Glioblastoma broadband power as a longitudinal biomarker for tumor progression

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

Summary

ID

NL-OMON54202

Source
ToetsingOnline

Brief title
GOALS2

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
brain tumor, glioblastoma

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: KWF kankerbestrijding

Intervention

Keyword: biomarker, brain activity, glioblastoma, glioma

Outcome measures

Primary outcome

(1) MEG/EEG brain activity at different timepoints during the disease, and (2)

radiological and clinical markers of tumor growth

Secondary outcome

(1) chemical exchange saturation transfer (CEST) MRI and resting-state

functional MRI (rsfMRI) at a number of timepoints

Study description

Background summary

Glioblastoma (grade IV glioma) is a devastating disease with dismal prognosis, for which individualized treatment through biomarkers is often aimed for, but rarely achieved. This lack of success necessitates a radically different way of thinking, which our group has been exploring in the past years. Recent work shows that glioma growth may not only depend on characteristics of the tumor itself, but is also determined by activity of the healthy tissue around it.
Higher activity of neurons surrounding glioma in an animal model has been shown to cause an acceleration of glioma growth, through glutamate-dependent *neurogliomal synapses*. Development of these synapses is promoted through increased neuroligin-3 (NLGN3) expression, which is also caused by higher neuronal activity. This causal relationship indicates that higher neuronal activity leads to faster tumor growth.
In patients, neuronal activity is difficult to measure directly, but the broadband power of electroencephalography (EEG) and magnetoencephalography (MEG) may most straightforwardly relate to neuronal activity. EEG and MEG allow for easy, non-invasive and low-burden measurement of brain activity: a five minute resting recording usually suffices.
We already translated some of these preclinical results, first showing that lower broadband power (indicating less neuronal activity) at the time of diagnosis relates to lower NLGN3 expression in resected tumor tissue in glioma patients.16 Moreover, lower broadband power relates to longer progression-free survival (PFS), with a hazard ratio (HR) of 2.1, adjusted for known predictors

of PFS. In a second study, we replicated these results in the postoperative phase of the disease, showing again that glioma patients with greater broadband power have shorter PFS (HR 2.5, adjusted for known predictors).
These promising results raise the question whether broadband power might be useful as a prognostic biomarker during the disease course of glioblastoma, and particularly during the standard first line treatment period comprised of chemoradiation and adjuvant chemotherapy. In this timeframe, distinguishing between pseudoprogression and actual tumor progression is an important clinical challenge, which limits optimization of treatment.

Study objective

We will investigate (1) whether broadband power can be measured repeatedly and accurately within this patient population with limited variation in case of stable disease, (2) whether meaningful changes in broadband power in the case of real progression exceed normal variations, and (3) whether it is possible to establish a cut-off score for broadband power that may provide clinically relevant diagnostic accuracy (taking the REMARK guidelines into account).

Study design

Longitudinal, observational study.

Study burden and risks

MEG/EEG does not bear any risks: this is a completely non-invasive measurement of brain activity, that does not make use of radiation. The additional MRI sequences do not present risks either: CEST is a safe sequence, which is already a clinical/commercial product of some vendors inside the Netherlands (e.g. Philips Healthcare). Task and rsfMRI are routinely performed in these patients and also do not bear any risk. Patients will be aware that they can refuse to undergo the extra scan times anytime including during the ongoing scan.
The burden of participation consists of undergoing these extra measurements at maximum five times. These measurements will be combined with necessary visits to the hospital as much as possible, to limit effort and time investment of the patients. There is no benefit of participation for patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

(1) age > 17 years, (2) histopathologically confirmed glioma, (3) eligible to start radiotherapy

Exclusion criteria

(1) psychiatric disease or symptoms at the time of inclusion, (2) other comorbidities of the central nervous system, particularly cerebrovascular accidents, multiple sclerosis, Alzheimer*s disease, (3) insufficient mastery of the Dutch language, (4) inability to communicate adequately. For the additional MRI sequences, an exclusion criterium is incompatibility with MRI.

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):	08-12-2021
Enrollment:	100
Type:	Actual

Ethics review

Approved WMO Date:	28-07-2021
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	31-01-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-02-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL76472.029.21
Other	NL9817