

# Cerebrovascular manifestations of Hereditary Hemorrhagic Telangiectasia: a look beyond AVMs | A study of the prevalence of structural brain changes in HHT and an assessment of the MR cerebrovascular reactivity of HHT patients

Published: 08-08-2012

Last updated: 17-08-2024

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<b>Ethical review</b>	Approved WMO
<b>Status</b>	Recruitment stopped
<b>Health condition type</b>	Chromosomal abnormalities, gene alterations and gene variants
<b>Study type</b>	Observational invasive

## Summary

### ID

NL-OMON41632

### Source

ToetsingOnline

### Brief title

Cerebrovascular manifestations of HHT: a look beyond AVMs

### Condition

- Chromosomal abnormalities, gene alterations and gene variants

### Synonym

Hereditary Hemorrhagic Telangiectasia, Rendu-Osler-Weber disease

## Research involving

Human

## Sponsors and support

**Primary sponsor:** Leids Universitair Medisch Centrum

**Source(s) of monetary or material Support:** Ministerie van OC&W, SWORO-fonds St. Antonius Ziekenhuis Nieuwegein

## Intervention

**Keyword:** AVM, cerebrovascular reactivity, Hereditary Hemorrhagic Telangiectasia, Small vessel disease

## Outcome measures

### Primary outcome

The prevalence and distribution of (i): lacunar infarcts, (ii): microbleeds, (iii): white matter hyperintensities (WMH), (iv) widened perivascular spaces, (v) cerebral AVMs, and (vi): cerebrovascular reactivity.

### Secondary outcome

No secondary parameters.

## Study description

### Background summary

The cerebrovascular manifestations of Hereditary Hemorrhagic Telangiectasia (HHT) have not been studied beyond the arteriovenous malformations (AVM) associated with this disease. From animal studies there are indications that in addition to these macrovascular pathologies the function of normal appearing vessels of HHT patients may also be affected. This may indicate that pathological changes in the brain of HHT patients occur that may show similarities to changes occurring in the brain of patients with small vessel disease, in which stiffening and fragility of the vessel wall results in white and grey matter abnormalities and reduced vascular reactivity. Furthermore, the cerebrovascular manifestations of HHT are more severe in patients with pulmonary AVMs (PAVMs) than those without PAVMs, and the source of this discrepancy is currently not known. Finally, mapping the cerebral expressions

of HHT is of interest not only to extend our knowledge of the pathological processes occurring in this particular disease but it may also offer the opportunity to explore mechanisms potentially relevant to other - more common - small vessel diseases.

## **Study objective**

The objectives of this study are:

1. to evaluate the occurrence and distribution of structural brain changes in HHT patients with and without pulmonary AVMs as compared to healthy age matched controls;
2. to evaluate the (autoregulatory) function of small brain vessels in HHT patients using CO<sub>2</sub> cerebrovascular reactivity measurements with MRI.

## **Study design**

This is an observational cross-sectional study comparing the prevalence and distribution of different small vessel disease markers in HHT patients with the prevalence and distribution of these markers in healthy age matched controls. This study consists of a single MRI scan session with a 3 Tesla clinical MRI scanner consisting of different MR image types (e.g. Time-of-flight (TOF) angiogram, T1-weighted, T2\*-weighted and fluid-attenuated inversion recovery (FLAIR) images) and CO<sub>2</sub> cerebrovascular reactivity measurements. The acquired images will be rated by trained radiologists for the aforementioned markers.

## **Study burden and risks**

The study is observational and aims to elucidate the expression of different small vessel disease markers in HHT patients with and without pulmonary AVMs. As such, HHT patients are required to be included in this study. After careful screening for contra indications for MRI and obtaining written informed consent, MRI scans will be made, with a negligible risk to the participants health. To further minimize the burden the total scan time is limited to 60 minutes.

## **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

- Endoglin gene mutation carriers (HHT type 1 patients)
- Ability and willingness to provide written informed consent
- Age: between 18 and 69 years
- Presence of pulmonary AVM (15 subjects)
- No pulmonary AVM present (15 subjects)

### Exclusion criteria

- Presence of other known cerebrovascular diseases not related to HHT: (overtly manifest hypertensive/atherosclerotic vascular disease, diabetes mellitus, previous head trauma, bleeding or ischemic stroke, CNS tumor, carotid artery stenosis)
- Contra indications to MR Imaging
- Contra indications to CO2 stimulation (Asthma/COPD, Change in hypertensive medication within the previous three months, Seizures within the previous year)
- Severe physical restriction / inability to be scanned, such as weight above 120 kg.

## 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): 08-02-2013

Enrollment: 45

Type: Actual

## Ethics review

Approved WMO

Date: 08-08-2012

Application type: First submission

Review commission: METC Leiden-Den Haag-Delft (Leiden)

metc-ldd@lumc.nl

Approved WMO

Date: 22-04-2014

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO

Date: 28-05-2015

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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## 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	NL41153.058.12