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Imaging glioblastoma pH using CEST-MRI

Submission date 07/08/2017	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 07/08/2017	**Overall study status** Completed	
Last Edited 10/09/2025	**Condition category** Cancer	

Plain English summary of protocol

Background and study aims
Several studies have demonstrated that acidity is greater within tumours that in normal tissue. This effect is predominantly driven by the hypoxic (low oxygen) environment in the tumour cells, and the build-up of lactic/carboxylic acid as the cells generate energy in the absence of oxygen. Extracellular acidity (outside cells) has been linked to increased tumour invasion and angiogenesis (blood vessel formation), reduced immune function and also resistance to radiation and systemic cytotoxic (anti-cancer drug) treatment. Chemical exchange saturation transfer (CEST) MRI is a non-invasive imaging technique that can give a readout of tissue pH (acidity). Besides pH there is evidence that this technique is also sensitive to protein concentration in tumours. This technique is already being assessed in stroke patients to aid the detection of areas with restricted blood supply and there is also a preclinical program in Oxford to develop this technique to evaluate tumours. The main aim of this study is to evaluate images obtained from CEST MRI in patients with glioblastoma, a type of brain cancer. The CEST-MRI data will also be compared with arterial spin labelling (ASL) perfusion MRI (a non-invasive imaging technique which assesses water and nutrient exchange) and tissue-based testing including pH, protein content and hypoxia markers.

Who can participate?
Patients aged 18 or over with glioblastoma who are scheduled for surgery

What does the study involve?
Participants undergo a CEST-MRI scan and ASL Perfusion MRI scan in addition to their standard care anatomical MRI scan. These may be repeated at the next standard care imaging visit if there are concerns over the time period between imaging and surgery. At surgery, biopsies (tissue samples) are taken for analysis. No visits additional to standard care are anticipated.

What are the possible benefits and risks of participating?
There is not expected to be a clinical benefit to those taking part in the study. There are no known risks or side effects to having a MRI, after proper safety considerations have been addressed. MRI is safe and non-invasive and does not involve any ionising radiation (x-rays). Participants are asked safety questions to help determine if they are able to take part. Some people find that the scanner makes them feel uncomfortable (because they have to keep still for a long time), gives them vertigo (dizziness) or claustrophobic (nervous in small spaces). Such feelings go away once the participant is outside the scanner and there are no after-effects of

having a MRI scan. The main risk associated with biopsy of glioblastoma is haemorrhage (bleeding). However in this setting, biopsy of the tumour during surgery should not carry any increased risk as the participant's tumour will be operated on immediately afterward.

Where is the study run from?
Churchill Hospital (UK)

When is the study starting and how long is it expected to run for?
February 2017 to June 2021

Who is funding the study?
Cancer Research UK

Who is the main contact?
Ms Stasya Ng

Contact information

Type(s)
Scientific

Contact name
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Contact details
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Additional identifiers

Protocol serial number
35083

Study information

Scientific Title
A single-arm exploratory study examining the feasibility of imaging glioblastoma pH using CEST-MRI

Study objectives
Several studies have demonstrated that acidity within tumours is greater that in normal tissue. This effect is predominantly driven by the hypoxic (low oxygen) environment in the tumour cells, and accumulation of lactic/carboxylic acid as the cells generate energy in the absence of oxygen.

Extracellular acidity has been linked to increased tumour invasion and angiogenesis (blood vessel formation), reduced immune function and also resistance to radiation and systemic cytotoxic (anti-cancer drug) therapy.

Chemical exchange saturation transfer (CEST) MRI is a non-invasive imaging technique that can give a readout of tissue pH (acidity). Besides pH there is evidence that this technique is also sensitive to protein concentration in tumour models. This technique is already being assessed in stroke patients to aid the detection of areas with restricted blood supply and there is also a preclinical program in Oxford to develop this technique to evaluate tumours.

The primary objective for this study is to evaluate CEST contrast image obtained from CEST MRI in glioblastoma, a type of brain cancer. As part of this study there are also several exploratory objectives in which the CEST-MRI signature will be correlated with tissue perfusion using arterial spin labelling/ASL perfusion MRI (a non-invasive imaging technique which assesses tissue perfusion/the extent of water and nutrient exchange with tissue) and tissue based testing including pH, protein content and immunohistochemistry to assess for hypoxia markers.

Ethics approval required
Old ethics approval format

Ethics approval(s)
South Central- Oxford A Research Ethics Committee, 18/07/2017, ref: 17/SC/0304

Study design
Non-randomised; Interventional; Design type: Diagnosis, Process of Care, Imaging

Primary study design
Interventional

Study type(s)
Diagnostic

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

Interventions
Current interventions as of 22/08/2019:
Study participants (previously untreated glioblastoma patients for resection/debulking surgery) will undergo a CEST-MRI scan and ASL Perfusion MRI scan in addition to their standard care anatomical MRI scan. These may be repeated at the next standard care imaging visit if there are concerns over the time period between imaging and surgery. At surgery, biopsies will be taken for analysis prior to tumour resection/debulking. No visits additional to standard care are anticipated.

Further analysis will explore, by carrying out genomic, transcriptomic and metabolomic profiling of the tumour samples, how the hypoxic tumour signature relates to the degree of CEST imaging contrast. This latter work will focus on transcriptomic metagene approaches to assess for example the expression of a validated hypoxia metagene and its relationship to the CEST MRI signature as well as characterisation of glutamine metabolism and its activation under hypoxic conditions (and hence relationship to the CEST MRI imaging signature).

Previous interventions:
Study participants (previously untreated glioblastoma patients for resection/debulking surgery) will undergo a CEST-MRI scan and ASL Perfusion MRI scan in addition to their standard care anatomical MRI scan. These may be repeated at the next standard care imaging visit if there are concerns over the time period between imaging and surgery. At surgery, biopsies will be taken for analysis prior to tumour resection/debulking. No visits additional to standard care are anticipated.

Intervention Type
Other

Primary outcome(s)
pH-weighted CEST MRI signal, assessed using amide proton transfer ratio analysis, taken at the patient's imaging visit

Key secondary outcome(s))
Current secondary outcome measures as of 22/08/2019:
1. Protein levels obtained from tissue-based assay using biopsies obtained on the surgery date
2. pH levels obtained from tissue-based assay using biopsies obtained on the surgery date
3. Hypoxia markers obtained from immunohistochemistry using biopsies obtained on the surgery date
4. Cerebral blood flow and bolus arrival time from ASL MRI perfusion scan, taken at the patient's imaging visit
5. Correlation of tumour metabolite levels and functional genetic pathway expression with CEST-MRI imaging signal

Previous secondary outcome measures:
1. Protein levels obtained from tissue-based assay using biopsies obtained on the surgery date
2. pH levels obtained from tissue-based assay using biopsies obtained on the surgery date
3. Hypoxia markers obtained from immunohistochemistry using biopsies obtained on the surgery date
4. Cerebral blood flow and bolus arrival time from ASL MRI perfusion scan, taken at the patient's imaging visit

Completion date
15/06/2021

Eligibility

Key inclusion criteria
1. Participant is willing, capable of cooperating with the protocol and able to give informed consent for participation in the study
2. Male or female, aged 18 years or above
3. Diagnosed with glioblastoma and scheduled for neurosurgical resection or debulking

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
19

Key exclusion criteria
Current exclusion criteria as of 16/02/2018:
1. Intolerant of MRI brain (for example: claustrophobia)
2. MRI brain contraindicated (for example: implanted electric and electronic devices, heart pacemakers, insulin pumps, implanted hearing aids, neurostimulators, intracranial metal clips, metallic bodies in the eye)
3. Neoadjuvant chemotherapy/radiotherapy treatment for glioblastoma which would interfere with the interpretation of trial results
4. Pregnancy
5. Other psychological, social or medical condition that the investigator considers would make the patient a poor trial candidate or could interfere with protocol compliance or the interpretation of trial results

Previous exclusion criteria:
1. Intolerant of MRI brain (for example: claustrophobia)
2. MRI brain contraindicated (for example: implanted electric and electronic devices, heart pacemakers, insulin pumps, implanted hearing aids, neurostimulators, intracranial metal clips, metallic bodies in the eye)
3. Prior treatment for glioblastoma
4. Pregnancy
5. Other psychological, social or medical condition that the investigator considers would make the patient a poor trial candidate or could interfere with protocol compliance or the interpretation of trial results

Date of first enrolment
24/10/2017

Date of final enrolment
31/05/2019

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Churchill Hospital
Old Road
Headington
Oxford
United Kingdom
OX3 7LE

Sponsor information

Organisation
University of Oxford

ROR
https://ror.org/052gg0110

Funder(s)

Funder type
Charity

Funder Name
Cancer Research UK

Alternative Name(s)
CR_UK, Cancer Research UK - London, Cancer Research UK (CRUK), CRUK

Funding Body Type
Private sector organisation

Funding Body Subtype
Other non-profit organizations

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The data sharing plans for the current study are unknown and will be made available at a later date.

IPD sharing plan summary

Data sharing statement to be made available at a later date

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Other publications	Human glioblastoma samples were obtained from this study	01/06/2022	10/09/2025	Yes	No
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes