Blood-Brain Barrier permeability quantification in cerebral small vessel disease -- reproducibility of dynamic contrast-enhanced MRI

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Primary Objective: To realize a clinically applicable quantification of BBB permeability using DCE-MRI by determining the reproducibility of the DCE-MRI methodSecondary Objective: To achieve the shortest scan duration without compromising the...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Central nervous system vascular disorders
Study type	Observational invasive

Summary

ID

NL-OMON38519

Source
ToetsingOnline

Brief title
Blood-brain barrier quantification in cerebral small vessel disease

Condition

- Central nervous system vascular disorders

Synonym
Cerebral small vessel disease; disease of the small brain arteries

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht

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

Intervention

Keyword: Blood-brain barrier permeability, Cerebral small vessel disease, Dynamic contrast enhanced MRI, Pharmacokinetic modeling

Outcome measures

Primary outcome

The primary study parameters are: Quantitative pharmacokinetic parameter values: Ki, linked to the BBB permeability, and vb linked to the blood volume.

Primary endpoint is to assess the reproducibiliy of the quantified pharmacokinetic parameters

Secondary outcome

The secondary study parameters are: Quantitative parameters: mean Ki and standard error in the mean Ki determined as a function of scan duration. Mean Ki is taken over all ROI*s or all subjects. The standard error is taken as a measure for the reliability.

Secondary endpoint is to assess the optimal scan duration without compromizing the reliability of the quantification of the pharmacokinetic parameters.

Study description

Background summary

Cerebral small vessel disease (cSVD) encompasses all pathological processes that affect the small vessels of the brain. On brain-MRI cSVD is characterized by structural brain abnormalities such as white matter lesions (WMLs). Clinically, cSVD is related to acute syndromes as lacunar stroke but also to more chronic health problems such as cognitive decline.
Recent literature suggests that a disrupted blood brain barrier (BBB), leading to elevated BBB permeability, may play a pivotal role in the aetiology of cSVD

and lacunar stroke. The BBB is a complex system of neuronal, glial and vascular cells which main function is to shield the brain from toxic components and regulate the homeostasis. Elucidating the role of the BBB may have far reaching consequences for the treatment of cSVD patients and the reduction of recurrence rate of the disease. This could lead to a better quality of life among cSVD patients and reduce the economic burden on society.
Currently the exact contribution and extent of a possibly defective BBB in cSVD remains largely unclear, due to the lack of a reliable method to accurately quantify the BBB permeability in cSVD patients. As a result, the current treatment consists of treating the cardiovascular risk factors, often with poor results.
Quantification of the BBB permeability provides an objective measure of the integrity of the BBB and as such aids the study of the role of the BBB. The aim of this study is to realize a clinically applicable MRI-method to quantify the BBB permeability. Moreover, the method can be used to study the involvement of BBB disruption in other neuropathologies including Alzheimer*s disease, vascular dementia, hypertension and diabetes.

Study objective

Primary Objective:
To realize a clinically applicable quantification of BBB permeability using DCE-MRI by determining the reproducibility of the DCE-MRI method

Secondary Objective:
To achieve the shortest scan duration without compromising the reliability of the BBB permeability quantification.

Study design

A prospective reproducibility and validation study

Study burden and risks

We do not expect the participants to be at any risk during the study and we do not expect them to benefit from this study directly.
Participants are asked to visit the hospital two times for a dynamic MRI scan. During these examinations a two-step intravascular injection of contrast agent is required. This may lead to an alergic reaction in rare cases. It is possible that participants will experience the MRI scans as uncomfortable due to the long scan duration, the small space inside the scanner, and the noise (hearing protection is obligatory).

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

All subjects:
- Age >18 years old
- The condition of the patient must be well enough to allow participation in the study, which is decided in consultation with the treating physician.;cSVD patients:
- patients who present with a transient ischemic attack (TIA) and cSVD related abnormalities on brain MRI. TIA patients are defined as patients with stroke like symptoms that last no longer than 24 hours. MRI abnormalities include extended white matter lesions, (asymptomatic) lacunar infarcts, microbleeds and enlarged Virchow-Robin spaces. The patients are eligible when the first DCE-MRI scan can be performed 8-12 weeks after the TIA to avoid the acute phase, and the second MRI-scan within four weeks after the first.;Cortical stroke or primary intracerebral hemorrhage patients:
- patients who have a clear clinical presentation of either cortical stroke or primary

intracerebral hemorrhage confirmed on brain CT. The patients are eligible when the DCE-MRI scans can be performed within 0-6 weeks of the vascular event and on two subsequent days as the vascular permeability may change significantly on the timescale of weeks.

Exclusion criteria

All subjects:
- History of cerebrovascular disease (e.g. ischemic/hemorrhagic stroke)
- History of other diseases of the central nervous system (e.g. epilepsy, brain tumor, multiple sclerosis)
- Contra-indications for MRI examination: e.g. pacemaker; neurostimulator; medication pump; cochlear or hearing implant; tattoos or other items that cannot be removed and include metal parts (for instance from operations in the past); metal splinter in the eye; pregnancy and claustrophobia; brain vessel clamps; denture, which contains magnets.
- Contra-indication for MRI contrast agent: e.g. strong suspicion for impaired kidney function, previous allergic reaction to contrast agent, dialysis patients
- Psychiatric co-morbidity and inability to perform the (DCE-)MRI scans.;cSVD patients
- Patients with a potential cardioembolic source (e.g. atrial fibrillation)
- Stenosis of *50% of one or both internal carotid arteries ;Cortical stroke or primary intracerebral hemorrhage patients:
- Extensive cSVD related abnormalities on brain MRI

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-06-2014
Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	11-09-2013
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL44496.068.13