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Using advanced MRI to explore metabolism and tissue structure in multiple sclerosis (MISSION MIMS)

Submission date
16/11/2023

Recruitment status
Recruiting

Registration date
21/11/2023

Overall study status
Ongoing

Last Edited
10/12/2025

Condition category
Nervous System Diseases

[_] Prospectively registered
[X] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Background and study aims
Multiple sclerosis (MS) is a brain degenerative condition caused by immune system changes. Magnetic Resonance Imaging (MRI) with contrast injection is the current standard for detection. In our study, we aim to use two new MRI techniques, 'Sodium MRI' and 'Carbon MRI,' to assess biological changes in MS-affected brains. Evidence suggests a buildup of 'lactate' in MS areas visible with 'Carbon MRI,' while 'Sodium MRI' images salt level changes. Another aspect of the study involves imaging glucose activity in the brain using Hyperpolarized Carbon and Deuterium MRI techniques. This substudy aims to compare the advantages of each method in measuring fast and slow glucose metabolism in MS patients.

We plan to compare brain images of both MS patients and healthy volunteers to understand normal versus abnormal brain patterns. The goal is to better understand MS-related brain changes, predicting treatment outcomes based on tissue lactate and glucose levels and blood vessel structure.

Who can participate?
Patients aged 18 years or older, with Multiple sclerosis. Healthy volunteers aged 18 years or older.

What does the study involve?
The MRI procedure involves a cylindrical machine with a plastic case over your head. 'Sodium MRI' is like a standard MRI, 'Carbon MRI' includes an injection of a natural sugar compound and 'Deuterium MRI' includes an administration of a sweet drink.
You might be offered an optional scan within 14 days to test the technique's repeatability. Other procedures may include basic health checks, blood tests, and pregnancy tests, conducted with your well-being in mind.
Fasting for up to six hours before a scan may be required.

What are the possible benefits and risks of participating?
Taking part in this study may not directly help you, but it could help doctors find better ways to

check for and keep track of brain tumours without using invasive methods. You will not be paid for taking part, we can cover your travel and parking costs.
MRI Scans: MRI scans are safe and do not involve X-rays or radioactivity. Some people might feel a bit closed-in (claustrophobic) or bothered by the noise, but you will be given earplugs and a squeeze-ball to help you feel more comfortable. The imaging software and hardware used are for research and not yet approved for routine diagnosis.
Incidental Findings: Although the scans are not part of your medical record, if we notice anything unusual, we will consult a specialist who may need to discuss it with you and your doctor.
Cannulation (inserting a small tube into a vein): This is a common procedure and is generally safe, but it might cause some discomfort or bruising at the insertion site. The cannula will be removed immediately after the scan.
Injection containing a substance called pyruvate: The injection is generally safe, with only mild and short-lasting side effects like flushing, feeling hot, dizziness or a metallic taste. Allergic reactions are highly unlikely, but we are prepared to manage any issues that may arise.
Sweet drink containing a substance called deuterated glucose: Glucose is a natural sugar that our body uses for energy, and deuterium is a safe form of hydrogen that is also found naturally in small amounts in our body. Scientists have previously studied water and glucose containing deuterium in people, and they did not find safety concerns. Any potential side effects will be managed by our team.

Where is the study run from?
Cambridge University Hospitals NHS Foundation Trust (UK).

When is the study starting and how long is it expected to run for?
July 2015 to June 2026

Who is funding the study?
Multiple Sclerosis Society (UK)

Who is the main contact?
cuh.radiologyresearch@nhs.net

Contact information

Type(s)
Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
166097

ClinicalTrials.gov (NCT)
Nil known

Central Portfolio Management System (CPMS)
19436

Study information

Scientific Title

Molecular Imaging and Spectroscopy with Stable Isotopes in Oncology and Neurology: Imaging metabolism and tissue structure in Multiple Sclerosis with MRI (MISSION: MIMS)

Acronym
MISSION: MIMS

Study objectives
The distribution of tissue sodium and the physiological metabolism of a glucose breakdown product, pyruvate can be assesed by hyperpolarised 13C-pyruvate MRI and sodium MRI.

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 08/09/2015, NRES Committee East of England - Cambridge South (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)115 883 9428; nrescommittee.eastofengland-cambridgesouth@nhs.net), ref: 15/EE/0255

Study design
Observational physiological imaging study

Primary study design
Observational

Study type(s)
Diagnostic

Health condition(s) or problem(s) studied
Multiple sclerosis

Interventions
Up to 15 patients with MS will be successfully imaged following injection with 13C pyruvate.
Up to 40 healthy volunteers will be successfully imaged following injection with 13C pyruvate. An optional second imaging study up to 14 days later will be offered. Some of these volunteers will be asked to fast for 6 hours prior to the scan taking place.
Up to 30 healthy volunteers will be recruited as part of the deuterium metabolic imaging (DMI) sub-study.
Up to 15 patients with MS will be recruited as part of the deuterium metabolic imaging (DMI) sub-study.

Intervention Type
Other

Primary outcome(s)
Using MRI imaging:
1. 13C. Spatial maps of area under the curve (AUC) timecourse sums of signals from hyperpolarized pyruvate, lactate, and any other metabolites detected, and ratios between these metabolite AUCs. Also estimates of the kinetic rate constants of conversion between injected tracer pyruvate and the metabolites formed (lactate, other). The timecourse typically covers approximately 1 minute beginning approximately 16 seconds after the start of injection.

2. DMI. Spectral peak intensity ratios between deuterated water, glucose, glutamate (brain only), lactate and lipids. These will be either in spatial maps derived from 3D spectroscopic imaging, or in unlocalized spectra from the whole sensitive volume of the coil.

Key secondary outcome(s))
Sensitivity and spatial resolution of carbon-13 imaging of pyruvate and lactate in the human brain as measured by computing the signal-to-noise ratio in images of the area-under-the-curve of the timecourse signals of pyruvate, lactate and bicarbonate.

Completion date
30/06/2026

Eligibility

Key inclusion criteria
MS patients (for C13 and DMI)
1. Be aged 18 years or older.
2. Have a confirmed diagnosis of MS.
3. Be aware of and understand their diagnosis.
4. Be able to provide written informed consent according to ICH/GCP, national and local regulations.
5. Be willing and able to comply with scheduled visits, laboratory tests, imaging and other study procedures.

Healthy volunteers (C13 and DMI)
1. Be aged 18 years or older
2. Be able to provide written informed consent according to ICH/GCP, national and local regulations
3. Be willing and able to comply with scheduled visits, laboratory tests, imaging and other study procedures

Participant type(s)
Healthy volunteer, Patient

Healthy volunteers allowed
Yes

Age group
Mixed

Lower age limit
18 years

Upper age limit
100 years

Sex
All

Total final enrolment

Key exclusion criteria
MS patients (for C13 and DMI)
1. Have uncontrolled diabetes or glucose deranging conditions, or treatment that would cause such effects.
2. Have any medical condition that may increase the risk associated with study participation or in the judgement of the investigators make it unsuitable for the patient to enter the study.
3. Have a known allergy, adverse reaction or contraindication to any of the injected contrast agents used in this study including gadolinium contrast agents or pyruvate.
4. Be otherwise unsuitable for MRI e.g. having a permanent pacemaker, severe obesity or inability to lie still.
5. Be pregnant or breastfeeding

Healthy volunteers (for C13 and DMI)
1. Have uncontrolled diabetes or glucose deranging conditions, or treatment that would cause such effects. The significance of this will be determined by the research team.
2. Have any medical condition that may increase the risk associated with study participation, or in the judgement of the investigators make it unsuitable for the patient to enter the study.
3. Have a known allergy, adverse reaction or contraindication to any of the injected contrast agents used in this study including gadolinium contrast agents or pyruvate.
4. Be otherwise unsuitable for MRI e.g. having a permanent pacemaker, severe obesity or inability to lie still.
5. Be pregnant or breastfeeding
6. Any previous or current neurological condition deemed to be significant by the research team.

Date of first enrolment
30/03/2016

Date of final enrolment
30/04/2026

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
Cambridge Biomedical Campus
Hills Road
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CB2 0QQ

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Not defined

Funder Name
Multiple Sclerosis Society

Alternative Name(s)
mssocietyuk, MS Society UK, Multiple Sclerosis Society UK, Multiple Sclerosis Society of Great Britain and Northern Ireland, The MS Society, MS Society

Funding Body Type
Private sector organisation

Funding Body Subtype
Associations and societies (private and public)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Data requests can be submitted starting 9 months after article publication and the data will be made accessible for up to 24 months. Extensions will be considered on a case-by-case basis. Access to trial IPD can be requested by qualified researchers engaging in independent scientific research and will be provided following review and approval of a research proposal and Statistical Analysis Plan (SAP) and execution of a Data Sharing Agreement (DSA). For more information or to submit a request, please contact cuh.radiologyresearch@nhs.net.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		01/04/2019	19/11/2024	Yes	No
Results article		15/08/2022	19/11/2024	Yes	No
Other publications		15/04/2018	19/11/2024	Yes	No
Other publications		01/02/2018	19/11/2024	Yes	No
Other publications		01/06/2020	19/11/2024	Yes	No
Other publications		18/01/2016	19/11/2024	Yes	No
Other publications		04/09/2017	19/11/2024	Yes	No
Other publications		22/10/2021	19/11/2024	Yes	No
Participant information sheet	C13 Patient Information Sheet version 6.0	06/05/2022	21/11/2023	No	Yes
Participant information sheet	C13 Volunteer Information Sheet version 6.0	06/05/2022	21/11/2023	No	Yes
Participant information sheet	DMI Patient Information Sheet version 6.0	06/05/2022	21/11/2023	No	Yes
Participant information sheet	DMI Volunteer Information Sheet version 6.0	06/05/2022	21/11/2023	No	Yes
Participant information sheet	Participant information sheet version 6.0	11/11/2025	11/11/2025	No	Yes
Protocol file		06/05/2022	21/11/2023	No	No