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Using advanced MRI to explore metabolism and tissue structure in prostate cancer

Submission date 06/12/2023	**Recruitment status** Recruiting	[_] Prospectively registered [X] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 08/12/2023	**Overall study status** Ongoing	
Last Edited 24/01/2025	**Condition category** Cancer	

Plain English summary of protocol
https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-new-ways-to-use-mri-scans-to-see-changes-in-prostate-cancer-mission-prostate

Background and study aims
We are conducting a study to better understand prostate cancer and improve future treatments. Evidence suggests a substance called 'lactate' builds up in cancer, including the prostate. A new imaging technique called hyperpolarised MRI is similar to a regular MRI but involves an injection of a natural sugar-like molecule called pyruvate. This helps the researchers to see how the body processes this sugar and understand prostate cancer better. The researchers will also use another technique called sodium MRI to check salt content in the prostate, as it may increase with cancer. Comparing tissue samples to MRI scans will enhance future MRI scans and may help predict treatment outcomes, guiding personalized treatment decisions.

Who can participate?
Males aged 18 years or older with prostate cancer

What does the study involve?
The MRI procedure involves a cylindrical machine and an endorectal coil - a small device which enhances the quality of prostate imaging. Before placing the coil, a digital (finger) rectal examination is done, similar to what you might have experienced during prostate biopsies. Although the initial placement can be a bit uncomfortable, it's generally well-tolerated afterwards, causing only mild pressure. The coil will be inserted and removed by an experienced doctor on our research team. If a second coil is considered, comfort is a priority, and participants can discuss whether to proceed with it before placement.
Sodium MRI is like a standard MRI and hyperpolarised MRI includes an injection of a natural sugar compound via a plastic tube called cannula.
Participants might be offered an optional scan within 7 days to test the technique's repeatability. Other procedures may include basic health checks, blood tests, and pregnancy tests, conducted with participants' well-being in mind.
The participants may be asked if they are comfortable with providing small tissue samples from their prostate, which will be collected during routine biopsies for research purposes only. These samples will be examined for changes in metabolism and may involve some genetic tests related

to the tumor for research.
If participants are undergoing cancer therapy, they will be asked to attend a post-therapy MRI scan.

What are the possible benefits and risks of participating?
Taking part in this study may not directly help participants, but it could help doctors find better ways to check for and keep track of prostate cancer without using invasive methods.
Participants will not be paid for taking part, but the researchers can cover travel and parking costs.
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 they will be given earplugs and a squeeze ball to help them feel more comfortable.
Endorectal coils are commonly used as part of standard prostate MRI imaging at many centres around the world. A disposable cover will be placed over the coil for hygiene and infection control.
Cannulation (inserting a small tube into a vein) 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.
The injection containing a substance called pyruvate 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 the researchers are prepared to manage any issues that may arise.
The injection containing a substance called gadolinium is part of a routine prostate MRI examination. It is considered safe but can have side effects such as headache, metallic taste, itching or rash. Serious reactions are rare.
Discomfort, small bleeding and bruising may happen during and after the biopsy, however, most patients cope well with this. Pain relief will be available in the unlikely event that discomfort becomes more severe.
Although the scans are not part of the participants' medical records, if the researchers notice anything unusual, they will consult a specialist who may need to discuss it with the participants and their doctor.

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?
November 2015 to March 2026

Who is funding the study?
Cancer Research UK

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

Contact information

Type(s)
Public, Scientific

Contact name
Dr Marta Wylot

Contact details
Cambridge Biomedical Campus
Cambridge
United Kingdom
CB2 0SP
+44 (0)1223767926
marta.wylot@nhs.net

Type(s)
Principal Investigator

Contact name
Dr Tristan Barrett

Contact details
Cambridge Biomedical Campus
Cambridge
United Kingdom
CB2 0SP
+44 (0)1223 336895
tristan.barrett@nhs.net

Type(s)
Scientific

Contact name
Ms Maria Zamora

Contact details
Box 218, Department of Radiology, Level 5
University of Cambridge School of Clinical Medicine
Cambridge Biomedical Campus
Cambridge
United Kingdom
CB2 0QQ
-
maria.zamoramorales@nhs.net

Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
196902

ClinicalTrials.gov number
Nil known

Secondary identifying numbers

Study information

Scientific Title
A physiological study comparing hyperpolarised carbon-13 labelled pyruvate (13C-pyruvate) metabolism and sodium MRI in prostate cancer and normal prostate tissue

Acronym
MISSION Prostate

Study objectives
1. Hyperpolarised 13C-lactate forms in prostate tumours after the intravenous injection of hyperpolarised 13C-pyruvate, and that this can be detected with 13C-Magnetic Resonance Spectroscopic Imaging (MRSI).
2. Alterations in 23Na-Magnetic Resonance Imaging (MRI) signal will correlate with the presence of prostate tumours, as a measure of underlying changes in tissue structure.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/07/2016, East of England - Cambridge South Research Ethics Committee (The Old Chapel, Royal Standard Place, Nottingham, NG1 6FS, United Kingdom; +44 (0)207 104 8104; nrescommittee.eastofengland-cambridgesouth@nhs.net), ref: 16/EE/0205

Study design
This is a physiological study to assess the metabolism of pyruvate and the spatial distribution of sodium in patients with prostate cancer. It is a single-site study to be carried out at the Addenbrooke's Hospital site.
1. Participants will be recruited through multidisciplinary team meetings and clinics.
2. Research study including proton MRI, 23Na-MRI, and hyperpolarised 13C-MRSI study performed. This will include the intravenous injection of hyperpolarised 13C-pyruvate.
3. A subset of patients will undergo an optional repeat hyperpolarised 13C-MRSI within 7 days of baseline imaging to assess for reproducibility of the imaging test.
4. Patients undergo surgery (where applicable) as part of standard-of-care. Alternatively, if the patient is not a surgical candidate the patient will undertake targeted biopsy or hormone therapy.
5. Where possible, peri-procedural biopsies will be performed to obtain tissue for biochemical, histological and genetic analysis. To reduce the number of biopsies a patient undergoes, we will ask the patient to consent to an additional biopsy core for research use being taken at the standard-of-care biopsy timepoint.
6. Completion of standard-of-care (i.e. prostatectomy or end of treatment) marks the end of patient involvement in the study.
7. Standard-of-care histopathological assessment will be performed on the biopsy or surgical specimen. In addition, immunohistochemistry and other analytical tests may be performed on the biopsy specimen to assess for tissue biochemistry and metabolism.

Primary study design
Observational

Secondary study design
Cross sectional study

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

Study type(s)
Diagnostic

Participant information sheet
Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied
Prostate cancer

Interventions
Patients will undergo up to three MRI scans lasting approximately 1 hour each, including placement of up to two separate endorectal coils. The study will necessitate one intravenous cannula for venous access and an intravenous injection of hyperpolarised 13C-pyruvate per 13C MRI scan.

Intervention Type
Other

Primary outcome measure
Measured by MRI before and after treatment:
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. Sodium. Maps of estimated millimolar sodium content over the 3D volume of tissue investigated. Optionally also maps of the ratio of intracellular-weighted signal to total sodium signal.

Secondary outcome measures
1. Levels of metabolites such as pyruvate, lactate in venous blood as measured by liquid chromatography mass spectrometry (LCMS) before and after treatment
2. Total activities of lactate dehydrogenase (LDH) in venous blood as measured by LDH assay before and after treatment
3. Levels of carbonic anhydrase IX, CD31, Hypoxia-Inducible Factor-1α (HIF-1α), Ki67, monocarboxylic acid (MCT1/4) transporters, LDH expression and lactate/pyruvate measured in prostatectomy or biopsy specimens by immunohistochemistry before and after treatment. Immunohistochemistry results will be converted into semi-quantitative data using an appropriate density measurement of staining.

Overall study start date
25/11/2015

Completion date

31/03/2026

Eligibility

Key inclusion criteria
1. Men aged >18 years
2. For surgery or hormone therapy patients, biopsy-proven intermediate-risk or high-risk prostate cancer (Appendix 1), with a clinical treatment plan
3. Previous diagnostic clinical MRI demonstrates a visible tumour

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Male

Target number of participants
85

Key exclusion criteria
1. Previous treatment for prostate cancer
2. Clinical contraindication to MRI
3. Renal impairment as defined by a glomerular filtration rate (GFR) <30 ml/min

Date of first enrolment
21/12/2016

Date of final enrolment
31/01/2026

Locations

Countries of recruitment
England

United Kingdom

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

United Kingdom
CB2 0QQ

Sponsor information

Organisation
Cambridge University Hospitals NHS Foundation Trust

Sponsor details
Cambridge Biomedical Campus
Cambridge
England
United Kingdom
CB2 0SP
+44 (0)1223 245151
cuh.research@nhs.net

Sponsor type
Hospital/treatment centre

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

ROR
https://ror.org/04v54gj93

Funder(s)

Funder type
Government

Funder Name
Cancer Research UK Cambridge Institute, University of Cambridge

Alternative Name(s)
Cancer Research UK Cambridge Institute, CRUK Cambridge Institute, CRUK CI, CRUK-CI

Funding Body Type
Government organisation

Funding Body Subtype
Research institutes and centers

Location

United Kingdom

Results and Publications

Publication and dissemination plan

Audiences for this research:
1. Scientific community
2. Funders, sponsors including NHS, ethics committees
3. Patients and the public

Dissemination activities will include:
1. Abstracts, posters and talks for national and international scientific conferences
2. PPI events
3. Use of electronic media such as websites and specialised social networks such as Linkedin and ResearchGate
4. Publications including Full, Executive Summary and Plain English Summary reports of the research, peer review journals and local NHS/University of Cambridge newsletters. Whenever possible, open access to publications will be sought.
This study may form part of a PhD thesis for a PhD student working in the research team.

Intention to publish date

01/11/2026

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?
Protocol file	version 3.0	22/11/2023	13/05/2024	No	No
Protocol file	version 5.0	17/12/2024	24/01/2025	No	No