS ESRs working with GE Vingmed Ultrasound are well aligned with ProCardio and have achieved interesting results relevant to the consortium. The MARCIUS project is an international collaboration involving GE Vingmed Ultrasound, UiO, the

universities of Maastricht (NL) and Leiden (B), as well as Jessa Hospital (B) and the company MedaPhor/Intelligent Ultrasound (UK). By this collaboration, the ProCardio consortium has access to highly reputed international researchers and domain experts within ultrasound simulation and deep learning.



#### SCIENTIFIC ACTIVITIES AND RESULTS

#### Validation study of the LMNA-risk VTA calculator

Rootwelt-Norberg C, Christensen A, Skjølsvik ET, Chivulescu M, Vissing CR, Bundgaard H, Aabel EW, Bogsrud MP, Hasselberg NE, Lie ØH, Haugaa KH

Cardiac laminopathies are highly malignant forms of familial dilated cardiomyopathy, caused by deleterious variants in the *LMNA* gene. A <u>risk calculator</u> for predicting life-threatening arrhythmias in laminopathies was introduced in 2019.

PhD-fellow Christine Rootwelt-Norberg, Professor Kristina Haugaa and co-authors published a paper validating the existing *LMNA*-risk VTA calculator.

The study was a multicentre collaboration with Rigshospitalet University Hospital in Copenhagen, including 118 *LMNA* genotype positive patients followed for 6 years.

#### Performance of the LMNA-risk VTA calculator

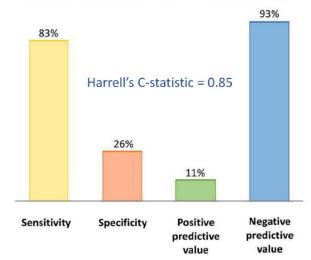


Figure from Rootwelt-Norberg, C. et al. Timing of cardioverter-defibrillator implantation in patients with cardiac laminopathies—External validation of the LMNA-risk ventricular tachyarrhythmia calculator. Heart Rhythm. 2023;20(3):423-429.



Twenty-three (19%) of patients experienced first-time life-threatening ventricular arrhythmias during follow-up. The previously published *LMNA*-risk calculator showed high sensitivity for detecting forthcoming ventricular arrhythmias, but low specificity.

Specifically, the *risk* calculator provided a 5-year sensitivity and specificity of 83% (95% CI 52%-98%) and 26% (95% CI 18%-35%), respectively, when applying the suggested  $\geq 7\%$  predicted 5-year risk as cutoff.

The 5-year positive predictive value was 11% (95% CI 6%–20%) and the negative predictive value was 93% (95% CI 78%–99%). Arrhythmic risk was more often overpredicted in male than in female patients.

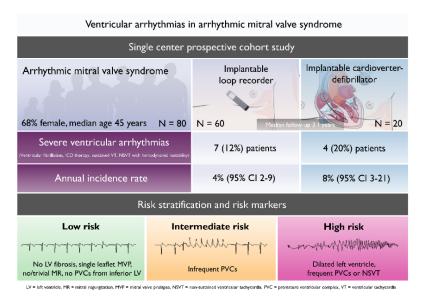
The study demonstrated that the *LMNA*-risk VTA calculator can provide valuable guidance in clinical practice when used frequently for reevaluation of patient risk. However, the previously proposed cutoff value of  $\geq$ 7% predicted 5-year risk for primary prevention ICD may result in premature implantation of devices.

# Ventricular arrhythmias in arrhythmic mitral valve syndrome – a prospective continuous long-term cardiac monitoring study

Aabel E, Chivulescu M, Lie ØH, Hopp E, Gjertsen E, Ribe M, Helle-Valle TM, Edvardsen T, Hegbom F, Dejgaard LA, Haugaa KH

Patients with arrhythmic mitral valve syndrome (AMVS) are at risk of life-threatening heart rhythm disturbances, but risk stratification is challenging due to lack of knowledge on incidence, mechanism and markers of arrhythmia.

In this prospective study, we implanted heart rhythm monitors in 60 patients with AMVS and follow them for 3 years to assess the incidence of heart rhythm disturbances. As a comparator, we also followed patients with survived cardiac arrest that had received implantable defibrillator.



Graphical abstract from the published article in the high impact journal EP Europace (doi: 10.1093/europace/euac182)

Furthermore, we explored possible risk markers to improve risk stratification. The study adds important information for clinicians caring for patients with AMVS.

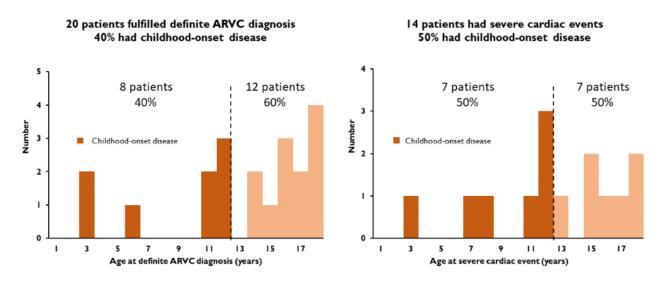
The study was published in the high impact journal EP Europace, and was presented at the ECS Congress 2022 in Barcelona by first author and PhD fellow Eivind Aabel, MD. Eivind also presented this work and won the Best Poster Award in the moderated poster session entitled "Genetics and arrhythmias" at the 20<sup>th</sup> Annual Oslo Symposium on Heart Research.

# Highly malignant disease in childhood-onset arrhythmogenic right ventricular cardiomyopathy

Smedsrud MK, Chivulescu M, Forså MI, Castrini I, Aabel E, Rootwelt-Norberg C, Bogsrud MP, Edvardsen T, Hasselberg NE, Früh A, Haugaa KH

Arrhythmogenic right ventricular cardiomyopathy (ARVC) is an inheritable and progressive heart muscle disease characterized by high risk of ventricular tachyarrhythmias and sudden cardiac death, in addition to morphological abnormalities and eventually heart failure. Penetrance of ARVC disease has been described in adolescents, but is currently considered to be extremely rare under the age of ten years. However, children with ARVC are underrepresented in research publications and the clinical characteristics of paediatric ARVC are largely unknown.

In a single-centre cohort study, we included all consecutive ARVC probands and genotype-positive relatives old followed at the Department of Paediatric Cardiology, Oslo University Hospital, Rikshospitalet between 2007 and 2021. In this paediatric ARVC cohort, there was a high incidence of severe cardiac events and half of them occurred in children ≤12 years of age. The ARVC penetrance in genotype positive paediatric relatives was 18%. These findings of a high-malignant phenotype in childhood-onset ARVC indicate a need for ARVC family screening at younger age than currently recommended.

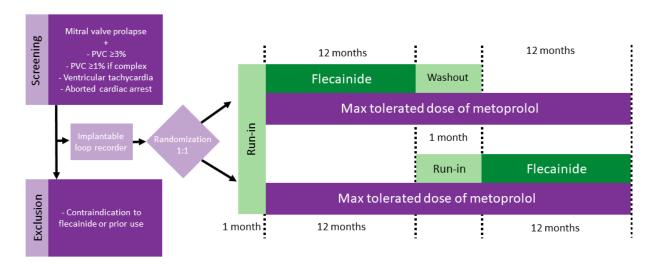


**Figure.** Age distribution of definite arrhythmogenic right ventricular cardiomyopathy and severe cardiac events. Smedsrud et al. Eur Heart J, Volume 43, 1 Dec 2022

The study was publishes in the highly ranked European Heart Journal in early August 2022 and presented at the ESC Congress in Barcelona. In an Editorial in European Heart Journal in December professor Juan Pablo Kaski at Great Ormond Street Hospital in London use the results of this study as an argument for considering changing international clinical screening guidelines.

#### **FLECAPRO**

FLECAPRO is an investigator-initiated, prospective, randomized, open-label, blinded-endpoint, crossover study with the goal to assess the efficacy and safety of adding flecainide to standard beta-blocker therapy in patients with arrhythmic mitral valve prolapse. The primary endpoint is the number of ventricular tachyarrhythmias (severe and life-threatening arrhythmias) on implantable heart rhythm monitors during 12 months in each treatment arm.

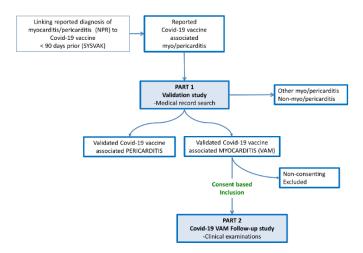


**Figure.** Age distribution of definite arrhythmogenic right ventricular cardiomyopathy and severe cardiac events. Smedsrud et al. Eur Heart J, Volume 43, 1 Dec 2022

Secondary endpoints are the number of premature ventricular beats on 24-hour home monitors, patient-reported health-related quality of life, and the number of life-threatening ventricular tachyarrhythmias. Oslo University Hospital is the only centre, and St. Olavs Hospital provides blinded primary endpoint adjudication and analyses of flecainide serum concentrations. All participants will be monitored by implantable heart rhythm monitors, as well as through clinical visits, physical examinations, blood samples, ECG, Holter monitoring and echocardiography.

#### Covid-19 vaccine associated myocarditis and pericarditis in Norway

Multiple studies have confirmed myocarditis and pericarditis as unexpected adverse events of Covid-19 vaccines administrated worldwide in mass vaccination campaigns to help combat the SARS-CoV-2 pandemic. There is uncertain data on the actual number of affected individuals and no data exists on potential long-term cardiac effects of vaccine associated myocarditis (VAM).



ProCardio has in 2022 initiated a national multicentre study, with postdoctoral researcher Nina Hasselberg as PI and PhD candidate Katarina Vlaisavljevic, in collaboration with the Norwegian Institute of Public Health (NIPH) and the Norwegian Medicines Agency (NoMA).

Part 1 of the study is a retrospective validation study of all reported cases of Covid-19 vaccineassociated myocarditis and pericarditis in Norway, including investigating for risk factors for developing these adverse events.

Part 2 of the study is a prospective clinical follow-up study examining patients 1 and 2 years after myocarditis to investigate for long-term cardiac effects.

Our study will provide data on the true incidence of pericarditis and myocarditis caused by Covid-19 vaccines, identify individuals at increased risk, and importantly provide follow-up and potentially treatment of patients with vaccine associated myocarditis. Furthermore, our study results will impact recommendations on the clinical follow-up of patients after vaccine-associated myocarditis. On a public health level, we expect our study to have immediate impact on global vaccination strategies for both the present and future pandemics.

#### Cardiac event detection in echocardiography with triplane data and deep learning

Fermann BS, Aase SA, Nyberg J, Grue JF, Grenne B, Dalen H, Remme E, Løvstakken L, Østvik A

This project demonstrates deep learning methods (3D CNN + LSTM) to detect six events in the cardiac cycle, thus adding more clinical information compared to previous timing networks using only two events. These additional events separate distinct physiological phases which may provide a less naïve representation of the cardiac cycle. We train this network on triplane recordings which provide multiple views of the heart with optimal synchronization for improved annotation accuracy.

The work was presented as a poster at the IEEE International Ultrasonics Symposium (IUS) 2022. The project is still ongoing, and the goal is to extend to a full paper and test integration in 2023.

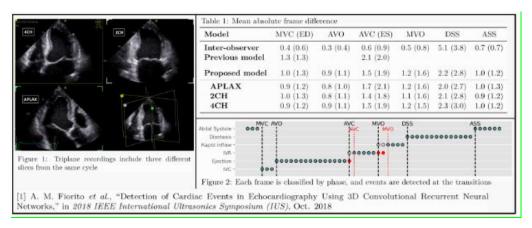


Figure 1 Results from cardiac event detection (from Fermann et. al. Cardiac event detection in echocardiography with triplane data and deep learning)

# Deep Learning for Multi-Level Detection and Localization of Myocardial Scars Based on Regional Strain Validated on Virtual Patients

Akdeniz M, Manetti CA, Koopsen T, Mirar HN, Snare, SR, Aase SA, Lumens J, Sprem J, McLeod KS

This project aims to assess heart function by quantification of myocardial deformation by echocardiography. Clinical assessment of cardiac function has generally focused on global indices of relative shortening; however, segmental strain indices have been shown to be abnormal in regions of myocardial disease such as scarring. In this work, a single framework to predict myocardial scars at global, territorial, and segmental levels using regional myocardial strain traces as input to a convolutional neural network (CNN) is proposed. A significant contribution is the proposal of an anatomically meaningful representation of the input data from the clinically standard bullseye representation to a multi-channel 2D image. This enabled the use of state-of-the-art neural network configurations.

A Fully Convolutional Network (FCN) was trained to detect and localize myocardial scar from regional left ventricular (LV) strain traces. Simulated regional strain data from a controlled dataset of virtual patients with varying degrees and locations of myocardial scar was used for training and validation. The proposed method successfully detected and localized the scars in 98% of the 5490 left ventricle (LV) segments of the 305 patients in the test set using strain traces only. Due to the sparse existence of scar in the dataset, only 10% of the LV segments were scarred. Taking the imbalance into account, the class balanced accuracy was calculated as 95%.

The proposed method proved successful on the strain traces of the virtual cohort and offers the potential to solve the regional myocardial scar detection problem on the strain traces of the real patient cohorts.

This work was submitted late 2022 and accepted for publication in IEEE Access Vol. 11. The project is currently being extended to also include real patient data.

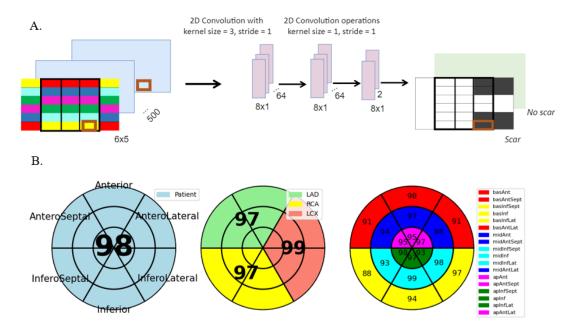


Figure 2 A. Local scar detection pipeline for LV segmental strain traces.B. The balanced accuracy scores for the top performing model. LAD = Left Anterior Descending, RCA = Right Coronary Artery, LCx = Left Circumflex Artery, bas = Basal, ap = Apical, Ant = Anterior. Inf = Inferior, Sept = Septal, Lat = Lateral

# A Data Augmentation Pipeline to Generate Synthetic Labeled Datasets of 3D Echocardiography Images using a GAN

Tiago C, Gilbert A, Beela AS, Aase SA, Snare SR, Sprem J, McLeod K

This project aims to generate synthetic images to be used for Deep Learning dataset generation. Due to privacy issues and limited amount of publicly available labeled datasets in the domain of medical imaging, an image generation pipeline to synthesize 3D echocardiographic images with corresponding ground truth labels was proposed.

This alleviates the need for data collection and for laborious and error-prone human labeling of images for subsequent Deep Learning (DL) tasks. The proposed method utilized detailed anatomical segmentations of the heart as ground truth label sources.

This initial dataset was combined with a second dataset made up of real 3D echocardiographic images to train a Generative Adversarial Network (GAN) to synthesize realistic 3D cardiovascular Ultrasound images paired with ground truth labels. To generate the synthetic 3D dataset, the trained GAN used high resolution anatomical models from Computed Tomography (CT) as input.

A qualitative analysis of the synthesized images showed that the main structures of the heart are well delineated and closely follow the labels obtained from the anatomical models.

To assess the usability of these synthetic images for DL tasks, segmentation algorithms were trained to delineate the left ventricle, left atrium, and myocardium.

A quantitative analysis of the 3D segmentations given by the models trained with the synthetic images

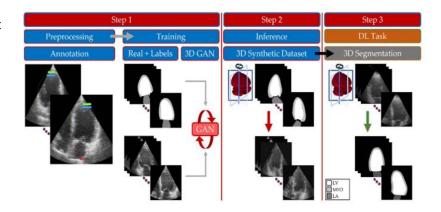


Figure 3 Illustration of the image generation pipeline and inference results. (from Tiago et. al. A Data Augmentation Pipeline to Generate Synthetic Labeled Datasets of 3D Echocardiography Images Using a GAN)

indicated the potential use of this GAN approach to generate 3D synthetic data, use the data to train DL models for different clinical tasks, and therefore tackle the problem of scarcity of 3D labeled echocardiography datasets.

This work was published in IEEE Access Vol. 10. In a follow-up project, other DL technologies for data generation is explored.

#### The Cardio-Oncology Dashboard application

In most hospitals around the world, different information relevant for cardio-oncologists, including chemotherapy type and doses, cardiac morphology and function data, blood sample results, etc. are stored in various data systems. Our goal is to collect all this information in one place and provide a quick overview of patient relevant data and give guideline directed diagnostic and therapeutic advice.

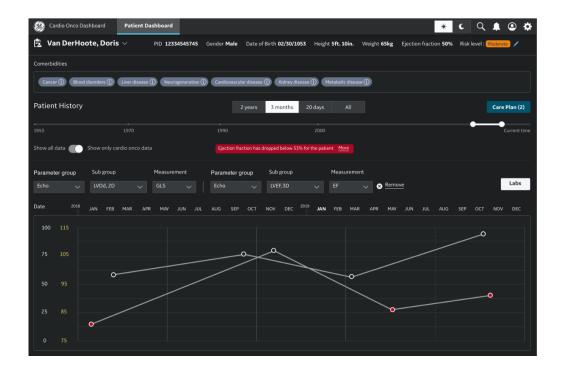
The Cardio-Oncology Dashboard application is a diagnostic tool designed to aid personnel in providing therapeutic care for their patients. Our project diverges from the Afib Dashboard, which concerns atrial fibrillation.

Some of the important tasks featured in the cardio-oncology dashboard are calculation of cumulative anthracycline doses and displaying doxorubicin equivalent doses of various anthracyclines. Another feature is a warning triggered by the change of various parameters relevant for cardio-oncology patients, such as myocardial function parameters assessed by echocardiography, blood sample results, electrocardiogram, etc.

Under development is a risk factor calculator based on the first cardio-oncology guidelines published in 2022 (ESC Guidelines on cardio-oncology developed in collaboration with the European Hematology Association (EHA), the European Society for Therapeutic Radiology and Oncology (ESTRO) and the International Cardio-Oncology Society (IC-OS)). The goal of the calculator is aiding cardio-oncologists in selecting a treatment plan in accordance to guidelines while taking relevant risk factors into consideration.

DIPS has mapped relevant patient data for the cardio-oncology tools, both in the electronic health record and in specialist systems. Data sources have been evaluated for reusability in the project. Test data has been tailored for testing the new ESC guidelines and made available in the development environment Open DIPS.

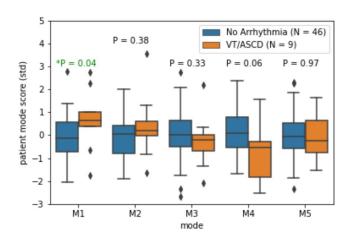
Initial framework for hosting third-party applications in the EHR (DIPS Arena) has been made ready for the cardio-oncology tools.



# Towards An Automated Pipeline to Create Patient Specific 3D LV Geometry Models of Patients with Mitral Annular Disjunction

Balaban G, Aabel EW, Ribe M, Castrini AI, Haugaa KH, Maleckar MM

Mitral annular disjunction (MAD) is characterized by an abnormal insertion of the posterior mitral leaflet on the atrial wall. Despite its often subtle presentation, the presence of MAD can be a warning sign of future ventricular tachycardia (VT) and sudden cardiac death (SCD), as recent studies have shown association among MAD-related imaging metrics and VT/SCA. Nevertheless, the precise mechanisms leading to VT/SCD in patients with MAD are poorly understood. A comprehensive 3D shape analysis of the left ventricles (LV) of patients with MAD may provide further insight and help to elucidate mechanisms. Towards this end, we created a patient-specific 3D LV geometry modelling pipeline for patients with MAD, to enable future morphological studies based on cardiac short axis magnetic resonance imaging (MRI). We applied our pipeline to derive personalized 3D LV geometries in a cohort of 69 patients with MAD originating from Oslo University Hospital. To demonstrate the utility of our pipeline, we perform a statistical comparison of the dominant modes of shape variation of our patient cohort with records of prior arrhythmia. The Figure shows that a statistical comparison of LV end-diastolic shape mode content between patients who suffered a VT or SCA versus patients who had no record of prior arrhythmia. The difference in mode M1 is statistically significant (P = 0.04). This project is ongoing and will yield new results in coming years.

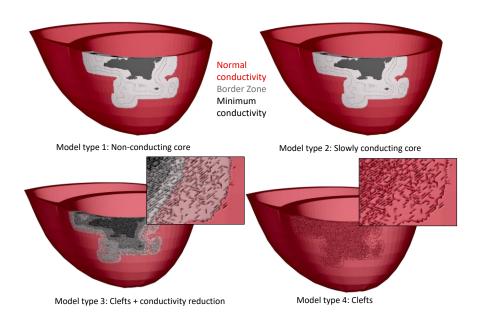


# Fibrosis Representation Affects Reentry in Ventricular Models of Non-Ischemic Cardiomyopathy

Myklebust L, Arevalo H

Non-ischemic cardiomyopathy (NICM) patients are at risk of ventricular arrhythmias, but diagnosis and treatment remain challenging. This study aims to explore arrhythmic mechanisms and predict risk using electrophysiological simulations.

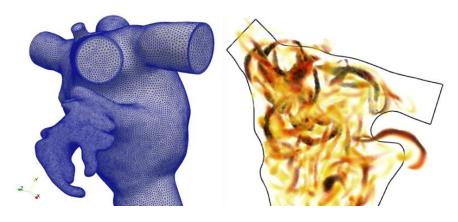
In particular, we focused on investigating different modalities of incorporating fibrosis and how it affects simulation outcomes. Preliminary results (see Figure below) show that reentrant circuits can be induced by in both continuous and discrete models. The reentry mechanisms and location are highly dependent on scaling of the tissue parameters.



#### Computational fluid dynamics towards stroke risk assessment in the setting of atrial fibrillation

Kjeldsberg H, Sendstad KV

Atrial fibrillation (AF) is the predominant type of cardiac arrhythmia that disrupts electrical signals and hampers the normal contractile function of the left atrium (LA), thereby affecting the blood flow's dynamic behavior. In approximately 99% of cases, strokes associated with AF result from a thrombus formed in the LA, more specifically, in the left atrial appendage (LAA). At Simula Research Laboratory, we have developed novel high-performance computational fluid dynamics (CFD) tools that allow for assessment of flow stasis in the LAA. The Figure below shows one example of a simulation based on dynamic computed tomography images that allows for in-silico stroke assessment to eventually supplement clinical decisions. At left, patient geometry of the LA and LAA; at right, 1 2D cross-section of results of the CFD simulation, permitting high-resolution visualization of blood flow in this patient.



#### INTERNATIONAL COOPERATION

ProCardio works with an international perspective where the research methods are of international interest and the innovation projects target the global market. The ProCardio partnership includes two partners outside Norway (Medtronic, the Netherlands and the Baker Heart and Diabetes Institute, Australia) in addition to GE HealthCare.

In 2022, the international collaboration in ProCardio resulted in the following applications/projects

- Within ProCardio we work with Prototype of wearable vest for electrophysiological utility (OUS Medtronic, Maastricht, NL)
- Kristina Haugaa participates centrally in an international registry group established by the European Heart Rhythm Association (EHRA) (national heart associations from 57 countries). In 2022, the group published guidelines for the diagnosis and treatment of patients with arrhythmogenic mitral valve prolapse.
- We collaborate with universities in Milan, Italy, and Utrecht/Maastricht, the Netherlands in connection with ultrasound-guided risk stratification for sudden death in an EU-funded project (EMPATHY) ERA-CVD.
- Kristina Haugaa is Professor at the Karolinska Institutet, Stockholm, SE where she worked part-time and laid the foundations for the collaborative project between the environments.
- We participate in an international cardiomyopathy registry established by Dr Lakdawala at Women Brigham, Boston Massachusetts, USA. ProCardio has published articles in 2022 as part of this collaboration.
- We participate in a Nordforsk-funded project on Personalized Medicine with participants from the Nordic countries.
- ProCardio at OUS is a central part of the Nordic ARVC register. Kristina Haugaa is in the steering committee. In 2022, Nina Hasselberg participated in the annual collaboration meeting in Copenhagen, and we have participated in several web-based meetings throughout the year.
- We collaborate with the University Hospital Brussels, Belgium on cardiac arrhythmias and sudden death.

#### International visiting researchers

Doctor Adrian Wassan, PhD candidate from Rennes Center Hospitalier Universitaire (CHU), was a new guest researcher at ProCardio for 7 months in 2022. He worked on a collaborative project between ProCardio and the University of Rennes where they have developed artificial intelligence/machine learning to be able to assess risk of serious cardiac arrhythmia and sudden death in patients with heart muscle disease. The work will result in a French master's degree and several scientific articles for international publication.

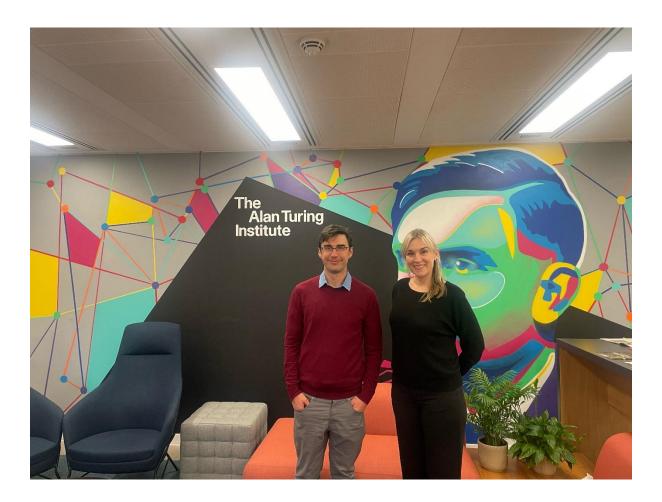
Doctor and cardiologist Esra Kaya from Turkey has been a guest researcher in ProCardio from 2021 and throughout 2022. She was funded by the European Association of Cardiovascular Imaging (EACVI) for the first 12 months and then with research funds from UiO. Dr. Kaya is working on a clinical ProCardio study on patients with aortic stenosis undergoing the TAVI procedure.

She has made great progress in 2022 with good presentations nationally and internationally, including an award for best presentation at the Norwegian Cardiology Spring Meeting in May 2022.

Doctor Feddo Kirkels is a PhD candidate from the Netherlands (financed by EMPATHY, ERA-CVD). After previous research stays in 2020 and 2021, he visited Norway in 2022 as a visiting researcher at ProCardio where he worked on ongoing innovative collaborative projects in artificial intelligence and imaging diagnostics between ProCardio and his home university in Utbrecht, the Netherlands.

Research Professor Mary (Molly) Maleckar from partner Simula was invited as a Visiting Scholar to the Alan Turing Institute in London, U.K., where she collaborates with local and international researchers to develop their strategic platform and research on cardiac digital twins designed to advance diagnostic technologies, longitudinal care, and therapies for those suffering from diverse cardiovascular diseases together with collaborators from King's College London and Imperial College London.

Molly Maleckar was given a Visiting Scholar award to The Alan Turing Institute in London England focuses on Digital Twins in Healthcare and specifically computational cardiology. This tenure occurred January-March 2023, and will continue longitudinally with collaborators at King's College London, Imperial College London, and the Turing Institute itself.



#### **NEW MEMBERS**



Henrik Agerup Kildahl MD, PhD fellow Focus: Valvular disease, automated measurements, artificial intelligence



**Sverre Høie** MD, PhD fellow **Focus**: Valvular disease



Katarina Vlaisavljevic MD, PhD fellow Focus: Covid-19 vaccine associated myocarditis



Jannike Ausland MSc, administrative coordinator



Bård Moseng
MSc, Engineering manager
GE Vingmed
Focus: Member of the
Board and Exploitation
Manager



Christiana Tiago MSc, PhD fellow Focus: Machine Learning



Müjde Akdeniz MSc, PhD fellow Focus: Machine Learning



Giulia Monopoli
MSc, PhD fellow
Focus: Image-based methods for
automatic detection of M.A.D.
Models for mechanistic insight
into arrhythmias

#### DISSERTATION

#### **Alessia Quattrone**

Risk stratification in adults operated for tetralogy of Fallot

September 23, 2022

#### **Adjudication committee**

First opponent: Assistant Professor Rafael Alonso-Gonzalez, Toronto General Hospital, Canada

Second opponent: Senior Consultant Assami Rösner,

UiT - The Arctic University of Norway

Third member and chair of the evaluation committee: Associate Professor John-Peder Escobar

Kvitting, University of Oslo



Professor Annetine Staff, University of Oslo

#### **Supervisors**

Main supervisor: Consultant cardiologist Mette-Elise Estensen, OUS

Co-supervisor: Professor Kristina Haugaa, University of Oslo Co-supervisor: Professor Thor Edvardsen, University of Oslo

#### **Summary**

Tetralogy of Fallot (TOF) is the most common cyanotic congenital heart diseases. It consists of a combination of four cardiac defects: ventricular septal defect, right ventricular outflow obstruction, right ventricular hypertrophy and over-riding of the aorta. The surgical correction of the anatomical defects is performed within the first months of life.

Life expectancy and quality of life in patients operated for TOF have increased importantly. In female patients pregnancy is usually well tolerated. However, adults operated for TOF are subject to higher mortality rate than in the general population, and complications as ventricular arrhythmias (VA) and sudden cardiac death represent major concerns. Despite yearly follow-up, it is not easy to identify patients with higher risk of complications, as well as it is not clear whether pregnancy have an influence on the long term. We aimed to improve the identification of risk factors that contribute to complications in adult operated for TOF. Furthermore, we aimed to investigate the influence of pregnancy on the long term outcome in females.

We selected patients >18 years old diagnosed for TOF and with history of complete surgical correction. A subgroup of patients was investigated with echocardiography and cardiac magnetic resonance.

We showed that almost one out of four adults operated for TOF experience VA about thirty years after surgical repair. The incidence of VA was similar in males and females. Males had more left ventricle (LV) and right ventricle (RV) dysfunction compared to females, expressed by lower RV and LV global longitudinal strain values and lower LV ejection fraction values. Experienced pregnancy was associated with higher prevalence of VA, being the increased risk expressed by higher RV mechanical dispersion and higher values of NT-proBNP, independently of age. Pregnancy seems not to cause alterations in RV and LV volumes, heart function, or grade of fibrosis.



#### DISSERTATION

#### **Christine Rootwelt-Norberg**

#### Disease manifestations and predictors of arrhythmia in patients with arrhythmogenic cardiomyopathy

December 15, 2022

#### **Adjudication committee**

First opponent: Professor David O. Arnar, University of

Iceland

Second opponent: Professor Charlotte B. Ingul, NTNU -Norwegian University of Science and Technology Third member and chair of the evaluation committee: Associate Professor Lars Fjellbirkeland, University of



#### Chair of the Defence

Professor II Jonny Hisdal, University of Oslo



Main supervisor: Professor Kristina Haugaa, University of Oslo

Co-supervisor: Dr. Øyvind Lie, MD PhD, OUS



Arrhythmogenic cardiomyopathy is a genetic cardiac disease associated with high risk of lifethreatening arrhythmias and sudden cardiac death. There is high variability between patients in regards to the severity of disease manifestations, with some patients going through life with no or mild symptoms, while others die at young age.

In the thesis Disease manifestations and predictors of arrhythmia in patients with arrhythmogenic cardiomyopathy, Christine Rootwelt-Norberg and co-authors demonstrated that in a Norwegian cohort of arrhythmogenic cardiomyopathy patients, almost half had experienced life-threatening arrhythmia by last follow-up. Risk of presenting with life-threatening arrhythmia as first disease manifestation was reduced after implementation of genetic testing in Norway in 2007, but was still considerable with close to half of families identified due to arrhythmic events in the proband.

Many arrhythmogenic cardiomyopathy patients end up with an implantable cardioverter defibrillator to prevent sudden cardiac death. However, the selection of patients to receive a defibrillator is highly challenging. During 4 years follow-up in patients without previous life-threatening events, precise risk prediction was achieved by applying a risk prediction model including exercise history, T-wave inversions on ECG and cardiac dysfunction by echocardiographic strain imaging.

Previous studies have reported worse outcome in male than in female arrhythmogenic cardiomyopathy patients. Rootwelt-Norberg and co-authors demonstrated more penetrant disease and worse phenotype in males, but this difference was confounded by sex differences in exercise habits. After implementation of exercise restrictions, disease progression was similar between the sexes. The studies of this thesis improve the understanding of disease manifestations of arrhythmogenic cardiomyopathy and provide new data relevant to risk stratification in clinical practice.



## SITE VISIT FROM THE RESEARCH COUNSIL OF NORWAY, Sept 30<sup>th</sup> 2022

The research council visited ProCardio on Sept 30<sup>th</sup>, 2022 at the center's locations at Oslo University Hospital (OUS). The purpose of a site visit is to make a review of the development and work in the center and of the ongoing plans. Johan Borge (department director HEALTH), Renate Simonsen (Senior adviser, case manager) and Liv Jorunn Jenssen (Special adviser, SFI coordinator) participated from the Research Council and SFI ProCardio was represented by the leadership, one representative from each partner and Topic leaders. Furthermore, we had the OUS vice-director of research showing the commitment from OUS.

We had a day of presentations leading up to fruitful discussions throughout the day as follows:

Responsible I	Description
<b>Kristina Haugaa</b> , Center leader	<ul> <li>Welcome</li> <li>Objectives, strategies, research plan</li> <li>International cooperation</li> <li>Budget and finances</li> </ul>
Thor Edvardsen, dissemination manager and Maria Rud, Admin coordinator	<ul> <li>Communication plan, website, profiling, and recruitment:         Achievements from 2022 were presented with scientific articles, and conference presentations. ProCardio's website is well visited (www.heart-sfi.no) and the center is active on Twitter with the account "ProCardioSFI". There is fluidity in the staff and there have been many new employees since the start.     </li> <li>Data management plan.</li> </ul>
<b>Eigil Samset</b> , Chair of Board, WP3	<ul> <li>Cooperation between partners, organization, governance, and management.</li> </ul>
Sebastian Sarvari, T5 leader Jorun Tangen, PhD candidate Linda Tangen Aaserud,	Presentations of research projects by ProCardio researchers.  Dashboard for cardio-oncology  Marcius Strain  NeuECG
PdD candidate	Tour of Rikshospitalet – Outpatient clinic - Domus Medica
<b>Maria Rud,</b> Admin coordinator	<ul> <li>Review of self-evaluation Areas for improvement:</li> <li>Mobility between the center's partners</li> <li>Routines for data management; active data management plan</li> <li>Work and routines for defining, mapping and following up research results with innovation potential.</li> </ul>
<b>Lillian Kramer-Johansen</b> Vice-Director of Researc OUS.	, Role and responsibilities of the host institution
Research council: Johan Borge, Renate Simonser Liv Jorunn Jenssen	Reflections and feedback
Everyone	Open dialogue and questions



#### After the visit the The Research Council summarized their view on ProCardio as follows:

SFI ProCardio has had a great start and is well organized with a competent board. Finances and reporting are under control. The partners in the center work well with the various work packages and research themes. The annual work plans are written with contribution from the entire center and are thus firmly anchored in the consortium.

The center has a good and deliberate plan for data management. Challenges with sharing data between partners is a national problem due to GDPR.

SFI ProCardio shows increasing awareness of innovation, and the center is a central and important part of Oslo University Hospital's (OUS) innovation initiative.

Recruitment of research fellows is well underway and the international collaboration is extensive. Visibility is good through the center website, a nice annual report and a strategy for communication. "World Heart Day", Sept 29th can be used to showcase SFI ProCardio.





The Norwegian research council visiting the Outpatient clinic at Department of Cardiology led by Kristina Haugaa. This is where the SFI plaquette is located. Many of the patients included in ProCardio's projects are recruited from the outpatient clinic.

From left to right: Johan Borge, Liv Jorunn Jenssen, Renate Simonsen, and Kristina Haugaa.

## **HIGHLIGHTS**



patients with cardiac laminopathies—External validation of the LMNA-risk ventricular tachyarrhythmia calculator 🧐

Timing of cardioverter-defibrillator imp

More than 50 scientific articles related to ProCardio were published in 2022. Over 70 dissemination activities took place and a few book chapters were also written.









The ProCardio Spring workshop was arranged at Rikshospitalet in April 2022.

The day included brief reviews from different partners on their projects and progress in ProCardio, followed by group work. Here, some focused on written work, others on new hands-on technology. Several new ideas were brought forward.







The ProCardio Fall meeting was held at Holmen Fjord Hotel, with scientific sessions to discuss the latest advancements in heart disease and

artificial intelligence. Highlights included the launch of the FLECAPRO clinical trial for patients with mitral valve prolapse, and new advancements in high frame rate ultrasound technology and automated valve tracking techniques. We celebrated the retirement of distinguished ultrasound engineer Gunnar Hansen, and held a highly competitive quiz competition. We also had the chance to discuss and develop startup company ideas in an entrepreneurship session held by Eigil Samset from GE HealthCare.



Center director Kristina Haugaa was installed as professor at Karolinska Institutet, Stockholm.

Gabriel Balaban presented shape modeling results at an awarded oral presentation at the Computing in Cardiology Conference in September 2022 in Tampere, Finland.

Marianne Forså and Eivind Aabel from ProCardio won the prizes for best abstract at the 20th Annual Norwegian Symposium on Heart Research. Marianne won in the category "Exercise, prevention and diagnostics", and Eivind in the category "Genetics and arrhythmias".





Esra Kaya, guest researcher at ProCardio, won the award for best abstract at the Cardiological Spring Meeting 2022 in Stavanger, with her abstract with results from the ProCardio study dealing with the use of ultrasound in patients with heart valve disease.



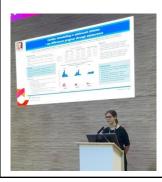
Helge Skulstad has been part of the working group for the new European guidelines for cardiac assessment of patients before and after surgery, published in the European Heart Journal (EHJ).



Kristina Haugaa has been part of the working group for the new European guidelines for cardiac arrhythmia and sudden death, published in the European Heart Journal (EHJ).











ProCardio actively participated with many lectures and abstract presentations during the European heart congress (ESC congress) in Barcelona in August 2022, the largest heart congress in the world.

#### PROCARDIO MEMBERS IN MEDIA

Faktisk.

Meny.

## Høyere antall hjertedødsfall knyttes ikke til vaksiner

Artikkel Embed artikkel

I 2021 døde det 1000-1500 flere enn forventet. Noen setter den økte dødeligheten i sammenheng med koronavaksinen. Det er det ingen grunn til - men pandemitiltakene kan ha vært medvirkende.



Det døde mellom 1000 og 1500 flere enn FHI hadde forventet i fjor. Det fikk noen til å tro at koronavaksinen var årsaken, noe FHI avviser. Foto: Stian Lysberg Solum / NTB.

Thor Edvardsen er hjertespesialist, professor og avdelingsleder ved Rikshospitalet. Han er ikke overrasket over den økte hjertedødeligheten. Foto: Kristin Ellefsen / OUS.



Thor Edvardsen, Source: Faktisk.no



























ProCardio at Holmenkollstafetten, Source: Collage by center members

## **APPENDIX**

## **Annual Accounts 2022**

Funding	Amount*
The Research Council	8 521
The Host Institution (Oslo University Hospital)	4 378
Research Partners	
University of Oslo	871
Simula Research Laboratory	348
Norwegian University of Science and Technology	1 590
Sørlandet Hospital	-
Baker Heart and Diabetes Institute	109
Enterprise partners	
GE HealthCare	1 937
GE Vingmed Ultrasound	3 656
Medtronic	1 062
Sesam AS	245
DIPS AS	1 600
Other Public Funding	4 863
Total	29 180

Costs	Amount*
The Host Institution (Oslo University Hospital)	13 800
Research Partners	
University of Oslo	871
Simula Research Laboratory	2 291
Norwegian University of Science and Technology	3 470
Sørlandet Hospital	139
Baker Heart and Diabetes Institute	109
Enterprise partners	
GE HealthCare	1 937
GE Vingmed Ultrasound	3 656
Medtronic	1 062
Sesam AS	245
DIPS AS	1 600
Total	29 180

### **Personnel**

Key Researchers			
Name	Institution	Main research area	
Kristina Hermann Haugaa	OUS	Cardiomyopathies, Cardiogenetics	
Thor Edvardsen	UiO	Cardiac imaging	
Helge Skulstad	OUS	Cardiac imaging	
Eigil Samset	GE	Data integration & platform development	
Sebastian Sarvari	OUS	Cardiac imaging, Cardiooncology	
Øyvind Haugen Lie	OUS	Athletes and arrhythmias	
Morgan Jakobsen	GE	Data integration & platform development	
Attila Vojtek	GE	Data integration & platform development	
Olivier Gerard	GE Vingmed	Data integration & platform development	
Jurica Sprem	GE Vingmed	Data integration & platform development	
Sten Roar Snare	GE Vingmed	Data integration & platform development	
Benjamin Fermann	GE Vingmed	Data integration & platform development	
Gunnar Hansen	GE Vingmed	Data integration & platform development	
Bård Moseng	GE Vingmed	Data integration & platform development	
Molly Maleckar	Simula	Simulation-based data augmentation and therapy optimization	
Joakim Sundnes	Simula	Simulation-based data augmentation and therapy optimization	
Samuel Wall	Simula	Simulation-based data augmentation and therapy optimization	
Gabriel Balaban	Simula	Simulation-based data augmentation and therapy optimization	
Hermenegild Arevalo	Simula	Simulation-based data augmentation and therapy optimization	
Trond Bertil Barstad	Sesam	Data integration & platform development	
Stein Håvard Pedersen	Sesam	Data integration & platform development	

Liv Bollvåg	DIPS	Data integration & platform development	
Bjørn Fjugstad	DIPS	Data integration & platform development	
Lasse Løvstakken	NTNU	Data science and machine learning	
Håvard Dalen	NTNU	Data science and machine learning	
Bjørnar Grenne	NTNU	Data science and machine learning	
Kristian Hveem	NTNU	Data science and machine learning	
Harald Brunvand	SS	Coronary artery disease	
Daniela Melichova	SS	Cardiomyopathies	
Pål Haugar Brekke	OUS/DIPS	Data integration & platform development	
Richard Cornelussen	Medtronic	Biomedical engineering	
Per Christiansen	Medtronic	Biomedical engineering	
Mirco de Melis	Medtronic	Biomedical engineering	
Anders Milch	Medtronic	Biomedical engineering	
Gunnar Morne	Medtronic	Biomedical engineering	
Kaspar Broch	OUS	Cardiac imaging, Heart failure	
Darian Rijbic	OUS	Cardiac imaging, Myocardial function	
Richard Massey	OUS	Cardiac imaging, Heart failure	
Lars Aaberge	OUS	Invasive cardiology, Acute cardiovascular care	
Thomas Helle Valle	OUS	Cardiac imaging, Myocardial function	
Finn Hegbom	OUS	Electrophysiology	
Mette-Elise Estensen	OUS	Cardiac imaging, Women's heart	
Klaus Mubræch	OUS	Cardiac imaging	
Christian Eek	OUS	Invasive cardiology, Acute cardiovascular care	
Njord Nordstrand	OUS	Acute cardiovascular care, Heart failure	
Kari Melberg	OUS	Cardiac imaging, Cardiomyopathy	
Jan Otto Beitnes	OUS	Cardiac imaging, Heart failure	
Lars Dejgaard	OUS	Electrophysiology	
Stian Ross	OUS	Electrophysiology	
Erik Kongsgård	OUS	Electrophysiology	
John Aalen	OUS	Cardiac imaging, Myocardial function	
Torbjørn Holm	OUS	Electrophysiology	
Kristin Nordvoll	OUS	Cardiogenetics	
Elin Bjurstrøm	OUS	Cardiogenetics	
Margareth Ribe	OUS	Cardiac imaging, Myocardial function	
Roger Håland	OUS	Cardiac imaging, Myocardial function	
Helen Storaker	OUS	Cardiac imaging, Myocardial function	
Eystein Skjølsvik	OUS	Cardiomyopathies, Cardiogenetics	
Johan Anzueles	OUS	Scientific programmer	
Tom Marwick	Baker institute	Cardiooncology	

Visiting Researchers					
Name	Affiliation	Nationality	Sex M/F	Duration	Topic
Esra Kaya	OUS/UiO	Turkish	F	1 year	Aortic stenosis
Feddo Kirkels	OUS/UiO	Dutch	М	1 week	Imaging and modelling of progression in arrhythmogenic cardiomyopathy
Adrian Wassan	OUS	French	М	7 months	Cardiac imaging and Al

Postdoctoral researchers with financial support from the Centre budget					
Name	Nationality	Period	Sex M/F	Topic	
Nina Hasselberg	Norwegian	01.05.2021- 30.04.2023	F	Disease progression and risk assessment in familial cardiomyopathies and arrhythmogenic mitral valve prolapse	
Gabriel Balaban	Norwegian	01.04.2021 - 28.02.2023	М	Disease progression and risk assessment in familial cardiomyopathies and arrhythmogenic mitral valve prolapse	

Postdoctoral researchers working on projects in the centre with financial support from other sources					
Name	Funding	Nationality	Period	Sex M/F	Topic
Marit Kristine Smedsrud	OUS	Norwegian	01.04.21-28.03.23	F	Early detection of genetic heart diseases – Prevention of sudden cardiac death in children

Name	Nationality	Period	Sex M/F	Topic
Christian Kullmann Five	Norwegian	06.09.2021- 05.09.2024	M	Disease progression and risk assessment in familial cardiomyopathies and arrhythmogenic mitral valve prolapse
Linda Tangen Aaserud	Norwegian	01.11.2021- 31.10.2024	F	Athletes and arrhythmias
Artem Chernyshov	Russian	06.09.2021- 05.09.2024	М	Functional Analysis of the Right Ventricle with Deep Learning
Mali Sæther	Norwegian	01.02.2021- 31.01.2024	F	Cardiooncology
Henrik Agerup Kihdahl	Norwegian	01.01.2022- 31.12.2027	М	Valvular disease, automated measurements, 50% PhD
Sverre Høie	Norwegian	21.11.2022- 20.11.2028	М	Valvular disease 50% PhD
Giulia Monopoli	Italian	16.11.2022- 15.11.2025	F	MAD, image-based diagnostics and mechanistic simulation 100%

Name	Funding	Nationality	Period	Sex M/F	Topic
Kristoffer Andresen	OUS/HSØ	Norwegian	01.06.2020-31.05.2026	М	Triplane speckle-tracking echocardiography of the right ventricle
Marianne Inngjerdingen Forså	OUS/HSØ	Norwegian	05.02.2018-04.12.2023	F	Cardiac remodelling in children and adolescents
Jorun Tangen	OUS/UIO	Norwegian	15.04.20-30.04.2024	F	Improved prediction of clinical outcome in patients with myocardial infarction and heart failure
Mi Nguyen	OUS/	Norwegian	01.12.2020-30.11.2023	F	Outcome after myocardial infarction
Alessia Quattrone	OUS/HSØ	Italian	01.02.2017-01.03.2021	F	Risk stratification in adults operated for tetrelogy of Fallot
Christine Rootwelt-Norberg	UiO/NFR/E U	Norwegian	01.05.2019-16.02.2023	F	Prevention of sudden cardiac death – Patient tailored recommandations in arrhythmogenic cardiomyopathy and long QT syndrome
Eivind Westrum Aabel	UiO/NFR	Norwegian	01.01.2020-28.02.2023	M	Arrhythmias and cardiomyopathies
Isotta Castrini	UiO/NFR	Italian	01.08.2019-31.03.2023	F	ARVC in pregnancy
Tove-Elizabeth Hunt	OUS/HSØ	Norwegian	01.09.2016-31.08.2023	F	Atrial fibrillation and sleep apnea
John Nyberg	NTNU	Swedish	25.08.2021-24.08.2024	M	Automated Measurements of Regional Left Ventricular Strain Based on Echocardiography and Artificial Intelligence in Patients with Ischemic Heart Disease
Lena Myklebust	SRL	Norwegian	01.10.2019-30.11.2023	F	Computational modeling of mitral annular disjunction
Katarina Vlaisaljevic	OUS/FHI	Serbisk	01.03.2022-28.02.2025	F	Covid-19 vaccine associated myocarditis
Benjamin Fermann	GE Vingmed/U iO	Norwegian	01.05.2020-30.04.2024	М	Noninvasive analysis of cardiac function using automated workflows
Müjde Akdeniz	GE Vingmed/ MARCIUS	Turkish	01.04.2020-31.03.2023	F	Pattern recognition of functional disease characteristics
Cristiana Tiago	GE Vingmed/ MARCIUS	Portuguese	01.03.2020-28.02.2023	F	Fully Automatic Anatomical and Functional Analysis of the Left Ventricle in 3D Echocardiography using Deep Learning

Master degrees						
Name	Sex M/F	Period	Topic			
Sigurd Zha	М	09.01.2020- 01.01.2023	Deep learning for automated left ventricular outflow tract diameter measurements in 2D echocardiography			
Magnus Rogstadtjernet	М	01.09.2019- 31.08.2022	Deep learning for automated left ventricular outflow tract diameter measurements in 2D echocardiography			

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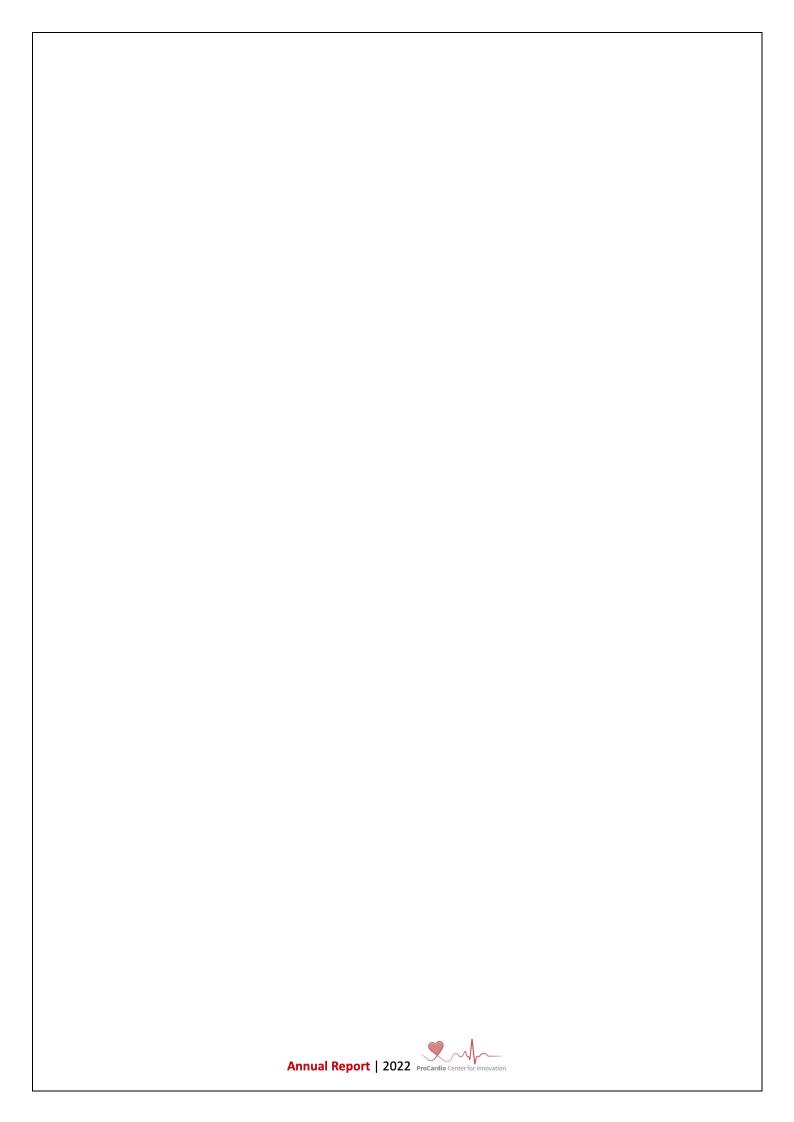
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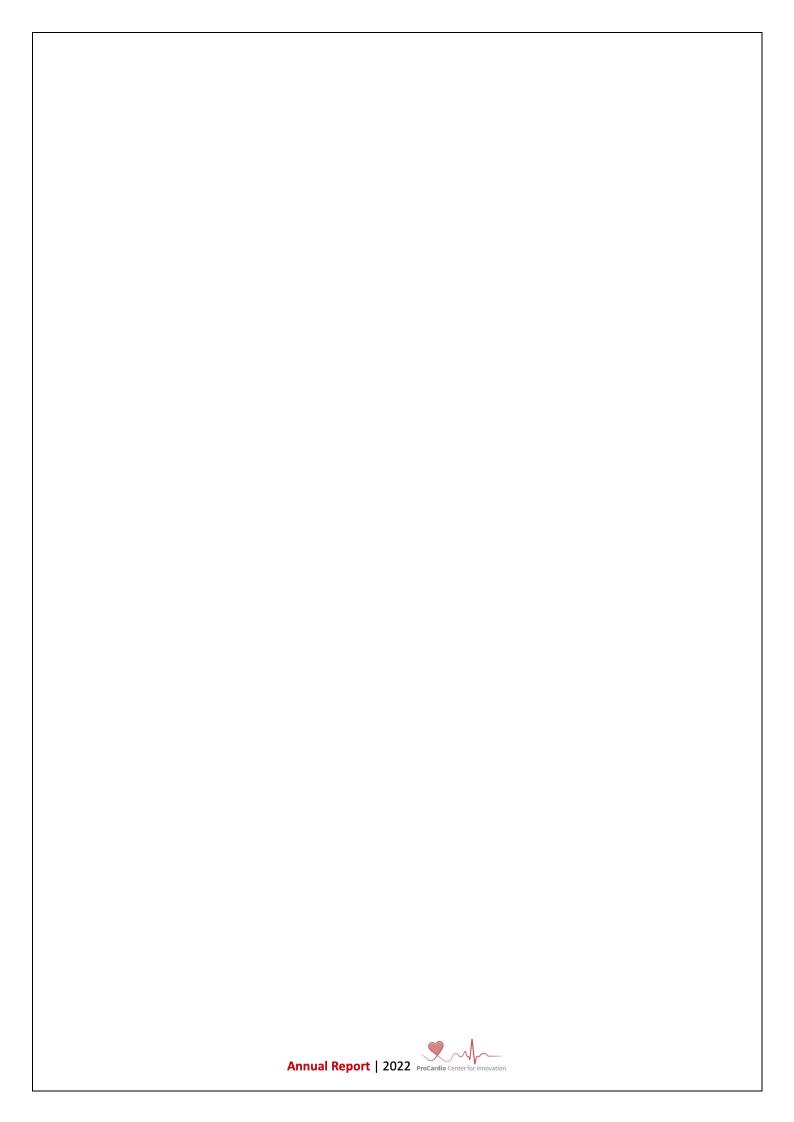
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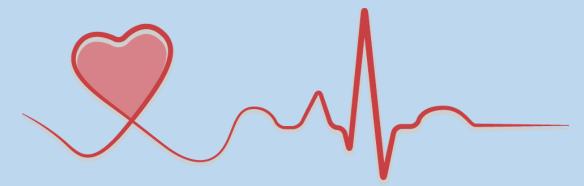
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