# New diagnostic tests in autonomic failure to improve diagnosis for PAF and MSA patients.

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Primary: To explore the diagnostic value to distinguish PAF and MSA of a variety of tests: corneal confocal microscopy optical coherence tomography (OCT) to measure the retinal nerve fibre layer thickness and total macular volume, corneal...

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Ocular structural change, deposit and degeneration NEC |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON43607

**Source**
ToetsingOnline

**Brief title**
New diagnostic tests in autonomic failure

### Condition

- Ocular structural change, deposit and degeneration NEC
- Peripheral neuropathies

**Synonym**
Autonomic failure, dysfunction of the autonomic nerve system

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Leids Universitair Medisch Centrum
**Source(s) of monetary or material Support:** Ministerie van OC&W

## Intervention

**Keyword:** autonomic failure, corneal nerve fibers, neurogenic orthostatic hypotension, sudomotor testing

## Outcome measures

### Primary outcome

- CCM : Difference in nerve fiber density in the cornea between patients with PAF, patients with MSA and controls. A difference of 14.2 fibers / mm2 between groups is regarded as a minimal clinically relevant difference .

- OCT: Difference in the RNFL (Retinal Nerve Fiber Layer) thickness between patients with PAF, patients with MSA and controls.

- WISW : Difference in the degree of wrinkling of the skin in the fingertips between patients with PAF, patients with MSA and controls. A difference of 1 ' grade ' between goups is considered a minimal clinically relevant difference .

- Sudoscan: Difference in electrochemical skin conductance in microsiemens (µS) between patients with PAF, patients with MSA and controls. A difference in skin conductance of 10 µS between groups is considered the minimal clinically relevant difference.

### Secondary outcome

ROX: difference in the arterial and venous oxygenation during a fall in blood pressure among patients with PAF, patients with MSA and controls.

# Study description

### Background summary

Two such rare disorders, pure autonomic failure (PAF) and multiple system

atrophy (MSA,) cause very severe autonomic failure as well as major diagnostic difficulties due to many clinical similarities: while both exhibit progressive autonomic failure, patients with MSA additionally develop movement disorders during the course of their disease and suffer the burden of a much less favourable prognosis than patients with PAF, with a mean survival of six years. Consensus criteria for MSA stipulate that a definite diagnosis of MSA can still only be made after death, leaving patients with autonomic failure to face years of uncertainty.

### Study objective

Primary: To explore the diagnostic value to distinguish PAF and MSA of a variety of tests: corneal confocal microscopy optical coherence tomography (OCT) to measure the retinal nerve fibre layer thickness and total macular volume, corneal sensitivity, a test of sweat production (Sudoscan) and water induced skin wrinkling (WISW).
Secondary: To explore whether measuring retinal perfusion in patients with autonomic failure using retinal oximetry (ROX) is suited as a pathophysiological tool.
With the help of one or more of these methods can be made a diagnosis hopefully earlier in the course of the disease in the future for PAF and MSA patients and thus years of uncertainty to be removed.

### Study design

Observational prospective study.

### Study burden and risks

There is a single, low risk for the participants, since all tests are non-invasive. PAF and MSA patients can get enough rest between the tests and at any time the tests can be paused.
There are hardly any risks associated with the study, only a very low risk of glaucoma. The pupil dilation with Phenylephrine HCL 2.5% en Tropicamide 0.5% is necessary to view the posterior segment of the eye. Side effects of these drops include photophobia and reduced accommodative power during 2 hours. We do not expect any adverse events or serious adverse events. There is a very low risk of acute angle-closure glaucoma due to pupil dilation: 3:10.000. If this occurs, we will examine and treat the patient according to standard car at Dept. Ophthalmology at LUMC.

## Contacts

### Public

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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 participants: older than 18 years and the ability to provide informed consent.
Patients with PAF are defined according to the consensus of the American Autonomic Society and the American Acedemy of Neurology (AAN):
- Presence of NOH AND
- Evidence of more widespread autonomic failure AND
- No other neurological features
Patients with MSA are defined according to the second consensus criteria of the AAN.
Healty controls: no signs of autonomic failure or other relevant neurological or other disorders.

## Exclusion criteria

For all participants: younger than 18 years or not able to provide informed consent.
Furthermore, a potential subject who meets any of the following criteria will be excluded from participation in this study:

- Diabetes Mellitus
- Inability to sustain the investigations due to the nature of their disease
- Ophtalmological morbidity: AMD, macular dystrophies, glaucoma, herpes keratitis, history of cornea surgery like refractive surgery

# Study design

## Design

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

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 04-07-2016 |
| Enrollment: | 33 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Generic name: | Sudoscan |
| Registration: | Yes - CE intended use |

# Ethics review

Approved WMO

| | |
|---|---|
| Date: | 08-06-2016 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

# 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 | NL54904.058.16 |