# MRS-based NAD+ quantification: Responsibility of a novel MRS-based method quantifying NAD+ in vivo

Published: 30-10-2019
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| **Ethical review** | Approved WMO |
| **Status** | Completed |
| **Health condition type** | Glucose metabolism disorders (incl diabetes mellitus) |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON49618

**Source**
ToetsingOnline

**Brief title**
NAD+ quantification with MRS

### Condition

- Glucose metabolism disorders (incl diabetes mellitus)

**Synonym**
diabetes, insulin resistance

**Research involving**
Human

### Sponsors and support

**Primary sponsor:** Universiteit Maastricht

**Source(s) of monetary or material Support:** ERC starting Grant 2017

## Intervention

**Keyword:** Fasting, Ischemia, MRS, NAD+

## Outcome measures

### Primary outcome

NAD+ concentration as measured by 31P-MRS before/after intervention.

### Secondary outcome

Secondary endpoint is NAD+ as determined in muscle biopsies.

# Study description

### Background summary

With increasing prevalence of cardiometabolic disease, the challenge of the coming years is to intervene at an earlier stage in the pathogenesis of such disease and discover new therapeutic targets. To identify and monitor the mechanisms responsible for blunted cardiometabolic health in humans, and progression to metabolic disease such as diabetes, non-invasive imaging methods are needed to investigate metabolism dynamically. Standard Magnetic Resonance Spectroscopy (MRS) methodology is nowadays commonly used to examine readily detectable biochemical compounds (like ectopic lipids). However, by dedicated design of novel*MRS sequences, more unique metabolites key in the development of metabolic*disorders, can be visualized and quantified*non-invasively.
Animal studies indicate that Nicotinamide Adenine Dinucleotide (NAD+), by being an activator of many intracellular enzymes and a co-regulator of mitochondrial function and biogenesis, may well play a role in regulating metabolic health. Human data on the relevance of NAD+ is still very scarce because investigation in humans requires rapidly processed tissue samples obtained via invasive procedures (muscle biopsies). Consequently, kinetic information is particularly difficult to obtain. 31P-MRS at high magnetic field (7T) was used to quantify NAD+ and NADH in the brain (Zhu, Lu et al. 2015). But at clinical field strength, the spectral resolution is lower, resulting in overlapping peaks of NAD+, NADH and ATP signals.
Therefore, to ensure robust quantification in muscle, design of tailored sequences for NAD+ detection are warranted in order to achieve the simultaneous suppression of ATP signals that are overlapping with NAD and enable

quantification at clinical field strength.

### Study objective

The objective of this study is to validate a novel MRS-based method to quantify NAD+ by selectively suppressing the coupled α-ATP spin system, which is overlapping with the NAD+/NADH signals in vivo. For NAD+/NADH quantification to be valuable in metabolic research, it should be possible to pick up changes in response to physiological stimuli. It is well known that NAD+ is increased upon fasting and ischemia. Therefore, in the current protocol, the measurement of NAD+ will be validated after such interventions. Furthermore, the in vivo measurements will be compared to NAD+ and NADH quantification in muscle biopsies.

### Study design

Proof of principle study with two short interventions making use of pre/post design.

### Intervention

ischemia (8 minutes) and prolonged fasting (36h)

### Study burden and risks

This study carries no benefits for the subjects and carries minor risks for the subjects. The major burdens consist of a moderate time commitment, staying fasted for a prolonged time and multiple muscle biopsies and blood sampling.

## 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

- Age: 18-40 years
- BMI: 18-25 kg/m2
- Generally healthy

## Exclusion criteria

- regular (every day more than three cigarettes) smoking Par-ticipants who smoke by occasion (for instance during a party) but not daily are not ex-cluded from participation
- Alcohol consumption (men > 4 units per day; women > 3 units per day)
- Use of anti-coagulants or other medication known to hamper blood coagulation
- Contraindications for MRI scans
- Participation in other (intervention) studies
- Subjects who do not want be informed about unexpected medical findings, or do not wish that their physician be informed cannot participate in the study
- Any condition, disease, abnormal laboratory test result or medication that, in the opinion of the investigator and the dependent physician, would interfere with the study outcome, affect trial participation or put the subject at undue risk.

# Study design

## Design

**Study type:** Interventional

| | |
|---|---|
| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Other |

## Recruitment

NL

| | |
|---|---|
| Recruitment status: | Completed |
| Start date (anticipated): | 09-07-2020 |
| Enrollment: | 20 |
| Type: | Actual |

## Medical products/devices used

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|---|---|
| Generic name: | 3.0T (Tesla) MRI scanner |
| Registration: | Yes - CE intended use |

# Ethics review

Approved WMO

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| Date: | 30-10-2019 |
| Application type: | First submission |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |

Approved WMO

| | |
|---|---|
| Date: | 20-05-2020 |
| Application type: | Amendment |
| Review commission: | METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht) |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

ID: 27957
Source: NTR
Title:

## In other registers

| Register | ID |
|---|---|
| CCMO | NL66905.068.19 |
| OMON | NL-OMON27957 |

# Study results

Date completed: 25-11-2021

**Summary results**
Trial ended prematurely