Subject information for participation in medical scientific research

Markers of CrAT protein activity and carnitine availability

Searching for non-invasive Magnetic Resonance-based markers for CrAT protein activity and carnitine availability in skeletal muscle

Introduction

Dear Sir,

You are asked to take part in a medical-scientific study. Participation is voluntary and requires your written consent. Before you decide whether you want to participate in this study, you will be given an explanation about what the study involves. Please read this information carefully and ask the investigator for an explanation if you have any questions. You can also ask the independent expert, who is mentioned at the end of this document, for additional information. You may also discuss it with your partner, friends or family.

Additional information about participating in a study can be found in the enclosed general brochure on medical research.

1. General information

This study takes place at the department of Nutrition and Movement Sciences at Maastricht University. Thirteen healthy male subjects are expected to participate in this study. The Medical Research Ethics Committee of the Academic Hospital Maastricht / Maastricht University has approved this study. General information about the assessment of research can be found in the general brochure on medical research.

2. Purpose of the study

The purpose of the study is to investigate the ability of muscle to activate mitochondria during exercise by monitoring a metabolite called phosphocreatine (PCr) through a non-invasive methodology known as Magnetic Resonance Spectroscopy (MRS). We will determine whether this mitochondrial activation event is associated with a protein expressed in muscle named CrAT and the ability of the muscle tissue to obtain oxygen from the circulation. This PCr metabolite, CrAT protein and oxygen supply to skeletal muscle are important factors for understanding exercise tolerance and muscle fatigue.

3. Background of the study

During exercise condition, our muscles need to produce huge amounts of energy. Previous investigations have shown that at the transition from a resting to exercise condition there is a lag on the energy production in subjects with poor health. This event may indeed lead to a low exercise tolerance and early muscle fatigue.

In this context, a molecule stored in the muscle called acetylcarnitine may be relevant, as it can provide extra energy during exercise by the function of a protein called CrAT. Similarly, another metabolite stored in muscle called phosphocreatine (PCr), which is used to produce energy during exercise, was also detectable only via the extraction of a piece of muscle. By monitoring PCr is possible to determine the rate of aerobic energy production of muscle. We are currently able to detect PCr levels in muscle over time by non-invasive methodologies, using magnetic resonance imaging/spectroscopy (MRI/MRS). By monitoring the reliance on PCr break down during and post exercise, we expect to determine whether CrAT protein is associated with the rate of aerobic energy production. Similarly, we will test whether the oxygen delivery to muscle tissue is associated with the ability to activate the aerobic energy production. Thus, we might be able to identify a possible target site to improve exercise tolerance, and early muscle fatigue.

4. What participation involves?

Your participation will last about 8 hours in total, divided over 3 different test days. The entire study consists of a preliminary examination to assess your eligibility (screening visit ~2h) and 2 MRS + exercise test days (~2-3h each day). There will be a rest period of at least 48 hours between the first and the second MRS + Exercise test days.

A global scheme of the entire study is shown in figure 1.

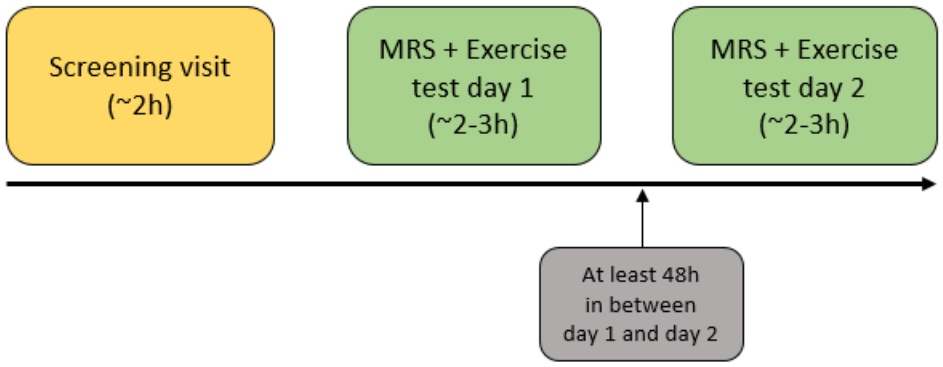

Figure1: Scheme overview of the entire study. The screening visit to assess elegibility is shown in yellow and the two MRS + Exercise test days are shown in green. There must be a minimum of 48h of resting time between MRS+Exercise test day 1 and 2, **period on which you go home.**

Screening: ˜2h.

Before you may participate in the study, your health status has must be assessed during a screening visit. For this visit, you will come at the University after remaining fasted for approximately 10 – 12 hours. Prior to starting the screening visit, you and the investigator will discuss the study and sign an informed consent. During the screening visit, the investigator will go through two questionnaires: one regarding you general health and the other to determine whether it is safe for you to undergo an MRS scan. Besides, the investigator will measure your body weight, height and will also take a blood sample to determine your health status. Moreover, the investigator will evaluate your maximal one-legged extension capacity and your maximal physical capacity (VO2max). Both maximal capacities will allow us to determine the exercise intensities for the next MRS+Exercise visits; if you participate in the study. More information can be found in appendix C.

MRS + Exercise test day 1:

For the study, you will visit the Metabolic Research Unit of the Maastricht University at 17.00h after a 5h fast (having your last meal at 12.00h).

The visit will take ~2-3h.

During this test day, the following will take place:

- We will measure your body composition using the Bod Pod technique (See appendix 2).
- We will measure the ability of your muscle tissue in the lower-upper leg to obtain oxygen form the circulation before and after exercise. For this purpose, you will perform one-legged exercise outside the scanner and we will use a cuff around your leg, which will be inflated (5 minutes) and released (5 minutes). You will lay inside an MRI/MRS scanner (your head will be outside the scanner), thus we can monitor dynamically the oxygen that your muscle contains upon inflation and release of the cuff.
- After finishing this test day, you can go home and be back at the university after at least 48 hours to continue with the second MRS + Exercise test day.

MRS+Exercise test day 2:

After at least 48 hours from the previous visit, you will again visit the Metabolic Research Unit of the University at 15.00h after a 4-5h fast (having your last meal at 11.00h).

The visit will take ~3h.

During this test day, the following will take place:

- We will ask you to lay back on a bed and medical doctor will take out a small piece of muscle from your upper leg under local anaesthesia (muscle biopsy; for more information see appendix 2, pag.10).
- You will again lay in the MRI/MRS scanner (your head will be outside of the scanner) and perform one-legged extensions. Here, we will measure a metabolite called phosphocreatine in the upper-leg at resting, during exercise (several minutes) and during the post–exercise recovery (~5-6 minutes).
- Subsequently, we will ask you to perform a cycling test for 30 minutes: 10 minutes cycling at 30%, 10 minutes at 50% and 10 minutes at 70% of your maximal physical capacity. Throughout the cycling exercise test, you will breathe through a mouthpiece, which is connected to a system that will analyse your respiration. This

is to determine if you burn fat or sugar during the exercise (and how much). Before starting the cycling test, we will insert a Teflon catheter in your arm to take four blood samples every 10 minutes while cycling (~10 ml per sample).

- After finishing the cycling test, you will again be place in the MRS/MRI scanner to measure the concentration of the metabolite acetylcarnitine formed in your muscle during exercise and the recovery after exercise. During the recovery post-exercise, we will take four extra blood samples (~10 ml each sample).

5. What is expected of you?

In order to carry out the study properly, we expect that you continue to follow your regular lifestyle during and between the screening visit and the exercise test days. We also expect that you refrain from alcohol consumption and strenuous physical activity 48h before the exercise test days. Besides, we expect that you consume the same light lunch before the exercise test days. In addition, we expect that you keep track of your food ingestion and physical activity for 2 days.

The study instructions require that you:

- Do not participate in another medical study
- Keep appointments for visits

It is important that you contact the investigator:

- Before you start using other medication. Even if they are homeopathic or natural remedies, vitamins and/or over-the-counter medicines.
- If you are admitted to a hospital or are going for treatment there.
- If you suddenly develop any health problems.
- If you no longer want to participate in the study.
- If your contact details change.

6. Possible advantages and disadvantages

It is important that you properly weigh up the possible benefits and disadvantages before you decide to participate.

Benefits:

You will not personally benefit from participation in this study. Your participation may contribute to increased knowledge about determining the activity of a key protein in muscle during exercise using non-invasive methodologies. In case you are interested in knowing your maximal physical capacity and cardiopulmonary fitness, we can provide

you the results of the maximal cycling test performed during the screening visit.

Disadvantages

- Before and during the test days, you are restricted to perform strenuous exercise, which could affect your regular physical activity or training regimen.

- You may develop a bruise near the insertion site of the cannulas (in your arm). Similarly, there is a (very small) chance of inflammation. In case you experience problems or develop a fever, you should contact the investigator or your general physician.

- At the MRS + Exercise test day 1, a cuff will be placed and inflated around your leg. This will be done for 5 minutes and afterwards the cuff will be released. This procedure can be a bit painful, but will only last a few minutes. You will be in contact with the researcher via an intercom all the time.

- At the beginning of the MRS + Exercise test day 2, you will undergo a muscle biopsy on the upper-leg. Obtaining the muscle biopsy may cause minor pain. By using anaesthesia, this can be prevented most of the times. There may occur an uncomfortable feeling after the muscle biopsy, or a bruise and/or swelling. In case the swelling increases in the hours or days after the biopsies, changes to a pink colour or if you develop a fever, you should contact the investigator or your general physician. There is a small chance that while obtaining the muscle biopsy, a small skin nerve can be affected, which may cause an unpleasant feeling at this spot that general disappears after a while. In addition, there is a chance you will have a small scar at the site where the muscle biopsy is taken on the upper leg.

- Before visiting the University for the screening test and for the MRS+Exercise test day 1 and 2, you will be asked to come at the University fasted. For the screening visit you will come after 10-12 hours fasted and for the other MRS+Exercise test days after a 4-5-hour fast.

- There is a small risk of detecting an unexpected medical finding that is revealed on the MRI images. In case of an unexpected finding, you, was well as your general physician, will be informed (as asked in the informed consent form).

- During the MRI imaging measurements, the noise may be somewhat unpleasant; therefore, we will provided you with headphones. The MRI bore has limited space in which your legs will be positioned. It can feel a little bit oppressive for you and create

a small discomfort.

- We will ask you to consume the same light lunch before the two MRS+Exercise test days. In addition, you will have to keep track of your daily food ingestion and physical activity using a diary between these two test days.

7. If you do not want to participate or you want to stop participating in the study.

It is up to you to decide whether or not to participate in the study. Participation is voluntary. If you do not want to participate, you do not have to do anything. You do not have to sign anything. You also do not have to say why you do not want to participate. If you do participate in the study, you can always change your mind and decide to stop, at any time during the study. You do not have to say why you are stopping, but you do need to tell the investigator immediately.
The data collected until that time will still be used for the study.
If you want, any bodily material collected can be destroyed.

If there is any new information about the study that is important for you, the investigator will let you know. You will then be asked whether you still want to continue your participation.

8. End of the study

Your participation in the study stops when:

- You have completed all the visits according to the schedule as described under point 4.
- You choose to stop
- The end of the study has been reached
- The investigator considers it best for you to stop
- Maastricht University, the government or Medical Research Ethics Committee, decides to stop the study

The study is concluded once all the participants have completed the study.

After processing the data, the investigator will inform you about the most important results of the study.

9. Usage and storage of your data and bodily material

Your personal data and bodily material will be collected, used and stored for this study. This concerns data such as your name, address, data of birth and data about your health. The collection, use and storage of your data and your bodily material is required to answer the questions asked in this study and to publish the results. We ask your permission for the use of your data and bodily material.

Confidentiality of your data and bodily material

To protect your privacy, your data and your bodily material will be given a code. Your name and other information that can directly identify you will be omitted. Data can only be traced back to you with the encryption key. The encryption key remains safely stored in the local research institute. The data and bodily material that is sent to the sponsor will only contain the code, not your name or other data with which you can be identified. The data cannot be traced back to you in reports and publications about the study.

Access to your data for verification

Some people can access all your data at the research location. Including the data without a code. This is necessary to check whether the study is being conducted in a good and reliable manner. Persons who have access to your data for review are: the team of investigators, the committee that monitors the safety of the study, a monitor hired by the sponsor of the study, and national and international supervisory authorities, such as the Health Care and Youth Inspectorate. They will keep your data confidential. We ask you to consent to this access.

Retention period of your data and bodily material

Your data must be kept for 15 years at the University of Maastricht. Your bodily material will not be destroyed immediately after use. It will be kept in order to be able to perform new assessments in connection with this study, in the course of this study.

Storage and use of data and bodily material for other research

You data and bodily material may also be of importance for other scientific research related with the main aim of this study. To this end, you data and bodily material will be stored for 15 years. You can indicate on the consent form whether or not you agree with

this. If you do not agree with this, you can still participate in the current study.

Information about unexpected findings

During this study, something may be found by chance that is not important for the study, but may be important to you. If this is important to your health, you and your general physician will be informed by the investigator. You can discuss with your doctor or specialist what needs to be done. You also consent to this.

Withdrawing consent

You can withdraw your consent to the use of your personal data at any time. This applies to this study and also to storage and use for future research. The study data collected until the moment you withdraw your consent will still be used in the study. Your bodily material will be destroyed after your consent has been withdrawn. If measurements have already been made with that bodily material, then this data will still be used.

More information about your rights when processing data

For general information about your rights when processing your personal data, you can consult the website of the Dutch Data Protection Authority.

If you have questions about your rights, please contact the person responsible for processing your personal data. For this study, that is the University Maastricht. See Appendix A for contact details.

If you have questions or complaints about the processing of your personal data, we advise you to first contact the research location. You can also contact the Data Protection Officer of the institution (see Appendix A) or the Dutch Data Protection Authority.

Registration of the study

Information about this study is included in a list of medical-scientific studies namely Clinicaltrials.gov. It does not contain any information that can be traced to you. After the study, the website my display a summary of the results of this study. You can find this study under the title “Markers of CrAT protein activity and carnitine availability”.

10. Study subjects insurance

Insurance has been taken out for everyone participating in this study. This insurance covers damage caused by the study. The insurance does not cover all damages. Appendix B contains more information about the insurance and the exclusions. It also tells you who to report damage to.

11. Will my GP be informed if I participate?

We will always send your GP a letter/email to let them know that you are participating in the study. This is for your own safety. If you do not agree to this, you cannot participate in the study. You cannot participate in the study if you do not have a GP. As unexpected medical finding can be revealed on the MRI images, you and your general physician will be informed (if you agree according to the informed consent).

12. Compensation for participation

For completion of the test days, you will receive an expense allowance (including travel costs) of €150. The compensation is calculated based on the time spent at the University during the Screening visit (if you are eligible), MRS+Exercise test day 1 and MRS+Execise test day 2. You will receive with compensation after the completion of the last test day. In addition, your travel costs will be reimbursed, based on the fares for the public transportation or costs for own motorized transport, of 19 cents per km. This reimbursement should be communicated to the Tax Authorities as income. In case of incomplete participation, you will receive a part of the compensation in accordance with the length of study participation and the tests performed.

13. Any questions?

If you have any question, please contact the investigator. If you would like any independent advice about participation in this study, you may contact the independent expert. She knows everything about the study, but she is not involved in it. If you have any complaints about the study, you can discuss this with the investigator. If you prefer not to do this, you may contact the complaints committee of the MUMC+. All the relevant details can be found in the **Appendix A:** Contact details.

14. Signing the consent form

When you have had sufficient time for reflection, you will be asked to decide on participation in this study. If you give permission, we will ask you to confirm this in writing on the appended consent form. By your written permission, you indicate that you have understood the information and consent to participation in the study. Both yourself and the investigator will receive a signed copy of the consent form.

Thank you for your attention.

15. Appendices to this information

A. Contact details

B. Insurance information

C. Overview/description of the study procedures

D. Informed Consent Form

Appendix A: Contact details

Executive Investigators:

Rodrigo Mancilla, MSc.
Department of Nutrition and Movement Sciences, Maastricht University
Telephone: 043 -388-1493 / 063 119 2862
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Department of Nutrition and Movement Sciences, Maastricht University
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Principal Investigator:

Dr. Vera Schrauwen-Hinderling
Department of Radiology – Nutrition and Movement Sciences, Maastricht University
Telephone: +31 43 3874951
Email: v.schrauwen@maastrichtuniversity.nl

Independent Doctor:

N.D Bouvy, M.D
Department of Surgery
Maastricht University Medical Centrum
Telephone: 043 387 5492
Email: n.bouvy@mumc.nl

Complaints:

Complaints about the research can best be discussed with the researchers (see above). If you prefer not to do so, you can contact the complaints committee of the MUMC+:
Maastricht UMC+
t.a.v de klachtencommissie
Postbus 5800
6202 AZ Maastricht

Data protection Officer of the Institution:

Mr. Raoul Winkens
Maastricht University
Telephone: 043 3883010
Email: fg@maastrichtuniversity.nl

Appendix B: Insurance information

Maastricht University (UM) is opdrachtgever

MODEL 2 POLICY STATEMENT
For the hereinafter specified Research

Title: Searching for non-invasive Magnetic Resonance-based markers for CrAT protein activity and carnitine availability in skeletal muscle

Insurance has been taken out by Maastricht University for everyone participating in this study. The insurance covers damage due to participation in the study. This applies for damage manifesting during the study or within four years of the end of your participation in the study. You must notify the insurance company about the damage within those four years.

The insurance does not cover all damages. The damages that are not covered are listed briefly at the end of this text.
This is set out in the Medical Research (Human Subjects) Compulsory Insurance Decree. This decree is listed on the website of the Central Committee on Research Involving Human Subjects www.ccmo.nl (see “Library” and then “Legislation and regulations”).

In the event of damage please contact the insurance company [or claims adjustor] directly.

The insurer of this study is: Name: CNA Insurance Company Ltd. Address: World Trade Centre, Strawinskylaan 703, 1077 XX Amsterdam Telephone number: 020-5737272 Policy number: 10193666 Contact person: Esther van Herk, Snr Claims Examiner E-mail: Esther.VanHerk@cnaeurope.com Telephone number: 020-5737274
The insurance claims handler of this study is: Name: Anissa El-Kaddouri, relatiebeheerder Meeùs Address: Meeùs, Paasheuvelweg 9C, 1105 BE Amsterdam E-mail: anissa.elkaddouri@meeus.com Telephone number: 020-3011810

The contact person at UM is:
Name: Treasury Department, Stefan Groenveld
Address: Maastricht University, Postbus 616 6200 MD MAASTRICHT
E-mail: um-verzekeringen@maastrichtuniversity.nl
Telephone number: 043-388204

The insurance offers a cover of at least € 650.000 per subject and at least €5.000.000 for the entire study (and at least € 7.500.000 per year for all research of UM).

The insurance **does not** cover the following damages:

- Damage as a result of a risk that you were informed in the written information. This does not apply if the risk occurs in a more severe form than envisaged, or if the risk was very unlikely to occur;
- Damage to your health that would also have occurred in case you did not participate in the study;
- Damage resulting from not or not entirely following directions or instructions;
- Damage to descendants as a result of a negative effect of the study on you or your descendants;
- Damage as a result of an existing treatment method for research into existing methods of treatment.

Appendix C: Overview/description of the study procedures.

		Day	Test / procedure	Duration	Comments
Screening		1	- Sign inform consent - General health questionnaire - MRI/MRS contra indication form - One blood sample - Body weight, height - Maximal one-legged extension capacity - VO2max test - ECG	~2h	Participant has to visit the University in fasting conditions (10-12h)
MRS+Exercise test day 1		1	- Measurement of body composition by BodPod technique - Measurement of Muscle tissue oxygenation inside the MRS scanner using a cuff on the upper-lower leg before and after one-legged exercise.	~2h	Participant has to visit the University in fasting conditions (5h)
MRS+Exercise test day 2		1	- One muscle biopsy at resting - Measurement of Acetylcarnitine at Resting and after cycling. - Measurement of Phosphocreatine during/post one-legged extension exercise inside the MRS scanner. - Standardized cycling test outside the scanner - 4 blood samples during exercise and 4 blood samples after exercise. - Substrate oxidation while cycling outside the scanner	~3h	Participant has to visit the University in fasting conditions (5h)

Information about the tests

Maximal aerobic capacity test:

The aim of this examination is to get valuable information about your physical fitness and to plan the future cycling tests. This examination will be performed using a bicycle ergometer. The test starts with a warm-up of 5 minutes and afterwards, you start cycling against an increasing resistance. You cycle until exhaustion, as we want to know your maximal physical capacity. Throughout the test, you will breathe through a mouthpiece that allows us to determine your maximal oxygen consumption. The test will be performed under the guidance of a research staff member.

Standardized cycling tests:

You will perform a standardize cycling test, cycling for a total of 30 minutes: 10 minutes at 30% of your maximal physical capacity, 10 minutes at 50% of your maximal physical capacity and 10 minutes at 70% of your maximal physical capacity. Throughout the cycling test, you will breathe through a mouthpiece that will determine whether you are burning fat or sugar during the exercise. Before starting the cycling test, we will insert a Teflon catheter in your arm to collect 4 blood samples at different time points: before starting the cycling test, at minute 8-10, 18-20 and 28-30. After exercise, we will also take 4 blood samples while you lay inside the scanner to measure your recovery after exercise. With these blood samples we can determine the concentration of some hormones in response to the exercise effort.

Muscle biopsy

As mentioned, at the beginning of the MRS+Exercise test day 2, an medical doctor will take one small muscle biopsy from your upper leg, towards the outer side of the thright, approximately 20 cm above the knee cap. The skin and the muscle will be locally numbed with a small syringe. After the anaesthetic has an effect (±10 minutes), a small incision will be made (0.5cm) into the skin and into the surrounding muscle sheath. Hereafter, with the use of a needle, a small piece of muscle will be removed.
After obtaining the muscle biopsy, the wound margin will be closed with a sterile Band-Aid (Steristrip). This will be covered in addition with a sterile permeable Band-Aid

(Tegaderm). Over that, a flexible bandage (Acrylastic) will be applied in order to keep the chance of bruising to a minimal. The Steristrip and Tagaderm Band-Aids should stay in place for 5 days. The flexible bandage may be removed after 24 hours. In general you can do everything afterwards, for example you can a shower, but do not take a bath or go to the sauna for the first 4 days, otherwise the Tegaderm may come loose and the wound margin may open. This will increase the chance of infection. In case you take medication that influences coagulation (such as ascal, cabasalaatcalcium, sintrom or marcumar) you are not allowed to undergo a biopsy due to increased risk of secondary bleeding. After the muscle biopsy, you may experience a numb feeling or muscle soreness for a number of days. The incisions from the biopsy may leave small scars. Most of the time this is barely visible. Furthermore, there is a small chance that a skin nerve is affected. This can cause a numb sensation in the skin of the leg, which may sometimes persist for a longer time (more than one month).

Magnetic resonance imaging/spectroscopy

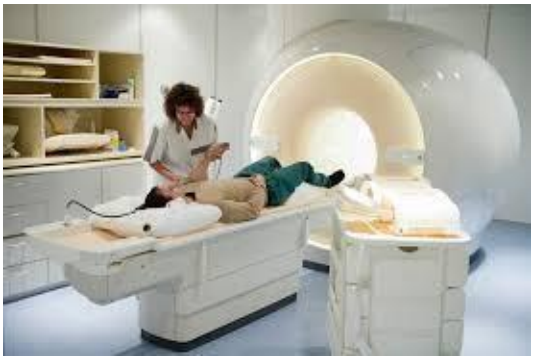
The magnetic resonance imaging/spectroscopy (MRI/MRS) is a completely painless, harmless and non-invasive method to measure specific components of a tissue in the body. MRI/MRS has the advantage of using radio waves instead of x-rays, which will not expose you to harmful radiation. Therefore, it is a modern and safe research technique.

However, there are cases when you cannot use a magnetic resonance imagining/spectroscopy scanner and you cannot participate in the research. This applies if you meet one of the following criteria:

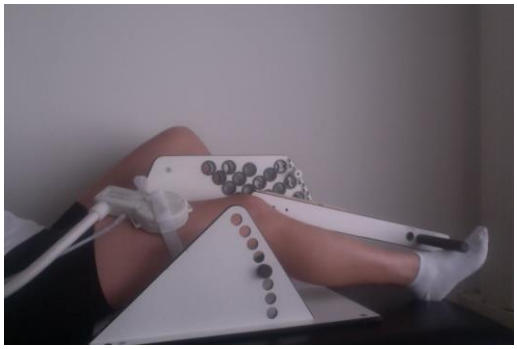
- Metal implant (for example; hip rot, pacemaker, neuro-stimulator, insulin pump,, hearing aid)
- Metal particles in the eyes (for example; splinters by welding) or brain (for example, after surgery)
- Claustrophobia; People with severe claustrophobia will experience the measurements in the MRI/MRS scanner as annoying.

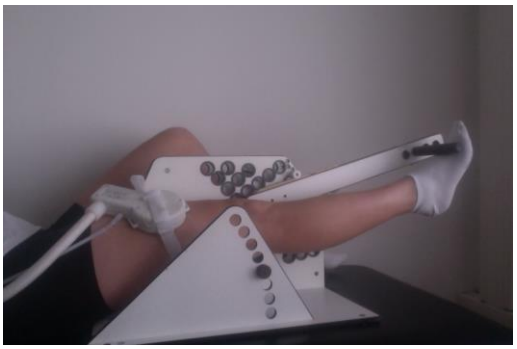
With the MRI/MRS scanner we will measure the phosphocreatine (PCr) and acetylcarnitine content at resting, during exercise and recovery after exercise. For these purposes, you will lie on a stretcher and you are pushed, with your feet first, into the scanner. In all the measurements you are on your back (supine position) and your head remains outside of the scanner. To perform the measurements, some pictures are taken by the scanner and analysed respectively. While performing the

measurements, you will hear a loud beating sound, which may be a little bit annoying, but that is part of the operation of the device. To measure the PCr and acetylcarnitine kinetic during exercise, you will perform consecutive one-legged knee extensions for several minutes (˜5 minutes). The exercise in the scanner looks like the following pictures.



Picture from a MRI/MRS measurement





Body composition:

Your body composition will be measured using a methodology called BodPod. The Bodpod is a kind of egg in which you will take place in sitting position. You will be asked to remove your clothes, except your underwear. Then you take a seat inside the BodPod and keep quiet. There will be at least 2 measurements, lasting around 2 minutes each. The BodPod can measure your body composition (amount of fat and muscle) through the displacement and density of air. During the measurement you will not feel anything.

This is an example of a bod pod measurement

Muscle tissue oxygenation by MRI:

Before performing the one-legged exercise and muscle tissue oxygenation assessment, your resting blood pressure and heart rate will be measured. Subsequently, you will be positioned in the MRI/MRS scanner and one leg will be secured to restrict movement. A blood pressure cuff will be secured around the thigh for rapid inflation (ischemia) and deflation (reactive hyperemia) using a MRI compatible Cuff Inflation System. Several images from your leg will be obtained in order to monitor the oxygen level of your muscle tissue during 15 minutes, using the first 5 minutes as baseline assessment, followed by 5 minutes of occlusion (cuff pressure inflated to 50 mmHg above resting systolic pressure) and finally 5 minutes of reactive hyperemia following cuff deflation.

Appendix D. Subject Consent Form

"Searching for non-invasive Magnetic Resonance-based markers for CrAT protein activity and carnitine availability in skeletal muscle"

- I have read the subject information form. I was also able to ask questions. My questions have been answered to my satisfaction. I had enough time to decide whether to participate.
- I know that participation is voluntary. I know that I may decide at any time not to participate after all or to withdraw from the study. I do not need to give a reason for this.
- I give permission for my GP to be informed that I am participating in this study and to inform them in case the investigator assumes it is necessary.
- I give permission for the collection and use of my data / blood samples / body material to answer the research question in this study.
- I know that some people may have access to all my data to verify the study. These people are listed in this information sheet. I consent to the inspection by them.
- I agree that my GP will be informed of coincidental findings that (may) be of interest for my health.
- I □ **do**

  □ **do not**

  consent to keeping my personal data longer and to use it for future research in the field of this study
- I □ **do**

  □ **do not**

  consent to being contacted again after this study for a follow-up study.
- I want to participate in this study.

Name of Participant:

Signature: Date:____/___/___

I hereby declare that I fully informed this study subject about this study.

If information comes to light during the course of the study that could affect the study subject's consent, I will inform him/her of this in a timely fashion.

Name of investigator (or his/her representative):

Signature: Date:___/___/_____

The study subject will receive the full information sheet, together with a signed copy of the consent form.