Accurate multiple sclerosis atrophy measurement system

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Ethical review	Approved WMO
Status	Completed
Health condition type	Demyelinating disorders
Study type	Observational non invasive

Summary

ID

NL-OMON51042

Source
ToetsingOnline

Brief title
AMS2

Condition

- Demyelinating disorders

Synonym
Multiple Sclerosis

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: ZonMW en Stichting MS Research

Intervention

Keyword: Atrophy, MRI, Multiple sclerosis (MS)

Outcome measures

Primary outcome

The main study endpoint is to create a proof-of-concept in a clinical setting: by validating the standardization directly in MS patients and controls. This allows us to measure the quantitative measures: inter-class correlation coefficient for absolute agreement and reduced volume differences between scanners, as well as the mean absolute differences and limits of agreement of inter- and intra-scanner variation. We will compare the volume of gray matter, white matter and the whole brain.

Secondary outcome

In the same format as the primary outcome measures, we will also look at the volume changes in gray matter, white matter and the whole brain. This allows us to measure the quantitative measures: inter-class correlation coefficient for absolute agreement and reduced volume differences between scanners, as well as the mean absolute differences and limits of agreement of inter- and intra-scanner variation.

Study description

Background summary

With the help of Magnetic resonance imaging (MRI) shrinkage of the brain can be monitored. This shrinkage is usually referred to as atrophy and has been observed to be 10 times faster in multiple sclerosis (MS) compared to normal aging of the brain. The responsible processes for this decline have not fully

been identified. However, several treatments for MS have recently shown to reduce brain atrophy rates. Although this seems promising, atrophy rates are rarely is used for the decision of treatment for patients. One of the reasons for this is that systematic differences between scanners arise, possible leading up to a 10% different measured volume on different scanners. Therefore, current volume measurement software cannot account for these differences and the measurements of the brain volume could be unreliable. We will develop a measurement system to remove differences between scanners, thus creating a reliable method to assess brain atrophy with the help of conventional MRI.

Study objective

The main objective of this project is to validate a standardized volume measurement system (using eight in-house 3D printed phantoms) to allow for reliable atrophy measurements in MS, by quantifying between-scanner and within-scanner reproducibility in volume measurements. Secondly, we will quantify between-scanner and within-scanner reproducibility in a longitudinal setup.

Study design

The method we are going to test uses so-called *phantoms*. Using 3D printing and precision mechanical techniques, we simulate brains with different severity of brain shrinkage. We use this as a standard (reference) to be able to align (standardize) the measurements in patients between different scanners and institutions. Such objects whose properties are known and which are used for reference are called *phantoms* in the MRI field. Our phantoms consist of compartments that are very precise throughout and mimic the cortex, the ventricles (chambers of cerebrospinal fluid), and white matter, ensuring that we know the volumes of all compartments very precisely. In a small pilot we made a first prototype of such a phantom. It turns out that we can produce the phantoms with this technology and that they are imagable on the MR scanner.

In this project, we will create a set of eight phantoms and use them to standardize volume measurements in 30 MS patients and 10 healthy subjects. These participants are all scanned on the same day on three different MRI scanners as much as possible. If that does not fit into the schedule, these three scans can also be spread over several days. We ask these participants back after 2 years ± 5 months for the same scans, to investigate the effect of the standardization on the measurement of volume change. No invasive procedures are performed or substances are administered. The volume measurements are standardized retrospectively, based on additional MRI measurements performed without the volunteer being present.

With the following scan procedure:
1. Scan and re-scan on scanner number 1.

2. Scan and re-scan on scanner number 2.
3. Scan and re-scan on scanner number 3.
Each pair of scan or re-scan takes approximately 50 minutes.

The scheduling of the various scans is done in consultation with the participant and based on the availability of the MRI scanners for this examination. The scan may, in consultation with the participant, be made on the same day or spread over a few days. Analysis: Intra- and inter-scanner reproducibility will be quantified using the median absolute difference as well as limits of agreement based on linear mixed model analyzes. These analyzes will be performed for both the corrected and uncorrected volumes measured with state-of-the-art methods: SIENA (X), FIRST and FreeSurfer.

Study burden and risks

Althoughthere are no immediate risks or side effects, and the patient undergoes the same clinical scan that he or she would otherwise have received, there is a significant burden. This is because all patients and healthy subjects undergo MRI scans for a total duration of 3 hours on one day. In the meantime, the movement from one scanner to another still has to take place (not all scanners are located in the same building section). All in all, this is a considerable burden, in addition to the usual inconveniences of undergoing an MRI scan, such as the noise and having to stay still in a narrow tunnel. We will explicitly inform potential participants about this, in order to prevent someone from starting the research insufficiently prepared and encountering unpleasant surprises. Because no contrast agent is administered, there is no additional burden on the MRI scans. The phantoms are scanned without the patient being present, so this also does not play a role. We will clearly advise participants about all possibly burdensome aspects, to avoid exposing anyone to this burden unknowingly. In a previous project, we have used a similar set-up to compare three scanners in 21 MS patients. The patients in that study indicated that although long, the burden was tolerable. No immediate benefits are expected for the patients.

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

MS patient group:
1. Clincally definite relapsing-remitting, secondary progressive, primary progressive MS, according to McDonald criteria (2017).
2. 18 to 70 years old.
3. Be able to undergo 6 MRI scans (scan and rescan on three different MR scanners) in one day
4. Written informed consent

Healthy controls:
1. 18 to 70 years old.
2. Written informed consent

Exclusion criteria

1. Inability to undergo MRI, e.g. metal objects in or around the body, claustrophobia or inability to lie still in the
scanner.
2. Pregnant
3. Past or current clinically relevant non-MS neurological or psychiatric disorder(s)
4. Past or current clinically relevant (auto)immune disorder(s)
5. Colleagues from the same department, people directly involved in the study or people with relevant relations to the aforementioned people (e.g. partner,

parent, sibling or child etc.).

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Other

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	18-01-2021
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO

Date:	21-04-2021
Application type:	First submission
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	NL75420.029.20