# Early prediction of Glioma Recurrence to Radiotherapy by 31P MRS and 1H CEST MRI

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To non-invasively measure metabolic alterations in GBM with 31P MRS at 7T and CEST MRI at 3T and 7T before and after radiotherapy (after the first session and after the whole treatment), and compare these results with Cx30 levels obtained from pre-...

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

## Summary

### ID

NL-OMON50558

**Source**
ToetsingOnline

**Brief title**
GRAPE

### Condition

- Nervous system neoplasms malignant and unspecified NEC

**Synonym**
Glioma Recurrence

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Universitair Medisch Centrum Utrecht
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** CEST, Glioma recurrence, MRI, Phosphorus Spectroscopy

## Outcome measures

### Primary outcome

The study endpoint will be the amount of ATP, protein level and pH change in GBM before and after single dose and complete course of radiotherapy with respect to background levels. Reproducibility is assessed in controls assuming no alteration in metabolite levels. In addition, the correlation between Cx30 and ATP as well as Cx30 and pH and protein level will be assessed.

### Secondary outcome

NA

# Study description

### Background summary

Resistance to radiotherapy is a common problem in patients with glioblastoma multiforme (GBM), one of the most common primary brain tumors in the adult population. In this study, molecular information from tumor tissue, e.g. level of Connexin30 (Cx30), will be used to predict radiotherapy efficacy and tumor recurrence. Overexpression of Cx30 inhibits proliferation of tumor cells but also renders them resistant to radiotherapy . Currently, there is no reliable method to predict resistance to radiotherapy in a non-invasive way. To this end, this study will be using non-invasive molecular profiling techniques at ultra-high field 7T.
In stress situations, e.g. shear stress, hypotonia, and hypoxia, cells release ATP (detectable non-invasively) into the extracellular space (ES). ATP possesses anti-tumor activity and can regulate proliferation of cancer cells. In addition, ATP can also act as a radio-protector. The similarity between Cx30 and ATP in the physiological effect exerted on the cells makes us hypothesize that ATP as measured by 31P magnetic resonance spectroscopy (MRS) may be a surrogate for Cx30, and therefore a marker of GBM resistance that can be measured non-invasively. A second potential method to detect the physiological response of tumor tissue to irradiation will be Chemical Exchange Saturation

Transfer (CEST) MR imaging. CEST MRI can probe tumor microenvironment, e.g. pH and protein content with high spatial resolution and recently it has been shown to be able to distinguish radiation necrosis from tumor recurrence. Changes in tumor physiology in response to radiotherapy will translate to changes in pH and/or protein content.
The primary aim of this study is to assess the feasibility of 31P magnetic resonance spectroscopy (MRS) to quantify changes of ATP levels in brain tumors in vivo before and after the first radiotherapy treatment. Our secondary aim is to investigate the correlation between MRS-based ATP measurements and CEST measurements before and after radiotherapy (after the first session and after the whole treatment course) with Cx30 levels from the pre-treatment biopsy samples measured by immunohistochemistry (IHC).

### Study objective

To non-invasively measure metabolic alterations in GBM with 31P MRS at 7T and CEST MRI at 3T and 7T before and after radiotherapy (after the first session and after the whole treatment), and compare these results with Cx30 levels obtained from pre-treatment biopsy.

### Study design

The study is designed as a single-center pilot study. A total of 20 brain tumor patients will be scanned with each patient being scanned three times (before biopsy, immediate after the first radiation dose and immediately after the whole radiotherapy treatment). In addition, a total of 20 healthy controls will be scanned twice to to establish normal values.

### Study burden and risks

The subjects participating in this study will not benefit from the results of the study, since the primary aim of this investigation is to collect feasibility data for a comparison between 31P MRS and CEST MRI and biopsy Cx30 values for patients treated for GBM. However, our ultimate aim is to use MRI to predict radiotherapy response without the need for a biopsy. Three visits to the 7T MRI facility will be required for each patient, before biopsy, after the first radiotherapy dose and after the complete course of treatment. The healthy volunteers will be scanned twice at 7T. The risk of undergoing MRI is low.

## Contacts

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

Main inclusion criteria for patients and healthy volunteers:
• Minimum age 18 years
Additional inclusion criteria for patients:
• Recently diagnosed with GBM using biopsy
• Scheduled for radiotherapy (no surgical resection possible or desirable)

## Exclusion criteria

Main exclusion criteria for patients and healthy volunteers:
• Standard contraindications for 7T MRI scanning, including claustrophobia and active metallic implants (see standard 7T screening form for contraindications)
• History of previously treated brain tumor
• History of previous partial or total brain radiotherapy
• Pregnancy
Additional exclusion criteria for patients:
• Altered consciousness prohibiting informed consent

• Recurrent GBM

# Study design

## Design

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| Study type: | Observational invasive |
| Intervention model: | Other |
| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Diagnostic |

## Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 26-03-2019 |
| Enrollment: | 40 |
| Type: | Actual |

# Ethics review

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| Approved WMO Date: | 02-05-2018 |
| Application type: | First submission |
| Review commission: | METC NedMec |
| Approved WMO Date: | 21-08-2020 |
| Application type: | Amendment |
| Review commission: | METC NedMec |

# 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 |
| --- | --- |
| CCMO | NL56019.041.17 |