Characterization of IDH1-mutational status in gliomas by 31P/H1 MRSI

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Primary objective: to non-invasively characterize the IDH1-mutational status of gliomas in patients by measuring the ratio of GPC/PE with 31P MRSI and 2HG content by 1H MRSI in the same examination. This is expected to make the identification of the…

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

Summary

ID

NL-OMON43436

Source
ToetsingOnline

Brief title
31P and 1H MRSI of brain tumors

Condition

- Nervous system neoplasms malignant and unspecified NEC

Synonym
brain tumor, glioblastoma, glioma

Research involving
Human

Sponsors and support

Primary sponsor: Radiologie en Nucleaire Geneeskunde
Source(s) of monetary or material Support: dept. Radiology and Nuclear Medicine;Radboudumc Nijmegen

Intervention

Keyword: biomarker, gliomas, IDH1, MRSI

Outcome measures

Primary outcome

The main parameters for the 1st objective are the integrated normalized peak areas of GPC and PE (31P MRS) and of 2HG (1H MRS). For the 2nd objective complete spectra will be evaluated. Outcomes will be correlated with IDH status which is available from clinical data.

Secondary outcome

n.a.

Study description

Background summary

About 70% of low grade gliomas and secondary glioblastomas harbor a gene mutation for isocitrate dehydrogenase (IDH1). Because these patients have a better clinical perspective and IDH1 is a potential therapy target it is important to identify the mutation. This can be done by analyzing tumor biopsies from the brain, but as this is a major burden to the patient a non-invasive biomarker is preferred.

It is known that tumors with the IDH1R132H mutation accumulate the oncometabolite D-2-hydroxy-glutarate (2HG) to a high level, detectable by non-invasive 1H MR spectroscopic imaging (MRSI). However, to uncover the signal of 2HG a special acquisition method is required that under unfavorable conditions may cause false positives. Hence it is necessary to find other MR biomarkers to improve the specificity of the non-invasive detection of IDH1 mutations.

In a recent 31P MRSI study of human tumors growing in the mouse brain we observed that the level of glycerophosphocholine (GPC) is increased and that of phosphoethanolamine (PE) is decreased in IDHR132H gliomas1. These specific changes were also observed in extracts of IDH1 mutated cell lines and in tumor biopsies of patients. The GPC and PE biomarker signals are better resolved and

less affected by field homogeneities than those of 2HG.

To monitor 31P compounds non-invasively in patients we use a dual 1H/31P detection probe for our clinical MR system with a much better signal-to-noise than commonly available. With this coil we already successfully obtained 31P MRS images with GPC and PC signals. The 31P spectra also show signals for important energy compounds such as phosphocreatine (PCr), ATP and inorganic phosphate (Pi) and from the resonance of Pi we can derive intracellular tumor pH. Moreover, in the same examination we obtained 1H MR spectra with signals that have been found to be of major interest to characterize brain tumors such as of choline (Cho).

Study objective

Primary objective: to non-invasively characterize the IDH1-mutational status of gliomas in patients by measuring the ratio of GPC/PE with 31P MRSI and 2HG content by 1H MRSI in the same examination. This is expected to make the identification of the mutation more reliable.

Secondary objective: to include the full information content of the 1H and 31P MR spectra in the characterization of the tumors. In particular the 31P MR spectra are of interest as we overcome partial volume effects that hampered previous 31P MR studies of brain tumors.

Study design

The study is observational. Patients will be examined after diagnosis and before the tumor is (partially) removed.
The measurements take place during the same session in which the neuro navigation MRI scan will be performed in the context of the treatment protocol.

Study burden and risks

Patients will be examined on a clinical 3T MR system. They will be in a supine position in the magnet with the head positioned in a double tuned 1H/31P birdcage head coil (Rapid Biomedical) equipped with an 8 channel 31P receive array insert. The measurements take about 60 minutes per patient. Risks of the examination are equal to the risks of regular clinical MRI exams without the use of contrast agents.

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

Patients must meet all of the following inclusion criteria:
- Adult (18+)
- Diagnosed low grade or secondary high grade glial brain tumor
- MR compatibility is verified using a questionnaire
Control group volunteers must meet all of the following inclusion criteria:
- Preferably age and sex matched
- have no indication of (prior) cerebral abnormalities
- MR compatibility is verified using a questionnaire

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- unable to provide informed consent
- any medical condition is present that might interfere with the study protocol, such as brain injuries, epilepsy, a major cardiovascular disease event or anxiety disorders.
- Use of any medication, except for oral contraceptives

- MR(I) contraindications (pregnancy, severe claustrophobia, metal parts in body)

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-02-2016
Enrollment:	45
Type:	Anticipated

Ethics review

Approved WMO

Date:	16-06-2016
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL56008.091.16