

Is it really mitochondrial Pi?

A study into the origin of the alkaline inorganic phosphate signal as observed by ^{31}P MRS at 7T

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The objective of the study is to be able to determine the contribution of blood inorganic phosphate to the signal observed in skeletal muscle.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Metabolic and nutritional disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON35595

Source

ToetsingOnline

Brief title

Using MRS to rule out blood origination of Pi signal

Condition

- Metabolic and nutritional disorders congenital
- Diabetic complications
- Muscle disorders

Synonym

Healthy controls

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: Magnetic resonance, Mitochondria, Muscle, Phosphorous

Outcome measures

Primary outcome

Peak intensity of the putative mitochondrial inorganic phosphate signal will be investigated, both before and during inflation of the cuff. In addition, the relative increase in the size of the leg as well as the blood vessels will be calculated, to obtain a measure for the expected increase in blood volume in the leg.

Secondary outcome

na

Study description

Background summary

Assessment of mitochondrial content and capacity in skeletal muscle is important in clinical research, for instance in diabetes, as well as in aging research and sports medicine. Current methods for determination of mitochondrial content are either invasive as they require a biopsy from the muscle tissue, or they are not feasible in a clinical setting, as exercise inside an MRI scanner is needed. Therefore, a non-invasive method to determine mitochondrial content that does not require exercise would offer a significant advantage for patients.

In a previous study at the LUMC, phosphorous magnetic resonance spectroscopy (31P MRS) of skeletal muscle was used to detect an extra signal for inorganic phosphate. This signal, which can only be detected at 7T due to the increased signal to noise ratio and increased spectral resolution, was attributed to the mitochondrial inorganic phosphate pool. If this signal really originates from

the mitochondria, this MR-tractable mitochondrial biomarker in resting muscle could offer a significant advantage because it offers a non-invasive determination of mitochondrial density.

A follow-up study showed a significant increase of this signal in endurance trained athletes, as well as a very high correlation with the phosphocreatine recovery time, a well accepted marker of mitochondrial capacity which requires in-magnet exercise. Both results provide further evidence for the origination of the signal from mitochondria because of the known increase in mitochondrial density in endurance trained athletes.

However, it could still be possible that a significant portion of the signal is originating from blood. Only when the blood contribution to the signal is known, further research can be done on the use of this signal as a biomarker for mitochondrial content. We propose to study this by reversibly increasing the blood volume in the tissue of interest by inflating a cuff around the upper leg resulting in venous occlusion, and acquiring ^{31}P MRS data in the lower leg before and during the inflation.

Study objective

The objective of the study is to be able to determine the contribution of blood inorganic phosphate to the signal observed in skeletal muscle.

Study design

The study will be performed on the 7 tesla Philips human MRI scanner in the C.J. Gorter Center for High Field MRI in the Department of Radiology at the Leiden University Medical Center. Subject will be placed in a supine position, with a MR surface coil placed on their calf muscle. An inflatable cuff will be placed around the upper leg, but the cuff will not be inflated at the start of the scan.

First some preparation scans will be made, and this will take about 15 minutes. Thereafter, a ^{31}P MR spectrum will be acquired, which takes about 10 minutes. Subsequently, the cuff will be inflated to a pressure of 60 mmHg, using a manual blood pressure Sphygmomanometer, which is located outside the scan room. The cuff will stay inflated for a maximum of 11 minutes, during which a 10 minute MR spectrum will be acquired. After that, the cuff will be deflated by opening the valve of the Sphygmomanometer, resulting in a gradually lowering of the pressure in the cuff.

Study burden and risks

There are no known risks associated with participating in an MRI study, as long as risk groups are excluded. Subjects with intracranial or intraocular metal, a pacemaker, and claustrophobia will be excluded because of potential contraindications of MRI in such subjects. The partial occlusion of the veins by using an inflatable cuff in healthy subjects for

about 11 minutes is not harmful or dangerous. In many previous studies partial or full venous occlusion has been performed in healthy subjects, without adverse effects.

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

Healthy adult volunteers

Exclusion criteria

- Claustrophobia

- Pacemakers and defibrillators
- Nerve stimulators
- Intracranial clips
- Intraorbital or intraocular metallic fragments
- Cochlear implants
- Ferromagnetic implants (e.g. thoracic implant for scoliosis)
- any muscle disease
- recent muscle trauma

Study design

Design

Study type: Observational invasive

Masking: Open (masking not used)

Control: Uncontrolled

Primary purpose: Other

Recruitment

NL

Recruitment status: Recruitment stopped

Start date (anticipated): 17-10-2011

Enrollment: 8

Type: Actual

Ethics review

Approved WMO

Date: 10-10-2011

Application type: First submission

Review commission: METC Leids Universitair Medisch Centrum (Leiden)

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	NL37548.058.11

Study results

Date completed:	04-06-2012
Actual enrolment:	4

Summary results

Trial is ongoing in other countries