[11C]MeDAS PET: an imaging tool for quantitative assessment of changes in myelin density over time in multiple sclerosis

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Demyelinating disorders
Study type	Interventional

Summary

ID

NL-OMON49461

Source
ToetsingOnline

Brief title
Changes in myelin density

Condition

- Demyelinating disorders

Synonym
MS, multiple sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen

Source(s) of monetary or material Support: ZonMW

Intervention

Keyword: Multiple sclerosis, Myelin, PET

Outcome measures

Primary outcome

The main study parameter is detection of changes in myelin density in MS lesions over time, indicative for myelin degradation or repair, as determined by [11C]MeDAS PET imaging.

Secondary outcome

Secondary study endpoints:

• The correlation between [11C]MeDAS PET and clinical characteristics

• The correlation between [11C]MeDAS PET results and specific MRI defined lesion types (black holes, normal appearing white matter, etc.)

• The correlation between [11C]MeDAS PET results and putative MRI correlates of myelin density

Study description

Background summary

Multiple sclerosis (MS) is a neurodegenerative disease, in which myelin sheaths in the brain and spinal cord are damaged. If repair of myelin damage is incomplete, nerve terminals will be irreversibly destroyed, leading to neurological symptoms. Ineffective remyelination is probably a major underlying mechanism resulting in irreversible neurological impairments in the progressive phase of MS. Most therapies aim to stop inflammatory processes associated with the myelin damage, but all lack efficacy in progressive MS so far. Strategies that promote myelin repair are promising, but still under investigation. Non-invasive imaging of myelin damage and repair could enable better disease characterization and accelerate evaluation of new interventions. Although MRI

is successfully used in MS diagnosis, it cannot quantify myelin changes. We have demonstrated in animal models for MS that damage and repair of myelin can be visualized and quantitatively measured by PET using the newly developed tracer [11C]MeDAS. In addition, our previous study showed the feasibility to image differences in myelin density using this tracer in human subjects. During the first in human [11C]MeDAS scans, no adverse events occurred and both the scan protocol as well as the scan itself were well tolerated. Preliminary results indicate that [11C]MeDAS binds primarily to white matter and is rapidly metabolised, which leads to a fast clearance from the body. The data suggests that [11C]MeDAS might have the potential to determine the efficacy of remyelination therapies, which has to be confirmed by performing scans in a longitudinal fashion. We now aim to investigate the applicability of [11C]MeDAS to image changes in myelin density over time and thereby determine the efficacy of [11C]MeDAS PET to image myelin degradation and repair. The scanning procedure will be performed in patients with progressive MS and results will be correlated to MRI results and (changes in) clinical symptoms. In progressive MS, myelin loss is expected to outweigh spontaneous remyelination.

Study objective

The objective of this study is to evaluate [11C]MeDAS PET as a quantitative method for assessment of changes in myelin density over time and thus the efficacy of [11C]MeDAS PET to image myelin degradation and repair.

Study design

The design of this study is a diagnostic intervention, validating [11C]MeDAS as a myelin tracer in MS patients for imaging changes in myelin density over time.

Intervention

The subjects will undergo two PET scans (with an interval of 9-12 months) with the myelin tracer [11C]MeDAS, which binds to β-sheet structures within intact Myelin Basic Protein (MBP). In addition, the subjects will undergo two MRI scans for comparison.

Study burden and risks

The subjects in this study will undergo two [11C]MeDAS PET scans with approximately 1 year interval. During the PET scans, 260 ml of blood is taken for radioactivity and radiometabolites measurements. At both time points, a MRI scans will also be made. For the PET scans, the subjects have to come to the UMCG two times. The MRI scans will be combined with these visits. The adverse events can be a bruise as a result of the arterial catheter or an idiosyncratic reaction to the tracer. The injected mass of [11C]MeDAS is negligible and idiosyncratic reactions are rare to occur for radioactive PET tracers.

Nevertheless, a physician will be available during each injection of the tracer. In addition, the radiation burden the subjects in this study are exposed to of 3.6 mSv, is within category IIb (1-10 mSv, minor to moderate risk), according to the International Commission on Radiological Protection (ICRP62). The subjects will not directly benefit from the study, but will help to evaluate the reliability of a measurement for myelin quantification. Such a method can aid the development of treatments that promote remyelination, by being able to directly quantify myelin density. For the MRI protocol, gadolinium is used, which can cause adverse events in 0.4% of cases. These adverse events are feeling warmth, brief headache or dizziness, all these events are reversible and disappear immediately after injection. During the first in human [11C]MeDAS scans, no adverse events occurred and both the scan protocol as the scan itself were well tolerated. Preliminary results indicate that [11C]MeDAS binds primarily to white matter and is rapidly metabolised, which leads to a fast clearance from the body. The data suggests that [11C]MeDAS might have the potential to determine the efficacy of remyelination therapies, which has to be confirmed by performing scans in a longitudinal fashion.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
• At least 18 years of age
• A diagnosis of primary or secondary progressive MS
• Sign an Institutional Review Board (IRB) approved informed consent form prior to any study procedures
• Subjects who, in the opinion of the principal investigator, can tolerate the [11C]MeDAS PET, MRI and blood sampling procedures

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
• Women who are pregnant or breast feeding
• Clinical history of diminished renal and/or liver function
• Inability to undergo MRI-scanning due to presence of materials in the body that can be magnetized and cannot be removed
• Claustrophobia
• Current clinically significant cerebrovascular disease
• Blood donation within 6 months prior to the [11C]MeDAS PET scan
• Current use of any investigational medications, or having participated in a trial with investigational medication within the last 30 days
• In the opinion of the investigator, otherwise unsuitable for a study of this type

Study design

Design

Study phase:	2
Study type:	Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-07-2020
Enrollment:	15
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	N-c-11-Methyldiaminostilbene
Generic name:	[11C]MeDAS

Ethics review

Approved WMO

Date:	23-06-2020
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2019-004636-33-NL
CCMO	NL72238.042.19