# Assessing brain hemodynamics using Arterial Spin Labeling.

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| **Ethical review** | Approved WMO |
| **Status** | Recruitment stopped |
| **Health condition type** | Arteriosclerosis, stenosis, vascular insufficiency and necrosis |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON37548

**Source**
ToetsingOnline

**Brief title**
A-CO2

### Condition

- Arteriosclerosis, stenosis, vascular insufficiency and necrosis

**Synonym**
Cerebrovascular disease, stroke

**Research involving**
Human

### Sponsors and support

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

## Intervention

**Keyword:** Arterial Spin Labeling, Cerebrovascular Reactivity, CO2-challenge, Oxygen Extraction fraction

## Outcome measures

### Primary outcome

The main endpoint in part 1 is to test the feasibility and safety of the

CO2-challenge in healthy volunteers. During this part we will also optimize the

sequences and the scan protocol.

In part 2 of this research the CVR and the OEF in the different patient

populations will be compared with the CVR and OEF in the control group.

### Secondary outcome

Not applicable

# Study description

### Background summary

The amount of oxygen that is extracted in the brain depends on the perfusion pressure in the brain tissue. In cerebrovascular diseases this perfusion pressure decreases. As a first reaction, the brain expands its vessels. When this is not sufficient the brain tissue extracts more oxygen than normal. Two parameters are used to describe this phenomenon; the Cerebrovascular Reactivity (CVR) and the Oxygen Extraction Fraction (OEF).
The CVR tells us how much brain vessels can dilate. The OEF tells us how much oxygen gets extracted from the blood. Both parameters are used to describe the severity of a cerebrovascular disease.
Vessels dilate when there is a higher concentration of carbondioxide in the blood. Arterial Spin Labeling (ASL) MRI enables us to measure perfusion in the brain tissue. Combining ASL MRI with an increase in concentration of carbondioxide enables us to measure the increase in perfusion, called the CVR.
The safest way to administer a higher carbondioxide concentration is with the Respiract device. This is a device which delivers accurately a preset

carbondioxide-and oxygen concentration. This device can as well be used to measure the OEF using a newly developed ASL technique.
Combining both parameters, the CVR and the OEF, enables us to get an insight in the hemodynamics of brain tissue in individual patients.

**Study objective**

This research consists of two parts.
In the first part we want to assess the the safety and feasibility of a CO2-challenge in 20 healthy volunteers. At this time MRI sequences and the scan protocol will be optimized as well.
After assessing the safety and feasibility of this CO2-challenge in healthy volunteers we will report back to the METC before starting the second part of this research.
In the second part of this research the CVR and the OEF will be measured in patients with a cerebrovascular disease and in a healthy control group. The CVR and OEF measured in the different patient populations will be compared with the healthy control group.

**Study design**

This is a single center prospective study which consists of two parts and will be performed in the UMC Utrecht.

In part 1 we will test the feasibility and safety of a CO2-challenge in 20 healthy volunteers. Furthermore, in these volunteers we will optimize the sequences and the scan protocol in order to make sure the amount of CO2-challenges is minimized were possible. After having finished this part of the protocol we will report back to the METC before progressing to the following part.

In part 2 the optimized scan protocol will be applied in 40 patients with asymptomatic extracranial vascular disease (stenosis of 70-100%), 40 patients with symptomatic extracranial vascular disease (stenosis of 70-100%) and 40 patients with symptomatic occlusion of the middle cerebral artery. In order to compare our findings in these 3 patients groups with a healthy control group we will apply the same scan protocol in a group of 40 healthy volunteers.

**Intervention**

All subjects will be exposed to a CO2- challenge during an ASL MRI research in which the CVR and OEF will be measured.
During this research 6 blocks of increased CO2-concentration will be administered. The maximum duration of each block will be 3 minutes and this will be interleaved by a block of normal air supply with a duration of minimum 3 minutes. The CO2-pressure will be increased to a maximum of 50 mmHg and this

in combination with a minimum O2-pressure of 100 mmHg.

**Study burden and risks**

The controlled gas breathing requires a closed breathing system. Therefore, subjects have to breath through a mask. Further, CO2 end-tidal levels of 50 mmHg can induce an increased breathing frequency due to physiological stress. However, end-tidal levels of 30-50 mmHg CO2 are within physiological ranges and are experienced repeatedly by most people over the day. If patients experience discomfort because of high arterial CO2 levels, they can open a valve in the mask or we can switch immediately to 100% oxygen by pushing the red button on the front of the gas blender. In the MRI they can squeeze as well the panic button.
Risks associated with controlled gas breathing of high levels of CO2 are minimized because the minimum O2 level in the gasses is 10% and the maximum concentration of CO2 is 10%. The blood gas is controlled by a digitally controlled gas blender steered by end-tidal blood gas PCO2 and PO2. So, CO2-, O2- levels and breathing frequency are monitored online. An independent blood oxygen saturation monitoring will be performed during the MRI measurements with fingertip pulse oxymetry, respiratory tracking during the MRI exam will be performed as well.
Before participating in this research all subjects will receive an extensive explanation about the device and the procedure. When after this explanation a subject decides to participate in this research, a second extensive explanation will be given before applying the device. In order to get the subject accustomed to the device and to the increase in CO2-values, a breathing test outside the scanner area will be performed. At this time we will also show and practice with the subject how to open the valve in the mask. When the subject is positioned on the MRI-table he or she will receive the panic button and will be able to practice squeezing in it.
The subject will be able to withdraw himself from this research at each moment in time.
The risk of this research is estimated as minimum excess of negligible risk.

# Contacts

**Public**
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
3584 CX Utrecht
NL
**Scientific**
Universitair Medisch Centrum Utrecht

Heidelberglaan 100
3584 CX Utrecht
NL

# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

Inclusion criteria for the healthy volunteers:
- 18 years or older
- male or female
- informed consent after extensive explanation about the device and the research protocol
- healthy;Inclusion criteria for patients:
- 18 years or older
- male or female
- (A)symptomatic extracranial vascular disease (stenosis of 70-100%)
or
Symptomatic middle cerebral artery occlusion
- Informed consent after extensive explanation about the device and the research protocol
- healthy

## Exclusion criteria

Exclusion criteria for the healthy volunteers:
- Contraindications for MRI (claustrophobia, or standard MRI contraindications such as pacemakers or specific metal objects in or around the body)
- Previous history of ischemic symptoms
- Minors or (legally) incompetent adults;Exclusion criteria for patients:
- Contraindications for MRI (claustrophobia, or standard MRI contraindications such as pacemakers or specific metal objects in or around the body)
- Unwilling or unable to co-operate with breathing manoeuvres

- Known cardiac or pulmonary disease
- altered consciousness
- Non compliance with prescribed anti-seizure medication
- Minors or (legally) incompetent adults

# Study design

## Design

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

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Recruitment stopped |
| Start date (anticipated): | 12-07-2012 |
| Enrollment: | 180 |
| Type: | Actual |

# Ethics review

Approved WMO

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|---|---|
| Date: | 06-06-2012 |
| Application type: | First submission |
| Review commission: | METC NedMec |

# 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 | NL39070.041.11 |