# Longitudinal study of biological surrogate markers in primary progressive Multiple Sclersosis.

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| **Ethical review** | Approved WMO |
| **Status** | Pending |
| **Health condition type** | Demyelinating disorders |
| **Study type** | Observational invasive |

## Summary

### ID

NL-OMON31170

**Source**
ToetsingOnline

**Brief title**
Biological surrogate markers in primary progressive MS

### Condition

- Demyelinating disorders

**Synonym**
MS

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Vrije Universiteit Medisch Centrum
**Source(s) of monetary or material Support:** de stichting MS Research

## Intervention

**Keyword:** Magnetic resonance imaging, Multiple Sclerosis, neuroaxonal damage, surrogate markers

## Outcome measures

### Primary outcome

To improve the sensitivity of surrogate markers for neuroaxonal damage for

clinical trials by combining MR measures longitudinally.

To assess if any baseline measures of atrophy, NAA/Cr, MTI or DTI predicts a

subgroup of patients who subsequently have greatest rates of atrophy.

### Secondary outcome

To assess whether potential serum and urine biomarkers of neurodegeneration may

have added value.

To produce data for powering neuroprotective studies for all of the different

combinations of MR and biological fluid markers. This would allow selection of

measures in the future depending on the study requirements.

To assess reproducibility and reliability of the data between centers.

# Study description

### Background summary

Patients with primary progressive multiple sclerosis represent a subgroup with clinical and MRI characteristics that differ from those of patients with relapsing-remitting multiple sclerosis / secondary progressive multiple sclerosis. They have less MRI lesion activity (lesion volume) and new lesions, more lesional neuroaxonal damage and less inflammation, more diffuse damage and spinal cord involvement. Thus, in PPMS patients the correlation between conventional MRI measures and clinical disease severity is poor.

### Study objective

This study aims at investigating in vivo the macroscopic and microscopic aspects of brain and cervical cord neuroaxonal pathology in multiple sclerosis in a cohort of PPMS patients, by measuring brain and cervical cord atrophy, the ratio of N- Acetyl aspartate (NAA) and Creatine (Cr), magnetization transfer variables and diffusion tensor metrics. Such measures will assess cortical and subcortical structures * total brain, white and gray matter, thalamic, corpus callosum and cervical cord volumes or area, thalamic and corpus callosum NAA/Cr, whole brain, thalamic and corpus callosum MT measures, whole brain, thalamic and corpus callosum diffusion tensor metrics.

This study will also collect clinical data in the form of EDSS and MSIS-29 scores. Furthermore, in order to relate MRI parameters of neuroaxonal degeneration to body fluid markers of neuroaxonal degeneration, blood and urine samples will be collected

**Study design**

Patients and healthy controls will be studied at baseline, 2 , 50 and 52 weeks. MRI scanning will be performed. Disability will be assessed in patients using Kurtzke*s Expanded Disability Status Scale (EDSS) (Kurtzke, 1983) and the Multiple Sclerosis Impact Scale (MSIS -29) at the same time points. Blood and urine samples will be collected from patients and healthy controls at the same frequency as the imaging.

**Study burden and risks**

Subjects participating to this study will undergo four MRI scans. Also, on same occasions urine and venous blood will be collected. Lastly, only patients undergo each time a neurological exam and a selftest. This will all be done in one year.
There are practically no risks associated with participation with this study.

The burden of the study will be primarily the boredom or inconvenience of lying in a MRI scanner. Also, there is the burden of the needle (four times).
Finally, patients also have the burden of being subject four times to a neurological exam and the selftest.

# 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 patients: disease type should be primary progressive and EDSS should be 0-6.5
Both patients and healthy controls should have an age between 18-60 years of age

## Exclusion criteria

Immunomodulatory medication
Claustrophobia or other contraindications to MRI
Neurological or psychiatric disease or history

# Study design

## Design

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|---|---|
| Study type: | Observational invasive |
| Intervention model: | Other |

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| Allocation: | Non-randomized controlled trial |
| Masking: | Open (masking not used) |
| Control: | Active |
| Primary purpose: | Diagnostic |

### Recruitment

NL

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|---|---|
| Recruitment status: | Pending |
| Start date (anticipated): | 01-01-2008 |
| Enrollment: | 20 |
| Type: | Anticipated |

## Ethics review

Approved WMO

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| 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 | NL19229.029.07 |