Beyond Observed Lesion Diameter (BOLD) glioblastoma surgery: a multicenter randomized controlled trial

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To investigate if resection with a margin, that is significantly beyond the radiological contrast enhancement, improves overall survival in selected patients with glioblastoma.

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

Summary

ID

NL-OMON56831

Source
ToetsingOnline

Brief title
BOLD trial

Condition

- Nervous system neoplasms malignant and unspecified NEC
- Nervous system, skull and spine therapeutic procedures

Synonym
brain tumor, glioblastoma

Research involving
Human

Sponsors and support

Primary sponsor: St. Olavs University Hospital
Source(s) of monetary or material Support: Ministerie van OC&W,The Norwegian Cancer Society and the Nordic union

Intervention

Keyword: Glioblastoma, Supramarginal, Surgery

Outcome measures

Primary outcome

The main study endpoint is overall survival according to intention-to-treat

principle 36 months after the last included and randomized patient.

Secondary outcome

• Investigate survival 24 and 36 months after randomization.

• Investigate the neurological function using the Neurological assessment in

Neuro-Oncology (NANO) at early postoperative control and at study closure.

• Determine health-related quality of life using EQ-5D 3L, EORTC QLQ C30 and

BN20 questionnaires.

• Determine Neurocognition according to Mini Mental Status Examination (MMSE).

• Investigate perioperative 30 day surgical complications grade 3, 4 and 5,

assessed using the Dindo-Clavien classification.

• Determine the extent of resection using unintended contrast remnant, T2/FLAIR

remnant and Cavity volume/contrast enhancement volume data

Study description

Background summary

Gliomas are the most common malignant brain tumor, and they result in more years of life lost than any other tumor group. Glioblastoma, WHO grade IV astrocytoma, is the most common subtype and unfortunately also the most aggressive subtype with median survival in population based cohorts being only 10 months. Extensive surgical resections followed by postoperative fractioned radiotherapy and concomitant and adjuvant temozolomide prolong survival and is

the standard treatment. We think there is significant potential in individualized surgical decision-making in glioblastoma management, as it is counterintuitive that one size fits all. The current concept in all patients with glioblastoma is *maximum safe resection of the contrast enhancing tumor*, but we think this may be extended to simply *maximum safe resection* tailored to the patient and extent of disease at hand. The BOLD trial will therefor investigate if resection with a margin, that is significantly beyond the radiological contrast enhancement, improves survival in selected patients with glioblastoma.

Study objective

To investigate if resection with a margin, that is significantly beyond the radiological contrast enhancement, improves overall survival in selected patients with glioblastoma.

Study design

This is a multicenter randomized controlled trial with parallel group design in newly diagnosed suspected glioblastoma amendable to supramarginal resection. Patients will be randomized 1:1 between surgical removal of tissue clearly beyond the contrast enhancement seen on magnetic resonance imaging (supramarginal surgery group) and surgical removal of the tissue corresponding to the contrast enhancement on MRI (conventional surgery group).

Intervention

Surgical removal of tissue clearly beyond the contrast enhancement seen on magnetic resonance imaging (supramarginal surgery).

Study burden and risks

Patients with glioblastoma have a very poor prognosis. Surgery is often the only way to remove most of the tumor. A supramarginal resection has almost the same risk of complications as a normal resection, while the chance of longer survival appears to be greater because more of the tumor can be removed. The additional questionnaires and cognitive examinations are a very minor burden for the patients.
This research can contribute to improving treatment for patients with GBM and therefore ensure longer survival with a better quality of life.

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

The subjects must fulfill all the following inclusion criteria to be eligible for participation in the study, unless otherwise specified:
1. A suspected diagnosis of supratentorial glioblastoma by MRI.(A)
2. Indication for surgical treatment and where supramarginal resection is considered possible according to the preoperative imaging. This consideration needs to be verified by two specialists in neurosurgery.
3. Negative work-up for other primary tumor(B)
4. Age 18 years or older.
5. Karnofsky performance status of 70 - 100.41

A) If randomized to supramarginal surgery, intraoperative frozen section must conclude with *high-grade glioma* to be able to proceed. Surgery in two sessions is also possible in supramarginal group if there is no intraoperative frozen section available or frozen section indicate another diagnosis, but final histopathology reveals a glioblastoma. In case of surgery in two session, there must be no more than 30 days between procedures. See flow-chart in

attachment 1.
B) No suspected primary tumor seen on CT chest, abdomen and pelvis. If relevant symptoms/clinical suspicion also supplement with mammography, dermatologist exam, relevant endoscopies etc.

Exclusion criteria

Potential study subjects who meet any of the following criteria are not eligible for participation in the study:
1. Not willing to be randomized.
2. Informed consent not possible (e.g. language barriers, aphasia, cognitive severely impaired).
3. Contrast enhancement volume bilateral OR involving corpus callosum.
4. Contrast enhancement along the ependymal lining of ventricles (contact is however not an exclusion criteria).
5. Contrast enhancement involving several lobes.
6. History of major psychiatric disorder such as psychosis, schizophrenia and/or mood disorder (e.g. depression and bipolar disorder) in need of hospitalization
7. Unfit for participation for any other reason judged by the including physician

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	03-03-2025

Enrollment:	30
Type:	Anticipated

Ethics review

Approved WMO Date:	20-06-2024
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
ClinicalTrials.gov	NCT04243005
CCMO	NL86360.078.24