Hitting the Mark: Introducing state-of-the-art MRI for precision radiotherapy of glioblastoma

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Primary objective:• To demonstrate that the probability for reduced coverage of the recurrence volume by a radiotherapy plan based on a CTVbio, compared to the clinical radiotherapy plan (1.5-cm CTV), is lower than 0.20.Secondary objectives:&...

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

Summary

ID

NL-OMON55947

Source
ToetsingOnline

Brief title
MOSAIC

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
brain tumor glioblastoma

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: NWO Mosaic 2.0

Intervention

- Other intervention

Keyword: glioblastoma, MRI, precision radiotherapy

Explanation

N.a.

Outcome measures

Primary outcome

Pattern of failure and dose to organs at risk by the radiotherapy plan based on the 1.5-cm CTV and the theoretical plan created with the CTVbio.

Secondary outcome

• The differences in tumor recurrence coverage and size between the CTVbio (based on all three aMRI-scans) and CTVs based on individual or other combinations of aMRI, i.e. based on two or one aMRI-scan(s).
• The difference in mean and maximum signal intensity on the individual aMRI-scans between the tumor recurrence site and the contralateral normal-appearing white matter.

Study description

Background summary

One of the fundamentals of glioblastoma management is radiotherapy, where ionizing radiation is aimed towards a specific target area in the brain to inhibit further tumor growth. As these brain tumors are notorious for their extensive tumor infiltration, where tumor grows beyond the tumor that is visible on conventional magnetic resonance imaging (MRI), this target area, defined as the clinical target volume (CTV), consists of the visible tumor plus a 1.5-cm isotropic safety margin. In the majority of cases, this unspecific CTV
margin adequately covers tumor infiltration, but inevitably also includes considerable amounts of healthy tissue. Radiation-induced side-effects like headaches, nausea, fatigue and cognitive decline can substantially affect the
quality of life for these patients. An opportunity arises to indirectly visualize tumor infiltration with
state-of-the-art advanced MRI (aMRI) techniques, providing additional information on physiology rather than only showing anatomical information through conventional MRI. A workflow has been developed to create a CTV based on these aMRI scans (CTVbio) rather than an isotropic expansion. With the additional information that aMRI provides, it could be

possible to more accurately define what needs to be targeted and thus minimize damage to healthy tissue. In this research, the aim is to assess the potential of integrating aMRI into radiotherapy target delineation for patients with a glioblastoma by comparing the pattern of failure (coverage of first tumor recurrence by the radiotherapy plan) and the expected radiation dose to organs at risk between
the CTVbio and the 1.5-cm CTV. It is hypothesized that the CTVbio can result in decreased radiation dose to organs at risk, whilst having similar pattern of failure.

Study objective

Primary objective:
• To demonstrate that the probability for reduced coverage of the recurrence volume by a radiotherapy plan based on a CTVbio, compared to the clinical radiotherapy plan (1.5-cm CTV), is lower than 0.20.

Secondary objectives:
• To illustrate a reduction in dose to organs at risk with a radiotherapy plan based on a conceptual CTVbio compared to the clinical radiotherapy plan (1.5-cm CTV).
• To evaluate the synergistic information that each individual aMRI-scan provides for the identification of tumor infiltration.
• To explore the association between pathophysiological changes on aMRI and future tumor recurrence.

Study design

In this prospective cohort study, the clinical standard MRI session used for radiotherapy planning of glioblastoma patients will be extended with aMRI techniques that assess altered oxygenation, angiogenesis and increased protein concentration. Patients who would not have received an MRI-scan prior to radiotherapy, will get an extra MRI-scan when they participate in this study. Radiation treatment (and patient follow-up) will occur according to the clinical standard, i.e. using the 1.5-cm CTV for radiotherapy planning. The aMRI-scans will be used to create a theoretical CTVbio and corresponding radiotherapy plan. Pattern-of-failure analysis and assessment of dose to organs at risk will be done to compare the radiotherapy plan based on the 1.5-cm CTV with the (theoretical) radiotherapy plan based on the CTVbio. Additionally, various theoretical CTVs based on different combinations of aMRI-scans are generated to explore the added value of the different aMRI techniques. Lastly, the signal intensities on the aMRI-scans at the site of tumor recurrence are compared with contralateral normal-appearing white matter.

Intervention

Four advanced MRI techniques (qBOLD, ASL, DSC and CEST) will be investigated in this research. These techniques provide information on various biological aspects. qBOLD in combination with ASL provides information on the cerebral metabolic rate of oxygen (CMRO2), DSC provides information on blood perfusion (rCBV), and CEST provides information on protein concentrations (APT).

Study burden and risks

For patients who will already undergo an MRI-scan for radiotherapy, the burden will be an extended MRI-scan (+20 minutes; the total scan time will be 45 minutes instead of 25 minutes). There is no benefit for these patients. Patients who would not have received an MRI-scan prior to radiotherapy, the burden of participation will be an extra MRI-scan (total scan time: 45 minutes) with additional contrast injection. The dosage and administration are similar to the standard Brain tumor MRI protocol, which has often already been acquired before in these patients. The radiation oncologist may decide to use the conventional MRI-scan from this study MRI for target delineation if they believe it has an added value. The use of the conventional MRI-scans is recommended in the ESTRO-EANO guidelines, but is not routinely done for all patients at Erasmus MC. The advanced MRI-scans investigated in this research will not be used by the radiation oncologist.

Contacts

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Trial sites

Trial sites in the Netherlands

Erasmus MC, Universitair Medisch Centrum Rotterdam
Target size: 53

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Written informed consent;
Adults (18 years or older);
Diagnosed with IDH-wildtype glioblastoma, as confirmed by pathology including molecular analysis post resection/biopsy;
Referred to the outpatient clinic of the Dept. of Radiotherapy to undergo standard treatment with radiotherapy (30x2 Gy or 15x2.67 Gy or 10x3.4 Gy);

Exclusion criteria

Contraindication for (3 Tesla) MRI;
Contraindication for use of gadolinium-based contrast agent (e.g. subject having renal deficiency or known allergy);
Referred for treatment of recurrent glioblastoma;
Previous radiotherapy to the brain;
Unable to give informed consent;

Study design

Design

Study phase:	N/A
Study type:	Observational invasive
Intervention model:	Single
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-01-2024
Enrollment:	53
Type:	Actual

Medical products/devices used

Product type:	N.a.
Registration:	No

IPD sharing statement

Plan to share IPD: Yes

Plan description
not yet decided

Ethics review

Approved WMO Date:	06-11-2023
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	13-08-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	15-05-2025
Application type:	Amendment
Review commission:	METC Erasmus MC

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
ClinicalTrials.gov	NCT06183983
CCMO	NL84994.078.23
Research portal	NL-005969