Unravelling the invisible infiltrating component of glioblastoma using MRI and a strong iron-like bloodpool contrast medium?

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This study has been transitioned to CTIS with ID 2024-514013-34-00 check the CTIS register for the current data. 1. Perform a feasibility study of USPIO neuro-imaging in healthy participants (n=6)2. Perform MR imaging of glioblastoma by use of a new…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Nervous system neoplasms malignant and unspecified NEC
Study type	Observational non invasive

Summary

ID

NL-OMON53350

Source
ToetsingOnline

Brief title
USPIO-MRI for GBM

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
Brain cancer

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: ZonMw Off Road programma

Intervention

Keyword: Glioblastoma, MRI, USPIO

Outcome measures

Primary outcome

Is it feasible to perform a study of USPIO neuro-imaging in healthy

participants (n=6)?

Secondary outcome

Can we robustly perform MR imaging of glioblastoma by use of a new Off Road

multi-sequence protocol (i.e., T1w, T2w, FLAIR, DWI/DTI, SWI, T1w- and T2*w

post-USPIO images) in 15 GBM patients to visualize tumor infiltration?

What is the diagostic accuracy of the Off Road imaging protocol to predict

tumor recurrence?

Study description

Background summary

The most common primary brain tumor - glioblastoma (GBM) - is invariably fatal with median survival of 15 months(1, 2). Regions with high GBM cell density promote the development of abnormal vasculature only as they proliferate further(3), which can be detected and visualized with conventional contrast-enhanced magnetic resonance imaging (MRI). However, before dense proliferation, GBM cells actively and extensively infiltrate the surrounding healthy brain tissue over relatively long distances along myelinated axons and blood vessels, co-opting on oxygen and nutrient supply(3-5). Without damage to the locoregional blood-brain-barrier (BBB) this GBM cell invasion cannot be visualized by conventional or contrast-enhanced MRI(6-8). Visualization of tumor spread is of crucial importance when treating patients suffering from GBM as the success of tumor resection depends strongly on the extent of tumor

infiltration(9, 10). For instance, incomplete resection often results in tumor recurrence(11). Thus, out-of-the-box MRI methods for visualization of infiltrating brain tumors are needed. The infiltrative growth of GBMs around existing vasculature slightly influences the local density of blood vessels. One would be able to visualize this small decrease in blood volume if a very strong blood pool contrast agent could be used.

Study objective

This study has been transitioned to CTIS with ID 2024-514013-34-00 check the CTIS register for the current data.

1. Perform a feasibility study of USPIO neuro-imaging in healthy participants (n=6)

2. Perform MR imaging of glioblastoma by use of a new Off Road multi-sequence protocol (i.e., T1w, T2w, FLAIR, DWI/DTI, SWI, T1w- and T2*w post-USPIO images) in 15 GBM patients.

3. Analyze the obtained images and characterize brain tissue using both a quantitative and qualitative methodology to delineate regions of tumor infiltration.

Study design

The design of this study regards a single-arm prospective observational study. The intention is to include 15 patients who are believed to suffer from glioblastoma preo-operatively and are scheduled to undergo neurosurgical treatment and/or chemoradiation therapy.
Prior to the inclusion of patients, a feasibility study will be carried out in six healthy participants. This is needed to optimize the dosage of USPIOs administered for adequate imaging.

Patients will be informed about this study and its objectives by a nurse practitioner/neurologist/neurosurgeon during regular consultations prior to surgery. Patients who meet all criteria and are willing to participate will be informed about this study and will receive a patient information letter (file E1) after which they will have a reflection period. Patients will have the possibility to consult an independent physician who is informed about the protocol but not actively involved in this study. After a maximum of 5 days, patients will be contacted to answer remaining questions. If they are willing to participate, they will sign a written informed consent (file E2).

Patients who are willing to participate in this study will be referred to the Dutch hospital where USPIO neuroimaging will take place (Radboudumc, Department of Radiology and Nuclear Medicine). The images will be taken by employees of

Radboudumc Nijmegen; Department of Nuclear Medicine following the available clinical protocols.
USPIO imaging of the brain will not delay the clinical progress of the patient to receive SCS. After USPIO imaging, patients will receive normal clinical and radiological follow-up and treatment schemes.

Study burden and risks

Adverse effects have been reported in most studies with ferumoxtran-10. Most of these were most likely unrelated to ferumoxtran-10 or were of mild severity (8). One case of anaphylactic shock resulting in death was reported. In this case ferumoxtran-10 was administered undiluted and within only several minutes as bolus injection. This patient also had a previous contrast reaction to another contrast agent.

In the present study, low dose of ferumoxtran-10 will be administered very slowly (>30 min) and diluted and subjects will be observed by a physician during this period. If any sign of a contrast reaction should occur, the administration of ferumoxtran-10 will be stopped and further medical steps will be undertaken if necessary. If the side effects have disappeared and it is medically justified, the administration of ferumoxtran-10 will be continued very slowly. In our hospital, between 2014 and 2016, 310 prostate cancer patients were administered the similar compound ferumoxtran-10 as we will use. Adverse effects occurred in 2.6% (n=8) of all subjects included of which 7 were considered contrast-related. Four patients experienced side-effects during administration (mild low back pain, flushing, and nausea) and three experienced a dry mouth after infusion was completed. All were considered minor effects and disappeared after temporary interruption or resolved spontaneously within several hours (8).

Conclusively, the administration of ferumoxtran-10 has been researched in many studies and shown to only pose small risks, particularly with the administration method (diluted, slow and under observation) that is employed in the clinic at our department.

We therefore feel that the possible benefits of this study (non-invasive visualization of tumor infiltration in GBM patients) outweigh the (small) risks involved in administering ferumoxtran-10

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Aged between 18 and 75 years
• Diagnosed with suspected glioblastoma
• Eligible for neurosurgical resection and/or chemoradiation therapy.

Exclusion criteria

• Younger than 18 years old
• Patients unfit for surgery or lesions unsuitable for neurosurgical treatment

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	16-01-2024
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Ferrotran (ferumoxtran-10) lyophilisate
Generic name:	Ferrotran (ferumoxtran-10) lyophilisate
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	09-02-2023
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Approved WMO

Date:	12-07-2023
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EU-CTR	CTIS2024-514013-34-00
EudraCT	EUCTR2023-000068-80-NL
ClinicalTrials.gov	NCT05656300
CCMO	NL83709.091.23