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Evaluation of a new 3D cardiac MRI sequence for the identification of myocardial scars and fibrosis

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Registration date 20/04/2021	**Overall study status** Completed	[_] Statistical analysis plan [_] Results
Last Edited 10/05/2021	**Condition category** Circulatory System	[_] Individual participant data [_] Record updated in last year

Plain English summary of protocol

Background and study aims
Scars and fibrotic changes in the heart muscle (myocardium) are important risk factors for cardiovascular events, especially cardiac arrhythmias (irregular heartbeat). The aim of this study is to evaluate a new 3D cardiac MRI sequence to assess scarring and fibrosis in all four heart chambers with a high spatial resolution, and their significance for the occurrence of arrhythmias.

Who can participate?
Patients referred for a cardiac MRI scan with a specific clinical indication (for example significant coronary artery disease [CAD], myocarditis, cardiomyopathy)

What does the study involve?
First, the researchers investigate the quality and capability of a new 3D sequence to detect myocardial scars in the left chamber of the heart in CAD and myocarditis as compared to the current 2D "gold standard". Second, they expand the evaluation of scar/fibrosis detection to the left atrium (important in atrial fibrillation, a highly common cardiac arrhythmia in older age) and the right ventricle (important in some cardiomyopathies with ventricular arrhythmias). Finally, the researchers will investigate the detectability of thrombus (blood clot) in the left atrial appendage, as this is an important risk factor for cardio-embolic strokes.

What are the possible benefits and risks of participating?
Benefits in the long run include providing higher spatial resolution images of the heart with the ability to detect more fine-grained structural changes. There are no specific risks to the study as only patients with an already existing need for a cardiac MRI (including the application of contrast agent) are included; the evaluation of the new 3D sequence adds another 7-12 minutes of scanning time, i.e., patients need to stay this amount of time longer in the MR scanner.

Where is the study run from?
The study is run as part of research of the Working Group of Cardiac MRI (Head: Prof. J. Schulz-Menger) of the Experimental and Clinical Research Center (a joint cooperation between the Charité MedicalFaculty and the Max-Delbrück Center for Molecular Medicine and HELIOS

Hospital Berlin-Buch, Germany) and conducted at the Cardiac MR facility of the HELIOS Hospital Berlin-Buch (Germany)

When is the study starting and how long is it expected to run for?
July 2018 to December 2024

Who is funding the study?
HELIOS Hospital Berlin-Buch (Germany)

Who is the main contact?
Dr Thomas Grandy
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Contact information

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Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Protocol serial number
3000200

Study information

Scientific Title
Delineation of myocardial scar or fibrosis with high spatial resolution by means of cardiac MRI – validation and application of a 3-dimensional compressed sensing (3DCS) sequence

Acronym
3DCS LGE

Study objectives
1. A new prototype 3DCS sequence for the detection of late gadolinium enhancement (LGE) is equivalent to an established sequence in clinical routine in detecting myocardial scar/fibrosis in coronary artery disease and myocarditis
2. A new prototype 3DCS sequence for the detection of provides:
2.1. Delineation of myocardial scar/fibrosis in the left atrium and right ventricle
2.2. Allows risk stratification regarding the occurrence of arrhythmic events
3. A new prototype 3DCS sequence allows detection of thrombus in the left atrial appendage

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 16/08/2018, Charité University Medicine ethics board (Charitéplatz 1, 10115 Berlin, Germany; +49 (0)30 450 517 222; ethikkommission@charite.de), ref: EA1/111/18

Study design
Single-center study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Myocardial scarring and fibrosis and its role in cardiovascular risk stratification

Interventions
Patients recruited for this study will undergo in addition to their clinical cardiac MRI examination one additional image acquisition sequence (3DCS LGE).

1. Data quality, scar size, scar localization, and signal-(contrast-)to-noise ratios will be compared between the clinical routine images and the 3DCS images (via parametric/non-parametric tests – Mann-Whitney-U, Student’s t, Spearman/Pearson correlation depending on scale properties and distribution of the data).

2. Qualitative and semi-quantitative description of scar in the left atrium and right ventricle (currently no gold-standard for quantification of scar in these structures) and development of manual, semi-automatic, and automatic tools for the segmentation of scar; prospective assessment of the ability of risk stratification by scar size for the (re-)occurrence of arrhythmias ("survival"/Kaplan-Meier estimates).
3. Investigation of the sensitivity and specificity of a new 3DCS LGE sequence to detect thrombus in the LAA, comparison to data from transoesophageal echocardiography.

Intervention Type
Procedure/Surgery

Primary outcome(s)
1. Image quality of the LGE images (short axis [SAX] package, 2D gold standard and 3DCS) visually assessed using a 4-point Likert scale at baseline
2. Scar/fibrosis volume or weight (ml or g) and fraction of the overall myocardial mass (in %) measured by means of manual segmentation of images of the "gold standard" sequence and images from a new 3DCS sequence at baseline
3. Signal/contrast-to-noise ratios estimated by means of manual selection of voxels representing myocardium, scar and blood pool, measured at baseline
4. Scar identified/segmented manually and automatically using (1) for LV: cvi42 with manual segmentation of endocardial/epicardial contours in the SAX images and (a) "full width half maximum" calculation relative to ischemic scar areas or (cf. Flett et al. 2011, JACC: CVI; doi: 10.1016/j.jcmg.2010.11.015) or (b) identification of myocarditis-scars by identifying areas of myocardium with higher signal intensity than 3 standard deviations from the distribution of signal intensities of normal myocardium (cf. Mühlberg et al. 2018, JCMR; doi: 10.1186/s12968-018-0434-2); and (2) using methods for automatic LA-segmentation and fibrosis-detection as described in Razeghi et al. 2020 (doi: 10.1016/j.softx.2020.100570) at baseline
5. Time to occurrence and frequency of occurrence of arrhythmias assessed using ECG documentation and Holter monitoring at 3 months and 6 months after baseline
6. Existence or absence of thrombus in the LAA assessed via visual inspection of the acquired images at baseline

Key secondary outcome(s))
1. Acquisition time for the new 3DCS sequence measured using the timestamps of the MR sequences (in sec) at baseline
2. Region-specific analyses of scar quantification and region-specific analysis of signal/contrast-to-noise ratios in the LV conducted using the above-mentioned scar quantification methods with subdividing the myocardium of the LV into six circular segments referenced to the anterior RV-insertion and three longitudinal segments (basal, midventricular, apical) at baseline
3. Long-term follow up of the occurrence of arrhythmias using ECG documentation and Holter monitoring after 1 year

Completion date
31/12/2024

Eligibility

Key inclusion criteria
Referral for cardiac MRI with clinical indication:
1. Existence of scar due to myocardial infarction or fibrosis due to myocarditis
2. (Paroxysmal) atrial fibrillation and referral for first pulmonary vein isolation; referral for the

evaluation of A(RV)C
3. LAA thrombus and indication for cardiac MRI

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
Relative and absolute contraindication for (cardiac) MRI

Date of first enrolment
01/08/2018

Date of final enrolment
31/12/2022

Locations

Countries of recruitment
Germany

Study participating centre
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Universitätsmedizin Charité Berlin, Campus Buch
Experimental and Clinical Research Center
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13125

Study participating centre
Helios Klinikum Berlin Buch
Schwanebecker Chaussee 50
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Sponsor information

Organisation
Charité

ROR
https://ror.org/001w7jn25

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
HELIOS Hospital Berlin-Buch

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Thomas Grandy (thomas.grandy@helios-gesundheit.de). Type of data that will be shared: anonymized DICOM data. Data will become available upon request after publication regarding the main study hypotheses; data sharing has to obey legal requirements in Germany and the EU. Consent of participants (with few exceptions) for data storage and secondary analyses was obtained.

IPD sharing plan summary
Available on request