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An imaging study investigating a new magnetic resonance imaging tracer for cancer detection and cancer treatment monitoring

Submission date
04/09/2023

Recruitment status
Recruiting

Registration date
05/10/2023

Overall study status
Ongoing

Last Edited
20/03/2025

Condition category
Cancer

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The study team is currently investigating the potential of detecting dying cancer cells using a novel imaging technique known as hyperpolarised magnetic resonance imaging (MRI). Patient imaging data will be meticulously analyzed and subsequently compared with tissue samples derived from biopsies obtained from the patient's tumours. This comparative analysis aims to assess the accuracy of this innovative test in identifying cell death. Furthermore, the research seeks to explore whether this new imaging technique can predict the long-term effectiveness of treatment, even at an early stage of the treatment process. The anticipated outcome of this study is the development of enhanced methods for imaging cancer patients and tailoring individualized treatment approaches. The rationale behind this research stems from the fact that while an MRI scanner can capture various tumour characteristics, many of these traits take time to change following the initiation of drug treatment. In contrast, the new technique offers insights into cancer metabolism, which may undergo alterations earlier than the changes detectable through conventional MRI. The team is currently focused on imaging a hyperpolarised molecule called fumarate, which, although not radioactive, exhibits significantly increased signal intensity compared to natural levels. This heightened signal allows the MRI scanner to more effectively identify these molecules within the body. Fumarate undergoes conversion into another molecule in the presence of dead cells, referred to as malate. The team's goal is to leverage the presence of malate as an indicator of deceased tissue.

Who can participate?
Adult patients aged over 18 years old who have been diagnosed with cancerous tumours or masses at the Cambridge University Hospitals (CUH) NHS Foundation Trust, and healthy volunteers to assist in test development and to gain a better understanding of the results obtained from patients

What does the study involve?
This is a first-in-human physiological imaging study conducted in two stages which may run in parallel:
Stage 1 - Injection of 13C-fumarate into healthy volunteers. This may take place either outside of

the MRI scanner in a clinical facility within the Cambridge University Hospitals (CUH) NHS Foundation Trust or within the MRI scanner with dynamic 13C-MRI to optimise the MRI technique in healthy vascularised tissue
Stage 2 - Dynamic 13C-MRI in patients to optimise the MRI technique in malignant tissue
This physiological study will not change the treatment that has been determined for the patients either as part of their standard of care treatment or another study.

What are the possible benefits and risks of participating?
Participation in this study offers several potential benefits. It is expected to contribute to the development of innovative tumour imaging techniques and methods for monitoring treatment response, reducing the need for invasive procedures such as biopsies. Additionally, it holds the promise of enhancing the accuracy of treatment selection, thereby increasing the likelihood of positive health outcomes for patients.

There are potential risks associated with:
MRI
MRI scans do not involve X-rays or radioactivity. There are very few risks associated with having an MRI scan. MRI scanners have been used for the past 25 years on millions of patients worldwide and are considered very safe. Some people (less than 5% or 1 in 20) experience a sense of being closed-in (claustrophobia). The MR system is noisy, but participants will be provided with headphones or earplugs to wear. The participant will be provided with a 'squeeze-ball' alarm, which they are free to use if they feel any discomfort. The radiographer conducting the scan can see and talk with the participant at all times and will stop the scan if necessary.

Cannulation
Placing a small plastic tube (cannula) into a vein can cause some discomfort and very rarely can lead to infection, but this is highly unlikely in the short time it will be in place. Some people may get bruising at the site where the cannula is inserted. This procedure is performed regularly in the hospital and is generally very safe. The cannula will be inserted just before the scan and will be removed immediately afterwards.

Fumarate injection
Although Hyperpolarised Carbon MRI is a new technology, tests up to now with pyruvate (a naturally occurring substance in the body) have demonstrated no significant safety issues. Fumarate is another naturally occurring substance in the body, so is not expected to cause any issues. Although it is unlikely that an allergic reaction or other side effect will occur, there are facilities in place within the MRI unit, and within the hospital, to manage these appropriately.

Other Studies
It is possible that if the participant is already contributing to or plans to contribute to other research studies, being part of this study may cause difficulties for them, the research study and other researchers. The study team will try to limit these difficulties as much as possible. If they are helping with other research studies or plan to and are interested in participating in this study, they need to let the study team know, so that they can discuss this. It is important for them to consider the time and other commitments required to participate in several studies simultaneously. The team are happy to discuss this with them and can also talk with their families if required.

Where is the study run from?
University of Cambridge, School of Clinical Medicine (UK)

When is the study starting and how long is it expected to run for?
February 2018 to June 2027

Who is funding the study?
1. National Cancer Imaging Translational Accelerator (NCITA) (UK)
2. Mark Foundation Institute for Integrative Cancer Medicine at the University of Cambridge (UK)

Who is the main contact?
Dr Marta Wylot, marta.wylot@nhs.net

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-improving-the-quality-of-images-taken-by-an-mri-scan-mission-fumarate

Study website
https://ncita.org.uk/mission-fumarate-study-ncita-exemplar-2/

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
266343

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 266343, CPMS 46873

Study information

Scientific Title
A physiological study of the metabolism of fumarate in cancer using hyperpolarised 13C magnetic resonance imaging

Acronym
MISSION-Fumarate

Study objectives
Animal studies have shown that there is a rapid conversion of 13C-fumarate into 13C malate within tumours compared to normal tissues. This imaging study will acquire dynamic data from human tissues following the injection of hyperpolarised 13C-fumarate and use 13C-MRI to monitor spatial and temporal changes in the ratio of 13C-malate to 13C-fumarate. In this way, this study aims to establish if altered fumarate metabolism is similar between human and animal studies (i.e. proof of concept).

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 22/06/2020, East of England - Essex Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)2071048227; Essex.REC@hra.nhs.uk), ref: 20/EE/0090

Study design
Non-randomized first-in-human physiological imaging study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital, University/medical school/dental school

Study type(s)
Diagnostic

Participant information sheet
Patient information material can be found at: https://ncita.org.uk/wp-content/uploads/2022/11/MISSION-Fumarate-Participant-HV-Information-Sheet-v1.1-1.pdf

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

Interventions
This is a non-randomised, first-in-human physiological imaging study with a study design that will be conducted in two stages which may run in parallel:
Stage 1 - Injection of 13C-fumarate into healthy volunteers. This may take place either outside of the MRI scanner in a clinical facility within the Cambridge University Hospitals (CUH) NHS Foundation Trust or within the MRI scanner with dynamic 13C-MRI to optimise the MRI technique in healthy vascularised tissue;
Stage 2 - Dynamic 13C-MRI in patients to optimise the MRI technique in malignant tissue.
This is a physiological study and will not change the treatment that has been determined for the patients either as part of their standard of care treatment or another study.
For healthy volunteers, any unexpected abnormalities found during any research MRI scans will be discussed with them or their GP by a clinical member of the research team to consider whether further investigations are required. For cancer patients, any unexpected abnormalities found during any research MRI scans will be reported to their clinical team and/or General Practitioner (GP).
Stage 1: Up to 20 healthy volunteers will be injected. Some of these healthy volunteers will be injected outside of an MRI scanner with this endogenous molecule and the remaining will be injected inside the MRI scanner to optimise MRI techniques.
Stage 2: Up to 70 cancer patients will be injected and scanned.

Healthy volunteers are to receive a 13C-fumarate injection inside or outside of the MRI scanner. The doses are as follows: 20 mM (at 0.4 mL/kg, 0.96 mg/kg), 40 mM (at 0.4 mL/kg, 1.92 mg/kg), and 80 mM (at 0.4 mL/kg, 3.84 mg/kg). If there is no MRI signal visible we may increase the highest dose (80 mM) to be administered at 0.6 mL/kg (5.76 mg/kg). Cancer patients are to receive at least one 13C-fumarate injection inside of the MRI scanner at the dose established in stage 1.

Intervention Type
Other

Primary outcome measure
MRI signal of hyperpolarised 13C-fumarate and its metabolite 13C-malate measured using dynamic MRI to study fumarate metabolism in normal tissue and in tumours at one timepoint

Secondary outcome measures
1. Optimal dose of injected hyperpolarised 13C-fumarate to enable the detection of hyperpolarised 13C-malate formation in tumours measured using dynamic MRI at one timepoint
2. Optimise 13C-MRI parameters to provide the optimal hyperpolarised 13C-fumarate and 13C-malate signal-to-noise ratios (SNR) measured using dynamic MRI at one timepoint
3. Correlations between serum fumarate, serum malate, fumarate hydratase (FH) and the MR signal acquired from the dynamic 13C-malate/13C-fumarate MRI data at one timepoint
4. Correlations between tissue expression (archival or fresh tissue) of metabolic and other markers (such as FH) and the MR signal acquired from the dynamic 13C malate/13C fumarate MRI data at one timepoint

Overall study start date
28/02/2018

Completion date
01/06/2027

Eligibility

Key inclusion criteria
All participants:
1. Over 18 years old
2. Able to and provide written informed consent to participate
3. If female, postmenopausal or if women of childbearing potential (WOCBP) using a suitable contraception
4. If male, using a suitable contraceptive method for the duration of the study

Healthy volunteers (Stage 1):
Not on any regular medications (except the oral contraceptive pill) that may impact the study results as determined by the researcher

Cancer patients (Stage 2):
1. Radiologically evaluable disease as established by clinical imaging
2. Capable of undergoing repeat study visits

Participant type(s)
Healthy volunteer, Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
20 healthy volunteers and 70 cancer patients

Key exclusion criteria
The presence of any of the following will preclude participation as determined by the delegated investigator:
1. Contraindication or inability to tolerate MRI
2. Pregnant or actively breast-feeding woman
3. If using an intrauterine contraceptive device (IUCD) as a method of contraception the device should be MRI-safe at 3 T (researcher to confirm)
4. Clinically significant cardiac, pulmonary or neurological diseases as determined by the investigators
5. Laboratory abnormalities that may impact the study results
6. Any other significant medical or psychiatric history rendering the subject ineligible as deemed by the investigators

Date of first enrolment
28/07/2023

Date of final enrolment
01/03/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
Cambridge University Hospitals NHS Foundation Trust
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Sponsor information

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CB2 0QQ
+44 (0)1223 245151
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Sponsor type
Hospital/treatment centre

Website
https://www.cuh.nhs.uk

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Research organisation

Funder Name
National Cancer Imaging Translational Accelerator (NCITA)

Funder Name
Mark Foundation Institute for Integrative Cancer Medicine at the University of Cambridge

Results and Publications

Publication and dissemination plan

Results of primary and final analyses will be shared at scientific meetings by a member of the Study Management Team, and publications of the study results will be written by the Study Team Members, on the basis of the primary and final analyses performed at the University of Cambridge. Draft manuscripts will be submitted by the study coordinators for review no later than six months after having received the final data reports. After revision by the co-authors, manuscripts will be sent to a major scientific journal.
Authors of the manuscripts will include all Study Team Members who have contributed to the study.
All manuscripts will include an appropriate acknowledgment section, mentioning all investigators who have contributed to the study, as well as supporting bodies. The Principle Investigators/Study Coordinators must approve all publications, abstracts and presentations based on patients included in this study. This is applicable to any individual healthy volunteer or patient registered in the study, or any subgroup of the study participants.

Intention to publish date
01/12/2025

Individual participant data (IPD) sharing plan
Only registered users from collaborating organisations explicitly authorised to, can access the data.
The users from participating centres are responsible for providing a list of collaborators who will be involved in the project and will use the data. The data collection will be made available only to authorised users. The data repository/data owner or its representatives will directly manage and give collaborators access to the data accordingly, which will remain private and inaccessible to other users with no explicit permissions granted by the data owner, or its representatives.

Added 17/07/2024:
The data will be available for academic researchers working in similar fields, after the end of the study, contact: cuh.radiologyresearch@nhs.net; study participant consent has been obtained, only anonymised data will be shared, imaging data will be available from NCITA, https://ncita.org.uk/, at the end of the study.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Supplementary information sheet for additional research biopsies version 1.1	20/05/2020	04/09/2023	No	Yes
Participant information sheet	version 1.1	20/05/2020	06/09/2023	No	Yes
Participant information sheet	version 1.1	20/05/2020	06/09/2023	No	Yes