# Ultrasound Navigation Guided Improvement of High Grade Glioma Resection and Quality of Life: a phase III Randomized Controlled Trial.

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Primary ObjectiveTo investigate whether ultrasound guided tumor resection succeeds gross total resection significantly more frequently, when compared with the conventional non-ultrasound guided tumor resection.Secondary Objective(s)To investigate...

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| **Ethical review** | Approved WMO |
| **Status** | Pending |
| **Health condition type** | Nervous system neoplasms malignant and unspecified NEC |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON41750

**Source**
ToetsingOnline

**Brief title**
US-GLIOMA Study

### Condition

- Nervous system neoplasms malignant and unspecified NEC

**Synonym**
aggressive brain tumor, high grade glioma

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Erasmus MC, Universitair Medisch Centrum Rotterdam

**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** Extent of resection, High grade glioma, Quality of life, Ultrasound

## Outcome measures

### Primary outcome

Primarystudy parameter/endpoint

* Extent of resection (gross-total resection or sub-total resection)

Gross-total resection: No residual contrast enhancement on post-operative MRI scans (within 48 hours); 100% of all enhancing tumor has been resected when compared to initial enhancing tumor on pre-operative MRI scans.

Sub-total resection: Residual contrast enhancement on post-operative MRI scans (within 48 hours); <100% of all enhancing tumor has been resected when compared to initial enhancing tumor on pre-operative MRI scans.

### Secondary outcome

Secondary study parameters/endpoints

* Extent of resection (%)

Initial and residual tumor volume (cm3) of all enhancing tissue on respectively pre and post-operative MRI scans will be volumetrically assessed.
The extent of resection (%) will be calculated with the formula: (initial tumor volume-residual tumor volume)/initial tumor volume x 100.

* Neurological status (KPS) (Pre-operative and post-operative on 1, 3, 6 months) 32

* Quality of Life (QLQ-C30 and QLQ-BN 20 questionnaire) (Pre and post-operative on 1, 3, 6 months)

* Surgery associated neurological deficits (National Institutes of Health Stroke Scale, NIHSS) (Pre-operative and 1 month post operative)

* Adverse Events (classified according to the US National Cancer Institute common toxicity criteria version 4.0)

* Time of survival (days)

## Study description

**Background summary**

Median survival of high grade glioma is only 15 months after surgery, radio- and chemotherapy. Prognosis of patients with HGG is independently associated with larger surgical resections of the tumour. However, larger resections also have the risk of damaging normal brain and could therefore have detrimental effect on quality of life of these patients. Achieving GTR without causing new neurological deficits is therefore still a great challenge in glioma surgery.

The term gross total resection (GTR) is used in the literature to indicate no residual tumour on post-operative MRI scans. GTR in newly diagnosed, untreated HGG patients varies in the literature from 33% to 85% in retrospective studies. GTR of HGG patients operated in Erasmus MC is around 30% and comparable to the only known published randomized controlled study, investigating the use of fluoro-guided resection16. The relatively low GTR*s are caused by the technical difficulty to identify interface during resection between tumour and white matter of the brain. The neurosurgeon is therefore not able to distinguish tumour from white matter clearly. New intraoperative high resolution imaging is needed to overcome this problem.

With the use of navigation equipment, pre-operative MRI scans are used to help neurosurgeons navigate to the destination of the glioma in the brain during surgery. However, due to brain and tumour shift during operation, these images do not reflect the real-time situation in the brain during surgery.

Intraoperative acquired, real-time images are therefore needed to correct for brain and tumour shift to optimize tumour resection. Nowadays, intraoperative MRI (iMRI) is an increasingly used as a tool to acquire real-time images and to improve extent of glioma resection during surgery. However, installing this technique in the operating room is highly expensive (between 3*5 million euros), has high maintenance costs, is extremely time consuming during operations (1-2 hours), and will not be available for most of the neurosurgical centres around the world. Intraoperative navigated high resolution ultrasound (US) could be an alternative.

Recently, a new intraoperative navigated high resolution US (developed by Brainlab and BK-medical) has been shown to be a promising cost-effective tool to acquire real-time intraoperative images to localize and to resect gliomas. Intraoperative US guidance costs a fraction of an MRI, has almost no maintenance costs, is much less time consuming and can be used to acquire real time images during surgery. With the use of (older) US, GTR percentages between 63% and 94% could be attained, but most of these published studies are biased by selection, where superficial small tumours have better resections as compared to more difficult to operate deeply seated larger tumours. The new intraoperative navigated high resolution US (developed by Brainlab and BK-medical) is a significant improvement as and has the potential to be incorporated standardly during resection of HGG in contrast to older (non-navigation fused) US devices.

The purpose of this study is to investigate the effectivity of the newly acquired intraoperative navigated US in achieving GTR in patients with HGG and to measure influence on quality of life. Our primary goal is to investigate whether the use of IOUS additional to neuronavigation improves after the extent of high grade glioma resection compared with the use of neuronavigation only. Our secondary goal is to investigate whether ultrasound guided tumor resection improves neurological outcome, quality of life and survival time, when compared with non-ultrasound guided tumor resection

**Study objective**

Primary Objective
To investigate whether ultrasound guided tumor resection succeeds gross total resection significantly more frequently, when compared with the conventional non-ultrasound guided tumor resection.

Secondary Objective(s)
To investigate whether ultrasound guided tumor resection improves the extent of resection , quality of life and survival time, without causing new neurological deficits more frequently, when compared with the conventional non-ultrasound guided tumor resection.

### Study design

Randomized Controlled Trial, Single Blinded
All newly diagnosed, untreated, contrast enhancing presumed high-grade glioma patients (18-75 year) will be randomized in two groups. In one group glioma surgery will be performed by using neuronavigation only (conventional treatment). In the other group, glioma surgery will be performed with the use of intraoperative ultrasound in addition to neuronavigation (ultrasound guided).

### Intervention

The study consists of two treatment arms: non-ultrasound guided glioma resection (conventional treatment) versus ultrasound guided glioma resection (intervention) .

### Study burden and risks

The standard treatment of glioblastoma patients consist of combined radiation and chemotherapy for a period of 6 weeks after surgery, followed by monthly cycles of chemotherapy alone, mostly during 6 months. Maximal and safe resection is the main goal of glioblastoma surgery and is currently still a great challenge. Finding an adjuvant neurosurgical tool to improve the extent of glioblastoma resection is of high importance. Ultrasound guided resection is a very low-risk alternative to a standard tumor resection procedure, which possibly shortly extends the time of surgery. In this study, patients will be randomised in two treatment arms: ultrasound guided or non-ultrasound guided glioblastoma surgery. During a follow up time of 6 months, patients will be called up 3 times to fill in 2 questionnaires to compare quality of life and neurological functioning. Both treatment arms will follow the standard treatment protocol for glioblastoma and no additional interventions will be done.

## Contacts

**Public**
Erasmus MC, Universitair Medisch Centrum Rotterdam

s-Gravendijkwal 230
Rotterdam 3015 CE
NL
**Scientific**
Erasmus MC, Universitair Medisch Centrum Rotterdam

s-Gravendijkwal 230
Rotterdam 3015 CE
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

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

## Inclusion criteria

- Individuals between 18-75 years
- Newly diagnosed, untreated, contrast enhancing presumed high-grade glioma
- KPS * 60
- Preoperative intention to perform gross-total resection of the enhancing tumor
- Written informed consent conform ICH-GCP

## Exclusion criteria

- Tumours crossing the midline basal ganglia, cerebellum, or brain stem prohibiting gross total resection
- Multifocal contrast enhancing lesions
- Pre-existing neurological deficit (e.g. aphasia, hemiparesis) due to neurological diseases (e.g. stroke)
- Inability to give consent because of dysphasia or language barrier

# Study design

### Design

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|---|---|
| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Single blinded (masking used) |
| Control: | Active |
| Primary purpose: | Diagnostic |

### Recruitment

NL

| | |
|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 01-09-2015 |
| Enrollment: | 50 |
| Type: | Anticipated |

## Ethics review

Approved WMO

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| Date: | 02-10-2015 |
| Application type: | First submission |
| Review commission: | METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam) |

## 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 | NL49175.078.15 |