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PreOperative Brain Irradiation in Glioblastoma

Submission date
27/03/2025

Recruitment status
Recruiting

Registration date
14/04/2025

Overall study status
Ongoing

Last Edited
06/06/2025

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 research evaluates a new approach to managing glioblastoma. Current treatment is not a cure and includes surgery followed by radiotherapy. Between surgery and radiotherapy patients have time to recover and wounds to heal. Glioblastoma is fast-growing and can grow in this time. This study tests if it is possible to give radiotherapy before the operation and whether this influences tumour growth.
The data collected will allow researchers to look at the effects of giving radiotherapy on the tumour before surgery, by studying tumour samples taken during surgery and looking at before and after scans.
There are two study aims:
1. Determine the safest method and dose of radiotherapy to give before the operation without affecting the surgery.
2. Assess whether giving radiotherapy before the operation reduces the growth of the tumour between surgery and radiotherapy.
There are two optional parts:
1. Looking at the oxygen levels within glioblastoma. Low oxygen levels are associated with a less-than-expected response to treatment. Therefore, we will measure the oxygen levels within the tumour to find out which areas have the lowest oxygen.
2. Collecting biofilms from the corner of the eye (tears). Data shows this could help diagnose brain tumours. Collecting and analysing this fluid could help the diagnosis of glioblastoma and monitoring response to preoperative radiotherapy. Currently this is done by a scan with/without surgery.

Who can participate?
Adults (aged 18 years or over) with a new radiological diagnosis of glioblastoma. Patients must be capable of all self-care, able to conduct work of a light or sedentary nature, be medically well enough to participate and able to have MRI scans. Their tumour size and location must meet treatment requirements. Patients must not have had any other type of cancer (except skin or fully removed cervical or prostate) for the last 3 years.

What does the study involve?
Clinic appointments and consent
At the first appointment, the study is discussed, and patients are given the information sheet. Patients have time to consider participation and ask questions.

During the following weeks appointment patients have another opportunity to find out more about the study and ask questions. If amenable, patients sign the informed consent form and are given a copy.
Blood tests: Four blood tests are taken to help look at the effects of radiotherapy. Where possible, these are taken before MRI scans when patients already have cannulas.
CT (computed tomography) scan: This involves a small dose of radiation that patients would not normally receive but is important for study radiotherapy planning.
MRI (magnetic resonance imaging) scan: Patients have four MRI scans.
Radiotherapy before the operation: Radiotherapy that patients receive is planned carefully before their operation. One day after radiotherapy patients are contacted to enquire about side effects.
Tumour oxygen levels (optional): If consented, patients take a pimonidazole hydrochloride tablet within 8 – 16 hours before their operation.
Pimonidazole hydrochloride usually leaves patients' bodies within 72 hours. A low dose that does not normally cause any side effects is used.
Pimonidazole is not a treatment and will not affect patients' cancer or the treatment they receive.
Biofilm collection (tears, optional): If consented, patients tear samples will be collected at the same four time points as the MRI scans. This involves putting a small strip of filter paper at the corner of the eyelid.
Surgery: Patients are admitted on the morning of their operation. During surgery diagnostic samples are taken. If sufficient tumour is removed, some will be used for research purposes.
After the operation: Patients have an MRI scan prior to discharge. They are seen in clinic to discuss the results. If a diagnosis of glioblastoma is confirmed patients continue in the study. Patients continue to be reviewed per their normal routine. Researchers contact them to monitor their progress and response to treatment.

What are the possible benefits and risks of participating?
Glioblastoma microscopically spreads through the brain and is incurable with surgery alone. In this study, parts of the tumour that cannot be removed during surgery receive radiotherapy several weeks earlier than they otherwise would. Earlier treatment could mean that the tumour grows less overall.
The possible risks of taking part include delaying surgery by about a week. The radiotherapy starts earlier and because of this the operation is delayed.
As inclusion is based on an MRI scan, there is a small chance that the tumour is not glioblastoma (i.e. misdiagnosis). The commonest alternative would be a tumour from elsewhere in the body. Treating such tumours with preoperative radiotherapy is safe.
Short-term risks: Radiotherapy-specific effects include, but are not limited to, brain swelling, headaches, nausea, vomiting, neurological deficits, fatigue, and hair loss. Patients are monitored closely and if they do experience side effects the study team can treat them. To reduce the chance of developing complications, patients are prescribed a slightly longer course of steroids to reduce swelling around the tumour. These can cause weight gain and raised blood sugar.
Long-term risks: The radiotherapy radiation dose patients receive may be higher than standard radiotherapy. The study investigates if this will increase the effectiveness of the radiotherapy. Patients have one extra CT scan (which uses ionising radiation) as part of the study. Ionising radiation may cause cancer many years or decades after the exposure. In patients with glioblastoma the chance of this happening is extremely small.
Biofilm collection: The main risk is short-term irritation. Very rare more serious risks include infection and ulceration.
Pimonidazole risks: Side effects experienced at high doses include feeling unwell, feeling disorientated and sweating. No side effects are expected at the doses in this study.

Where is the study run from?
The study is sponsored by the Christie NHS Foundation Trust with support from Liverpool Clinical Trials Unit (UK)

When is the study starting and how long is it expected to run for?
March 2021 to April 2026

Who is funding the study?
1. Cancer Research UK RadNet Manchester (UK) [C1994/A28701]
2. Medical Research Council (UK) [MR/X014088/1]

Who is the main contact?
Melanie Oddy, melanie.oddy@nhs.net

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-study-looking-at-additional-radiotherapy-for-glioblastoma-before-surgery-to-improve-the-outcome-of

Contact information

Type(s)
Public, Scientific

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Scientific, Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
288337

ClinicalTrials.gov number
NCT03582514

Secondary identifying numbers
CPMS 49203

Study information

Scientific Title
PreOperative Brain Irradiation in Glioblastoma

Acronym
POBIG

Study objectives
It is hypothesised that preoperative radiotherapy will reduce the rate of rapid early progression and improve patient outcome.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 05/07/2021, North West - Greater Manchester South Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, United Kingdom; +44 (0) 2071048065; gmsouth.rec@hra.nhs.uk), ref: 21/NW/0121

Study design
Phase I multicentre dose-escalation study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment, Safety

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

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

Interventions
This is a study of early intervention (preoperative radiotherapy)

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Surgery: Patients are admitted on the morning of their operation. During surgery, diagnostic samples are taken. If sufficient tumour is removed, some will be used for research purposes.
After the operation: Patients have an MRI scan prior to discharge. They are seen in clinic to discuss the results. If a diagnosis of glioblastoma is confirmed patients continue in the study. Patients continue to be reviewed per their normal routine. Researchers contact them to monitor their progress and response to treatment.

Intervention Type
Procedure/Surgery

Primary outcome measure
Maximum tolerated dose and maximum tolerated irradiated volume of a single fraction of preoperative radiotherapy, measured by:
1. Radiotherapy-related swelling leading to a change of the scheduled date of surgery
2. Post-operative radiotherapy commencement delayed to beyond 6 weeks after surgery due to radiation-related symptoms and/or complications from surgery
3. Interruption of post-operative radiotherapy >5 days

Secondary outcome measures
1. The use of MRI to select patients without pathological confirmation measured using concordance between MRI-based diagnosis and definitive histological diagnosis at the pre-op MRI timepoint.

2. The effect of a single fraction of preoperative radiotherapy on rapid early progression, measured using tumour volume difference between the postoperative MRI and pre-radiotherapy MRI scans.
3. The safety of a single dose of preoperative radiotherapy given in addition to routine postoperative chemotherapy/radiotherapy. Measured by safety data throughout the study up to and including the date of death.
4. The effect of a single fraction of preoperative radiotherapy on the pathological and molecular biology of glioblastoma, measured by confirmation of GBM and the prognostication still feasible on a selection of patients at the post-surgery timepoint
5. (Exploratory) The effect of a single fraction of preoperative radiotherapy on the microenvironment of glioblastoma and relate this to clinical outcome at the post-surgery timepoint
6. (Exploratory) The use of tears as a form of liquid biopsy in glioblastoma patients both for diagnosis and treatment response at the post-surgery timepoint
7. (Exploratory) The relationship between hypoxia and radiotherapy response in glioblastoma at the post-surgery timepoint

Overall study start date
14/03/2021

Completion date
30/04/2026

Eligibility

Key inclusion criteria
1. Age ≥18 years
2. Male or female
3. New radiological diagnosis of glioblastoma
4. Performance status judged by World Health Organisation, Eastern Cooperative Oncology Group [ECOG] score = 0-1
5. Case has been reviewed by the neuro-oncology multidisciplinary team (MDT - neurosurgeon, clinical oncologist, radiologist and pathologist); MDT consensus that offering study entry is clinically appropriate and safe i.e. patient unlikely to come to harm (e.g. hydrocephalus) from delayed surgery and pre-operative radiotherapy based on available clinical information and imaging.
6. Confirmation at first clinic visit that study entry is clinically appropriate and safe (e.g. lack of severe and debilitating symptoms of raised intracranial pressure).
7. Intention to treat with surgical resection and postoperative adjuvant therapy as per current standard of care (Stupp regimen).
8. Tumour size, location and configuration meet radiotherapy treatment planning criteria (e.g. meets dose constraints for organs at risk when accounting for post-operative radiotherapy).
9. Adequate haematological and biochemical parameters for surgery and contrast agent administration (full blood count and coagulation profile deemed acceptable by clinical team, eGFR >30 ml/min)
10. Mental capacity to consent for treatment
11. Able and willing to give informed consent

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
18

Key exclusion criteria
1. Planned biopsy procedure only.
2. Suspicion of other tumour on CT body scan or known malignancy except non-melanoma skin cancer, completely resected cervical or prostate cancer (with Prostate Specific Antigen of less than or equal to 0.1 ng/ml) within the past 3 years.
3. Contraindications to contrast-enhanced MRI scanning (e.g. claustrophobia, gadolinium allergy).

Date of first enrolment
23/05/2022

Date of final enrolment
30/11/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
The Christie NHS Foundation Trust
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Manchester
United Kingdom
M20 4BX

Study participating centre
Northern Care Alliance NHS Foundation Trust
Salford Royal
Stott Lane
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United Kingdom
M6 8HD

Sponsor information

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the-christie.sponsoredresearch@nhs.net

Sponsor type
Hospital/treatment centre

Website
http://www.christie.nhs.uk/

ROR
https://ror.org/03v9efr22

Funder(s)

Funder type
University/education

Funder Name
MRC-PHE Centre for Environment and Health

Alternative Name(s)
MRC PHE Centre for Environment and Health, MRC-PHE Centre for Environment & Health, MRC Centre for Environment & Health, MRC Centre for Environment and Health, MRC CE&H

Funding Body Type
Private sector organisation

Funding Body Subtype
Universities (academic only)

Location
United Kingdom

Results and Publications

Publication and dissemination plan
The data arising from the study will belong to the sponsor, The Christie NHS Foundation Trust. The Operational Director for Research will act as the data custodian for this study. The main study results will be published in a peer reviewed journal, on behalf of all collaborators. Participants will be given the option to request a summary of the study results should they so wish.

Intention to publish date
30/06/2026

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