Metabolic MRI in brain cancer and epilepsy

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Develop a fast metabolic MRI protocol, based on DMI and 31P-MRSI at ultra-high field MRI, to investigate the Warburg effect and phospholipid metabolism in glioblastoma and to asses metabolic disruption in epilepsy.

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

Summary

ID

NL-OMON53308

Source
ToetsingOnline

Brief title
MINT

Condition

- Nervous system neoplasms malignant and unspecified NEC
- Cranial nerve disorders (excl neoplasms)

Synonym
glioma; brain tumor

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Utrecht
Source(s) of monetary or material Support: namelijk VENI beurs

Intervention

Keyword: 31P, Deuterium, Glioma, Metabolic MRI

Outcome measures

Primary outcome

Part 1: Quantified rates of brain glucose metabolism; a scan is successfull if an SNR>5 for 2H-Glx is reached

Part 2a: Quantified levels of phospholipid metabolites and glucose metabolism in the tumor compared to those levels in healthy brain tissue from the same subject

Part 2b: Quantified levels of glucose metabolism in the epileptogenic cortex (determined by either a structural lesion, PET or neurophysiology) compared to healthy brain tissue from the same subject

Secondary outcome

Part 1:

Optimal dose of [6,6*-2H2]-glucose

Optimal timing between administration of [6,6*-2H2]-glucose and static DMI

Plasma glucose levels

Deuterium enrichment of plasma water, lactate and glucose

Part 2a:

Change in glucose metabolism and phospholipid levels in response to treatment

pH levels of the tissue, assed by 31P MRSI

redox status of the tissue, assed by 31P MRSI

Change in tumor volume, measured on conventional imaging according to RECIST

criteria

Part 2b:

Glucose metabolism compared to FDG-PET metabolism

Glucose metabolism in areas with invasive neurophysiological abnormalities

Study description

Background summary

Glioblastoma is the most common brain tumor in adults. Glioblastoma patients face a dismal prognosis, with a median overall survival of only 12-18 months after diagnosis. Despite extensive research on new therapies, this survival rate has not changed significantly over decades. Better understanding of glioblastoma pathophysiology is of utmost importance.

Metabolic reprogramming is the central hallmark of cancer, and itis thought that metabolic alterations precede morphological tissue changes in cancerous tissue. Imaging tumor metabolism will give insights in brain tumor pathophysiology. Here we aim to develop a fast, repeatable and non-invasive metabolic MRI protocol to detect two important aspects of metabolic reprogramming in glioblastoma: (1) the Warburg effect and (2) altered phospholipid metabolism. The metabolic MRI protocol will be dedicated to image these altered metabolic pathways, using two complementary techniques: deuterium metabolic imaging (DMI) and 31P-MR spectroscopic imaging (31P-MRSI), respectively.

In order to assess the extent of measurable metabolic disruption, we will also include patients with epilepsy in this study. Epilepsy results in disrupted brain metabolism (glutamate, glutamine, GABA), but likely in a more subtle way than in glioblastomas. Furthermore, epilepsy patients with PET hypometabolism exhibit a disturbance in glucose metabolism and epilepsy often occurs as a symptom of glioblastomas. Therefore, it is useful to have an idea of the degree of (measurable) metabolic disruption resulting from epilepsy alone.

Study objective

Develop a fast metabolic MRI protocol, based on DMI and 31P-MRSI at ultra-high field MRI, to investigate the Warburg effect and phospholipid metabolism in glioblastoma and to asses metabolic disruption in epilepsy.

Study design

Observational study. The study consist of two parts. First scan parameters will be evaluated, optimized an validated in a optimization study (part 1). Then we will characterize brain tumor metabolism and evaluate treatment effects (part 2a) and characterize metabolic disruptions in epilepsy (part 2b).

Study burden and risks

Subjects participating in part 1 will visit the UMC Utrecht once or twice. Subjects will be subjected to 4-hour fast and upon arrival an intravenous access site will be installed in a vein in the arm for frequent blood sampling (i.e. every 10 min, 5-10 ml). Only in part 1 The metabolic MRI scan will take 120-150 min.

Glioblastoma patients participating in part 2 will visit the UMC Utrecht three times. Epilepsy patients in part 2 will vist the UMC Utrecht once. Subjects will be subjected to 4-hour fast. During each visit they will undergo a 7T metabolic MRI scan of ~60 minutes. Before each scan, they will receive an oral dose of deuterated glucose (max 0.75 g/kg, with a maximum of 60 g) dissolved in water (0.2 g/ml).

The intake of above mentioned amounts of deuterated glucose, and drawing of the above mentioned amount of blood (only in part 1) does not affect the health of participants. Deuterium (2H) is a stable, non-radioactive, isotope of hydrogen, and biologically, deuterated glucose behave similarly to normal glucose. No adverse effects have been observed with oral administration of deuterated glucose at the dosage which will be used in this study.

MRI is a safe and reliable technique for subjects without contra-indications for undergoing MRI and is widely used in clinical examinations and scientific research. Subjects included in the study will have no contra-indications for MRI and they will be screened again for standard contra-indications before undergoing the MRI examination(s).

Patients will not have a direct benefit from participating. However, the outcome of this study will aid in better understanding of tumor physiology, which may improve diagnosis and treatment evaluation and the consequent individual treatment decisions

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

All subjects: - Aged >18 years
- Ability to give informed consent
- Ability to follow test instructions
- Sufficient understanding of the Dutch or English language

Glioblastoma Patients in part 2a
- Patients who are newly diagnosed with a (suspected) glioblastoma IDH wild type and with a relevant lesion (>1 cm3; prior to surgery) on conventional MRI
- Patients who will start treatment according to the Stupp regimen (for part 2a only)

Epilepsy Patients in part 1
- Patients diagnosed with epilepsy with a relevant lesion detected by FDG PET

Epilepsy Patients in part 2b
- Patients diagnosed with epilepsy with or without a lesion on conventional MRI

Exclusion criteria

- The presence of claustrophobia;
- MRI-specific exclusion criteria, such as metal implants.
- Refusal or inability to provide informed consent
- Pregnant or lactating
The presence of diabetes mellitus type 1 and 2;
The presence of a medical condition which influences brain metabolism

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-09-2023
Enrollment:	56
Type:	Actual

Medical products/devices used

Generic name:	7T MRI with 2H1H head coil and 31P2H borecoil
Registration:	No

Ethics review

Approved WMO Date:	19-07-2023
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	17-04-2024
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	NL83501.041.23