

# Multi-centre MRI study of the heart microstructure in healthy volunteers

<b>Submission date</b> 30/04/2025	<b>Recruitment status</b> Not yet recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
<b>Registration date</b> 12/05/2025	<b>Overall study status</b> Ongoing	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 02/12/2025	<b>Condition category</b> Circulatory System	<input type="checkbox"/> Individual participant data <input checked="" type="checkbox"/> Record updated in last year

## Plain English summary of protocol

### Background and study aims

Cardiac diffusion tensor imaging (cDTI) is an emerging magnetic resonance imaging (MRI) based technique for examining the microstructure of the heart. The cardiac function and microstructure are highly interconnected. The adult heart comprises more than a billion heart muscle cells that are intricately connected and that contract in a highly coordinated manner to support the beating of the heart. Changes to the heart microstructure are an important feature in conditions such as heart attack or myocardial infarction (MI) and hypertrophic cardiomyopathy (HCM), where the heart muscle wall thickens. For example, an increase in collagen and scar following changes in microstructure following MI, and cell disarray in HCM, which can be assessed with cDTI. The microscopic displacement of water molecules due to diffusion is heavily influenced by the presence of cells and by the properties of these cells such as size, shape, orientation, integrity and so forth. Thus, by encoding the water diffusion information in the MRI image, one can evaluate the cardiac microstructure. In cDTI, several diffusion directions are encoded and then diffusion tensors (a mathematical model that can be pictured in 3D as an American football in shape) are fitted. From the diffusion tensor, several quantitative values can be derived such as the mean diffusivity (MD) that describes the average apparent diffusion, the fractional anisotropy (FA) that describes how pointed the tensor is, and the helix angle (HA) and sheetlet angle (E2A) that reflect the orientations of the heart muscle cells and their arrangement in sheetlets.

The links between the diffusion tensor and cardiac microstructure have been verified in numerous preclinical ex vivo and in vivo studies. Early clinical studies have reported diffusion parameters in the pathologic heart. In particular, higher myocardial MD and lower FA have been reported in pathologies such as MI, HCM and aortic stenosis (AS). Similarly, differences in HA and E2A angles have been reported in conditions such as MI, HCM, AS and dilated cardiomyopathy (DCM). This is thought to be related to the underlying changes in the cardiac microstructure. The field of cardiac diffusion MRI remains technologically challenging due to a number of factors such as motion from the heart beating and breathing, distorted images and long scan times. Nonetheless, the field has been rapidly expanding over the past years, with publications in cDTI more than doubling over the decade up to 2020, and whole-heart cDTI within clinically feasible scan times looks increasingly likely to be achievable within the foreseeable future.

The study aims to:

1. Evaluate variation in cDTI data due to differences in (i) site/operator/scanner, (ii) subject, (iii)

acquisition and (iv) post-processing methods.

2. Identify the greatest sources of variation and inform strategies for optimisation, standardisation and harmonisation of cDTI.

3. Inform power calculations and data interpretation in future larger studies, in particular, where different sites/methods are used.

Who can participate?

Healthy volunteers aged 18 to 65 years old with a body mass index (BMI) of 18.5 to 29.9 kg/m<sup>2</sup>.

For the travelling volunteer study: Ability to travel independently between sites and to have all scans done within 2 months from first scan; possession of valid documentation (e.g. passport and visa) to travel between sites with validity extending to at least 8 months following first MRI scan, and with a passport no older than 10 years at the time of the last scan.

What does the study involve?

Non-travelling healthy volunteers will be identified, approached and recruited by non-travelling volunteer sites in accordance with site-specific ethics for sites outside the UK. Non-travelling volunteers will only be consented under the respective site-specific ethics. These are non-NHS sites and non-HRA-relevant.

Travelling volunteers will be recruited and consented by the study team at Royal Brompton Hospital to travel to multiple sites for a single MRI scan at each site. Potential volunteers who express interest in participating will be sent the participant information sheet (PIS) and research volunteer checklist. Before consent/scan, volunteers who wish to participate in the study will be asked to complete and return the research volunteer checklist for the study team to assess eligibility. Participants who meet eligibility requirements and are interested in participation will be invited to provide written consent. Consent will also be sought for the sharing and storing of personal information for study oversight, scan scheduling, safety monitoring, booking travel and reimbursement.

Volunteers will be invited to undergo a single MRI examination at each site. Before each scan, the participant's height and weight will be measured. A site-specific MRI screening questionnaire shall be completed to help ensure safety in the MRI scanner. The MRI scan will typically last between 60 to 90 minutes. Surface electrodes (stickers) will be placed on the chest to monitor heart beat during the scan.

What are the possible benefits and risks of participating?

This study is done solely for research purposes and participants will not benefit from taking part. Their participation may, however, benefit future care. The scans will be for research purposes only and cannot be used for clinical diagnosis.

MRI is safe and no ionising radiation (energy that can potentially cause damage to cells) is used for this scan. There are no known risks from the technique. Some people may experience claustrophobia (fear of confined spaces). The MRI staff will do all that they can to make participants feel comfortable during the scan. Participants may withdraw from the study at any time. For travelling volunteers, there is a small risk associated with travel. Participants are asked to highlight any concerns they may have about such travel. Travel and accommodation will be arranged through reputable vendors, and participants will be kept updated on any travel advisories at the time.

Where is the study run from?

This is an international multi-centre initiative, initiated by the Society of Cardiovascular Magnetic Resonance Cardiac Diffusion Special Interest Group. The Project Management Committee responsible for taking decisions on the study has members based in Switzerland, the UK and the USA.

When is the study starting and how long is it expected to run for?  
July 2024 to August 2029

Who is funding the study?  
Investigator initiated and funded

Who is the main contact?  
Dr Irvin Teh, i.teh@leeds.ac.uk

## Contact information

**Type(s)**  
Scientific, Principal investigator

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Public

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## Additional identifiers

**Clinical Trials Information System (CTIS)**  
Nil known

**Integrated Research Application System (IRAS)**  
343837

**ClinicalTrials.gov (NCT)**

Nil known

**Protocol serial number**

Nil known

## Study information

### Scientific Title

Multi-centre investigation of cardiac diffusion tensor imaging (DTI) in healthy volunteers by SCMR Cardiac Diffusion Special Interest Group NETwork

### Acronym

SIGNET

### Study objectives

There exists a wide range of reported diffusion tensor imaging (DTI) metrics in the literature, including reports that are potentially artifactual, which have been previously highlighted. This will be influenced by the subject cohort, e.g. health vs disease. Other potential sources of variation include differences in sites/operators/scanners, acquisition and post-processing methods. This variation needs to be better understood to support clinical validation of the technique.

Early work has evaluated reproducibility in a ten-site study in isotropic phantoms and in a two-site study in healthy volunteers. In this study, we propose a broad multi-centre collaborative effort to evaluate inter-site variation due to differences in (i) site/operator/scanner, (ii) acquisition and (iii) post-processing methods. The results will guide the interpretation of the cardiac diffusion MRI literature, and help to refine strategies for standardisation and harmonisation of protocols. We propose in the first instance to study healthy volunteers to establish a baseline of variation due to technical (non-pathology related) factors.

### Ethics approval required

Ethics approval required

### Ethics approval(s)

approved 31/07/2024, University of Leeds School of Medicine Research Ethics Committee (SoMREC) (Worsley Building, University of Leeds, Leeds, LS2 9JT, United Kingdom; -; FMHUniEthics@leeds.ac.uk), ref: MREC 23-027

### Study design

Multi-centre prospective observational study

### Primary study design

Observational

### Study type(s)

Diagnostic

### Health condition(s) or problem(s) studied

Evaluation of cardiac microstructure with cardiac DTI

## **Interventions**

Single MRI scan for non-travelling volunteers

Single MRI scan for travelling volunteers at each site, over multiple sites

Non-travelling healthy volunteers will be identified, approached and recruited by non-travelling volunteer sites in accordance with site-specific ethics for sites outside the UK. Non-travelling volunteers will only be consented under the respective site-specific ethics. These are non-NHS sites and non-HRA-relevant.

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## **Intervention Type**

Other

## **Primary outcome(s)**

Cardiac DTI data including mean diffusivity, fractional anisotropy, helix angle and E2 angle. For non-travelling volunteers, these will be acquired at baseline. For travelling volunteers, these will be acquired at all travelling volunteer sites within 2 months of baseline.

## **Key secondary outcome(s)**

Signal-to-noise ratio and potential non-compliance of scans with the protocol collected during each scan

## **Completion date**

31/08/2029

## **Eligibility**

### **Key inclusion criteria**

1. Healthy volunteer
2. Male or female; sites shall aim to recruit equal numbers, i.e. male (n = 6) / female (n = 6)
3. Age 18 to 65 years old
4. Body mass index (BMI) 18.5 to 29.9 kg/m<sup>2</sup>
5. For travelling volunteer study: Ability to travel independently between sites, and to have all

scans done within 2 months from first scan; possession of valid documentation (e.g. passport and visa) to travel between sites with validity extending to at least 8 months following first MRI scan, and with passport no older than 10 years at time of last scan.

**Participant type(s)**

Healthy volunteer

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Lower age limit**

18 years

**Upper age limit**

65 years

**Sex**

All

**Total final enrolment**

0

**Key exclusion criteria**

1. Safety or clinical concerns precluding participation
2. Any history of health conditions that may affect the heart (e.g. hypertension, diabetes, arrhythmias, angina, myocardial, valve and vessel disease)
3. Pregnancy or breastfeeding, including suspected pregnancy
4. Claustrophobia that limits/prevents participants from remaining in the MRI scanner
5. Inability to lie flat on the scanner table
6. Physical frailty
7. Contraindications to MRI (some pacemakers, intraorbital debris, intraauricular implants, intracranial clips, etc)
8. Those who could be considered to have a particularly dependent relationship with an investigator, e.g. members of staff or students
9. Involvement with the research apart from volunteering
10. Any relevant health conditions precluding safe travel between sites within 2 2-month time frame (For travelling volunteer study)

**Date of first enrolment**

15/01/2026

**Date of final enrolment**

31/05/2026

**Locations****Countries of recruitment**

United Kingdom

England

Wales

Belgium

Denmark

France

Japan

Poland

Switzerland

United States of America

**Study participating centre**

**Barts Health NHS Trust**

The Royal London Hospital

80 Newark Street

London

England

E1 2ES

**Study participating centre**

**Cardiff University Brain Research Imaging Centre**

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Cardiff

Wales

CF24 4HQ

**Study participating centre**

**Royal Brompton Hospital**

Sydney Street

London

England

SW3 6NP

**Study participating centre**

**University College London**  
Gower Street  
London  
England  
WC1E 6BT

**Study participating centre**  
**University of Leeds**  
Woodhouse Lane  
Leeds  
England  
LS2 9JT

**Study participating centre**  
**University of Oxford**  
University Offices  
Oxford  
England  
OX1 2JD

**Study participating centre**  
**Aarhus University Hospital**  
Aarhus  
Denmark  
8200

**Study participating centre**  
**Beth Israel Deaconess Medical Center**  
Boston  
United States of America  
MA 02215

**Study participating centre**  
**Boston Children's Hospital**  
Boston  
United States of America  
MA 02115

**Study participating centre**



**Brussels University Hospital**  
Brussels  
Belgium  
1090 Jette

**Study participating centre**  
**Cleveland Clinic**  
Cleveland  
United States of America  
OH 44195

**Study participating centre**  
**Copenhagen University**  
Copenhagen  
Denmark  
1172 København

**Study participating centre**  
**CREATIS-Lyon**  
Lyon  
France  
69100 Villeurbanne

**Study participating centre**  
**Emory University**  
Atlanta  
United States of America  
GA 30322

**Study participating centre**  
**ETH Zurich**  
Zurich  
Switzerland  
8092 Zürich

**Study participating centre**

**Geneva University Hospital**  
Geneva  
Switzerland  
1205 Genève

**Study participating centre**  
**Hokkaido University Hospital**  
Hokkaido  
Japan  
060-8648

**Study participating centre**  
**Live Healthy Imaging**  
Houston  
United States of America  
TX 77401

**Study participating centre**  
**Medical University of Gdansk**  
Gdansk  
Poland  
80-210

**Study participating centre**  
**Massachusetts General Hospital**  
Boston  
United States of America  
MA 02114

**Study participating centre**  
**National Heart, Lung, and Blood Institute - Medstar Washington Hospital**  
Bethesda  
United States of America  
MD 20892

**Study participating centre**

**Poznan University of Medical Sciences**

Poznan

Poland

61-701

**Study participating centre****Rigshospitalet**

Copenhagen

Denmark

2100 København

**Study participating centre****Stanford University**

Stanford

United States of America

CA 94305

**Study participating centre****Texas A&M University**

Houston

United States of America

TX 77840

**Study participating centre****University of Bordeaux**

Bordeaux

France

33076

**Study participating centre****Imelda Hospital**

Bonheiden

Belgium

2820 Bonheiden

**Sponsor information**

## Organisation

University of Leeds

## ROR

<https://ror.org/024mrxd33>

## Funder(s)

### Funder type

Other

### Funder Name

Investigator initiated and funded

## Results and Publications

### Individual participant data (IPD) sharing plan

The datasets generated during and/or analysed during the current study will be stored in a publicly available repository.

Anonymised research data will be made available by UoL to the research community for the current study and future research as governed by the Collaboration Agreement.

Access to publicly available data by third parties will be governed by an agreement with an End User / Data Sharing Agreement.

### IPD sharing plan summary

Stored in publicly available repository

### Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<a href="#">Protocol article</a>		25/08/2025	02/12/2025	Yes	No
<a href="#">Study website</a>		11/11/2025	11/11/2025	No	Yes