

Brain imaging to predict toxicity in elderly patients after radiotherapy

Submission date 18/04/2023	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 31/05/2023	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 08/03/2024	Condition category Cancer	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

The aim of this study is to produce a way of predicting who might be more or less likely to suffer side effects from radiotherapy prior to starting treatment for a glioblastoma, a type of brain tumour. This will enable doctors and patients to make more individual, tailored treatment plans, exploring other treatment options or recognising the need for extra support in certain cases.

Glioblastoma (GBM) is the commonest primary malignant brain tumour. The chances of developing a GBM peak in your 70s and 80s. Outcomes from this disease in older patients are poor. Part of the reason is the lack of good clinical trials for this age group. Treatment options are best supportive care where the focus is on maintaining a good quality of life for as long as possible.

Treatment of GBMs can involve chemotherapy and radiotherapy. Research has shown that there is a particular test oncologists can perform on the tumours which suggests whether that particular tumour is more or less sensitive to chemotherapy. This test is used to guide whether chemotherapy is offered. As yet there is no such test to guide radiotherapy treatment.

Radiotherapy to the brain is an effective treatment. However, it does often produce side effects. These can include fatigue, nausea, problems with memory and sometimes a worsening of the original symptoms that led to the discovery of the tumour. The degree of side effects which different patients experience can vary widely. Some of this due to the amount of radiotherapy given and how it's given but there is a lot that we don't understand as to why certain patients are much more affected than others. It has been thought that if the patient's underlying normal brain (i.e. not the part affected by the tumour) is fragile due to an underlying mild dementia or problems associated with high blood pressure or cholesterol then this might make them more vulnerable.

MRI scans can be used to assess whether there are changes in the normal brain from these background conditions. This study aims to use MRI scans to see whether we can predict those patients who might be more at risk of side effects caused by radiotherapy.

Who can participate?

Patients aged 65 or over who have been newly diagnosed with a GBM and are going to receive radiotherapy as part of their treatment.

What does the study involve?

Patients who agree to take part in the study will have already had an MRI scan as part of their normal diagnosis. They will undertake some questionnaires before starting their radiotherapy which will aim to assess their quality of life and their mental processes of perception, memory, judgment, and reasoning (called cognitive function).

They will then repeat these questionnaires 4 and 8 weeks after their treatment has finished when they come for their follow-up appointments. The results of these questionnaires will be compared to measurements made on their pre-treatment MRI scan. Occasionally the MRI scan the patients had as part of their diagnosis will not have quite enough information on it and some patients may need to have an extra scan before starting their radiotherapy treatment.

What are the possible benefits and risks of participating?

Participation in the study does not change the treatment the patient receives. There are no direct benefits to the participants in undergoing this study. The risk of significant harm to the participant is unlikely within this study.

Participants who require a further MRI scan may require the administration of gadolinium contrast. This is generally safe and well tolerated however the risk profile of this will be discussed with the patient prior to administration and local policies will be followed if the patient has a reaction to the contrast agent. MRI scans do not involve ionising radiation therefore do not carry with them any increased risk of cancer.

Participants will be attending clinic for their routine follow-up visits when they complete the assessments and therefore will not need any extra visits to the hospital. During their clinic visit, they may need to spend slightly more time than they would usually do in order to complete the questionnaires. In order to minimise this, we have allowed for carers/family/a member of the trial team to assist with the self-reported questionnaires or for the patient to take the questionnaire home with them to complete and post back to the trial team.

The participant's GP will be informed of their involvement in the study. If there are concerns from the answers to the questionnaires that the participants may be at risk of harm to themselves or to others then this will be discussed with the participant's GP or other teams. The participants will be aware of this. In the unlikely event that any psychological distress is caused to the participants by completing the questionnaires, we would address this within the clinic visit and if necessary refer to their GP or local psychiatric services for further support. Participants who require a further MRI scan may require the administration of gadolinium contrast. This is generally safe and well tolerated however the risk profile of this will be discussed with the patient prior to administration and local policies will be followed if the patient has a reaction to the contrast agent. MRI scans are in general well tolerated and do not involve ionising radiation therefore do not carry with them any increased risk of cancer.

Where is the study run from?

The study is run from University Hospitals Sussex NHS Trust as lead and sponsor but is open in a number of centres across the UK.

When is the study starting and how long is it expected to run for?

May 2018 to December 2022

Who is funding the study?

1. The Sussex Cancer Fund (UK)
2. BrainsTrust (UK)

Who is the main contact?

Dr Cressida Lorimer, cressida.lorimer@nhs.net

Contact information

Type(s)

Principal investigator

Contact name

Dr Cressida Lorimer

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Additional identifiers

Clinical Trials Information System (CTIS)

Nil known

Integrated Research Application System (IRAS)

216343

Protocol serial number

CPMS 38723, IRAS 216343

Study information

Scientific Title

Brain Imaging to predict Toxicity in Elderly patients after Radiotherapy (BRITER): an observational cohort study

Acronym

BRITER

Study objectives

The BRITER study is being performed on patients aged 65 or over who have a new diagnosis of glioblastoma (GBM). It tests the hypothesis that there is a relationship between 5 scores of a 'vulnerable' brain seen on pre-treatment MRI and a clinically significant change in patient quality of life, as defined by a 10-point change in the EORTC QLQ questionnaire from baseline to 8 weeks post-treatment.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 15/06/2018, London - Bloomsbury Research Ethics Committee (Barlow House, 3rd Floor, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8285; bloomsbury.rec@hra.nhs.uk), ref: 18/LO/0997

Study design

Observational cohort study

Primary study design

Observational

Study type(s)

Quality of life

Health condition(s) or problem(s) studied

Glioblastoma

Interventions

All participants received an extra pre-treatment MRI scan and undertook a series of questionnaires at time points through their treatment. Study participants were eligible if they were receiving radiotherapy to their brain for a Glioblastoma. The type of radiotherapy or dose is at the discretion of the treating physician.

Data will be gathered on patient quality of life via toxicity assessments and completion of EORTC QoL questionnaires

Intervention Type

Other

Primary outcome(s)

The proportion of patients with a 10-point change in the EORCT QLQ C30 quality of life questionnaire (with the BN-20 brain and ELD14 elderly patient subsets of questions added) from baseline to 8 weeks

Key secondary outcome(s)

The impact of side effects from cranial radiotherapy will also be assessed by:

1. MoCA cognitive screening questionnaire, scored as impaired (< 25) or unimpaired (>25), at baseline and at 8 weeks
2. Corticosteroid dose, recorded in milligrams at baseline and at 8 weeks
3. Treatment-associated toxicities of fatigue, headache, confusion, nausea, vomiting and seizures, measured using the Common Terminology Criteria for Adverse Events (CTCAE) at baseline and 8 weeks. Those scoring >3 will be recorded.
4. Overall survival, measured from the date of diagnosis (defined as the first imaging modality reviewed by a neuroradiology consultant within the multidisciplinary team meeting (MDM) setting which shows changes consistent with a GBM) until the date of death or censoring of the study
5. Progression-free survival, measured from the date of diagnosis (defined as the first imaging modality reviewed by a neuroradiology consultant within the MDM setting which shows changes consistent with a GBM) until the date of progression as confirmed by imaging reviewed by a neuroradiologist

Completion date

31/12/2022

Eligibility

Key inclusion criteria

1. Patients aged >65 years with a new diagnosis of GBM. Diagnosis made via histological confirmation following biopsy or debulking surgery or radiologically during an MDM meeting confirmed by a consultant neuroradiologist. This lower age limit is due to previous clinical trials which have established gold-standard treatment regimes for patients under the age of 65 years. Patients aged 65 years or over have less clinical trial data available to them and treatment decisions are more nuanced with a greater emphasis on quality of life given the poorer prognosis of older patients.
2. Patients undergoing radiotherapy treatment to the brain for the treatment of their GBM
3. Patients able to undergo an MRI scan
4. Patients undergoing treatment at one of the study centres
5. Patients have the capacity to participate in the study
6. Patients with physical impairments that prevent them from filling in their questionnaires involved in the study may still participate if they are able to communicate their answers through a third party

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Senior

Sex

All

Total final enrolment

120

Key exclusion criteria

1. Patients not fit for radiotherapy treatment or having single-agent chemotherapy with no radiotherapy
2. Patients lacking capacity
3. Patients who do not have a sufficient grasp of the English language to be able to complete the questionnaires
4. Patients unable to communicate their responses to the questionnaires
5. Patients who are concurrently enrolled in a Clinical Trial of an Investigational Medicinal Product (CTIMP)

Date of first enrolment

05/11/2018

Date of final enrolment

31/12/2021

Locations

Countries of recruitment

United Kingdom

England

Scotland

Study participating centre

Royal Sussex County Hospital

University Hospitals Sussex

Sussex Cancer Centre

Eastern Road

Brighton

United Kingdom

BN2 5BE

Study participating centre

Beatson West of Scotland Cancer Centre

1053 Great Western Road

Glasgow

United Kingdom

G12 0YN

Study participating centre

Royal Marsden Hospital

Downs Road

Sutton

United Kingdom

SM2 5PT

Study participating centre

Nottingham Hospital

Nottingham University Hospitals NHS Trust

City Campus

Hucknall Road

Nottingham

United Kingdom

NG5 1PB

Study participating centre

Addenbrookes Hospital

Cambridge University Hospitals NHS Trust
Hills Road
Cambridge
United Kingdom
CB2 0QQ

Study participating centre

Castle Hill Hospital

Hull University Teaching Hospitals NHS Trust
Queens Centre
Castle Road
Cottingham, Hull
United Kingdom
HU16 5JQ

Study participating centre

The Christie

The Christie NHS Foundation Trust
Wilmslow Road
Manchester
United Kingdom
M20 4BX

Study participating centre

Norfolk & Norwich University Hospital

Colney Lane
Norwich, Norfolk
United Kingdom
NR4 7UY

Study participating centre

Mount Vernon Hospital

Rickmansworth Road
North Middlesex
United Kingdom
HA6 2RN

Study participating centre**Maidstone Hospital**

Kent Oncology Centre

Meritage Lane

Maidstone, Kent

United Kingdom

ME16 9QQ

Study participating centre**Queen Elizabeth Hospital**

University Hospitals Birmingham NHS Foundation Trust

Oncology

Mindelsohn Way

Edgebaston

Birmingham

United Kingdom

B15 2WB

Study participating centre**Charing Cross Hospital**

Imperial College Healthcare NHS Trust

Fulham Palace Road

London

United Kingdom

W6 8RF

Study participating centre**Western General Hospital**

Edinburgh Cancer Centre

Crewe Road South

Edinburgh

United Kingdom

EH4 2XU

Sponsor information**Organisation**

University Hospitals Sussex NHS Foundation Trust

ROR

<https://ror.org/03wvsyq85>

Funder(s)

Funder type

Charity

Funder Name

Sussex Cancer Fund

Funder Name

BrainsTrust

Results and Publications

Individual participant data (IPD) sharing plan

The datasets from this study are stored in a non-publicly available repository. The results will be published in peer-reviewed journals and presented at international conferences. The trial participants consented to their data being available only to members of the trial team in order to respect confidentiality. As this is an important repository of anonymised images and quality-of-life data, if requests are made for raw data to the BRITER study email address the researchers can assess these on an individual basis and seek advice from the HRA as to whether they can share anonymised datasets on a case-by-case basis.

IPD sharing plan summary

Stored in non-publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No
Participant information sheet	version 0.5	03/04/2019	28/04/2023	No	Yes
Poster results	Abstract submitted to European Association of Neuro-Oncology April 2023		19/01/2024	No	No
Protocol file	version 0.8	03/04/2019	28/04/2023	No	No